Table 2.76. Studies of *ALDH2*, *ADH1B* and *ADH1C* genotype-associated risk for sites other than cancer of the upper aerodigestive tract

Reference, study location, period	Genes involved	Relative risk (95% CI)	Comments
Stomach			
Yokoyama *et al*. (1998), Kanagawa, Japan, 1987–97	***ALDH2***		Male alcoholics; because the differences in odds ratio between the incident cases and the prevalent cases were slight, the cases were combined. Adjusted for age, alcohol drinking and cigarette smoking.
	**1/*1*	1.00	
	**1/*2*	3.49 (1.64–7.44)	
Yokoyama *et al*. (2001), Kanagawa, Japan, 1993–2000	***ALDH2*** **1/*2*		Male alcoholics. Adjusted for age, drinking, smoking, *ALDH2* and *ADH1B* genotypes. Possible partial overlap with Yokoyama *et al*. (1998). There were 38 cases of gastric cancer, of which 9 cases had also oropharyngolaryngeal cancer or oesophageal cancer (multiple cancers).
	All stomach cancer	4.35 (1.90–9.93)	
	Without UADT cancer	1.34 (0.38–4.72)	
	With UADT cancer	110.58 (13.71–891.67)	
Yokoyama *et al*. (2007b) Kanagawa, Japan, 1993–2004	***ALDH2***		Alcoholic participants only. Adjusted for age, daily alcohol drinking, daily cigarette smoking. Multivariate model with H. Pylori, CAG, MCV, concurrent carcinoma.
	*1/*1	1.0	
	*1/*2	3.7 (1.4–9.5)	
Nan *et al*. (2005) Republic of Korea, 1997–2002	***ALDH2***		Adjusted for age and sex.
	*1/*1	1.00	
	*1/*2 + *2/*2		
	Cases without hMLH1 promoter hypermethylation	1.45 (0.83–2.52)	
	Cases with hMLH1 promoter hypermethylation	0.73 (0.34–1.56)	
Terry *et al*. (2007a), Connecticut, New Jersey and Washington, USA, 1993–1995	***ADH1C***		Adjusted for age, gender and geographic site
	**2/*2*	1.0	
	**1/*2*	1.3 (0.5–3.3)	
	**1/*1*	3.3 (1.3–8.5)	

Table 2.76. Studies of *ALDH2*, *ADH1B* and *ADH1C* genotype-associated risk for sites other than cancer of the upper aerodigestive tract

Reference, study location, period	Genes involved	Relative risk (95% CI)	Comments
Zhang *et al*. (2007) Poland, 1994–1996	***ALDH2*** *+82A > G* *AA* Non-drinkers Drinkers Intensity < 7 drinks/wk > 7 drinks/wk Duration < 40 yr of drinking > 40 yr of drinking *AA + GG* Non-drinkers Drinkers Intensity < 7 drinks/wk > 7 drinks/wk Duration < 40 yr of drinking > 40 yr of drinking For *ADH1B* and *ADH1C*,see comments	 1.00 0.65 (0.39–1.07) 0.59 (0.35–0.99) 1.01 (0.52–1.96) 0.62 (0.37–1.05) 0.90 (0.44–1.86) 1.00 1.53 (0.76–3.08) 1.39 (0.67–2.88) 2.63 (1.00–6.88) 1.31 (0.63–2.69) 3.66 (1.19–11.24)	Model includes age, gender, education, cigarette smoking, fresh vegetable and fruits intake, family history of stomach cancer and interaction terms between the ALDH2 polymorphism and each alcohol intake exposure categories. No significant association between *ADH1B* Ex3123A > G (rs1229984), *ADH1B* Ex9177A > G (rs17033), *ADH1C* Ex8–56A > G (rs698), and *ADH1C* Ex6–14G > A (rs1693482) polymorphisms and risk of gastric cancer. No/few participants had *ADH1B* Ex915C > T (rs2066702) and *ADH1B* Ex3158A > T (rs6413413) polymorphisms
Pancreas			
Miyasaka *et al*. (2005) Japan, not reported	***ALDH2***	Frequency of active form lower in cases than in controls ($P = 0.018$) in men: 37.1% versus 51.8%. No difference in women (50% in cancer cases versus 49.7% in controls).	No risk estimates provided

Table 2.76. Studies of *ALDH2*, *ADH1B* and *ADH1C* genotype-associated risk for sites other than cancer of the upper aerodigestive tract

