### ORIGINAL ARTICLE

# Updated epidemiological study of workers at two California petroleum refineries, 1950–95

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Accepted 17 October 2001 **Objectives:** To further assess the potential role of occupational exposures on mortality, a second update of a cohort study of workers at two petroleum refineries in California was undertaken. **Methods:** Mortality analyses were based on standardised mortality ratios (SMRs) and 95% confidence intervals (95% CIs) using the general population of California as a reference. Additional analyses of lymphatic and haematopoietic cancer deaths and diseases related to asbestos were undertaken.

**Results:** The update consisted of 18 512 employees, who contributed 456 425 person-years of observation between 1950 and 1995. Both overall mortality and total cancer mortality were significantly lower than expected, as were several site specific cancers and non-malignant diseases. In particular, no significant increases were reported for leukaemia cell types or non-Hodgkin's lymphoma. Mortality excess from multiple myeloma was marginally significant. The excess was confined to employees enrolled before 1949. Furthermore, there was no significant upward trend based on duration of employment, which argues against a causal interpretation relative to employment or exposures at the refineries. No increase was found for diseases related to asbestos: pulmonary fibrosis; lung cancer; or malignant mesothelioma. There was no significant increase in mortality from any other cancers or non-malignant diseases.

**Conclusion:** This second update provides additional reassurance that employment at these two refineries is not associated with increased risk of mortality.

This report presents the results of a second update of a historical cohort mortality study of Chevron employees at the Richmond and El Segundo refineries in California. Although both the original study¹ and the first update² showed a generally healthy workforce, the current update was undertaken for several reasons: (a) to follow up on the previous study findings, (b) to find whether any new health risks have emerged (recognising that some diseases may take many years to develop), (c) to assess health risks relative to more contemporary levels of exposure and work environments at the refinery, and (d) to assess mortality patterns in the context of recently reported findings among other petroleum industry cohorts.

#### MATERIAL AND METHODS

The cohort consisted of employees who had completed 1 year of work by 31 December 1995 at either the Richmond or El Segundo refinery and who had worked for at least 1 day between 1 January 1950 and 31 December 1995. This update includes additional employees who entered the workforce after the cut off of the original study, 31 December 1980.

Vital status was determined through company pension benefits records, the Social Security Administration's Death Master File, and the National Center for Health Statistics' National Death Index. Death certificates for people identified to have died were obtained from state health departments and the underlying causes of death were based on the 8th revision of the international classification of disease (ICD-8) were assigned by a trained nosologist.

Statistical analyses were based on cause specific standardised mortality ratios (SMRs) adjusted for age (5 year groups), sex, race, and calendar year (5 year groups). Expected deaths were based on California mortalities. Ninety five per cent confidence intervals (95% CIs) were also computed. The calculations were performed with the University of Pittsburgh's OCMAP program.<sup>3</sup> For male employees (92% of the cohort),

stratified analyses by refinery, duration of employment, time since first employment at the refineries, and period of enrollment (before 1949 and 1949 and after) were also performed.

Additional analyses were conducted for the following lymphatic and haematopoietic cancers (LHC) in light of initial interest: non-Hodgkin's lymphoma (NHL, ICD-8 200, 202), multiple myeloma (MM, ICD-8 203), and the major cell types of leukaemia: acute lymphatic (ALL, ICD-8 204.0), chronic lymphatic (CLL, ICD-8 204.1), acute myeloid (AML, ICD-8 205.0), and chronic myeloid leukaemia (CML, ICD-8 205.1). Expected deaths for the cell type specific leukaemias were based on rates compiled by the National Center for Health Statistics.<sup>4</sup> For NHL and MM, United States mortality rates compiled by the National Cancer Institute based on data derived from the surveillance, epidemiology, and end results (SEER) programme were used in computing the expected deaths.<sup>5</sup>

Also, because of the use of asbestos at the refinery in the past, separate analyses for diseases related to asbestos were also performed. Because a certifying physician might not be aware of the decedent's exposure to asbestos (if any), asbestosis could have been coded simply as pulmonary fibrosis or pneumoconiosis (ICD-8 515–517). Therefore, the category pulmonary fibrosis or pneumoconiosis was analyzed. Expected deaths were based on United States rates for pulmonary fibrosis obtained from the National Center for Health Statistics (unpublished data by special request). For malignant mesothelioma, expected deaths were based on United States incidences compiled by the National Cancer

Abbreviations: ICD-8, 8th revision of the international classification of disease; LHCs, lymphatic and haematopoietic cancers; NHL, non-Hodgkin's lymphoma; MM, multiple myeloma; ALL, acute lymphatic leukaemia; CLL, chronic lymphatic leukaemia; AML, acute myeloid leukaemia; CML, chronic myeloid leukaemia; SEER surveillance, epidemiology, and end results; TWA, 8 hour time weighted average

