疫学文献におけるばく露期間と膀胱がん発症との関係

No.2

Bladder cancer incidence among workers exposed to o-toluidine, aniline and nitrobenzene at a rubber chemical manufacturing plant.

ゴム薬品製造工場でo-トルイジン、ニトロベンゼンにばく露した従業員の膀胱がん発生率

Carreón T, Hein MJ, Hanley KW, Viet SM, Ruder AM.

Occup Environ Med. 2014 Mar;71(3):175-82. doi: 10.1136/oemed-2013-101873. Epub 2013 Dec 24

Table 2

Observed and expected numbers of bladder cancer cases, SIRs, and directly standardised rate ratios among chemical workers, by exposure category

Group	PYAR	OBS	SIR	95% CI	SRR	95% CI
Exposure category						
Probably not exposed	10 534	<5*	0.59	0.07 to 2.12	1	(referent)
Probably exposed (low and irregularly/occasionally)	3020	<5	2.47	0.67 to 6.33	2.50	0.42 to 14.8
Probably exposed (low and regularly)	2852	<5	4.21	1.15 to 10.8	4.85	0.81 to 29.0
Definitely exposed (moderate/high)	18 749	27	3.90	2.57 to 5.68	4.28	1.02 to 18.0
Overall	35 155	37	2.87	2.02 to 3.96		
Duration of exposure among definitely exposed (moderate/high) workers						
<5 years	13 604	<10	1.98	0.80 to 4.08	1	(referent)
5-<10 years	1834	<5	4.52	0.93 to 13.2	2.56	0.60 to 10.9
≥10 years	3312	17	6.24	3.63 to 9.99	4.50	1.74 to 11.6
						P_{trend}=<0.001
Time since first exposure among definitely exposed (moderate/high) workers						
<10 years	5614	<5	1.74	0.04 to 9.68	1	(referent)
10-<20 years	5697	<5	3.41	0.93 to 8.72	7.09	0.76 to 66.2
20-<30 years	4545	9	4.75	2.17 to 9.02	13.4	1.59 to 11.3
≥30 years	2892	13	3.97	2.11 to 6.79	8.61	1.11 to 67.0
						P_{trend}=<0.001
Cumulative rank quartile—unlagged‡						
1: <15 000 unit-days	26 907	10	1.47	0.71 to 2.71	1	(referent)
2: 15 000-<35 000 unit-days	4886	8	2.33	1.01 to 4.59	1.91	0.60 to 6.11
3: 35 000-<61 000 unit-days	2118	9	6.24	2.86 to 11.8	5.74	2.18 to 15.1
4: 61 000+ unit-days	1243	10	8.20	3.93 to 15.1	8.12	2.71 to 24.4
						P_{trend}=<0.001
Cumulative rank quartile—10-year lag‡						
1: <11 000 unit-days	28 335	9	1.32	0.61 to 2.51	1	(referent)
2: 11 000-<27 000 unit-days	3815	10	3.37	1.62 to 6.20	3.05	1.13 to 8.22
3: 27 000-<48 000 unit-days	1885	9	5.44	2.49 to 10.3	6.37	2.30 to 17.7
4: 48 000+ unit-days	1120	9	6.13	2.80 to 11.6	7.34	2.44 to 22.1
						P_{trend}=<0.001
Cumulative rank quartile—20-year lag‡						
1: <2800 unit-days	28 178	9	1.46	0.67 to 2.78	1	(referent)
2: 2800-<11 000 unit-days	3653	10	4.26	2.04 to 7.83	2.95	1.00 to 8.70
3: 11 000-<28 000 unit-days	2211	9	3.42	1.56 to 6.49	2.22	0.78 to 6.37
4: 28 000+ unit-days	1114	9	5.11	2.34 to 9.70	6.70	2.09 to 21.5
						P_{trend}=0.037

No.9

Bladder cancer risks in workers manufacturing chemicals for the rubber industry.

ゴム産業用化学品製造作業員の膀胱がんリスク

Sorahan T.

Occup Med (Lond). 2008 Oct;58(7):496–501. doi: 10.1093/occmed/kqn104. Epub 2008 Aug 25.