Reference, study location, period	Genes involved	Relative risk (95% CI)	Comments
Kanda *et al*. (2009), Nagoya, Japan, 2001–2005	*By alcohol intake*		
	ALDH2*1/*1*		
	None	1.00	
	< 30 g/d	1.35 (0.58–3.18)	
	≥ 30 g/d	1.98 (0.77–5.13)	
	ALDH2*1/*2 or *2/*2*		
	None	1.67 (0.75–3.75)	
	< 30 g/d	2.26 (0.93–5.46)	
	≥ 30 g/d	3.27 (1.03–10.44)	
	ADH1B*2/*2*		
	None	1.00	
	< 30 g/d	1.35 (0.58–3.18)	
	≥ 30 g/d	2.99 (1.39–6.44)	
	ADH1B*1/*1 or *1/*2*		
	None	1.17 (0.61–0.61)	
	< 30 g/d	1.42 (0.75–2.70)	
	≥ 30 g/d	1.30 (0.54–3.17)	
Hepatocellular carcinoma			
Shibata *et al*. (1998), Kurume, Japan, 1992–95	***ALDH2*** **2/*2* or **1/*2* versus **1/*1*		No adjustments. The frequency (38%) of *ALDH2*1/*1* in the community controls was lower than that generally reported in Japan.
	versus hospital controls	1.1 (0.6–2.5)	
	versus community controls	0.5 (0.2–1.0)	
Yokoyama *et al*. (1998), Kanagawa, Japan, 1987–97	***ALDH2***		Alcoholic participants only. Adjusted for age, drinking, smoking.
	**1/*1*	1.00	
	**1/*2*	0.71 (0.09–5.60)	

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Table 2.76. Studies of *ALDH2*, *ADH1B* and *ADH1C* genotype-associated risk for sites other than cancer of the upper aerodigestive tract

Reference, study location, period	Genes involved	Relative risk (95% CI)	Comments
Koide *et al*. (2000), Nagoya, Japan, 1994	***ALDH2***		Alcoholic beverage drinking was not a significant risk factor. Adjusted for age, sex.
	**1/*2 + *2/*2*	1.00	
	**1/*1*	1.24 (0.70–2.20)	
Takeshita *et al*. (2000b), Hyogo, Japan, 1993–96	***ALDH2***		Alcoholic beverage drinking was a significant risk factor. Adjusted for age, smoking.
	**1/*1*	1.0	
	**1/*2*	1.1 (0.6–2.1)	
	**2/*2*	0.3 (0.1–1.3)	
	ADH1B		
	*1/*1 + *1/*2	1.0	
	*2/*2	0.8 (0.5–1.5)	
Yu *et al*. (2002), Haimen, China, 1995–97	***ALDH2***		Alcoholic beverage drinking was not a significant risk factor. Matched analyses (matched for age and sex).
	**1/*2 + *2/*2*	1.00	
	**1/*1*	1.36 (0.81–2.28)	
Kato *et al*. (2003), Tokyo, Japan, 1993–99	***ALDH2***		20% of patients had *ALDH2*2/*2*. The rate is much higher than in the other studies (2–10%). No adjustments.
	**1/*1*	*1.0*	
	**1/*2 + *2/*2*	5.4 (2.1–14.0)	
Munaka *et al*. (2003), Fukuoka, Japan, 1997–98	***ALDH2***		Alcoholic beverage drinking was a significant risk factor. Adjusted for age, sex Adjusted for age, sex, drinking, HCV, HBV
	**1/*1*		
	**1/*2 + *2/*2*	1.00 9.77 (1.63–58.60)	
Covolo *et al*. (2005), Brescia, Pordenone, Italy, 1999–02	***ADH1C***		Alcoholic beverage drinking was a significant risk factor. Adjusted for age, sex, area of recruitment, HCV, HBV.
	**1/*2 + *2/*2*	1.0	
	**1/*1*	0.8 (0.5–1.3)	

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Table 2.76. Studies of *ALDH2*, *ADH1B* and *ADH1C* genotype-associated risk for sites other than cancer of the upper aerodigestive tract