	Richmond	refinery		El Segundo	o refinery		Combined cohorts		
Cause of death (ICDA-8)	Obs	SMR	95% CI	Obs	SMR	95% CI	Obs	SMR	95% CI
At risk (n)	10584			6594			17003		
Person-years	278454.3			157271.2			432422.7		
All causes of death (001 to 999)	3091	84.6**	1.6 to 87.6	1748	82.5**	78.7 to 86.5	4822	84.1**	81.8 to 86.6
All malignant neoplasms (140 to 209)	740	89.7**	83.4 to 96.4	397	83.6**	75.6 to 92.2	1129	87.6**	82.6 to 92.9
Cancer of buccal cavity and pharynx (140 to 149)	14	61.0	33.3 to 102.3	8	61.2	26.4 to 120.7	22	61.6*	38.6 to 93.3
Cancer of digestive organs and peritoneum (150 to 159)	181	85.9*	73.9 to 99.4	88	72.9**	58.5 to 89.8	267	81.2**	71.8 to 91.6
Cancer of oesophagus (150)	22	107.8	67.6 to 163.2	15	129.8	72.7 to 214.1	37	116.8	82.3 to 161
Cancer of stomach (151)	36	99.2	69.5 to 137.4	10	48.8*	23.4 to 89.7	46	81.6	59.7 to 108
Cancer of large intestine (153)	60	85.7	65.4 to 110.4	30	<i>7</i> 3.8	49.8 to 105.3	88	80.2*	64.3 to 98.8
Cancer of rectum (154)	22	111.1	69.6 to 168.1	8	70.6	30.5 to 139.1	30	97.0	65.5 to 138
Cancer of biliary passages and liver (155 to 156)	6	33.3**	12.2 to 72.4	5	48.3	15.7 to 112.8	11	39.1**	19.5 to 70.0
Cancer of pancreas (157)	31	70.7	48.1 to 100.4	15	59.7*	33.4 to 98.5	46	67.3**	49.3 to 89.8
Cancer of respiratory system (160 to 163)	239	85.7*	75.1 to 97.2	141	88.0	74.1 to 103.8	378	86.9**	78.3 to 96.
Cancer of larynx (161)	11	114.2	57.0 to 204.3	7	127.1	51.1 to 261.8	18	119.9	71.0 to 189
Cancer of bronchus, trachea, lung (162)	222	83.4**	72.8 to 95.1	129	84.4	70.5 to 100.3	349	84.1**	75.5 to 93.4
Cancer of prostate (men only) (185)	75	96.7	76.0 to 121.2	35	76.2	53.1 to 105.9	109	89.0	73.0 to 107
Cancer of kidney (189)	21	106.6	66.0 to 162.9	10	88.3	42.3 to 162.4	30	97.6	65.8 to 139
Cancer of bladder and other urinary organs (188, 189.9)	21	84.7	52.5 to 129.5	8	55.0	23.7 to 108.3	29	74.3	49.7 to 106
Malignant melanoma of skin (172 except scrotum)	1 <i>7</i>	122.9	71.6 to 196.7	8	100.5	43.4 to 197.9	25	115.8	75.0 to 171
Cancer of nervous system (191 to 192)	28	124.0	82.4 to 179.1	16	124.2	71.0 to 201.7	43	122.4	88.5 to 164
Cancer of bone (170)	0	-	0.0 to 170.1	0	-	0.0 to 300.5	0	-	0.0 to 109.4
Cancer of all lymphatic, haematopoietic tissue (200 to 209)	92	113.9	91.8 to 139.6	39	83.8	59.6 to 114.5	131	103.8	86.7 to 123
Lymphosarcoma and reticulosarcoma (200)	17	144.2	84.0 to 230.9	5	75.2	24.4 to 175.4	22	120.0	75.2 to 181
Hodgkin's disease (201)	5	91.9	29.8 to 214.5	3	98.9	20.4 to 288.9	8	95.0	41.0 to 187
Leukaemia and aleukaemia (204 to 207)	32	99.8	68.2 to 140.9	15	80.8	45.2 to 133.3	47	93.6	68.8 to 124
Cancer of all other lymphopoietic tissue (202, 203, 208, and 209)	38	120.4	85.2 to 165.3	16	87.3	49.9 to 141.7	54	109.4	82.1 to 142
Benign neoplasms (210 to 239)	9	98.4	45.0 to 186.8	8	151.2	65.3 to 297.9	1 <i>7</i>	118. <i>7</i>	69.1 to 190
Diabetes mellitus (250)	30	65.0*	43.9 to 92.8	15	56.7*	31.8 to 93.6	45	62.5**	45.6 to 83.6
Cerebrovascular disease (430 to 438)	183	79.3**	68.2 to 91.7	114	85.1	70.2 to 102.2	294	81.1**	72.1 to 90.9
All heart disease (390 to 398, 400.1, 400.9, 402, 404, 410 to 414, 420 to 429)	1196	86.9**	82.0 to 92.0	720	90.1**	83.6 to 96.9	1913	88.6**	84.6 to 92.6
Ischaemic heart disease (410 to 414)	1066	87.4**	82.3 to 92.8	638	90.2**	83.4 to 97.5	1 <i>7</i> 01	88.9**	84.7 to 93.2
Hypertension with heart disease (400.1, 400.9, 402, 404)	20	60.7*	37.1 to 93.7	11	58.3	29.1 to 104.4	31	60.3**	41.0 to 85.0
Hypertension without heart disease (400, 400.2, 400.3, 401, 403)	6	63.6	23.3 to 138.4	2	36.6	4.4 to 132.1	8	54.0	23.3 to 106
Non-malignant respiratory disease (460 to 519)	238	82.4**	72.3 to 93.6	121	70.5**	58.5 to 84.2	358	78.3**	70.4 to 86.9
Influenza and pneumonia (470 to 474 and 480 to 486)	93	81.8	66.1 to 100.3	54	78.8	59.2 to 102.8	146	80.7**	68.1 to 94.9
Emphysema (492)	29	49.1**	32.9 to 70.5	18	52.8**	31.3 to 83.5	47	50.8**	37.3 to 67.5
Cirrhosis (571)	82	67.3**	53.5 to 83.5	42	60.9**	43.9 to 82.3	124	65.5**	54.5 to 78.
All external causes of death (e800 to e999)	251	73.9**	65.0 to 83.6	150	78.4**	66.3 to 92.0	400	75.8**	68.6 to 83.6
Motor vehicle accidents (e810 to e823)	74	78.1*	61.3 to 98.0	37	70.7*	49.8 to 97.4	111	75.9**	62.4 to 91.4
Suicides (e950 to e959)	81	88.5	70.3 to 110.0	55	105.3	79.3 to 137.0	135	94.6	79.3 to 112

 Table 2
 Cause specific mortality by duration of employment, men only, Richmond and El Segundo refineries, 1950–95