Table 3. Relative risk of bladder cancer (all notifications of malignant or benign tumours[a]) by potential exposure to four chemicals

Variable with levels	*n*	RR[b]	95% CI	RR[c]	95% CI
Cumulative exposure to MBT (mg m^{-3} years)					
None	41	1.0		1.0	
0.01–21.24	6	1.39	0.59–3.30	0.97	0.38–2.43
21.25–63.74	6	2.40*	1.02–5.66	1.70	0.65–4.41
≥63.75	3	2.71	0.84–8.76	2.12	0.64–7.06
P-value for trend[d]		$P < 0.05$		$P = 0.16$	
Duration of employment in PBN department (years)					
None	49	1.0		1.0	
0.1–4.9	3	1.88	0.59–6.06	1.03	0.26–4.05
≥5.0	4	4.55**	1.63–12.8	2.10	0.55–8.04
P-value for trend[e]		$P < 0.01$		$P = 0.37$	
Duration of employment in aniline-exposed departments (years)					
None	37	1.0		1.0	
0.1–4.9	8	1.55	0.72–3.33	1.24	0.52–3.00
≥5.0	11	2.22*	1.13–4.36	1.35	0.56–3.25
P-value for trend[d]		$P < 0.05$		$P = 0.44$	
Duration of employment in *ortho*-toluidine-exposed department (years)					
None	50	1.0		1.0	
0.1–4.9	4	4.68**	1.66–13.2	3.72*	1.21–11.4
≥5.0	2	6.99**	1.69–28.9	3.38	0.67–17.0
P-value for trend[d]		$P < 0.001$		$P < 0.05$	

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

[a]Reported on death certificates or by cancer registry: ICD-8: 188, 223.3, 237.6, ICD-9: 188, 223.3, 233.7, 236.7, 239.4, ICD-10: C67, D09.9, D30.3, D41.4.

[b]Column summarizes four analyses, adjusting for age (40–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79 and 80–84 years) and calendar period (1955–71, 1972–81, 1982–91, 1992–96 and 1997–2005).

[c]Column summarizes a single analysis in which the four chemical exposure variables are analysed simultaneously with age and calendar period.

[d]Four exposure categories scored 1–4 and treated as a continuous measure.

[e]Three exposure categories scored 1–3 and treated as a continuous measure.

No.14

Continued epidemic of bladder cancer in workers exposed to ortho-toluidine in a chemical factory.

化学工場でo-トルイジンにばく露した作業員の長期にわたる膀胱がんの発生異常

Markowitz SB, Levin K..

J Occup Environ Med. 2004 Feb;46(2):154-60.

TABLE 1

Newly Identified Cases of Bladder Cancer Among Workers in a Rubber Antioxidant Manufacturing Plant[a]

Exposure Group	Case No.	Year of First Exposure	Exposure Duration, Years[b]	Latency, Years	Year of Diagnosis	Age at Diagnosis	Source of Case	Pathology, Bladder Cancer	Vital Status/Year
Definitely exposed (Dept. 245)	1	1957	2	25	1982	54	A[c]	Grade 1, TCC[d]	A-2002[e]
	2	1957	28	34	1991	68	A	Grade 1, TCC	A-1993
	3	1957	23	35	1992	57	A	Grade 1, TCC	A-1998
	4	1963	27	32	1995	54	A	Grade 1–2, TCC	A-1998
	5	1976	13	21	1997	43	A	Grade 2–3, TCC	A-1999
	6	1957	20	41	1998	73	A	Grade 3, TCC; carcinoma in situ	A-1999
	7	1969	16	31	2000	50	A	Grade 3, TCC carcinoma in situ	A-2000
	8	1958	8	44	2002	65	A	Low grade papillary TCC	A-2002
	9	1965	3	38	2003	59	A	Grade 1–2/3 papillary TCC	A-2003
	10	1965	2	38	2003	63	A	Grade 1 papillary TCC	A-2003
Possibly exposed: worked in maintenance, janitorial/yard, or shipping	11	1969	21	28	1997	59	A	Carcinoma in situ, TCC	A-1999
	12	1969	0.5	28	1997	49	A	Grade 1–2, TCC	A-1998
	13	1958	20	41	1999	84	C	Grade 1, TCC	A-2000
	14	1957	29	43	2000	76	A	Low grade TCC	D-2001
	15	1969	20	32	2001	54	A	Grade 1, TCC	A-2000
	16	1952	35	16	2003	75	A	Grade 2 papillary TCC	A-2003
	17	1971	32	32	2003	57	A	Low grade papillary TCC	A-2003
Probably not exposed	18	1975	12[2]	21	1996	43	A	Grade 1, TCC	A-1999
	19	1962	20[2]	37	1999	85	C	Grade 1–2, TCC	A-2000

[a] Newly identified since the publication of Ward et al. *JNCI*, 1991.