Reference, study location, period	Genes involved	Relative risk (95% CI)	Comments
Sakamoto *et al*. (2006), Saga, Japan, 2001–04	*Light-to-moderate drinkers (< 69 g /d)*		Alcoholic beverage drinking was a significant risk factor; no *ALDH2*-associated risk observed in non-drinkers or heavy drinkers; there were no significant interactions between current drinking status and *ADH1B* genotype. Adjusted for age, sex, smoking, HCV, HBV
	ALDH2*1/*2 vs *1/*1		
	versus hospital controls	4.4 (1.2–15.4)	
	versus chronic liver disease controls	1.8 (0.8–3.7)	
	ADH1B	No association	
Homann *et al*. (2006) Germany, 1999–2003	***ADH1C**1/*1* in heavy drinkers		[The reference group was not reported: *ADH1C*2/*2* or *ADH1C*2/*2 + ADH1C*1/*1*.]
	Alcohol associated HCC versus benign tumour	3.56 (1.33–9.53)	
	Alcohol associated HCC versus liver cirrhosis	3.53 (1.31–9.47)	
Ding *et al*. (2008), Taixing, Jiangsu Province, China, 1998–2002	*By alcohol intake*		208 cases and 208 population-based controls. Adjusted for age, sex, HBsAg, hepatocirrhosis, and schistosmiasis
	***ALDH2**1/*1*		
	None	1.00	
	> 0 – ≤ 3 kg/yr	0.89 (0.45–1.76)	
	> 30 kg/yr	1.20 (0.85–1.71)	
	***ALDH2**1/*2 or *2/*2*		
	None	1.44 (0.74–2.81)	
	> 0 – ≤ 3 kg/yr	1.37 (0.56–3.36)	
	> 30 kg/yr	3.30 (1.24–8.83)	
	***ADH1B**1/*1*		
	None	1.00	
	> 0 – ≤ 3 kg/yr	0.54 (0.09–3.51)	
	> 30 kg/yr	1.10 (0.28–3.19)	
	***ADH1B**1/*2 or *2/*2*		
	None	0.85 (0.25–2.87)	
	> 0 – ≤ 3 kg/yr	0.65 (0.18–2.45)	
	> 30 kg/yr	1.46 (0.39–5.47)	

Table 2.76. Studies of *ALDH2*, *ADH1B* and *ADH1C* genotype-associated risk for sites other than cancer of the upper aerodigestive tract

Reference, study location, period	Genes involved	Relative risk (95% CI)	Comments
Colorectal cancer			
Yokoyama *et al*. (1998), Kanagawa, Japan, 1987–97	***ALDH2***		All study participants were alcoholics: 46 cases of colon cancer and 487 controls. Adjusted for age, drinking, smoking.
	**1/*1*	1.00	
	**1/*2*	3.35 (1.51–7.45)	
Murata *et al*. (1999), Chiba, Japan, 1989–95	Colon cancer		Study in men
	ALDH2**1/*1*		The number of *ALDH2*2* allele was more frequent in colon cancer cases (trend $P = 0.04$), but not rectal cancer cases (trend $P = 0.21$), compared with controls; trend *p* adjusted for sex only; odds ratios for each genotype not shown. Adjusted for age.
	(ml ethanol /d)		
	0	1.0	
	2.7–27	1.3 (0.2–8.6)	
	≥ 27	1.9 (0.4–8.6)	
	**1/*2*		
	0	1.0	
	0.1–1.0	1.6 (0.3–7.8)	
	≥ 1.0	3.1 (0.7–14.0)	
	Rectal cancer		
	ALDH2 **1/*1*		
	(ml ethanol /d)		
	0	1.0	
	2.7–27	0.9 (0.1–5.8)	
	≥ 27	1.4 (0.4–5.1)	
	**1/*2*		
	0	1.0	
	2.7–27	0.7 (0.1–3.7)	
	≥ 27	1.3 (0.2–7.0)	

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Table 2.76. Studies of *ALDH2*, *ADH1B* and *ADH1C* genotype-associated risk for sites other than cancer of the upper aerodigestive tract

Reference, study location, period	Genes involved	Relative risk (95% CI)	Comments
Matsuo *et al.* (2002), Aichi, Japan, 1999	Alcohol drinking ***ALDH2** *1/*1* Low Moderate High **1/*2* Low Moderate High **2/*2* Low Moderate High	 1.0 1.2 (0.5–2.6) 1.9 (0.8–4.8) Trend $P = 0.14$ 1.0 0.8 (0.3–2.0) 3.6 (1.0–13.0) Trend $P = 0.16$ 1.0 24.5 (0.8–787) Not calculated Trend $P = 0.07$	Alcohol category: low (less than once), moderate (≥ 1 per wk with < 50 mL of ethanol), and high (≥ 1 per wk with ≥ 50 mL of ethanol); increased risk associated with alcohol in *ALDH2*1/*2* was seen for rectal cancer (trend $P = 0.01$), not for colon cancer (trend $P = 0.44$). Adjusted for age and smoking in the overall analysis; age and sex in the stratified analysis.
Giovannucci *et al.* (2003), Boston, USA, 1986–95	***ADH1C*** **1/*1* **1/*2* **2/*2* **1/*1* **1/*2* **2/*2* **1/*1* **1/*2* **2/*2*	*Alcohol intake* *≤5 g/d* 1.0 1.0 (0.6–1.8) 1.1 (0.6–2.0) *5–30 g/d* 1.3 (0.9–2.1) 1.0 (0.7–1.6) 0.8 (0.5–1.5) *> 30 g/d* 1.3 (0.6–2.5) 1.8 (1.0–3.3) 2.9 (1.2–6.9)	Case–control study, Health Professional Follow-up Study (HPFS). Cases ($n = 397$) with colorectal adenomas and 727 controls. ORs controlled for matching variables (previous endoscopy, yr of endoscopy, age) and smoking history, aspirin use, body-mass index, physical activity, and intakes of red meat and alcohol or folate.

