16. SIX YEARS LATER

16.1 Introduction

All results presented so far have been based on follow-up of the cohort of 3 915 workers until 1977-01-01. In this chapter, follow-up has been extended by another six years. Here we will specifically address the question whether the mortality pattern (cf Fig. 7.1 and 7.3) has changed but will also analyze trends in cancer incidence. In particular it may be of interest to study whether lung cancer mortality (cf Fig. 7.2) now is still more unfavourable or whether some levelling off can be traced. Up-dated analysis also aims to stabilize previous risk assessments, especially for internal comparisons between work sites.

16.2 A growing data set

Up-dating the cohort for the period 1977–82 has meant an increase of the total follow-period from 113 816 to 130 503 person-years. The ageing of the cohort is shown in Fig. 16.1.

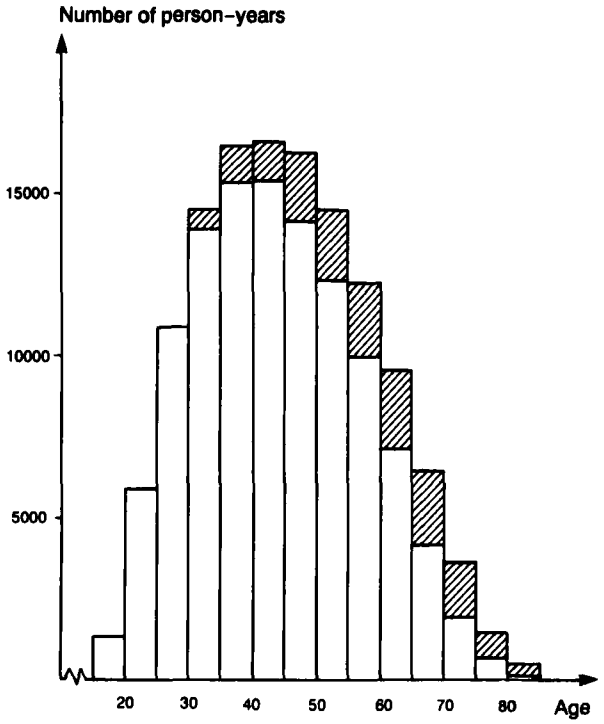

Fig. 16.1. Change in person-time distribution after up-dating the cohort (shaded areas).

Six additional years of follow-up have also meant another 406 deaths in the cohort. A distribution of the additional cases by main cause of death is shown in Table 16.1. Due to a later revision of death certificates there may be some instances where a previous code has been changed at up-date. This explains why in some few cases the frequency of a sub-group may have decreased.

The growing material gives an increased power to 'detect' statistically a certain excess risk relative to the external standard. Thus, the additional 16 613 person-years have yielded about 45 expected lung cancer deaths, instead of the previous 29, based on national rates. The power to detect a 50% excess lung cancer risk (5% significance level) has then increased from 78% to 91% (Breslow 1987). Alternatively, the smallest detectable relative risk, assuming a power of 80%, has changed from about 1.5 to 1.4.

Schlesselman (1982) has shown that the statistical power of a case-referent study is a function not only of the number of cases, the number of referents/case and the relative risk 'worthy' of detection, but also of the proportion P_0 of exposed individuals among the referents.

Assuming a one-sided test to detect RR = 2.0 at 5% significance level when $P_0 = 0.25$ (approximately as for roaster exposure in Table 11.2), the statistical power will increase from 75% to 86% by having 102 cases instead of 76 if still using two referents per case. For a fixed power of 80%, the smallest detectable relative lung cancer risk decreases from 2.1 to 1.9 after the cohort up-date, i.e when the case-group has increased from 76 to 102, again assuming $P_0 = 0.25$.

