Int Arch Occup Environ Health (1993) 65:163–169

International Archives of
Occupational and Environmental Health

Mortality and tumour morbidity among Swedish market gardeners and orchardists

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Received December 14, 1992 / Accepted March 29, 1993

Summary. In order to investigate possible effects of exposure to pesticides, mainly fungicides and insecticides, we studied a cohort of 2370 subjects, who, during the period 1965–1982, had been members of a horticulturists' trade association (market gardeners and orchardists). Compared to a regional reference population, total mortality (542 deaths; standardized mortality morbidity ratio, SMR = 0.8; 95% confidence limits, CLs = 0.7, 0.9) and mortality due to malignant tumours (133 deaths, SMR = 0.9; CLs = 0.7, 1.0), and cardiovascular and respiratory deaths were somewhat decreased. Suggestive excesses in mortality were seen for mental disorders and tumours of the stomach, skin and nervous system. The tumours of the nervous system were in particular excess in the young and middle-aged horticulturists (below age 60; six cases, SMR = 2.9; CLs = 1.1, 6.2). During the period 1965–1986, the total tumour morbidity was slightly decreased (255 cases; SMR = 0.9; CLs = 0.8, 1.0), as were gastrointestinal and respiratory tract tumours. The incidence of melanomas was increased (15 cases, SMR = 2.1; CLs = 1.2, 3.5), and tumours of the female genital organs, myelomas, and brain tumours (12 cases, SMR = 1.5; CLs = 0.8, 2.7) were slightly numerically elevated. Brain tumours in the young and middle-aged horticulturists (11 cases, SMR = 3.2; CLs = 1.6, 5.7), including meningiomas (four observed, SMR = 6.8; CLs = 1.9, 17.4), were increased, especially in the period 1975–1979. The mortality and tumour morbidity patterns in gardeners and orchardists, analysed separately, were similar to the patterns in all the horticulturists. The risk for brain tumours in the young and middle-aged subjects was increased about threefold in the gardeners, and about fivefold in the orchardists; in particular, meningiomas were in excess among the gardeners.

Key words: Brain tumour – Morbidity – Mortality – Horticulturists – Pesticides

Introduction

Horticulturists, like orchardists and market gardeners, who work in confined spaces, are at risk of significant pesticide exposure via the skin, lungs and gastro-intestinal tract. Some pesticides are genotoxic and/or immunotoxic, and some are definite or suspected animal carcinogens. In epidemiological studies, insecticides have been associated with tumours of the lung, brain and lymphatic system and with soft tissue sarcomas (STSs) [19]. Furthermore, fungicides have been associated with non-Hodgkin's lymphomas (NHLs) [16] and brain neoplasms [23], and herbicides with myelomas [7] and NHLs [16]. In particular, an association has been observed between chlorophenoxy herbicides and malignant lymphomas and STSs [18, 28]. However, the carcinogenicity of pesticides in humans is still a matter of debate [3, 4, 9, 17, 19], which could be due to, for example, use of different substances, climate and/or variations in work practice. Epidemiological literature in the field of horticulture is rather scarce. Orchardists have been claimed to be at increased risk of respiratory cancer [33] and lymphomas/multiple myelomas [25], including NHLs [26]. The incidence of lip cancer [10] and melanomas [14] has been reported to be elevated in gardeners. In a group of farmers, farm managers and market gardeners in the United Kingdom, but not in gardeners and groundsmen, there was a moderate excess of STSs [2]. Danish [30] and Swedish [40] gardeners were found to have an increased risk of STSs; Danish gardeners also had an increased risk of chronic lymphatic leukaemia (and NHLs) [30], and Swedish female gardeners an increased risk of bladder cancer [29]. However, census-based studies of Swedish market gardeners did not show an excess risk of STSs [34] or malignant lymphomas [35], and there was no increase in malignant lymphomas or myelomas in horticultural workers [12].