Table 2.76. Studies of *ALDH2*, *ADH1B* and *ADH1C* genotype-associated risk for sites other than cancer of the upper aerodigestive tract

Reference, study location, period	Genes involved	Relative risk (95% CI)	Comments
Tiemersma *et al*. (2003) Bithoven, Wageningen, Netherlands, 1997–2000	***ADH1C***	*Alcohol intake*	Patients (n = 433) with adenomatous polyps and 436 polyp-free controls undergoing endoscopy in 1995–2000. Adjusted for sex, age, and indication for endoscopy (complaints related, screening, other/unknown).
		< 1 drinks/wk	
	**1/*2 + *2/*2*	1	
	**1/*1*	0.9 (0.5–1.6)	
		1–10 drinks/wk	
	**1/*2 + *2/*2*	1.0 (0.6–1.6)	
	**1/*1*	1.0 (0.6–1.8)	
		≥ 10 drinks/wk	
	**1/*2 +* 2*/2*	1.2 (0.7–1.9)	
	**1/*1*	1.8 (1.0–3.1)	
Landi *et al*. (2005), Barcelona, Spain	Overall		Alcohol beverage intake not ascertained. Adjusted for age and sex.
	ADH1B		
	**1/*1*	1.00 (ref)	
	**1/*2*	1.04 (0.68–1.59)	
	**2/*2*	0.57 (0.09–3.50)	
Otani *et al*. (2005), Nagano, Japan; 1998–2002	Overall		No stratification with alcohol intake. Adjusted for age, sex, residence and hospital.
	ALDH2		
	**1/*1*	1.0 (ref)	
	**1/*2*	1.1 (0.7–1.9)	
	**2/*2*	1.2 (0.5–2.9)	

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Table 2.76. Studies of *ALDH2*, *ADH1B* and *ADH1C* genotype-associated risk for sites other than cancer of the upper aerodigestive tract

Reference, study location, period	Genes involved	Relative risk (95% CI)	Comments
Matsuo *et al.* (2006), Aichi, Japan, 2001–04	*Overall* ***ALDH2*** **1/*1* **1/*2* **2/*2* ***ADH1B*** **2/*2* **1/*2* **1/*1* *Stratified analyses* *ALDH2*1/*1+ ADH1B*2/*2* *ALDH2*1/*1+ ADH1B*1* *ALDH2*2+ ADH1B*2/*2* *ALDH2*2+ ADH1B*1*	 1.00 (ref) 0.99 (0.71–1.37) 0.98 (0.54–1.75) 1.00 (ref) 1.35 (1.00–1.84) 1.93 (1.06–3.53) 1.00 0.10 (0.04–0.21) 0.10 (0.06–0.19) 1.36 (0.94–1.97)	In stratified analyses, *ALDH2*1* refers to *ALDH2*1/*2 + ALDH2*2/*2* and *ADH1B*1* refers to *ADH1B*1/*1 + ADH1B*1/*2*. A strong interaction between *ALDH2* and *ADH1B* was noted ($P < 0.001$). Adjusted for age, sex, drinking, smoking, BMI, family history, estrogen use; conditions with potential use of NSAIDs
Hirose *et al.* (2005) Japan, 1997–2001 colorectal	***ALDH2*** **1/*1* **1/*2* **2/*2*	 1.0 0.81 (0.62–1.05) 0.67 (0.35–1.27)	Adjusted for age, hospital, rank, cigarette smoking, alcohol consumption, BMI.
van der Logt *et al.* (2006) the Netherlands	***ADH1C*** rare homo	0.83 (0.54–1.3)	Adjusted for age and gender

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Table 2.76. Studies of *ALDH2, ADH1B* and *ADH1C* genotype-associated risk for sites other than cancer of the upper aerodigestive tract