	Years wor	ked at the R	lichmond ref	inery	Years wor	ked at the E	El Segundo re	finery	Years worked at either refinery			
Cause of death (ICDA-8)	<5	5–14	15–29	≥30	<5	5–14	15–29	≥30	<5	5–14	15–29	≥30
At risk (n)	8766	6698	4028	2060	5566	3887	2276	971	14162	10511	6338	3052
Person-years	91054.6	95120.2	61042.2	38336.2	55645.5	50131.9	33613. <i>7</i>	17880.1	141839.1	141419.2	93513.7	55643.3
All causes of death (001 to 999)	88.7*	85.4**	* 84.5**	82.8**	83.5*	* 90.5	84.0**	76.2**	88.1**	87.9*	* 84.5**	80.3
All malignant neoplasms (140 to 209)	98.4	93.2	85.1*	88.8*	88.6	91. <i>7</i>	84.1	76.2**	95.4	93.0	84.9**	84.3
Cancer of buccal cavity and pharynx (140 to 149)	34.5	81.2	56.4	62.2	_	_	92.8	99.3	20.7	54.0	70.4	74.
Cancer of digestive organs and peritoneum (150 to 159)	55.6*	84.2	85.0	96.1	64.5	58.1*	84.9	73.0	61.2*	73.8*	85.4	87.8
Cancer of oesophagus (150)	37.9	142.1	133.4	92.7	158.4	221.3	137.0	53.3	91.1	174.2	135.5	79.
Cancer of stomach (151)	26.7	55.0	146.4	104.7	37.0	26.2	75.8	40.6	31.9	46.1	120.3	82.6
Cancer of large intestine (153)	67.9	83.6	70.4	103.0	91.4	55.5	53.1	94.6	80.5	65.6	64.1*	99.0
Cancer of rectum (154)	51.9	155.8	83.3	124.5	_	-	135.3	71.9	30.8	104.1	103.5	106.
Cancer of biliary passages and liver (155 to 156)	-	26.5	39.0	46.2	54.1	_	63.9	60.5	22.9	17.6*	48.7	50.7
Cancer of pancreas (157)	100.2	56.9	59.9	77.9	27.3	21.0	98.0	58.7	71.6	45.4*	74.8	71.0
Cancer of respiratory system (160 to 163)	140.5*	116.6	68.1**		115.5	109.8	80.5	69.3*	134.2*	114.9	74.0**	
Cancer of larynx (161)	-	103.0	67.7	192.4	-	95.7	219.9	108.5	-	103.0	126.2	163.
Cancer of bronchus, trachea, lung (162)	144.1*	116.8	64.0**		120.9	105.0	72.4	66.7*	138.7**		68.3**	
Cancer of prostate (men only) (185)	75.1	75.1	111.9	96.8	93.3	106.1	52.8	80.3	86.5	83.4	89.8	90.
Cancer of kidney (189)	149.0	70.8	85.8	129.3	104.2	43.6	111.1	85.5	112.0	62.8	85.2	123.
Cancer of kidney (189) Cancer of bladder and other urinary organs (188, 189.9)	53.2	48.2	91.4	99.1	104.2	89.0	41.5	66.4	31.0	64.3	72.5	87.
	104.4	108.7	109.3	165.7	51.4	99.0	134.9	112.7	85.2	107.4	119.3	147.
Malignant melanoma of skin (172 except scrotum)	97.4										119.3	
Cancer of nervous system (191 to 192)		120.7	122.4	146.4	178.1	94.5	127.6	100.5	118.8	113.7		130.
Cancer of bone (170)	-	-	-	-	-	-	-	-	_	-	-	
Cancer of all lymphatic, haematopoietic tissue (200 to 209)	60.0	78.8	136.3	139.8	73.8	72.3	104.8	76.2	67.5	78.3	124.9	117.
Lymphosarcoma and reticulosarcoma (200)	73.9	73.9	131.5	229.2*	-	139.3	89.5	49.2	44.5	98.2	116.1	167.
Hodgkin's disease (201)	83.4	122.4	138.3		131.3	116.3	121.6		103.8	121.6	132.2	_
Leukaemia and aleukaemia (204 to 207)	22.1	72.4	97.8	148.6	<del>.</del> .	79.8	123.9	83.4	13.4**		108.2	125.
Cancer of all other lymphopoietic tissue (202, 203, 208, and 209)	87.2	76.4	1 <i>7</i> 6.9*	114.2	152.8	27.5	89.1	86.0	118.2	60.7	144.2	104.
Benign neoplasms (210 to 239)	164.8	99.7	35.7	128.0	118.4	91.5	1 <i>77</i> .6	180.1	149.6	98.8	89.5	145.
Diabetes mellitus (250)	67.5	62.1	52.4	75.6	-*	<i>77</i> .1	61.6	67.0	40.7	68.9	56.1*	72.
Cerebrovascular disease (430 to 438)	106.5	72.9	75.4*	80.1*	101.3	75.5	106.7	69.3*	107.5	68.4*	87.7	76.
All heart disease (390 to 398, 400.1, 400.9, 402, 404, 410 to 414, 420 to 429)	88.1	89.1	88.3*	84.5**	89.5	108.9	89.1	82.5**	91.1	97.5	88.9**	83.
Ischaemic heart disease (410 to 414)	97.5	91.1	87.7*	83.5**	89.3	108.6	89.9	82.5**	96.5	98.5	88.9**	83.
Hypertension with heart disease (400.1, 400.9, 402, 404)	23.5	14.8*	85.2	79.7	102.0	55.6	52.0	45.8	57.1	29.7*	72.9	67.
Hypertension without heart disease (400, 400.2, 400.3, 401, 403)	129.1	115.1	35.1	49.1	_	111.1	57.0	_	77.2	116.2	43.7	31.
Non-malignant respiratory disease (460 to 519)	108.3	111.0	84.6	64.4**	71.0	73.5	89.0	53.7**	92.8	100.5	86.8	60.
Influenza and pneumonia (470 to 474 and 480 to 486)	89.6	66.4	103.0	71.2*	45.0	66.4	113.8	63.2*	66.2	68.1	107.7	68.
Emphysema (492)	80.9	61.6	37.6**	48.2**	68.0	77.0	60.5	34.8**	77.9	68.6	46.6**	43.4
Cirrhosis (571)	111. <i>7</i>	63.8*	47.8**		65.7	72.5	31.8**	86.7	95.5	68.1*	41.9**	69.8
All external causes of death (e800 to e999)	75.9*	68.7**	* 83.1	67.3*	85.7	80.6	71.1	68.5	80.9*	72.9*	* 78.7*	67.4
Motor vehicle accidents (e810 to e823)	101.1	45.5**		46.9	79.3	105.0	27.6*	31.3	94.2	66.5*	82.1	41.
Suicides (e950 to e959)	80.1	71.5	117.5	89.2	91.4	85.2	150.6	95.4	86.1	74.9	129.5	90.8