Table 16.1

Additional number of cases after up-dating the cohort by main causes of death

Cause of death	No. of cases		Total
	1928–1976	1977–1982	1928–1982
Infective and parasitic diseases	18	2	20
Neoplasms	245	99	344
Digestive system	89	29	118
Respiratory system	79	35	114
Genito-urinary system	30	20	50
Brain, nervous system, UNS	20	6	26
Leukaemias	25	7	32
Remaining sites	2	2	4
Endocrine system, metabolic and nutritional dis.	7	8	15
Diseases of blood and bloodforming organs	2	−1*	1
Mental disorders	5	3	8
Disorders of nervous system and sense organs	6	3	9
Diseases of the circulatory system	488	233	721
Ischaemic heart disease	312	170	482
Cerebrovascular disease	99	30	129
Chronic, Rheumatic dis.	6	1	7
Others	71	32	103
Diseases of the respiratory system	24	15	39
Diseases of the digestive system	38	7	45
Diseases of the genito-urinary system	15	12	27
Accidents, poisoning and violence death	89	20	109
Suicide	12	2	14
Remaining causes	77	18	95
Other causes	16	1	17
Total	953	402	1,355

(* due to revised classifications)

16.3 Mortality 1928–82

Similar to the analysis in Chapter 7, the mortality of the up-dated cohort has been compared with the general Swedish population in terms of SMR-values. In Table 16.2 the changes in total mortality after up-dating the cohort are shown.

Thus, the overall SMR-value is somewhat increased, mainly due to changes in lower ages. Obviously a change in SMR also reflects the ageing of the cohort and despite the increased SMR, survival of the cohort is improved: In terms of survival from various ages, a gain of 1/4 to 1/2 year is shown in Table 16.3.

From Table 16.4 we note that the SMR-values of most causes of death have actually decreased after the up-dating.

A direct comparison in terms of age-adjusted rates using the cohort of 1928–76 as a standard population reveals that the overall changes are mostly decreases and marginal. Changes, however, are due to older ages almost exclusively. Thus the decline of total mortality is about 6% above 65 years. For cancer and circulatory diseases these figures are 5 and 6% respectively. For violent deaths there is a certain increase in older ages.

In Fig. 16.2 and 16.3 mortality trends previously shown in Fig. 7.1 and 7.2 have been up-dated. It seems as if the increasing total mortality during the period 1961–75 is now levelling off. It is encouraging to note that this seems to hold also for lung cancer, although substantial excess figures still prevail.

16.4 Cancer incidence 1958–82

The analysis of cancer incidence was made possible by using the Swedish cancer register, which contains all new cases of cancer diagnosed from 1958 onwards. Thus, the

Table 16.2

Change in total mortality relative to the general Swedish male population after up-dating the cohort

Age (years)	1928–1976			1928–1982		
	Obs. no. of cases	SMR (%)	95% C.L	Obs. no. of cases	SMR (%)	95% C.L
15–44	105	74	(60; 88)	108	91	(74; 108)
45–54	159	108	(91; 125)	190	115	(99; 131)
55–64	278	115	(102; 129)	359	117	(105; 129)
65–74	291	128	(114; 143)	455	112	(111; 133)
75–	120	114	(94; 135)	243	111	(97; 125)
Total	953	111	(104; 118)	1355	115	(109; 129)

Table 16.3

Estimated changes in survival after up-dating the cohort

Study period	Remaining life expectancy			Remaining median life-time		
	15–	45–	65–	15–	45–	65–
1928–76	56.83	28.59	12.69	58.71	29.36	12.12
1928–82	57.09	28.85	13.09	59.05	29.69	12.50
Change	0.26	0.26	0.40	0.34	0.33	0.38

study cohort is here defined as those of the original cohort alive at this date or first employed thereafter but before 1 January 1967. This comprised a total of 3 710 workers. An analysis of cancer incidence in the Rönnskär cohort was also performed (Sandström et al. 1989).

Table 16.4

Changes in cause-specific mortality relative to the general Swedish male population after up-dating the cohort

Cause of death	SMR-value	
	1928–76	1928–82
All causes	111	115
All cancer	134	129
Circulatory diseases	130	126
Violent deaths/suicides	81	83
Other causes	83	84
Digestive cancer	127	117
Respiratory cancer	263	224
Genito-urinary cancer	97	98
Cancer of brain, nervous system	231	226
Leukemias	128	117
Ischaemic heart disease	126	120
Cerebrovascular disease	150	134
Digestive diseases	92	80
Respiratory diseases	71	73
Genito-urinary diseases	72	104