In order to investigate further the possible carcinogenic effects of exposure to pesticides, primarily fungicides and insecticides (Table 1), we here present a study of deaths and tumours among Swedish self-employed market gardeners and orchardists. Tumours of the respiratory system, skin (including melanomas) and nervous system, STSs and malignant lymphomas/myelomas were of special interest.

Materials and methods

Swedish horticulture and pesticide use. The extent of the horticultural trade in Sweden has fluctuated greatly since the 1940s, but in

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Table 1. Main pesticides used in Swedish horticulture, 1920–1982

Pesticide		Time period[a]						
Type	Substance	1920	1930	1940	1950	1960	1970	1980
Fungicides	Benomyl							
	Binapacryl							
	Captan							
	Chinomethionate							
	Copper sulphate							
	Copper oxychloride							
	Difolatan							
	Dimethirimol							
	Dinobuton							
	Dinocap							
	Ditalimfos							
	Dithianon							
	Dithiocarbamates							
	Dodin							
	Dodemorph							
	Folpet							
	Mercuric chloride							
	Orthophenylphenol							
	Oxycarboxin							
	Prothiocarb							
	Pyrazofos							
	Quintozene							
	Sulphur							
	Technazene							
	Tolylfluanid							
	Triadimefon							
	Vinclozolin							
Insecticides	Aldicarb							
	Azobensol							
	Carbaryl							
	DDT							
	Dieldrin							
	Endosulfan							
	Lead arsenate							
	Lindan							
	Methoxychlor							
	Naphthalene							
	Nicotine							
	Organophosphates							
	Pyrethrins							
	Pyrethroids, synthetic							
	Quassia							
	Rotenone							
	Tetrachloroethane							
	Zinc arsenate							
Herbicides	Diquat							
	Glyphosate							
	Lenacil							
	Paraquat							
	Phenoxy acids (MCPA, 2,4-D, 2,4-DP)							
	Terbacil							
	Triazines (atrazine, simazine, terbutylazine)							

Table 1 (continued)

Pesticide		Time period[a]						
Type	Substance	1920	1930	1940	1950	1960	1970	1980
Other	Carbolineum	—	—	—	—	—	—	—
	2-Chloroethyltrimethyl-ammonium chloride						—	—
	Chloroethylphosphonic acid						—	—
	Daminozide						—	—
	Dazomet					—	—	—
	Diatomaceous silica	—	—	—				
	Dicofol					—	—	—
	Dienochlor					—	—	—
	Dinitro-ortho-cresol			—	—			
	Formaldehyde			---	---	—	—	—
	Hydrocyanic acid	---	---	---				
	Mercaptodimethur						—	—
	Metam					—	—	—
	Tetradifon					—	—	—

[a] Solid line denotes substantial use, dotted line less extensive use

Table 2. Vital status on 31 December 1986 of the total cohort of members of the horticulturists' association 1965–1982

Vital status	Male		Female		All	
	No.	%	No.	%	No.	%
Living	1683	75.6	136	90.1	1819	76.5
Dead	527	23.7	15	9.9	542	22.8
Emigrated	9	0.4	0	0	9	0.4
Unknown	8	0.4	0	0	8	0.3
Total	2227	100	151	100	2378	100

1985 about 21000 persons, 0.5% of the working population, were employed, full-time or seasonally, in horticulture. Of all horticultural products in Sweden, about 50% were ornamental plants, 30% vegetables and 20% fruits and berries.

Swedish orchardists have used pesticides since the beginning of the century, and market gardeners since the late 1940s. Thereafter, the use has rapidly increased, especially in southern Sweden. Fungicides, like benomyl, bisdithiocarbamates, captan, copper salts, folpet, quintozene and sulphur, as well as insecticides, mainly carbamates, DDT, lindan, organophosphates and pyrethroids, have been predominant (Table 1). Some of the most harmful (for man and/or environment) ones have been banned (by 1982 DDT, dieldrin, difolatan, dinitro-ortho-cresol, monuron, nitrophene, parathion, 2,4,5-trichlorophenoxy acetic acid); others have been abandoned for other reasons. However, more than a hundred generic substances were still in use in Swedish horticulture in 1982. Between 94 and 188 tons of pesticides (active substance), more than half of which was fungicides, were sold annually for horticultural use in the 1980s.