	Richmond refinery interval since hire (y)					lo refinery i	nterval sinc	e hire (y)	Combined cohorts interval since hire (y)			
Cause of death (ICDA-8)	<10	10–19	20–29	≥30	<10	10–19	20–29	≥30	<10	10–19	20–29	≥30
At risk (n)	9499	8824	7029	5285	6005	5088	3990	2765	15321	13791	10943	8007
Person-years	72137.4				44724.9		30934.8		115528.9			
All causes of death (001 to 999)	54.4*	68.7**		92.2**	56.5*	* 82.6*	* 72.0**	87.7**	55.4**	74.1*		
All malignant neoplasms (140 to 209)	70.3	75.5*	80.7*	94.7	27.8*	* 87.2	78.8	87.3*	53.1**	79.7*	80.7**	92.
Cancer of buccal cavity and pharynx (140 to 149)	-	-	59.7	<i>77</i> .1	-	_	-	101.4	-	-*	37.9	86.
Cancer of digestive organs and peritoneum (150 to 159)	31.5	46.5*	83.2	94.0	24.9	53.4	76.0	<i>77</i> .0*	29.8*	46.7*	* 81. <i>7</i>	87
Cancer of oesophagus (150)	_	54.9	111.0	117.9	284.5	93.9	187.1	112.5	113.2	70.9	141.5	116
Cancer of stomach (151)	_	50.4	165.0	94.5	_	_	79.0	51.1	_	32.8	135.2	79
Cancer of large intestine (153)	113.5	18.9	46.5	99.7	_	63.3	63.4	79.8	<i>7</i> 1.1	24.2*	53.6	91
Cancer of rectum (154)	_	99.2	111.2	117.9	_	262.3	_	65.0	_	160.8	70.9	99
Cancer of biliary passages and liver (155 to 156)	_	_	_	46.1	_	_	_	68.1	_	_	_*	54
Cancer of pancreas (157)	_	73.1	75.9	72.0	_	_	107.4	58.1	_	46.9	88.8	67
Cancer of respiratory system (160 to 163)	118. <i>7</i>	102.0	86.0	82.2*	41.2	114.8	78.4	89.2	91.4	106.7	84.4	84
Cancer of larynx (161)	_	105.1	52.6	138.2	_	179.3	_	164.9	_	135.2	33.2	148
Cancer of bronchus, trachea, lung (162)	126.6	103.7	88.4	78.0**	43.9	107.1	79.0	84.7	97.5	104.7	86.2	80
Cancer of prostate (men only) (185)	-	-	73.9	103.3	_	_	102.1	76.9	-	_*	86.3	93
Cancer of kidney (189)	148.5	150.9	_*	128.0	_	165.9	-	107.6	_	159.8	_**	12
Cancer of bladder and other urinary organs (188, 189.9)	-	-	58.2	97.4	_	-	_	69.8	_	-	37.2	87
Malignant melanoma of skin (172 except scrotum)	81.9	88.1	70.5	159.9	_	214.3	122.7	72.5	50.7	138.2	90.6	129
Cancer of nervous system (191 to 192)	108.1	134.8	157.8	108.7	_	179.4	134.9	122.7	67.6	153.8	138.4	114
Cancer of bone (170)	100.1	-	-	100.7	_	-	-	-	07.0	-	-	
Cancer of Botte (170)  Cancer of all lymphatic, haematopoietic tissue (200 to 209)	19.6	83.7	94.2	133.7*	_	71.5	62.5	100.7	12.3**		83. <i>7</i>	122
Lymphosarcoma and reticulosarcoma (200)	-	195.9	70.1	185.6		174.9	-	90.4	-	190.4	45.0	15
Hodgkin's disease (201)	_	73.8	256.8	54.7	_	-	310.2	99.6	_	48.0	277.4	70
Leukaemia and aleukaemia (204 to 207)		27.2	78.3	127.4	_	93.6	68.2	90.3	_	52.4	75.6	114
Cancer of all other lymphopoietic tissue (202, 203, 208, and 209)	104.2	80.0	85.3	132.4	_	75.0	35.7	112.8	63.8	50.3	68.0	120
Benign neoplasms (210 to 239)	154.8	-	60.3	132.4	_	_	105.2	215.8	98.2	-	77.5	158
Diabetes mellitus (250)	134.0	_*	67.8	78.6			119.2	55.3		_**	77.3 87.6	70
	- 74.8	56.5	56.2*	78.6 85.7	-	- 46.1	80.3	91. <i>7</i>	- 47.5	49.5*		87
Cerebrovascular disease (430 to 438)			78.1**		-	103.5	77.6**		47.5 57.6**		78.8**	
All heart disease (390 to 398, 400.1, 400.9, 402, 404, 410 to 414, 420 to 429)	54.4**		82.0**		69.2 69.6	103.5	72.9**		60.1**		79.5**	
Ischaemic heart disease (410 to 414)												
Hypertension with heart disease (400.1, 400.9, 402, 404)	-	- 024.0	21.6	79.2 42.5	-	111.1 222.2	74.9	51.3	-	41.2	41.8	69
Hypertension without heart disease (400, 400.2, 400.3, 401, 403)	15.5*	236.8	83.5	42.5 86.1*	-		-	24.0	-	234.4	54.5	35
Non-malignant respiratory disease (460 to 519)	15.5*	65.4	79.4		25.3	57.0	55.1*	75.0**	19.6**		71.6*	82
Influenza and pneumonia (470 to 474 and 480 to 486)	32.5	25.6*	91.2	87.1	53.1	45.2	87.1	81.3	41.1	33.1*	91.0	. 84
Emphysema (492)	- 20 4*	107.8	29.4*	48.7**	-	118.5	50.6	48.0**		113.4	37.5**	
Cirrhosis (571)	30.4*	32.5**		93.8	31.2	40.2*	40.1**		31.5**	35.9*		
All external causes of death (e800 to e999)	58.5*			89.8	68.8*	89.0	66.6*	86.2	62.3**			88
Motor vehicle accidents (e810 to e823)	84.3	51.9*	76.6	100.4	67.6	101.7	55.4	50.8	78.8	70.0	69.6	83
Suicides (e950 to e959)	48.7*	96.1	107.2	95.0	77.7	90.9	111.0	132.1	57.3*	95.0	109.3	108