[b] For cases classified as "probably not exposed," the exposure duration is the duration of time spent working at the plant.

[c] A, attorney; C, company.

[d] TCC, transitional cell carcinoma.

[e] A, alive; D, dead.

No.14

TABLE 2
Trends in Bladder Cancer of Definitely and Possibly Exposed Workers by Age, Exposure Duration, Duration From Onset of Exposure, and Decade of Diagnosis

Variable	Newly Identified Bladder Cancer Cases (n = 17)		Previously Reported Bladder Cancer Cases (n = 11)		All Bladder Cancer Cases (n = 28)	
	Number	%	Number	%	Number	%
Age (years)						
40–49	2	11.8	1	9.1	3	10.7
50–59	8	47.1	5	45.5	13	46.4
60–69	3	17.6	4	36.4	7	25.0
70–79	3	17.6	1	9.1	4	14.2
80–89	1	5.9	0	0	1	3.6
Duration of exposure (years)						
0–5	4	23.5	2	18.2	6	21.4
6–10	1	5.9	3	27.3	4	14.2
11–20	5	29.4	4	36.4	9	32.1
21–30	7	41.2	2	18.2	9	32.1
Duration from onset of exposure (years)						
0–5	0	0	1	9.1	1	3.6
6–10	0	0	2	18.2	2	7.1
11–20	1	5.9	1	9.1	2	7.1
21–30	4	23.5	6	54.5	10	35.7
31+	12	70.6	1	9.1	13	46.4
Decade of first exposure						
1950–1959	8	47.1	6	54.5	14	50.0
1960–1969	7	41.2	3	27.3	10	35.7
1970–1979	2	11.8	2	18.2	4	14.2

No.31

Carcinomas of the urinary bladder in a 4-chloro-o-toluidine cohort..

4-クロロ-o-トルイジンばく露作業者と膀胱がんに関するコホート調査

Stasik MJ...

Int Arch Occup Environ Health. 1988;60(1):21-4.

Table 2. Ages at start of exposure and at bladder carcinoma diagnosis; durations of exposure and of latency ($n = 8$)

Parameter	Median	Min.	Max.
Age at beginning of exposure (years)	35.5	31.0	41.0
Age at diagnosis of bladder carcinoma (years)	64.0	58.0	78.0
Duration of exposure (years)			
(a) before 1970	14.0	1.5	20.0
(b) total	25.5	1.5	30.0
Latency (years)	27.5	17.0	38.0

No.41

A further cohort study of workers employed at a factory manufacturing chemicals for the rubber industry, with special reference to the chemicals 2-mercaptobenzothiazole (MBT), aniline, phenyl-beta-naphthylamine and o-toluidine..

ゴム工場向けの化学物質を製造しているある工場の作業従事者の追加コホート研究：とりわけ化学物質2-メルカプトベンゾチアゾール(MBT)、アニリン、フェニル-β-ナフチルアミン、o-トルイジンに関して

Sorahan T, Hamilton L, Jackson JR.

Occup Environ Med. 2000 Feb;57(2):106-15.

Table 8 Relative risks of mortality from bladder cancer and all causes excluding bladder cancer by potential exposure to various chemicals, employment histories are unlagged

