

**Table 2.1. Cohort studies of populations exposed to benzidine derivatives and azo dyes metabolized to benzidine and cancer**

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)*	Adjustment factors	Comments
<i>Benzidine derivatives</i>								
Schulte et al. (1985); Schulte et al. (1986) Georgia, USA	Nested case-control study from cohort of 1385 workers employed in a chemical plant during 1940–72	Workers potentially exposed to 3,3'-dimethylbenzidine, BZ and BNA. Questionnaire used to obtain occupational history and other risk factors; workers considered exposed if employed > 1 year or any time in any 2 departments with potential BNA exposure	Bladder	Exposed Duration of employment	13 13	<b>OR</b> 7.0 (3.9–12.4) 4.3 (1.8–10.3)	Smoking, source of drinking water	

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Sinks et al. (1992) Georgia, USA	Cohort of 2050 workers (1 828 men, 222 women) employed >1 day at a paperboard printing manufacturing plant during 1957–88; mortality follow up 1957–88; incidence follow-up to 1990; vital status 90%; cause of death 82%; nested case–control study of 6 renal cell cancer cases and 48 controls	Length of employment and department from plant records; materials used from review of MSDS and supplier information	Renal cell	Overall	1	<b>SMR</b> 1.4 (0.0–7.7)	Age, sex	Mortality, national reference; incidence, local reference; which workers were exposed to DCB was not determined
			Bladder	Overall	1	2.6 (0.1–14.7)		
			Renal cell	Overall	6	<b>SIR</b> 3.7 (1.4–8.1)		
			Bladder	Overall		1.1 (0.2–3.1)		
			Renal cell	<i>Department (&gt;5 years)</i>		<b>OR</b>		
				Finishing	3	16.6 (1.7–453.1)		
				Maintenance	1	5.3 (0.1–223.4)		

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Naito et al. (1995) Urban area, Japan	Cohort of 442 workers of a BZ production and dye manufacturing plant (437 men, 5 women) during 1935–88; mortality and incidence follow-up 1935–92; vital status 100%	Workers exposed to one or more substance, including 3,3'-dimethoxybenzidine, BZ and BNA. Duration of employment at BZ manufacture or use facility as surrogate of duration of exposure	Urinary tract (188, 189) Bladder	Dye manufacture	6	<b>SMR</b> 15.8 (5.8–34.3)		National reference; incidence rates reported by duration of exposure; PPE reportedly used among all workers
				Dye manufacture	5	27.0 (8.8–63.0)		
Ouellet-Hellstrom & Rench (1996) Connecticut, USA	Cohort of 704 workers (585 men, 119 women) first employed at a chemical plant between 1965 (when BZ production was discontinued) and 1989; incidence follow-up 1965–94; vital status 96%	Personnel records for occupational history; exposure scoring for arylamines (3,3'-dimethoxybenzidine, 3,3'-dimethylbenzidine, DCB, <i>o</i> -toluidine, <i>o</i> -chloroaniline) for each job title based on expert judgement	Bladder	<b>Men</b>		<b>SIR</b>		State reference; workers with testicular cancer had no exposure to arylamines
				Overall	7	8.3 (3.3–17.1)		
				<i>Annual cumulative exposure score (CES)</i>				
				No exposure	0	0		
				<2.5	2	5.5 (0.7–19.8)		
				2.5+	5	16.4 (5.3–38.2)		
<i>CES among smokers</i>								
<2.5		11.6 (1.4–41.8)						
2.5+		23.6 (7.7–55.2)						
Overall	2	11.4 (1.4–41.1)						
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Rosenman & Reilly (2004) Michigan, USA	Cohort of 488 white men employed in a chemical manufacturing facility during 1960–77; mortality follow-up 1979–2001; incidence follow-up 1981–2002 (Michigan Tumor Registry)	Workers classified as exposed to BZ and DCB if employed before 1973, those employed during or after 1973 were exposed to DCB only. Time and length of employment estimated from social security records.	Bladder	Overall	3	<b>SMR</b> 8.3 (1.7–24.4)		National reference for SMR and SEER for SIR
				<i>Year started work</i>				
				<1973	3	9.6 (2.0–28.1)		
				≥1973	0	0		
			Lymphohaematopoietic cancer	Overall	6	2.8 (1.4–6.2)		
				<i>Year started work</i>				
				<1973	3	6.6 (1.4–19.4)		
				≥1973	3	5.1 (1.4–12.9)		
Leukemia	Overall	4	<b>SIR</b> 6.9 (4.3–10.4)					
	Bladder	22						
<i>Azo dyes metabolized to benzidine</i>								
Stern (2003) Minnesota and Wisconsin, USA	Cohort of 9365 tannery production workers (7085 men, 2280 women), employed during 1940–79 at tannery A and 1940–80 at tannery B; mortality follow-up 1940–82; vital status 95%; cause of death 97%	Occupational history from plant records; duration of employment as surrogate for cumulative exposure; BZ measured in 2 samples of bulk dyes: 2.0 & 55 ppm	Bladder	Latency (15+ years)	4	<b>SMR</b> 0.5 (0.1–1.3)	State reference; no increased SMR for other cancers	
				<i>Department</i>				
				Retan, colour, fat-liquor	2	1.0 (0.2–3.2)		
				Finishing	3	0.9 (0.2–2.5)		
			Leukemia (ICD-7, 204)	Latency (15+ years)	10	1.0 (0.5–1.9)		
				<i>Department</i>				
				Retan, colour, fat-liquor	3	1.0 (0.2–2.9)		
			Lymphomas (ICD-7, 200–203, 205)	Finishing	7	1.3 (0.5–2.6)		
				Latency (15+ years)	12	0.9 (0.5–1.5)		
				<i>Department</i>				
Retan, colour, fat-liquor	1	ND						
Finishing	7	0.9 (0.4–1.9)						