Different methods have been applied to spread the chemicals: in earlier days backpack, and later handgun spraying, as well as application from tractor ramp. Fumigation, high-volume airblast application and lately ultralow-volume application have also been used. In the past, handling of pesticides involved more powdered material than nowadays, when liquids predominate. In Sweden, there are no TLV values for pesticides and no compulsory regulation concerning re-entry periods or safe levels of foliar residues following pesticide application. Since 1965, however, pesticide applicators are obliged to have a certificate for pesticide handling, which gradually has resulted in an increased understanding of protective measures.

Cohort. We investigated the southern region members of a nationwide Swedish association of horticulturists, which was founded in 1903 and originally included self-employed market gardeners and nurserymen (growing ornamental plants and vegetables, mainly in greenhouses) and later also orchardists and some berry growers (growing mainly apples, pears and strawberries). The proportion of horticulturists joining the association has varied between roughly 50% and 80% since the late 1940s. The association register, complete from 1965 to 1982, contained information on name, address, often birth date, job title, type and size of culture, and entry into and exit from the association. Missing information was supplemented from annually published membership books and membership lists. The study population comprised 1856 subjects registered as market gardeners/nurserymen and 547 subjects registered as orchardists (and/or berry growers). (Thirty-three subjects were registered as both gardener and orchardist). All were members for at least 1 year from 1965 onwards. A few had been members since 1903, and some were honoured by a life-long membership. Economic considerations and opinions on policies, not status of work, often determined entries and exits. Thus, the period of membership was not judged to be a suitable substitute for work/exposure.

Vital status for 2378 subjects, 2227 men and 151 women, was determined up to 31 December 1986 (Table 2). Only eight subjects were lost to follow-up. The median year of birth was 1921 for the men, and 1925 for the women.

Information on deaths and tumours. Information on causes of death between 1965 and 1986 was obtained from the National Swedish Central Bureau of Statistics (NSCBS), which is responsible for the coding of all Swedish death certificates. All codes were amended according to the 8th revision of the International Classification of Diseases (ICD). The proportion of death certificate diagnoses, based on autopsies, was similar in the cohort and the reference population (44.6% vs 40.7%).

Information on up to at most two tumours, coded according to the 7th revision of the ICD, and diagnosed from 1965 to 1986, was obtained from the National Swedish Tumour Registry and the Southern Swedish Regional Tumour Registry. 87.6% of the tumours in the cohort were verified with patho-anatomical diagnosis vs 82.8% in the reference population.

Table 3. Observed and expected mortality and specific causes of death in a cohort of horticulturists, 1965–1986[a]

Cause of death	ICD-8	O	E	SMR	CLs
Malignant neoplasms	140–209	133	156.7	0.9	0.7, 1.0
Gastro-intestinal	150–159	49	59.4	0.8	0.6, 1.1
Stomach	151	23	17.1	1.4	0.9, 2.1
Intestine	152–153	10	13.6	0.7	0.4, 1.4
Respiratory tract	160–163	14	29.2	0.5	0.3, 0.8
Soft tissue	171	1	0.6	1.7	0.0, 9.6
Skin	172–173	4	2.9	1.4	0.4, 3.5
Male genital organs	185–187	24	21.5	1.1	0.7, 1.7
Urinary tract	188–189	10	11.3	0.9	0.4, 1.6
Nervous system	191–192	7	4.6	1.5	0.6, 3.1
Brain	191	4	4.0	1.0	0.3, 2.6
Blood, lymph	200–209	18	14.7	1.2	0.7, 2.0
Lymphomas/myelomas	200–203	10	8.4	1.2	0.6, 2.2
Mental disorders	290–315	5	2.9	1.7	0.6, 4.1
Nervous system	320–389	7	6.8	1.0	0.4, 2.1
Cardiovascular diseases	390–458	286	366.1	0.8	0.7, 0.9
Respiratory diseases	460–519	28	43.0	0.7	0.4, 1.0
Bronchial	490–493	6	14.4	0.4	0.2, 0.9
Violence, intoxication	800–999	42	44.8	0.9	0.7, 1.3
All causes	000–999	542	676.5	0.8	0.7, 0.9