	Bladder cancer†		*All other causes*	
Variable with levels	*n*	*RR (95% CI) simultaneous analysis‡*	*n*	*RR (95% CI) simultaneous analysis‡*
Cumulative exposure to MBT (mg.μ³y):				
None	14	1.0	959	1.0
0.01–21.24	4	2.69 (0.77 to 9.48)	83	1.06 (0.84 to 1.34)
21.25–63.74	3	2.69 (0.68 to 10.58)	47	0.94 (0.69 to 1.28)
≥63.75	1	2.10 (0.27 to 16.43)	20	0.79 (0.51 to 1.24)
p Value for trend§		p=0.24		p=0.43
Duration of employment in PBN department (y):				
None	18	1.0	1044	1.0
1–4	0	} 1.75 (0.42 to 7.35)	38	1.23 (0.88 to 1.73)
≥5	4		27	1.27 (0.85 to 1.88)
p Value for trend§		p=0.048		p=0.09
Duration of employment in aniline department (y):				
None	17	1.0	938	1.0
1–4	1	0.34 (0.04 to 2.73)	101	1.04 (0.84 to 1.29)
≥5	4	1.31 (0.39 to 4.39)	70	0.79 (0.61 to 1.02)
p Value for trend§		p>0.50		p=0.15
Duration of employment in o-toluidine department (y):				
None	19	1.0	1095	1.0
1–4	2	4.44 (0.76 to 25.79	7	0.48 (0.22 to 1.02)
≥5	1	5.48 (0.51 to 59.14)	7	1.23 (0.57 to 2.65)
p Value for trend§		p=0.08		p>0.50

*p<0.05.
†Any part of death certificate coded to ICD-8 188 (table 3, first column).
‡Column summarises a single analysis in which the four chemical exposure variables are analysed simultaneously with age.
§See text.

Table 9 Relative risk of bladder cancer (all notifications of malignant neoplasms†) by potential exposure to various chemicals: employment histories are unlagged

Variable with levels	*n*	*RR (95% CI) separate analysis‡*		*RR (95% CI) simultaneous analysis§*	
Cumulative exposure to MBT (mg.μ³y):					
None	21	1.0		1.0	
0.01–21.24	5	2.96*	(1.11 to 7.86)	2.24	(0.76 to 6.60)
21.25–63.74	3	2.50	(0.74 to 8.48)	1.46	(0.38 to 5.63)
≥63.75	1	1.72	(0.23 to 12.82)	1.21	(0.15 to 9.54)
p Value for trend¶		p=0.06		p=0.18	
Duration of employment in PBN department (y):					
None	25	1.0		1.0	
1–4	1	1.26	(0.17 to 9.32)	0.58	(0.06 to 5.46)
≥5	4	7.48**	(2.60 to 21.52)	4.35*	(1.30 to 11.57)
p Value for trend¶		p<0.001		p=0.03	
Duration of employment in aniline department (y):					
None	23	1.0		1.0	
1–4	2	0.85	(0.20 to 3.61)	0.61	(0.14 to 2.76)
≥5	5	2.20	(0.84 to 5.79)	1.50	(0.52 to 4.35)
p Value for trend¶		p=0.17		p>0.50	
Duration of employment in o-toluidine department (y):					
None	27	1.0		1.0	
1–4	2	6.73*	(1.59 to 28.41)	5.18*	(1.04 to 25.80)
≥5	1	7.65*	(1.03 to 56.87)	2.73	(0.29 to 25.45)
p Value for trend¶		p=0.002		p=0.31	

*p<0.05; **p<0.01; ***p<0.001.
†See table 3, second column.
‡Column summarises four analyses, only adjusting for age.
§Column summarises a single analysis in which the four chemical exposure variables are analysed simultaneously with age.
¶See text.

No.41

Table 10 Relative risk of bladder cancer (all notifications of malignant and benign neoplasms†) by potential exposure to various chemicals; employment histories are lagged by 15 years

Variable with levels	*n*	*RR (95% CI) separate analysis‡*	*RR (95% CI) simultaneous analysis§*
Cumulative exposure to MBT (mg.μ'y):			
None	34	1.0	1.0
0.01–21.24	3	1.40 (0.43 to 4.54)	1.18 (0.34 to 4.07)
21.25–63.74	4	2.16 (0.76 to 6.12)	1.84 (0.58 to 5.86)
≥63.75	0		
p Value for trend¶		p=0.23	p=0.49
Duration of employment in PBN department (y):			
None	36	1.0	1.0
1–4	2	2.01 (0.48 to 8.36)	1.46 (0.31 to 6.95)
≥5	3	4.73* (1.45 to 15.42)	3.48 (0.98 to 12.40)
p Value for trend¶		p=0.007	p=0.059
Duration of employment in aniline department (y):			
None	35	1.0	1.0
1–4	3	1.03 (0.32 to 3.34)	0.86 (0.25 to 2.90)
≥5	3	1.23 (0.38 to 4.01)	0.94 (0.26 to 3.37)
p Value for trend¶		p>0.50	p>0.50
Duration of employment in *o*-toluidine department (y):			
None	39	1.0	1.0
1–4	1	3.11 (0.43 to 22.65)	2.05 (0.24 to 17.28)
≥5	1	13.43* (1.84 to 98.06)	7.64 (0.90 to 65.14)
p Value for trend¶		p=0.007	p=0.076