The risk population for the analysis of cancer incidence was defined by the person-time distribution of follow-up from first employment (or 1 January 1958, for individuals

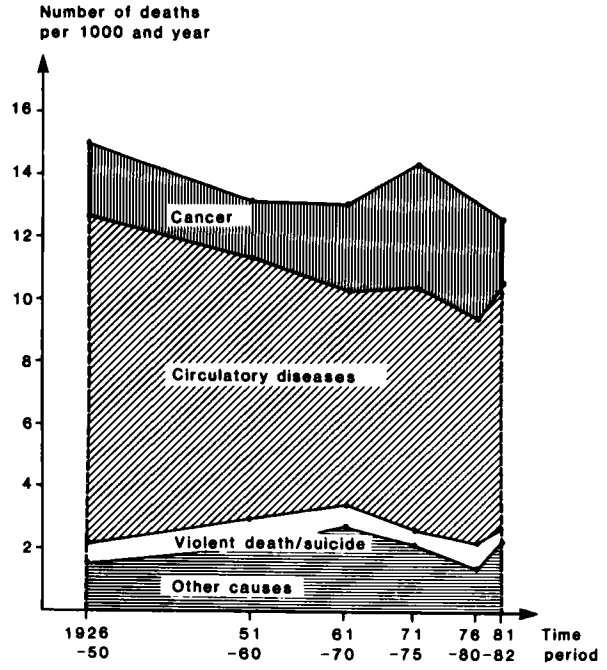

Fig. 16.2. Mortality trends in the Rönnskär cohort for main causes of death after up-dating the cohort. Directly standardized mortality rates using Swedish men 1951–1955 as standard population.

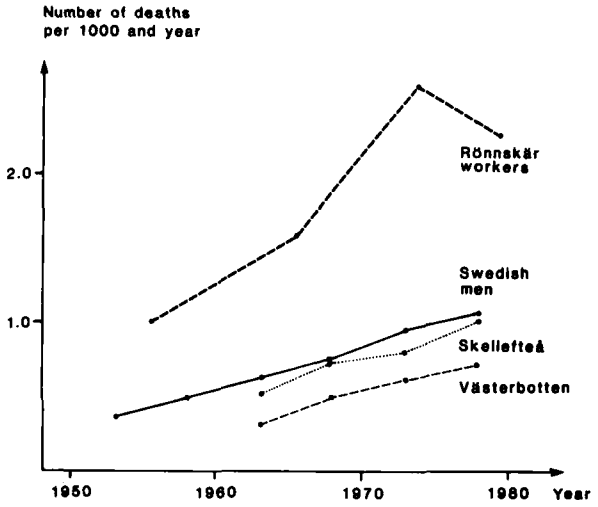

Fig. 16.3. Lung cancer mortality trends in the Rönnskär cohort and the three reference populations after up-dating the cohort. Directly standardized mortality rates using Swedish men 1951–1955 as standard population.

employed before 1958) to the study end-point or prior death. When analyzing lung cancer, person-time is accumulated to the diagnosis of lung cancer or death. For the study of all cancer or site categories, diagnosis of cancer will not qualify for withdrawal. This follow-up has resulted in a total lived through risk time of 79 319 person-years (which was about 300 person-years more than for the analysis of lung cancer).

For external comparisons the expected number of cases of cancer was calculated using age- and calendar time-specific incidence rates for the general Swedish male population, for the male populations of Västerbotten county and of Skellefteå municipality. The corresponding incidence rates were applied to the observed person-time experience of the entire cohort. Internal comparisons were made specifically to validate previous findings on hazardous work sites and to judge whether excess risks still prevail for those later employed. When analyzing specific work sites, person-years were accumulated from first employment at the actual work site.

16.4.1 *Cancer incidence in the Rönnskär cohort*

Between 1958 and 1982, a total of 467 diagnoses of cancer within the cohort were registered in the Swedish Cancer Register, of which 33 had more than one cancer. A classification of cases by age and site categories is shown in Table 16.5. 50% of all cancer cases occurred before 1970.