 Table 3
 Cause specific mortality by interval since hire, men only, Richmond and El Segundo refineries, 1950–95

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 Table 4
 Cause specific mortality by period of hire, men only, Richmond and El Segundo refineries, 1950–95

	Hired before 1	949	Hired on or after 1949			
Cause of death (ICDA-8)	Obs	SMR	Obs	SMR		
At risk (n)	5334		11669			
Person-years	178755.6		253664.9			
All causes of death (001 to 999)	3600	84.6**	1222	82.7**		
All malignant neoplasms (140 to 209)	804	85.2**	325	94.2		
Cancer of buccal cavity and pharynx (140 to 149)	18	70.1	4	39.8		
Cancer of digestive organs and peritoneum (150 to 159)	203	82.2**	64	78.5		
Cancer of oesophagus (150)	24	107.9	13	137.8		
Cancer of stomach (151)	39	89.6	7	54.4		
Cancer of large intestine (153)	66	78.5*	22	85.7		
	27	111.2	3	45.2		
Cancer of rectum (154)	8	42.8**	3	31.8*		
Cancer of biliary passages and liver (155 to 156)	34					
Cancer of pancreas (157)		66.8*	12	68.7		
Cancer of respiratory system (160 to 163)	243	77.5**	135	111.2		
Cancer of larynx (161)	16	143.9	2	51.3		
Cancer of bronchus, trachea, lung (162)	218	72.9**	131	112.9		
Cancer of prostate (men only) (185)	91	87.4	18	97.5		
Cancer of kidney (189)	16	75.3	14	147.3		
Cancer of bladder and other urinary organs (188, 189.9)	28	86.1	1	15.3*		
Malignant melanoma of skin (172 except scrotum)	16	134.0	9	93.3		
Cancer of nervous system (191 to 192)	27	125.3	16	11 <i>7.7</i>		
Cancer of bone (170)	0	-	0	-		
Cancer of all lymphatic, haematopoietic tissue (200 to 209)	103	117.0	28	<i>7</i> 3.3		
Lymphosarcoma and reticulosarcoma (200)	18	125.9	4	99.1		
Hodgkin's disease (201)	3	58.8	5	150.6		
Leukaemia and aleukaemia (204 to 207)	41	115.3	6	41.0*		
Cancer of all other lymphopoietic tissue (202, 203, 208, and 209)	41	123.6	13	80.1		
Benign neoplasms (210 to 239)	12	114.5	5	130.0		
Diabetes mellitus (250)	36	69.4*	9	44.8**		
Cerebrovascular disease (430 to 438)	265	85.5*	29	54.9**		
All heart disease (390 to 398, 400.1, 400.9, 402, 404, 410 to 414, 420 to 429)	1516	87.3**	397	93.8		
Ischaemic heart disease (410 to 414)	1361	86.9**	340	98.2		
Hypertension with heart disease (400.1, 400.9, 402, 404)	26	<i>7</i> 1.1	5	33.7**		
Hypertension without heart disease (400, 400.2, 400.3, 401, 403)	7	57.0	1	39.5		
Non-malignant respiratory disease (460 to 519)	285	75.8**	73	90.4		
Influenza and pneumonia (470 to 474 and 480 to 486)	122	80.4*	24	82.3		
Emphysema (492)	38	47.5**	9	71.8		
Cirrhosis (571)	75	65.9**	49	65.0**		
All external causes of death (e800 to e999)	188	75.3**	212	76.3**		
Motor vehicle accidents (e810 to e823)	42	63.9**	69	85.7		
Suicides (e950 to e959)	73	99.4	62	89.6		

Institute SEER program.<sup>6 7</sup> Because malignant mesothelioma is a rapidly fatal disease, these incidences will closely estimate the expected number of deaths.

#### **RESULTS**

Included in the current update were 18 512 employees (88% white and 12% non-white) at the two refineries, who contributed 456 425 person-years of observation between 1950 and 1995. About 27% (n=4941) of the cohort members are dead, and death certificates were obtained for all but 0.8% (n=40). The vital status of 3% of cohort members could not be determined, and, therefore, their observation was truncated on their last known date alive (usually the last date of employment). The average duration of employment at the Richmond refinery (15 years) was slightly longer than at El Segundo (13 years). Among male employees, more than 32% at Richmond and close to 28% at El Segundo had worked for more than 20 years at the refineries. The average interval since first employment was 29 years at Richmond and 27 years at El Segundo. For employees enrolled after 1948, the mean duration of employment was 10 years, and the mean interval since first employment was 23 years.

#### Mortality among male cohort members

Only 8% of cohort members were women, and they accounted for a total of 119 deaths. The overall SMR from all causes for women was 92.0 (95% CI 76.2 to 110.1). For most causes of death, the number of deaths among female employees was relatively small and only mortality from suicide was significantly increased (seven observed deaths; SMR 249.3, 95% CI 100.2 to 513.6).

Table 1 shows the observed deaths and SMRs for men by cause for each refinery as well as both refineries combined. For both refineries, the total mortality from all causes was significantly lower at the Richmond refinery (SMR 84.6, 95% CI 81.6 to 87.6), the El Segundo refinery (SMR 82.5, 95% CI 78.7 to 86.5), and for the two refineries combined (SMR 84.1, 95% CI 81.8 to 86.6). For the major causes of death, including all cancers combined, heart disease, non-malignant respiratory disease, and external causes, the SMRs at the two refineries were similar and significantly below 100.

For causes of death which have been found to be increased in some studies of petroleum refinery workers, the SMRs for the combined cohort were as follows: cancer of the skin 115.8 (95% CI 75.0 to 171.0), cancer of the nervous system 122.4 (95% CI 88.5 to 164.8), kidney cancer 97.6 (95% CI 65.8 to 139.3), leukaemia 93.6 (95% CI 68.8 to 124.5), lymphosarcoma and reticulosarcoma 120.0 (95% CI 75.2 to 181.7), and other lymphatic tissue cancer 109.4 (95% CI 82.1 to 142.7).