[a] Calculations were based on 2370 subjects and 38460 person-years. ICD, International classification of diseases; O, observed mortality; E, expected mortality; SMR, standardized mortality ratio; CLs, 95% confidence limits

Risk estimates. The regional expected mortality for the period 1965–1986 was calculated using calender year-, 5-year age-group- and cause-specific mortality rates for males and females in the five southern counties. These rates were calculated from deaths and population counts obtained from the NSCBS. Similarly, cancer rates for the period 1965–1986 were obtained from the Southern Swedish Regional Tumour Registry, and the expected morbidity was calculated.

The calculation of person-years started at entry into the association, or on 1 January 1965 for subjects who entered before that date. Dates of death or emigration were used as individual end points. Subjects whose vital status was unknown were not included in the comparisons. In the tumour morbidity analyses, accumulation of person-years ceased at first or second tumour, emigration, death or end of follow-up. Deaths and tumours at all ages were included in the main analyses.

Cause-specific standardized mortality/morbidity ratios (SMRs), as well as 95% confidence limits (CLs), according to the Poisson distribution, were calculated.

Results

Mortality and causes of death

The all-cause mortality was somewhat decreased (Table 3), and the total tumour mortality was close to unity. As to cause-specific mortality, there was a decrease in tumours of the respiratory system and in cardiovascular and bronchial diseases. Slight numerical excesses were seen for tumours of the stomach, skin and nervous system and for mental disorders. One case of STS was observed.

Separate analyses in 5-year calendar periods showed similar patterns, as did separate analyses of gardeners and orchardists.

In other Swedish agriculturists, the disease pattern seems to differ in young as compared to old age groups [32, 39]. In the present study, mortality analyses in different age groups, as a substitute for work/exposure, did not reveal significant exposure-response patterns, but below the age of 60 the mortality due to tumours of the nervous system (ICD 8: 191–192) was increased (six observed, SMR = 2.9; CLs = 1.1, 6.2).

Tumour morbidity

The total tumour incidence was close to the expected incidence (Table 4). An increase in malignant melanomas and suggestive excesses of tumours of female genital organs, myelomas and brain tumours were observed. The brain tumours were all diagnosed ante mortem in males aged 33–61. There were six astrocytomas (five histologically classified as grade III–IV, one as grade I–II), four meningiomas and two acoustic neuromas. Slight deficits of respiratory tract and of all gastro-intestinal tumours were seen and no case of STS.

Tumour morbidity analysed separately in 5-year calendar periods between 1965 and 1986 showed that lymphomas/myelomas (ICD 7 = 200–203) were in excess in 1965–1969 (five observed, SMR = 2.9; CLs = 1.0, 6.8), skin tumours (20 observed, SMR = 1.9; CLs = 1.2, 3.0)

Table 4. Observed and expected tumour morbidity in a cohort of horticulturists, 1965–1986[a]