16.4.2 *Cancer incidence in reference populations*

In terms of directly standardized incidence rate ratios (SRR), a comparison was made between the three reference populations (Table 16.6). The greatest differences were found for lung and stomach cancer. Rates of stomach cancer for both Skellefteå and Västerbotten were remarkably higher than the rate for Sweden (Nyström et al. 1986). For lung cancer, however, the rate for Västerbotten was much lower than the rates for Sweden and Skellefteå. In Skellefteå 290 cases of lung cancer occurred during 1959–1982, whereas the corresponding figure for the Rönnskär cohort was 105. This was probably the major reason why the rate for Skellefteå was more similar to that of Sweden than to that of its own county, Västerbotten, and indicates that the incidence of lung cancer in the male population in Skellefteå municipality was highly affected by the incidence among Rönnskär workers.

16.4.3 *External comparisons*

When comparing the incidence of cancer among Rönnskär workers with general and local populations, in terms of standardized incidence ratios and accounting for

Table 16.5

Number of cancer cases 1958–82 among 3 710 workers by age and cancer site

ICD-7	Cancer site	Age group (years)			All ages
		15–44	45–64	65–	
140–149	Lip, oral cavity and pharynx	0	2	5	7
150–159	Digestive organs	3	49	78	130
151	Stomach	1	27	25	53
160–164	Respiratory organs	3	57	60	120
162	Trachea, bronchus, lung and pleura, primary	2	50	56	108
177–181	Urogenital organs	4	39	81	124
200–209	Blood, bone marrow, and lymphatic system	2	17	17	36
190–199	Others and unspecified	3	24	23	50
140–209	All sites	15	188	264	467

Table 16.6

A comparison between the three reference populations in terms of directly standardized rate ratios (SRR)

Cancer site	Sweden	Västerbotten county	Skellefteå municipality
Digestive organs	100	102	106
Stomach	100	136	130
Colon and rectum	100	87	89
Trachea, bronchus and pleura, primary	100	71	95
Uro-genital organs	100	98	93
Prostate	100	102	87
Kidney	100	101	114
Urinary organs (excl. kidney)	100	90	98
Blood, bone marrow and lymphatic system	100	111	123
All sites	100	94	100

age and calendar time (Table 16.7), a 24–34% excess of the incidence of all cancer was found. This was mainly due to the 120 respiratory cancers, 70–85 more cases than would be expected from reference figures.

Excess SMR values for all cancer and respiratory cancer were significant, whichever reference population was used (Fig. 16.4). Excluding respiratory cancer from the all cancer category resulted in a SMR value of 111 compared with Swedish males. Respiratory cancer was almost synonymous with lung cancer (108 out of 120 cases). Owing mainly to stomach cancer, the observed excess figure for digestive cancer was eliminated when comparing with local populations.

Trends in the cancer incidence pattern during 1958–1982 for Rönnskär workers were compared with those of Swedish men in Fig. 16.5. Starting from an almost equal level in the early 1960s, a significantly increasing trend was shown for Rönnskär workers towards the mid-seventies, followed by a levelling off thereafter.

For lung cancer in particular, a decreasing rate was shown from the late 1970s. In terms of SMR values, using moving 5-year calendar periods (1973–77, 1974–78 etc), the 3-fold or 4-fold increase relative to general and local populations during the mid-seventies were followed by five successive decreasing values, down to 1.5- and 2-fold respectively. For 1979–1983 and 1980–1984, incidence figures were estimated using the regional cancer register.

Table 16.7

Age and site-specific cancer incidence among Rönnskär workers in terms expected number of cases and standardized morbidity ratios relative to three different reference populations (SMR = 100 for reference populations)

Site	Age (years)	Obs cases	Reference populations:					
			Sweden		Västerbotten		Skellefteå	
			Exp cases	SMR (%)	Exp cases	SMR (%)	Exp cases	SMR (%)
Digestive organs	15–44	3	3.3		3.7		3.0	
	45–64	49	47.7		51.4		51.3	
	65+	78	60.4		62.7		63.5	
	15+	130	111.4	117	117.8	110	117.8	110
Respiratory organs	15–44	3	1.2		1.0		0.6	
	45–64	57	24.9		16.1		22.6	
	65+	60	25.6		18.7		22.0	
	15+	120	51.7	232	35.8	335	45.2	265
Urogenital organs	15–44	4	3.2		2.6		2.5	
	45–64	39	39.3		35.4		34.6	
	65+	81	71.3		68.2		54.9	
	15+	124	113.8	109	106.2	117	92.0	135
Blood, bone marrow, lymphatic system	15–44	2	2.9		3.3		4.1	
	45–64	17	15.3		16.7		17.9	
	65+	17	14.2		15.9		15.0	
	15+	36	32.4	111	35.9	100	36.9	98
All sites	15–44	15	17.1		16.3		15.2	
	45–64	188	161.1		148.6		155.8	
	65+	264	198.5		185.9		177.3	
	15+	467	376.7	124	350.8	133	348.3	134