Table 2 shows cause specific SMRs by duration of employment (<5, 5–14, 15–29, and  $\ge 30$  years) for each refinery as well as both refineries combined. In the case of

	Richmond			El Segundo			Combined			
	<1949	≥1949	Total	<1949	≥1949	Total	<1949	≥1949	Total	
Acute lymphatic leukaemia (ALL, ICD-8 204.0)			10101	***			***			
Observed	0	2	2	2	0	2	2	2	4	
Expected	1.16	0.68	1.83	0.64	0.41	1.02	1.79	1.07	2.86	
SMR	0	294.9	109	312.5	0	195.4	111.6	187.7	140.0	
95% CI	0 to 316.2	33 to 1061.9	12.3 to 394.6	35 to 1128.3	0 to 894.6	22.0 to 707.9	12.6 to 403.4	21.0 to 674.9	37.2 to 358.1	
Chronic lymphatic leukaemia (CLL, ICD-8	0 10 3 10.2	33 10 1001.7	12.5 10 574.0	33 10 1120.3	0 10 074.0	22.0 10 7 07 .7	12.0 10 403.4	21.0 10 07 4.7	37 .2 10 330.1	
204.1):										
Observed	6	0	6	3	0	3	9	0	9	
Expected	4.83	1.34	6.16	2.73	0.85	3.47	7.54	2.12	9.66	
SMR	124.3	0	97.3	110	0.03	86.5	119.3	0	93.1	
95% CI	45.4 to 270.4	0 to 431.5	35.6 to 202.0	22.1 to 321.1	0 to 431.5	17.4 to 252.6	54.5 to 226.6	0 to 173.0	42.5 to 176.9	
Acute myeloid leukaemia (AML, ICD-8 205.0)		0 10 451.5	33.0 10 202.0	22.1 10 321.1	0 10 45 1.5	17.4 10 232.0	34.3 10 220.0	0 10 17 3.0	42.5 10 17 0.7	
Observed	9	2	11	5	1	6	14	3	17	
	6.27	3.31	9.57	3.43	2.04	5.37	9.68	5.24	14.92	
Expected SMR	143.6	60.5	114.9	145.7	29	111.7	144.6	57.3	114.0	
95% CI	65.5 to 272.5	6.8 to 218.2		47.0 to 340.2	0.6 to 272.7	40.8 to 243.2	79.0 to 242.7	11.5 to 167.3	66.3 to 182.4	
	03.3 to 2/2.3	0.8 10 218.2	57.3 to 205.7	47.0 to 340.2	U.O TO 2/2./	40.8 to 243.2	/9.0 to 242./	11.5 10 107.3	00.3 to 182.4	
Chronic myeloid leukaemia (CML, ICD-8										
205.1): Observed	2	0	2	1	0	1	3	0	3	
	2.79	1.51		1 54	0.93	2.42	-	2.4		
Expected			4.3	1.54			4.31		6.71	
SMR	71.7	0	46.5	65.1	0	41.3	69.5	0	44.7	
95% CI	8.1 to 258.8	0 to 242.9	5.2 to 167.9	0.9 to 361.3	0 to 394.4	0.5 to 229.9	14.0 to 203.4	0 to 152.8	9.9 to 130.6	
Non-Hodgkin's lymphoma (NHL, ICD-8 200, 202):										
Observed	26	4	30	6	5	11	32	9	41	
Expected	17.14	8.12	25.26	9.38	5.05	14.17	26.47	12.87	39.34	
SMR	151.7	49.3	118.8	64	99.1	77.6	120.9	69.9	104.2	
95% CI	99.1 to 222.3	13.3 to 126.1	80.1 to 169.6	23.4 to 139.2	31.9 to 231.1	38.8 to 139.4	82.7 to 170.7	31.9 to 132.8	74.8 to 141.4	
Multiple myeloma (MM, ICD-8 203):										
Observed	15	5	20	7	2	9	22	7	29	
Expected	8.67	3.02	11.68	4.79	1.91	6.55	13.43	4.79	18.22	
SMR	173.1	165.6	171.2	146.1	104.9	137.4	163.8	146.1	159.2	
95% CI	96.8 to 285.4	53.4 to 386.4	104.6 to 264.5	58.6 to 301.1	11.8 to 378.1	62.7 to 260.9	102.6 to 248.0	58.6 to 301.1	106.7 to 228.9	

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Richmond, three cause of death categories seemed to show increasing trends: cancer of the nervous system (97.4 to 146.4), lymphosarcoma and reticulosarcoma (73.9 to 229.2), and leukaemia (22.1 to 148.6). However, upon formal testing, only the trend for leukaemia was significant ( $\chi^2_{\text{trend (idf)}}$ =0.42, p=0.52;  $\chi^2_{\text{trend (idf)}}$ =3.08, p=0.08;  $\chi^2_{\text{trend (idf)}}$ =5.75, p=0.02; respectively). Only lymphosarcoma and reticulosarcoma in workers with 30 or more years of employment at Richmond, and lung cancer in workers with less than 5 years of employment at Richmond and both refineries combined, were significantly increased. At El Segundo, no cause of death showed a trend with increasing duration of employment.

Mortality analysis by interval since first employment (latency) is presented in table 3. Only mortality from the broad category LHC among male employees at Richmond with a latency of 30 years or longer was significantly increased. No other causes of death for any latency interval were significantly increased.

Table 4 shows SMRs by period of first employment (<1949  $\nu$  1949 and after) for the two refineries combined. Several cause specific SMRs were significantly low, in each period and no SMR exceeding 100 was significant. Only two refinery specific results (data not shown) had noticeably higher SMRs among workers first employed in or after 1949: kidney cancer at Richmond (SMR 166.9, 95% CI 80.0 to 306.8) and oesophageal cancer at El Segundo (SMR 215.0, 95% CI 92.8 to 423.5). For both cancers, neither refinery specific SMR was significant (nor was the SMR for the two refineries combined), and neither showed a significantly increasing trend with duration of employment ( $\chi^2_{\rm trend~(1df)}$ =0.73, p=0.39 for kidney cancer, and  $\chi^2_{\rm trend~(1df)}$ =0.30, p=0.59 for oesophageal cancer).