Reference, study location, period	Genes involved	Relative risk (95% CI)	Comments
Yin *et al*. (2007) Fokuoda, Japan, 2000–2003	***ADH1B*** **2/*2*		One unit of alcohol corresponds to 1 go (180ml) of sake, 0.5 go (90 ml) of shochu, 1 large bottle (633ml) of beer, 2 drinks (60ml) of whiskey, or 2 glasses (200ml) of wine. Adjusted for sex, age and area. Note: individual s with ALDH2*2/*2 were excluded because alcohol drinkers were few. No significant gene-gene interaction
	0 unit/d	1.0	
	< 2 units/d	0.97 (0.69–1.37)	
	> 2 units/d	1.52 (1.02–2.25)	
	**1/*2 or *1/*1*		
	0 unit/d	1.46 (1.04–2.03)	
	< 2 units/d	1.30 (0.92–1.85)	
	> 2 units/d	1.69 (1.14–2.52)	
	ADH1C **1/*1*		
	0 unit/d	1.0	
	< 2 units/d	0.98 (0.74–1.28)	
	> 2 units/d	1.44 (1.05–1.98)	
	**1/*2 or *2/*2*		
	0 unit/d	1.49 (0.89–2.50)	
	< 2 units/d	1.29 (0.70–2.40)	
	> 2 units/d	1.27 (0.62–2.57)	
	ALDH2		
	**1/*1*	1.00	
	**1/*2*	0.89 (0.71–1.13	
	**2/*2*	0.55 (0.33–0.93)	
	By alcohol drinking		
	**1/*1*		
	0 unit/d	1.0	
	< 2 units/d	1.04 (0.71–1.53)	
	> 2 units/d	1.24 (0.81–1.90)	
	**1/*2*		
	0 unit/d	1.02 (0.71–1.48)	
	< 2 units/d	0.74 (0.47–1.17)	
	> 2 units/d	1.33 (0.74–2.39)	

Table 2.76. Studies of *ALDH2*, *ADH1B* and *ADH1C* genotype-associated risk for sites other than cancer of the upper aerodigestive tract

Reference, study location, period	Genes involved	Relative risk (95% CI)	Comments
Curtin *et al*. (2007), Utah, Northern California, and Minnesota, USA, 1991–1994	***ADH1C***	No association	916 cases of colon cancer (excluding cases with rectosigmoid junction or rectum cancer, with known familial adenomatous polyposis, ulcerative colitis or crohn's disease) and 1972 population-based controls
Gao *et al*. (2008), Huian and Jintan, Jiangsu Province, China, 2000–2002	*Overall* ***ALDH2*** **1/*1* **1/*2* **2/*2* ***ADH1B*** **2/*2 or *1/*2* **1/*1* *Stratified analyses* *ALDH2*2+ ADH1B*2* *ALDH2*2+ ADH1B*1/*1* *ALDH2*1/*1+ ADH1B*2* *ALDH2*1/*1+ ADH1B*1/*1*	 1.00 0.56 (0.37–0.86) 0.52 (0.37–0.84) 1.00 1.60 (1.08–2.36) 1.00 1.64 (0.85–3.18) 1.87 (1.05–3.35) 3.05 (1.67–5.57)	In stratified analyses, *ALDH2*2* refers to *ALDH2*1/*2 + ALDH2*2/*2* and *ADH1B*2* refers to *ADH1B*1/*2 + ADH1B*2/*2*. Adjusted for age and smoking status

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Table 2.76. Studies of *ALDH2*, *ADH1B* and *ADH1C* genotype-associated risk for sites other than cancer of the upper aerodigestive tract

Reference, study location, period	Genes involved	Relative risk (95% CI)	Comments
Jung *et al*. (2008), Minneapolis, USA, 1991–1994	*Overall* ***ADH1C*** **1/*1* **1/*2* **2/*2* *By alcohol intake* ***ADH1C*****1/*1* None 1–7 g/d 8–25 g/d > 26 g/d **1/*2* None 1–7 g/d 8–25 g/d > 26 g/d **2/*2* None 1–7 g/d 8–25 g/d > 26 g/d	 1.00 1.15 (0.86–1.55) 1.23 (0.83–1.81) 1.00 0.62 (0.35–1.09) 0.76 (0.39–1.48) 1.09 (0.38–3.08) 0.75 (0.48–1.17) 1.00 (0.61–1.65) 1.12 (0.62–2.01) 2.25 (0.72–7.01) 0.61 (0.32–1.15) 1.15 (0.58–2.28) 1.71 (0.74–3.96) 1.95 (0.60–6.30)	530 cases with adenomatous polyps and 649 clinic-based controls with no polyps in colonoscopy. Adjusted for age, sex, body mass index, caloric intake, dietary fibre intake, hormone use (females only), smoking, and vitamin B12, B6, riboflavin, methionine, and folate intake
Homann *et al*. (2009), Heidelberg, Germany, 2000–2005	***ADH1C*** **1/*2 + *2/*2* **1/*1*	 1.00 1.67 (1.11–2.52)	173 cases with high-grade intraepithelial dysplasia (*n* = 37) or colorectal carcinoma (*n* = 136). The control group (*n* = 788) consisted of 537 patients with alcohol dependency and 251 community-based (laboratory and hospital staff) healthy individuals. Adjusted for age, sex, and alcohol intake