*p<0.05, **p<0.01.
†See table 3, third column.
‡Column summarises four analyses, only adjusting for age.
§Column summarises a single analysis in which the four chemical exposure variables are analysed simultaneously with age.
¶See text.

No.42

Excess number of bladder cancers in workers exposed to ortho-toluidine and aniline.

o-トルイジンならびにアニリンにばく露した労働者における膀胱がんの症例過剰

J Natl Cancer Inst. 1991 Apr 3;83(7):501-6.

Ward E, Carpenter A, Markowitz S, Roberts D, Halperin W.

Table 1. Characteristics of bladder cancer cases among chemical workers by exposure group

Exposure group	Case No.	Year of first exposure	Duration of exposure,* y	Latency, y	Year of diagnosis	Age at diagnosis	Stage	Source of case†	Pathology	Vital statistics/y
Definitely exposed	1	1970	11	16	1986	71	1	R	Unknown	Alive/1989
	2	1957	18	23	1980	61	1	P, R	Grade 1 papillary tumor	Alive/1989
	3	1957	25	25	1982	57	3	P, R	Adenocarcinoma	Died/1983
	4	1957	21	21	1978	43	1	P, R	Grade 2 papillary transitional cell carcinoma	Died/1982
	5	1961	10	25	1986	53	1	P, R	Grade 2 papillary transitional cell carcinoma	Alive/1989
	6	1957	13	23	1980	56	2	P, R	Grade 2 papillary transitional cell carcinoma	Alive/1989
	7	1957	7	31	1988	64		P	Multiple grade 2 or 3 papillary transitional cell carcinoma	Alive/1989
Possibly exposed: worked in maintenance, janitorial/yard, shipping	8	1957	11	25	1986	60	3	R	Grade 2 papillary transitional cell carcinoma	Alive/1989
	9	1963	9	10	1973	56	1	P, R	Unknown	Died/1989
	10	1979	5	5	1984	52	1	P, R	Grade 1 or 2 papillay transitional cell carcinoma	Alive/1989
	11	1968	1	9	1978	64	1	R	Unknown	Alive/19
Probably not exposed	12				1975	46		R	Unknown	Alive/19
	13				1983	64	3	R	Unknown	Alive/1988
Not included in analysis	14	1957	15	15	1972	44		P, R	Grade 3 transitional cell carcinoma	Died/1986
	15	1979	8	9	1989	60	1	P	Grade 2 papillary transitional cell carcinoma	Alive/1989

*Duration of exposure includes only the period before diagnosis. For individuals who worked in the exposed department, duration of exposure includes only time in that department. For workers in "possibly exposed" jobs, duration of exposure includes only time spent in those jobs.

†R = case identified from the New York State Cancer Registry; P = case reported by company or union.

No.42

Table 2. Observed and expected numbers of bladder cancers among chemical workers by exposure group

Probability of exposure to *o*-toluidine and aniline	No. of persons	Bladder cancers		SIR	90% CI
		Observed	Expected		
Definitely exposed	708	7	1.08	6.48	3.04-12.2
Possibly exposed	288	4	1.09	3.66	1.25-8.37
Probably unexposed	753	2	1.43	1.39	0.25-4.39
Total	1749	13	3.61	3.60	2.13-5.73

Table 3. Trends in bladder cancer risk by duration of employment in exposed department

Duration of exposure, y	No. of persons*	Bladder cancers		SIR†	90% CI
		Observed	Expected		
<5	584	0	0.75	—	—
5-9.99	51	1	0.11	8.8	0.45-41.7
10+	73	6	0.22	27.2	11.8-53.7

*No. of persons whose duration of employment (as of the study end date, the date of diagnosis, or date of death) was in the category stated.