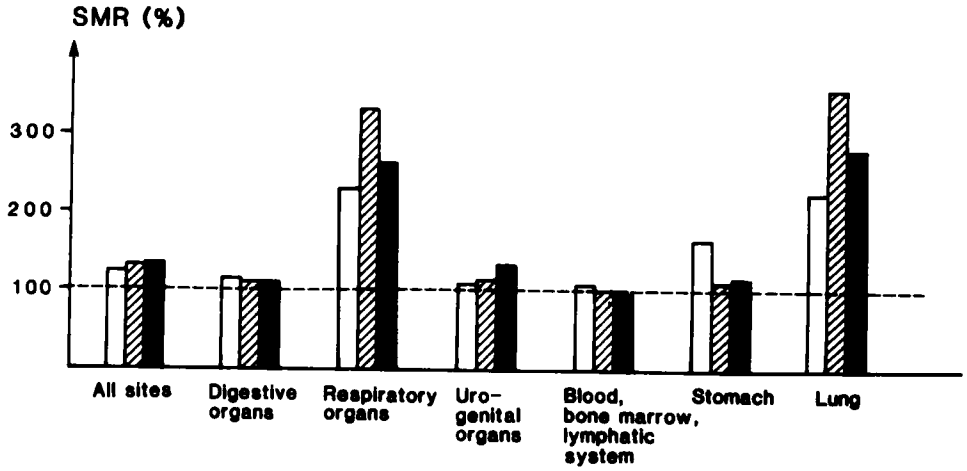

Fig. 16.4. Cancer incidence among Rönnskär workers in terms of standardized morbidity ratios (SMR = 100 for reference populations) for different site categories. □ Sweden; ▨ Västerbotten county; ■ Skellefteå municipality.

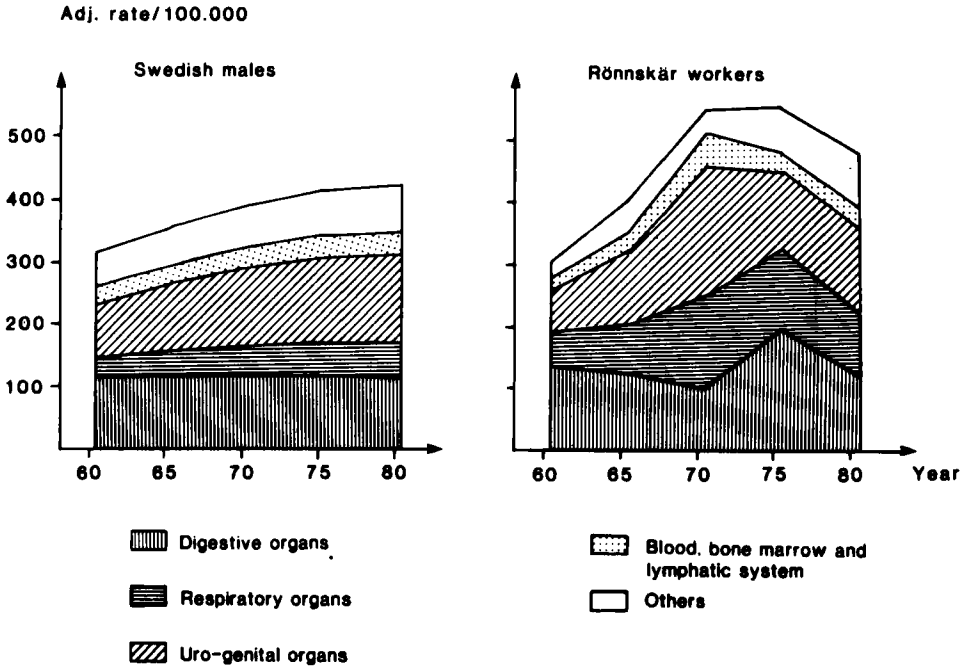

Fig. 16.5. Cancer incidence pattern among Rönnskär workers and the Swedish male population 1958–1982. (Adjusted rates calculated using the Swedish male population 1951–1955 as standard.)