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Table 2.76. Studies of *ALDH2*, *ADH1B* and *ADH1C* genotype-associated risk for sites other than cancer of the upper aerodigestive tract

Reference, study location, period	Genes involved	Relative risk (95% CI)	Comments
Breast cancer			
Freudenheim *et al*. (1999), New York, USA, 1986–91	**Premenopausal**		The cut-off between lower and higher alcoholic beverage intake was 6.5 and 4.5 drinks per mo on average over the past 20 yr for the pre- and postmetnopausal women, respectively. Adjusted for age, education, body mass index, parity, age at first birth, age at menarche, fruit and vegetable intake, duration of lactation, benign breast disease, age at menopause.
	ADH1C1/*1*		
	Lower	1.0 (0.4–2.5)	
	Higher	3.6 (1.5–8.8)	
		Interaction $P = 0.16$	
	**1/*2* or **2/*2*		
	Lower	1	
	Higher	0.8 (0.4–1.7)	
	Postmenopausal		
	ADH1C1/*1*		
	Lower	0.9 (0.5–1.6)	
	Higher	1.2 (1.1–2.2)	
	**1/*2* or **2/*2*		
	Lower	1	
	Higher	0.8 (0.5–1.4)	
Hines *et al*. (2000), 11 states, USA, 1989–94	*By alcohol intake*		Adjusted for age of birth, drinking, body mass index, parity, age at menarche, family history, benign breast disease
	ADH1C1/*1*		
	0 g ethanol/d	1	
	≤ 10 g /d	0.8 (0.5–1.3)	
	> 10 g/d	0.8 (0.4–1.5)	
		Interaction $P = 0.15$	
	**1/*2*		
	0 g/d	0.7 (0.4–1.2)	
	≤ 10 g /d	1.1 (0.7–1.8)	
	> 100 g/d	0.8 (0.4–1.4)	
	*2/*2*		
	0 g/d	0.6 (0.3–1.2)	
	≤ 10 g /d	0.6 (0.3–1.2)	
	> 100 g/d	1.1 (0.5–2.4)	

Table 2.76. Studies of *ALDH2*, *ADH1B* and *ADH1C* genotype-associated risk for sites other than cancer of the upper aerodigestive tract

Reference, study location, period	Genes involved	Relative risk (95% CI)	Comments
Choi *et al*. (2003), Seoul, Republic of Korea, 1995–2001	Overall *ALDH2*	 0.8 (0.6–1.2)	Adjusted for age, family history
Coutelle *et al*. (2004), Heidelberg, Germany, study period was not reported	Overall *ADH1C* **1/*2* or **2/*2* **1/*1*	 1 1.8 (1.4–2.3)	Alcohol intake: cases, 17 ± 22 g/d; alcoholic controls, 110 ± 89 g/d. No adjustment was reported.
Lilla *et al*. (2005), Southern Germany, 1992–95	*By alcohol intake* ***ADH1B*1/*1*** 0 g ethanol/d ≥ 12 g/d ****1/*2 + *2/*2*** 0 g/d ≥ 12 g /d	 1 1.1 (0.8–1.6) 1 0.3 (0.1–1.0) Interaction *P* = 0.05	Interactions between other drinking categories and *ADH1B* genotype not significant. Adjusted for age, education, smoking, family history, menopausal status, breast-feeding.
Terry *et al*. (2006), New York, USA, 1996–97	*Lifetime alcohol intake* ***ADH1C***1/*1* 0 g ethanol/d 15–30 g /d ≥ 30 g/d **1/*2* 0 g/d 15–30 g /d ≥ 30 g/d **2/*2* 0 g/d 15–30 g /d ≥ 30 g/d	 1.00 1.97 (1.10–3.54) 0.84 (0.42–1.68) Interaction *P* = 0.20 1.00 1.49 (0.91–2.41) 0.80 (0.44–1.45) 1.00 1.34 (0.51–3.54) 0.90 (0.24–3.39)	The association for *ADH1C*1/*1* carriers who drank 15–30 g/d was more pronounced among premenopausal women (odds ratio = 2.9; 95% CI: 1.2–7.1) versus postmenopausal women (odds ratio = 1.8; 95% CI: 0.9–3.8). Adjusted for age, education, race, caloric intake, smoking, body mass index, history of benign breast disease, parity, age at first birth, age at menarche, menopausal and lactation status.