Site of tumour	ICD-7	O	E	SMR	CLs
Gastro-instestinal tract	150–155, 157, 158	63	78.6	0.8	0.6, 1.0
Stomach	151	24	20.0	1.2	0.8, 1.8
Intestine	152–153	14	23.0	0.6	0.3, 1.0
Rectum	154	15	16.3	0.9	0.5, 1.5
Respiratory tract	160–164	20	34.4	0.6	0.4, 0.9
Female genital organs	171–176	5	2.2	2.3	0.7, 5.3
Male genital organs	177–179	62	54.1	1.2	0.9, 1.5
Urinary tract	180–181	25	30.8	0.8	0.5, 1.2
Bladder	1810	18	19.7	0.9	0.6, 1.5
Skin	190–191	29	20.2	1.4	1.0, 2.1
Melanomas	190	15	7.1	2.1	1.2, 3.5
Nervous system	192–193	13	9.1	1.4	0.8, 2.5
Brain	1930	12	7.8	1.5	0.8, 2.7
Soft tissue	197	0	2.0	0.0	0.0, 1.8
Blood and lymph	200–209	23	21.6	1.1	0.7, 1.6
Lymphomas/myelomas	200–203	15	13.2	1.1	0.6, 1.9
Non-Hodgkin's lymphomas	200, 202	6	7.8	0.8	0.3, 1.7
Hodgkin's lymphomas	201	3	1.5	2.1	0.4, 6.0
Myelomas	203	6	3.9	1.5	0.6, 3.3
Lymphatic leukaemia	204	4	3.8	1.0	0.3, 2.7
Myeloic leukaemia	205	3	2.7	1.1	0.2, 3.3
All	140–209	255	279.4	0.9	0.8, 1.0

[a] Calculations were based on 2370 subjects and 38444 person-years. ICD, International classification of diseases; O, observed morbidity; E, expected morbidity; SMR, standardized morbidity ratio; CLs, 95% confidence limits

and melanomas (15 observed, SMR = 2.1; CLS = 1.2, 3.5) in 1980–1986, and brain tumours in 1975–1979 (six observed, SMR = 3.5; CLs = 1.3, 7.7).

In general, the tumour morbidity among market gardeners and orchardists, analysed separately, did not differ markedly from the morbidity among all the horticulturists.

The analysis of tumour morbidity by age groups did not disclose exposure-response patterns, but below the age of 60, brain tumours (ICD 7: 1930; 11 observed, SMR = 3.2; CLs = 1.6, 5.7), as well as the three histological subtypes, were in excess, meningiomas significantly so (four observed, SMR = 6.8; CLs = 1.9, 17.4). Below age 50, brain tumours (six observed, SMR = 4.8; CLs = 1.8, 10.5) and meningiomas (three observed, SMR = 17.7; CLs = 3.6, 51.6) were still increased. Brain tumours were in excess below age 60 in both the market gardeners (eight observed, SMR = 2.8; CLs = 1.2, 5.5) and the orchardists (three observed, SMR = 5.1; CLs = 1.1, 14.8), and meningiomas were increased among the gardeners (three observed, SMR = 6.0; CLs = 1.2, 17.5). In the ages below 50, brain tumours (five observed, SMR = 4.5; Cls = 1.5, 10.6) and meningiomas (two observed, SMR = 13.3; CLs = 1.6, 48.2) were still significantly elevated among the gardeners.

Discussion

The results of the present study suggest no major health effects of horticulture, (including application of pesticides), as reflected by deaths and tumours. Although the horticulturists are more exposed to pesticides, in particular to fungicides and insecticides, than other Swedish agriculturists, the low overall risk estimates of disease are in agreement with findings in other agricultural groups [5, 34, 37, 39]. This might be due to a selection of healthy persons into the trades, and/or to the healthy countryside life-style concerning smoking [24], diet, physical activity and pollution.

Skin tumours, including melanomas, were increased in accordance with earlier observations in gardeners [14] and farmers [5], possibly due to UV radiation. There was no excess of STSs or lymphoproliferative diseases, which is consistent with the findings in some [12, 34, 35] but not in other [25, 26, 30, 40] studies of agricultural groups, which differ as to, for example, extension, type, intensity and duration of exposure. In our cohort, the use of, for instance, chlorophenoxy herbicides, has probably been moderate. The use of DDT and other organochlorine insecticides has been more extensive, or at least this was the case in the 1950s and 1960s, which might account for the peak incidence of lymphomas/myelomas in 1965–1969 [cf. 19].