Less attention to the values should be paid here for the municipality of Skellefteå in view of the impact of the cohort itself (Fig. 16.6).

16.4.4 *Internal comparisons*

The effects of latency were expected to be small in this study since follow-up did not start until 1958. When, therefore, a latency period of 15 years was used for external comparisons, the SMR value was 255 for lung cancer instead of 234 without latency criteria.

Similarly, the effects of total exposure time were estimated in terms of standardized rate ratios for those employed less than 5 years and for those employed 5 years or more. Table 16.8 (including only the age range 45–64 years to enable valid comparisons) shows that risk gradients were particularly evident for lung cancer incidence.

The 'exposure' of 'total employment time' was not specified. Probably a 'survivor population effect' (Fox et al. 1976) also operated and job-specific exposure time was therefore more relevant. Such an analysis confirmed the previous mortality analysis (Table 16.9), with excess lung cancer risks among roasters, arsenic workers, nickel smelters and workers at the machine shop. When 'eliminating' these sites SMR values of 172 remained for inci-

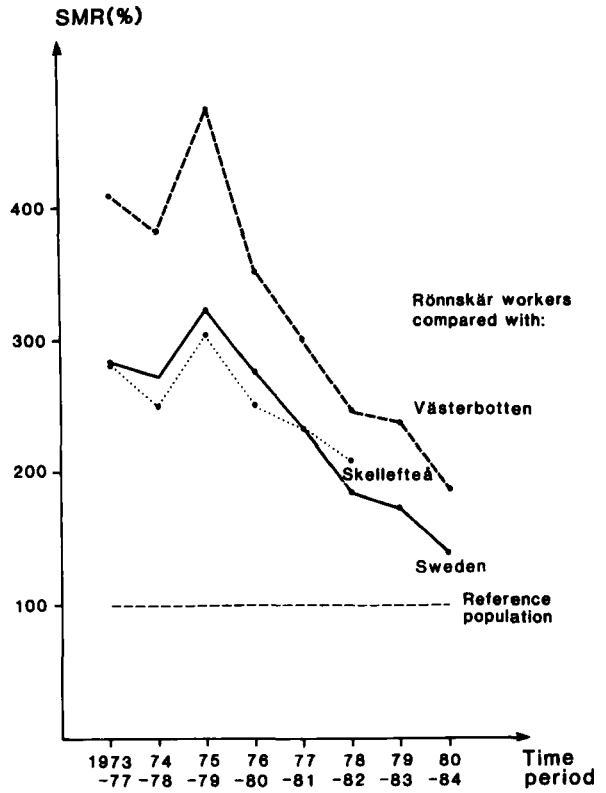

Fig. 16.6. Lung cancer incidence among Rönnskär workers relative to the reference populations (SMR = 100) by 5-year moving calendar periods for the period 1973–1984. (The figures for the years 1983 and 1984 are estimated using data from the regional cancer register.)

Table 16.8

Site-specific cancer incidence (ages 45–64) among Rönnskär workers, for different total exposure times in terms of age-standardized rates and rate ratios (SRR)

	Adjusted rate per 100 000			
	The cohort	Employed <5 years	Employed ≥5 years	SRR (%)
Digestive organs	312.7	226.6	338.7	149
Respiratory organs	250.9	157.9	270.8	172
Lung	230.6	139.0	248.5	179
Uro-genital organs	297.6	262.6	295.1	112
Blood, bone marrow, lymphatic system	76.1	97.9	76.8	79
All sites	1 055.7	891.5	1 085.5	122

dence and 140 for mortality relative to the Swedish male population.