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Costantini et al. (1989) Florence and Pisa, Italy	Cohort of 2926 male workers newly employed in tanneries during 1950–81; at least one period of employment of >6 months; mortality follow-up 1950–83; vital status 99%	Employment in the tannery industry from municipal records	Bladder	Overall	5	<b>SMR</b> 1.5 (0.5–3.5)		National reference
				<i>Latency (years)</i>				
				<15		0		
				15–19		1.6		
				20–24		2.8		
25–29		3.9						
			<i>p</i> for trend			>0.05		
You et al. (1990) Shanghai, China	Cohort of 1210 workers (1060 men and 150 women) employed >1 year in weighing and formulating or dyeing at textile printing and dyeing plants during 1949–83; vital status 98%	Workers divided in 2 groups based on BZ-based dyes usage: high exposure (>500 kg/month) and low exposure (<500 kg/month)	Bladder	Overall	1	ND		Local reference
Montanaro et al. (1997) Genoa, Italy	Cohort of 1244 workers at a tannery (870 men, 374 women) employed >6 months during 1955–88; mortality follow-up to 1994; vital status 96%; cause of death 98%	Length of employment from plant records; information on department only for 25% workers	Bladder	Overall	10	<b>SMR</b> 2.4 (1.2–4.5)		National and regional reference
				<i>Duration of exposure (years)</i>				
				<5	3	4.4 (0.9–12.8)		
				5–14	0	0 (0–2.8)		
				15+	7	3.0 (1.2–6.1)		
		Lymphoma (200–202)	Overall	1	0.4 (0.01–2.0)			
		Leukemia (204–208)	Overall	0	0 (0.0–0.9)			

BNA, 2-naphthylamine; BZ, benzidine; DCB, 3,3'-dichlorobenzidine; MSDS, material safety data sheets; ND, not determined; SIR, standardized incidence ratio; SMR, standardized mortality ratio