In agreement with earlier observations in pesticide-exposed groups (as mentioned above), we observed a slightly increased risk of brain tumours, and also of meningiomas (and gliomas), particularly in the young and middle-aged horticulturists. However, caution in interpreting these results is proposed, since we only have observed a given age group during a limited age interval. Interestingly, though, Swedish farmers below age 50 might have an increased risk of cancer [32]. Also, Swedish pesticide applicators born in 1935 or later were found to have a slightly increased total tumour morbidity, and certain tumours, e.g. those of the nervous system, were non-significantly in excess [38, 39]. Swedish agricultural research workers were identified as being at risk for gliomas [21], but alkyl mercury-exposed seed disinfectant appliers [36] and Swedish agriculturists in general seemed not to be at risk for tumours of the nervous system [34] or for menigiomas [20] or gliomas [21]. Further in accordance with our study are the observations of an increased risk of brain tumours in middle-aged males from fruit-producing and pesticide-using parts of Italy [13], and of brain tumours [5, 27] and gliomas in agriculturists, especially those active after 1960 [22] and those using fungicides and insecticides [23]. In our study, the peak incidence of brain tumours occurred in 1975–1979, which might likewise suggest a possible role for chemicals in common use after 1960. An increase in brain tumours has also been observed in other pesticide applicators [4, 9], farm and nursery workers [11] and wood workers [8], all of whom were exposed to insecticides and fungicides, and among American agricultural extension agents, a dose-resonse pattern for brain cancer with duration of exposure was seen [1]. It is noteworthy that many pesticides can react with nitrite to form N-nitroso compounds [17], which have been associated with brain tumours (most commonly of glial origin), in animals [31]. Further, the herbicide 2,4-dichloro-phenoxyacetic acid (2,4-D) has caused astrocytomas in rats [15]; however, brain tumours have not been increased in workers exposed to chlorophenoxy herbicides [18, 28], including potentially 2,4-D-exposed workers [6].

We also found small non-significant excesses of tumours of the stomach (in agreement with the findings in other agriculturists, including horticulturists [5], and female genital organs. However, the study sample was too small to allow for the detection of discrete changes of risk concerning some of the tumours of special interest: Even though the power to detect an increase in incidence of one and a half for tumours of the respiratory system was 75%, it was only 37% for malignant lymphomas/myelomas, 24% for brain tumours and 9% for STSs. Furthermore, the length of follow-up (mean: 16.1 years) is hardly sufficient to reveal a late rise in tumour morbidity, especially with respect to pesticides introduced in the 1970s or later.

In the present study, information on an individual basis regarding substances used and the duration and intensity of exposure was lacking. Thus, no true dose-response analyses could be performed. For reasons stated above, the entry/exit period of association was found to be a poor approximation of duration of work/time of assumed exposure. Since horticulture (in Sweden) used to be a life-long occupation, age was tentatively applied as a substitute for exposure, but significant exposure-response patterns were not revealed.

In conclusion, our findings suggest that Swedish self-employed horticulturists live an unusually healthy life. However, there is an increased relative risk of brain tumours among the middle-aged which might be related to the use of certain pesticides. Pesticides are widespread in the environment, and the brain tumour excess seen among a subgroup of horticulturists in the present study, as well as in other occupationally pesticide-exposed groups, may give one clue as to the reason for the recent increase in these tumours in many industrialized countries.

Acknowledgements. This study was supported by grants from the Swedish Work Environment Fund (AMFO 88-0127). The authors especially wish to thank members and officials of the horticulturists' organization for kind assistance, and Nordisk Alkali A/S, Malmö, for additional information on pesticides used in horticulture.

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