If interpreted as the effects of a changing work environment, the decreasing trends of lung cancer shown in Fig. 16.6 might partially be validated by an analysis of different employment cohorts. From Fig. 16.7 we see that the later the date of first employment, the lower the cancer incidence (especially for lung cancer). For all cancer, the

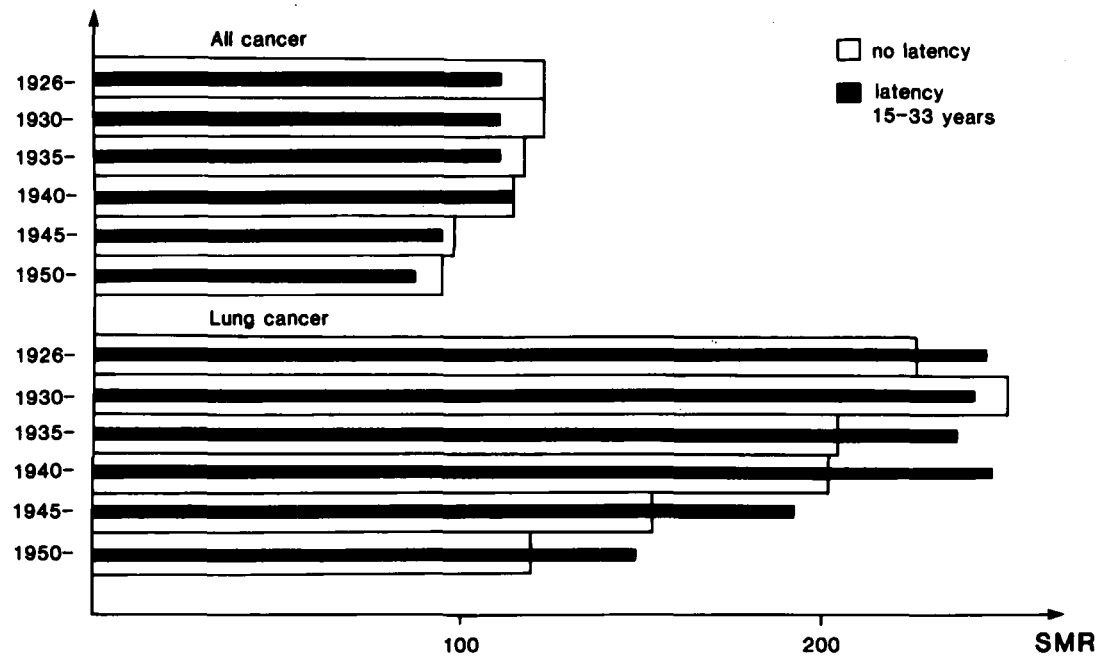

Fig. 16.7. Cancer incidence among Rönnskär workers by year of first employment for the entire cohort and with latency 15–33 years, relative to Swedish males (SMR = 100). □ No latency; ■ Latency 15–33 years.

Table 16.9

Lung cancer mortality and incidence during 1958–1982 for those who had ever worked at different work sites relative to Swedish males (SMR = 100). Latency 15 years

Work site	Lung cancer mortality			Lung cancer incidence		
	Obs cases	Exp cases	SMR (%)	Obs cases	Exp cases	SMR (%)
Roaster dept	30	7.2	417	35	7.5	467
Roaster gas purifier	22	5.1	431	22	5.3	415
Nickel smelter	11	3.9	282	12	4.3	279
Arsenic depts	22	7.7	286	23	8.1	284
Machine shop	26	7.0	371	25	7.1	352
Other depts	25	17.9	140	33	19.2	172
All work sites	95	39.2	242	107	41.9	255

excess risk relative to the Swedish male population no longer prevailed for workers employed 1945 or after. For lung cancer, however, 17 observed cases occurred in this cohort, compared with 11.2 expected. In relation to local populations (8.0 and 9.8 expected cases) the excess risks were statistically significant, but not, however, among those employed in 1950 or thereafter. Owing to varying latency periods, comparisons between different employment cohorts might not be easily interpreted. To improve validity in comparisons between employment cohorts, follow-up was restricted to the range 15–33 years (Fig. 16.7). To some extent this increased the SMR values for lung cancer among those later employed, but the overall pattern did not change.