Refinery specific trends for the periods before and after 1949 for the broad category LHC were similar. For the combined refineries, the SMR for Hodgkin's disease increased among workers employed in or after 1949 (from 58.5 to 150.6); however, it was based on a very few deaths (five deaths total). Conversely, declines in the SMRs for deaths from leukaemia (from 115.3 to 41.0), lymphosarcoma and reticulosarcoma (from 125.9 to 99.1), and other lymphatic tissue cancers (from 123.6 to 80.1) were found.

## Mortality from specific lymphatic and haematopoietic cancer (LHC) categories

From a biological and aetiological perspective it is important to evaluate ALL, CLL, AML, CML, NHL, and MM as separate diseases. 9 10 Analyses on these specific categories of LHC were carried out and results are reported in table 5. There were non-significant deficits for CLL and CML at both refineries. For ALL, the number of deaths was very small (two at each refinery), and the combined SMR of 140.0 (95% CI 37.2 to 358.1) was based on a single excess death. Acute myeloid leukaemia was similarly slightly increased at each refinery, with a combined SMR of 114.0 (95% CI 66.3 to 182.4; 17 observed v 14.9 expected). For NHL, there was a non-significant increase at Richmond (SMR 118.8; 95% CI 80.1 to 169.6), which was contrasted with a non-significant deficit at El Segundo (SMR 77.6; 95% CI 38.8 to 139.4). This resulted in a combined SMR of 104.2 (95% CI 74.8 to 141.4). A marginally significant increase of MM was found at Richmond (SMR 171.2; 95% CI 104.6 to 264.5) and a non-significant increase at El Segundo (SMR 137.4; 95% CI 62.7 to 260.9). The combined SMR for MM of 159.2 was significant (95% CI 106.7 to 228.9).

Stratified analysis by period of employment showed that SMRs were generally higher among men first employed before 1949. For ALL (El Segundo only), CLL, AML, and CML, the SMRs among male employees enrolled after 1948 were all below 100. For NHL, the only increase was found at Richmond among employees enrolled before 1949 (SMR 151.7; 95% CI 99.1 to 222.3). For MM, increased risks were found at both refineries, and for both periods of employment, although the

increase among men employed after 1948 was based on a total of only seven deaths. The significant increase among men employed before 1949 (SMR 163.8; 95% CI 102.6 to 248.0) was primarily driven by Richmond. The overall data for MM showed no significant trend by duration of employment (SMRs of 1.32, 0, 2.31, and 1.89 for <5, 5–14, 14–29, and  $\geq$ 30 years, respectively;  $\chi^2_{\text{trend (ldf)}}$ =3.07, p= 0.08).

#### Mortality from diseases related to asbestos

In the entire cohort, only one death was coded as asbestosis on the death certificate. For the broader category of pulmonary fibrosis or pneumoconiosis, a total of 22 deaths were found compared with 28.4 expected (SMR 77.5, 95% CI 48.6 to 117.4)

For malignant diseases related to asbestos (lung cancer and malignant mesothelioma), table 1 shows that mortality from lung cancer was significantly decreased at both refineries. Also, there was a clear inverse trend with duration of employment (table 2) at both refineries ( $\chi^2_{\rm trend\ (ldf)} = 36.5$ , p<0.0001). Employees with the longest employment histories ( $\geqslant 30$  years) had the lowest risks for lung cancer (significantly low at both refineries).

For mesothelioma, to be consistent with the SEER rate derivation, only death certificates specifying malignant mesothelioma were included in the analysis. There were two deaths labelled as malignant pleural mesothelioma and a third as malignant mesothelioma of the left chest wall, right lung, and left hemidiaphram. Based on these three malignant pleural mesotheliomas, the SMR was 39.6 (95% CI 8.2 to 115.8). Also, there were three deaths listed simply as malignant mesothelioma (ICD-8 199.1), without specifying the organ involved. If we were to further assume that these three additional deaths were from malignant pleural mesothelioma, the corresponding SMR would have been 79.2 (95% CI 29.0 to 172.5). One additional death was coded as ICD-8 158.9 and the cause of death on the death certificate was massive malignant diffuse peritoneal mesothelioma. Neither Connelly et al6 nor Spirtas et al7 presented age specific SEER rates for malignant peritoneal mesothelioma. Connelly et al, however, stated that malignant pleural mesothelioma rate in men was about nine times that for malignant peritoneal mesothelioma. Thus, less than one case (about 0.84 (7.58/9)) of malignant peritoneal mesothelioma was expected in the current cohort. Based on this estimate, there was no increased risk of malignant peritoneal mesothelioma in the current update (SMR 119.1, 95% CI 1.56 to 662.3).

#### **DISCUSSION**

Overall, the findings from this update closely parallel those of the previous update.<sup>2</sup> Most causes of death examined continued to show fewer deaths than expected based on a comparison with California mortalities. Also, several individual causes were significantly low, including lung and digestive cancers, ischaemic heart disease, non-malignant respiratory disease, and external causes of death. The "healthy worker effect," as previously described in these cohorts,<sup>2</sup> continued to have an influence, although it has diminished slightly with increased duration of follow up. This finding is consistent with the general observation in occupational epidemiological studies that the impact of the healthy worker effect is most prominent immediately after the start of employment but diminishes over time.

The significant increase reported in the previous update in Richmond for LHC (among employees enrolled before 1949) was still present. Further analyses showed that most of the increase was driven by deaths due to lymphoreticulosarcoma and reticulosarcoma (ICD-8 200) and cancer of other lymphatic tissue (ICD-8 202, 203, and 208). The previously reported significant increase in oesophageal cancer at El Segundo (among workers employed after 1948) was also still

present, but was no longer significant. Nor was there an upward trend by duration of employment. Overall, the SMR for cancer of the oesophagus among workers employed after 1948 at both refineries combined was not significantly increased (SMR 138, 95% CI 73.4 to 235.7). To our knowledge, no other studies of refinery workers have reported a significant increase in oesophageal cancer. Few, if any, occupational exposures have been linked to oesophageal cancer. Suspected risk factors include diet (especially the intake of hot and caustic beverages), low socioeconomic status, and family history. Unfortunately, no information on these risk factors was available in this study.