†Directly standardized rate ratios were 1.00, 3.31, and 16.0 (with low exposure group as referent). Test for linear trend was highly significant ($P < .001$).

Table 4. Trends in bladder cancer risk by time since first employment in exposed department

Time since first employment in exposed department, y	No. of persons*	Bladder cancers		SIR	90% CI
		Observed	Expected		
<10	196	0	0.22	—	—
10-20	364	1	0.49	2.03	0.10-9.64
20+	148	6	0.37	16.4	7.13-32.3

*No. of persons whose time since first employment (as of the study end date, the date of diagnosis, or date of death) was in the category stated.

No.43

The carcinogenic effect of aromatic amines: an epidemiological study on the role of o-toluidine and 4,4'-methylene bis (2-methylaniline) in inducing bladder cancer in man.

芳香族アミン類の発がん作用：男性に膀胱がんを誘発する際のo-トルイジンならびに4,4'メチレン ビス(2-メチルアニリン)の役割に関する研究

Rubino GF. Scansetti G, Piolatto G, Pira E..

Environ Res. 1982 Apr;27(2):241-54.

TABLE 5
OBSERVED AND EXPECTED DEATHS BY DURATION OF EXPOSURE AND SELECTED NEOPLASMS

Duration of exposure (years):	Up to 10			11–20			21 and over		
Number in study:	581			161			126		
Person-years of observation:	11,089			3261			1618		
	Observed	Expected	Ratio obs./exp.	Observed	Expected	Ratio obs./exp.	Observed	Expected	Ratio obs./exp.
Lung cancer	8	4.24	1.89	3	2.10	1.43	3	1.53	1.96
Laryngeal cancer	5	0.78	6.41**	0	0.39	—	0	0.24	—
Esophageal cancer	4	0.54	7.41**	1	0.33	3.03	0	0.19	—
Bladder cancer	8	0.64	12.50***	13	0.38	34.21***	15	0.21	71.43***

* $P < 0.05$.
** $P < 0.01$.
*** $P < 0.001$.

TABLE 6
MEAN LATENT PERIOD FOR BLADDER CANCER BY DURATION OF EXPOSURE

Category of duration of exposure (years)	No. in study	Mean duration and range (years)	Number of deaths from bladder cancer	Years since first exposure (mean and range)
Up to 5	377	<1	2	26.5 (25–28)
6–10	204	7.5 (6–10)	6	18.7 (12–27)
11–20	161	13.9 (11–19)	13	21.1 (12–30)
21 and over	126	27.7 (21–38)	15	30.4 (21–41)
All exposures	868	17.9 (<1–38)	36	24.9 (12–41)

TABLE 7
MORTALITY FROM BLADDER CANCER BY AGE AT ENTRY

Age at entry	Number in study	Number of deaths from bladder cancer	Years since first exposure (mean and range)	Age at death (mean and range)
Up to 25	275	10	31.6 (22–41)	54.1 (43–63)
26–35	252	12	24.9 (14–33)	56.4 (48–63)
36 and over	341	14	20.1 (12–28)	65.1 (57–76)
Total	868	36	24.9 (12–41)	59.2 (43–76)

TABLE 8
OBSERVED AND EXPECTED DEATHS, LATENT PERIOD, AND AGE AT DEATH FROM BLADDER CANCER BY CATEGORY OF EXPOSURE

Category	Observed	Expected	Ratio obs./exp.	Years since first exposure (mean and range)	Age at death (mean and range)
A	1	0.05	20.00	41	63
B	6	0.04	150.00***	24.7 (22–27)	55.5 (43–72)
C	5	0.06	83.33***	23.4 (12–30)	62.4 (48–73)
D	11	0.04	275.00***	24.2 (13–35)	56.4 (49–63)
E	3	0.24	12.50**	21.7 (12–34)	62.3 (57–71)
F	5	0.44	11.36***	24.2 (17–30)	63.0 (53–76)
G	5	0.08	62.50***	27.4 (12–40)	60.0 (54–64)
H	0	0.10	—	—	—
I	0	0.12	—	—	—
L	0	0.06	—	—	—
All	36	1.23	29.27***	24.9 (12–41)	59.2 (43–76)

* $P < 0.05$.
** $P < 0.01$.
*** $P < 0.001$.