Table 2.76. Studies of *ALDH2, ADH1B* and *ADH1C* genotype-associated risk for sites other than cancer of the upper aerodigestive tract

Reference, study location, period	Genes involved	Relative risk (95% CI)	Comments
Breast Cancer Association Consortium (2006), international multicenter study	***ADH1C***		7320 cases and 7805 controls with genotyping for *ADH1C*. No adjustment was reported.
	*1/*1	1.00	
	*1/*2	1.00 (0.93–1.07)	
	*2/*2	1.07 (0.97–1.18)	
Terry *et al*. (2007b), Australia, Canada and USA, study period not reported	***ADH1C***		Only women with at least one sister affected with breast cancer and one sister unaffected with breast cancer were enrolled. Adjusted for age. For ADH1C genotype, there were no statistically significant association by genotype and alcohol consumption
	**1/*1)*	1.0	
	**1/*2)*	1.04 (0.81–1.33)	
	**2/*2*	1.04 (0.71–1.52)	
	ADH1B		
	**1/*1*	1.0	
	**1/*2*	1.15 (0.80–1.66)	
	**2/*2*	0.91 (0.40–2.11)	

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Table 2.76. Studies of *ALDH2*, *ADH1B* and *ADH1C* genotype-associated risk for sites other than cancer of the upper aerodigestive tract

Reference, study location, period	Genes involved	Relative risk (95% CI)	Comments
Visvanathan *et al*. (2007) USA, 1989–2002	*By alcohol intake* ***ADH1C*** 56A > G **2/*2* Non-drinker Drinker **1/*2 + *1/*1* Non-drinker Drinker ***ADH1C*** 14G > A **2/*2* Non-drinker Drinker **1/*2 + *1/*1* Non-drinker Drinker ***ADH1B*** 23A > G **1/*1* Non-drinker Drinker **1/*2 + *2/*2* Non-drinker Drinker	 1.0 0.86 (0.36–2.05) 0.96 (0.53–1.72) 1.63 (0.86–3.11) 1.0 0.75 (0.24–2.32) 0.98 (0.44–2.21) 1.58 (0.67–3.74) 1.0 1.44 (0.95–2.17) 0.9 (0.25–3.26) 6.0 (0.69–52.3)	
Cox *et al*. (2007), multicenter international genome-wide study	***ADH1B*** *1/*1 *1/*2 *2/*2	 1.00 0.99 (0.90–1.10) 1.04 (0.95–1.14)	11 391 cases and 15 570 controls. Results presented here are from random-effects models. No adjustment
Ribas *et al*. (2008) Spain, 2000–2004	***ALDH2***	No association	No risk estimates provided. No association between *ALDH2* and risk of breast cancer.

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Table 2.76. Studies of *ALDH2, ADH1B* and *ADH1C* genotype-associated risk for sites other than cancer of the upper aerodigestive tract

Reference, study location, period	Genes involved	Relative risk (95% CI)	Comments
Kawase *et al*. (2009), Aichi, Japan, 2001–2005	***ADH1B*****2/*2*		Adjusted for matching factors, alcohol consumption, smoking status, BMI, exercise, family history of breast cancer, age at menarche, parity, HRT, mode of referral to hospital. All cases and controls with ALDH*2/*2 allele (cases, 38, controls, 92) were never-drinkers, except for one control who was a moderate drinker.
	never drinker	1.0	
	former drinker	1.78 (0.59–5.34)	
	light drinker	0.93 (0.61–1.43)	
	moderate drinker	1.06 (0.66–1.72)	
	heavy drinker	1.61 (0.85–3.02)	
	**1/*2*		
	never drinker	1.0	
	former drinker	0.91 (0.16–5.11)	
	light drinker	0.85 (0.5–1.45)	
	moderate drinker	0.88 (0.45–1.71)	
	heavy drinker	1.12 (0.52–2.4)	
	**1/*1*		
	never drinker	1.0	
	former drinker	NA	
	light drinker	0.82 (0.21–3.25)	
	moderate drinker	0.59 (0.09–3.93)	
	heavy drinker	1.7 (0.16–17.69)	
	ALDH2**1/*1*		
	never drinker	1.0	
	former drinker	1.03 (0.34–3.16)	
	light drinker	0.88 (0.57–1.36)	
	moderate drinker	0.98 (0.61–1.59)	
	heavy drinker	1.21 (0.7–2.11)	
	**1/*2*		
	never drinker	1.0	
	former drinker	1.94 (0.4–9.27)	
	light drinker	0.97 (0.57–1.67)	
	moderate drinker	0.85 (0.41–1.76)	
	heavy drinker	1.82 (0.52–6.36)	

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Table 2.76. Studies of *ALDH2, ADH1B* and *ADH1C* genotype-associated risk for sites other than cancer of the upper aerodigestive tract