The analyses by duration of employment showed that the increasing trends in the earlier updates of this cohort for the categories all lymphatic and haematopoietic tissue cancers, and more specifically, leukaemia, were not as apparent for the broader category, but still present for leukaemia. Further analysis by period of employment showed that risk of leukaemia decreased among workers employed in or after 1949 compared with those first employed earlier, and was well below that expected. Similarly, the significantly increased SMR for lymphosarcoma and reticulosarcoma among people with ≥30 years of service was confined to male workers employed before 1949. This suggests that even if certain exposures in the refinery environment were related to these increases, it seemed that they had dissipated substantially or disappeared. The average of 23 years of follow up, among workers employed enrolled in or after 1949, indicates that if there was an effect there was likely to be sufficient follow up to detect it.

When data for MM and NHL were analyzed, only mortality from MM (ICD-8 203) was significantly increased, with the increase being confined to men employed before 1949. Mortality from NHL (ICD-8 200 and 202) was not increased, although similar to MM, the SMR among employees at Richmond employed before 1949 was of borderline significance. Relatively few studies of petroleum refinery workers have reported results specifically for NHL and MM. Those that have analyzed LHC categories have not reported significant increases.12-15 Also, recent reviews and meta-analyses of NHL and MM among some 250 000 petroleum workers found no overall increase in risk of mortality from these causes (meta-SMRs of 90 and 93, respectively). 16 17 Although a recent study in China has reported an increased risk of NHL among workers exposed to various industrial chemicals including both benzene and agricultural chemicals,18 the preponderance of epidemiological data does not support an association between exposure to benzene and NHL. 16 19 Based on these findings, we are unable to conclude that employment at the refineries was responsible for the increases in MM or NHL among workers employed before 1949. The lack of an upward trend by duration of employment for cancers of other lymphatic tissue (MM, NHL, myelofibrosis, and polycythemia vera) argues against a causal interpretation. Furthermore, the lack of any increase in AML, which is known to be caused by long term, high exposure to benzene, argues against benzene's role in the increases of MM and NHL found here.

Increased risks of pulmonary fibrosis, lung cancer, and malignant mesothelioma of the pleura or peritoneum have been reported among workers exposed to asbestos. Although historically, asbestos was used at the refineries, we found no increase in either malignant or non-malignant diseases related to asbestos. Among the three deaths with specific diagnostic information, two were malignant pleural mesotheliomas and one was a malignant peritoneal mesothelioma. Of these cases, one was a former shipyard worker; the other two had no available previous work histories (before joining Chevron). It is quite likely that the former shipyard worker was exposed to asbestos before his employment at the refinery. In any event, there was no increased mortality from malignant pleural mesothelioma (7.58 deaths were expected based on SEER rates for malignant mesothelioma). Although asbestos

monitoring data for these two refineries are not available before the early 1970s, exposure data obtained between 1973 and 1986 during work to remove asbestos and routine maintenance work involving materials containing asbestos showed the average 8 hour time weighted average (TWA) concentrations to range from 0.001 to 0.09 fiber/ml. This would indicate that exposures were well within the permissible levels, and would not be likely to pose a risk of fibrosis or cancer.

In the current update, there were 43 deaths from cancer of the nervous system including the brain, comparable to the 35.13 expected (SMR 122.4, 95% CI 88.5 to 164.8). There was no upward trend by duration of employment, nor significant increase among workers with more than 30 years of employment. In a recent review, Wong and Raabe20 reported the results of brain cancer from studies of petroleum workers. None of the studies reported a significantly increased SMR overall. In fact, all large studies reported SMRs from brain cancer below or close to 100. Only the large United States study of Texaco employees,21 which reported an overall SMR of 109 (95% CI 85 to 138), also reported significant increases among certain subgroups of employees who worked 5 or more years in laboratory jobs or within the motor oil units. However, based on a subsequent review of chemical exposures and an analysis by duration of employment, the authors concluded that there were no patterns suggestive of a relation with workplace exposures. We performed a case review among our cases with brain cancer and found no similar job assignments or work patterns. Interestingly, the Mobil Paulsboro refinery study<sup>15</sup> reported a significant decreasing trend for brain cancer by duration of employment: SMRs of 197 (six deaths), 96 (two deaths) and 29 (one death) for <20, 20–29, and ≥30 years of employment ( $\chi^2_{trend~(1~df)}$ =4.36, p<0.05). The largest study of refinery workers, which was performed in the United Kingdom,22 reported an overall brain cancer SMR of 88 (95% CI 69 to 111), based on a total of 74 deaths. For all petroleum worker studies combined, the meta-SMR was 101 (95% CI 93 to 109). 19 Thus, the brain cancer finding from the current update of workers at the Richmond and El Segundo refineries is consistent with the conclusion reached by Wong and Raabe<sup>16</sup> that the current epidemiological data do not support an association with employment at petroleum refineries.

As with any historical cohort study, there are some inherent limitations in the available data. These include the lack of exposure measurements of specific chemicals, the lack of data on smoking and other potential confounding factors, and the potential inaccuracy of diagnostic information on death certificates. Furthermore, because of incomplete computerised work history information, we were unable to analyze mortality patterns by specific job categories or work locations within the refineries. Finally, in the light of the multiple comparisons (analyses) performed, some significant increases or deficits in SMRs would be expected by chance alone.

#### CONCLUSION

This second update (with vital status follow up to the end of 1995) of cause specific mortality patterns at the Richmond and El Segundo refineries has confirmed the continuing favorable mortality experience of current and former employees. Mortality from most causes was lower than expected based on mortalities for the general population in California. More than 40 individual causes of death were examined, and hundreds of SMRs were computed. Only mortality from MM was significantly increased. However, the increase was confined to employees enrolled before 1949. Furthermore, there was no significant upward trend by duration of employment, which argues against the interpretation that the historical increase was associated with employment at the refineries. There were no significant increases in mortality from either leukaemia overall or its major specific cell types. There was no significant mortality from any other causes or non-malignant diseases. 256 Satin, Bailey, Newton, et al

Overall, this second update provides additional reassurance that employment in these two refineries is not associated with increased risk of mortality.

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