Reference, study location, period	Genes involved	Relative risk (95% CI)	Comments
Lung			
Yokoyama *et al*. (1998), Kanagawa, Japan, 1987–97	***ALDH2***		Male alcoholics; because the differences in odds ratio between the incident cases and the prevalent cases were slight, the cases were combined. Adjusted for age, alcohol drinking and cigarette smoking.
	**1/*1*	1.00	
	**1/*2*	8.20 (1.27–53.15)	
Freudenheim *et al*., (2003). New York State, 02–1996 until 11–1998.	***ADH1C***	Alcohol intake Results for men	Cases (n = 273) were newly diagnosed lung cancers that were identified in two counties of NY State. There were 3 351 controls. Alcohol intake given as 'lower' and 'higher'. ORs adjusted for education, packs smoked per yr, yr smoked, passive exposure to smoke at home, work and in other settings, and vegetable and fruit intake.
		Lower	
	**1/*1*	0.7 (0.3–1.6)	
	**1/*2 + *2/*2*	1.0	
		Higher	
	**1/*1*	0.4 (0.2–1.0)	
	**1/*2 + *2/*2*	0.6 (0.3–1.2)	
		Results for women	
		Lower	
	**1/*1*	1.0 (0.3–3.6)	
	**1/*2 + *2/*2*	1.0	
		Higher	
	**1/*1*	2.6 (0.8–8.0)	
	**1/*2 + *2/*2*	2.3 (0.9–6.0)	

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Table 2.76. Studies of *ALDH2*, *ADH1B* and *ADH1C* genotype-associated risk for sites other than cancer of the upper aerodigestive tract

Reference, study location, period	Genes involved	Relative risk (95% CI)	Comments
Minegishi *et al*., (2007). Chiba and East-Tokyo, Japan, 1997–2000.	***ADH1C***	*Alcohol intake*	Patients (*n* = 505) with primary lung cancer, newly diagnosed, histologically and cytologically confirmed. Unmatched controls (*n* = 256) with no history of cancer, were recruited from the population between 2002 and 2003. Adjusted for age, sex, and smoking pack-yr.
	**1/*1*		
	Non-drinkers	1.00	
	≤ 31.6 g/d	1.59 (0.99–2.55)	
	> 31.6 g/d	1.88 (1.10–3.21)	
	**1/*2, + *2/*2*		
	Non-drinkers	1.00	
	≤ 31.6 g/d	4.31 (0.91–20.38)	
	> 31.6 g/d	3.28 (0.74–14.55)	
	Overall		
	**1/*1*	1.00	
	**1/*2, + *2/*2*	0.78 (0.48–1.28)	
	ALDH2		
	**1/*1*		
	Non-drinkers	1.00	
	≤ 31.6 g/d	0.75 (0.39–1.42)	
	> 31.6 g/d	0.46 (0.2–0.99)	
	**1/*2 + *2/*2*		
	Non-drinkers	1.00	
	≤ 31.6 g/d	3.63 (1.76–7.46)	
	> 31.6 g/d	6.15 (2.77–13.65)	

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Table 2.76. Studies of *ALDH2*, *ADH1B* and *ADH1C* genotype-associated risk for sites other than cancer of the upper aerodigestive tract

Reference, study location, period	Genes involved	Relative risk (95% CI)	Comments
Eom *et al*. (2009), Cheongju and Cheonan, Korea (Republic of), 2001–2006	***ALDH2***		Adjusted for age, sex and smoking.
	Non-drinkers		
	**1/*1*	1.00	
	**1/*2 + *2/*2*	0.48 (0.29–0.79)	
	< 108 g/wk		
	**1/*1*	1.00	
	**1/*2 + *2/*2*	0.78 (0.36–1.69)	
	≥ 108 g/wk		
	**1/*1*	1.00	
	**1/*2 + *2/*2*	1.69 (0.73–3.91)	
Bladder			
van Dijk *et al*., (2001). Nijmegen, the Netherlands, 1997–2000.	***ADH1C***	*Alcohol intake*	Hospital-based case–control study. Patients with histologically confirmed bladder cancer (n = 115) and convenience controls (n = 131) with benign prostate hyperplasia. Control group for alcohol intake were moderate drinkers. Adjusted for age, sex, and smoking pack-yr.
		1–14 glasses/wk	
	**1/*2 + *2/*2*	1.00	
	**1/*1*	3.33 (1.26–8.80)	
		< 14 glasses/wk	
	**1/*2 + *2/*2*	1.95 (0.85–4.48)	
	**1/*1*	2.18 (0.82–5.77)	

ADH, alcohol dehydrogenase; *ALDH, aldehyde dehydrogenase*; CI, confidence interval; HbsAg, hepatits B virus surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; NSAIDS, non-steroidal anti-inflammatory drugs; UADT, upper aerodigestive tract

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