

## The AGRiculture and CANcer (AGRICAN) cohort study: enrollment and causes of death for the 2005–2009 period

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### Abstract

**Objective** To elaborate and describe a large prospective agricultural cohort including males and females in France with various agricultural activities and to study causes of death.

**Methods** To date, few large prospective cohorts have been conducted among agricultural population. AGRiculture and CANcer cohort is a large prospective cohort of subjects in agriculture studying cancer among active and retired males and females, farm owners and workers, living in eleven areas of France with a population-based cancer registry.

**Results** Enrollment was conducted from 2005 to 2007 with a postal questionnaire. In January 2008, 180,060 individuals (54 % males, 54 % farm owners, 50 % retired) were enrolled. Mortality was studied until December 2009 (605,956 person-years with standardized mortality ratio (SMR) by comparison with the general population of the areas. Over this period, 11,450 deaths 6,741 in men and 4,709 in women were observed, including 3,405 cancer-

related deaths. SMRs were significantly reduced for global mortality (SMR = 0.68, 95 % CI 0.67–0.70 in males and SMR = 0.71, 95 % CI 0.69–0.73 in females) and for death by cancer (SMR = 0.67, 95 % CI 0.65, 0.70 in males and SMR = 0.76, 95 % C: 0.71, 0.80 in females). These results were mainly explained by less frequent smoking-related causes of death (lung cancer, cardiovascular diseases). Nonsignificant excesses of death were observed only for rheumatoid arthritis and arthrosis, suicides (in females), death for event of undetermined intent (in males) and breast cancer in male agricultural workers.

**Conclusions** These first results are the first ones obtained in France based on a large prospective agricultural cohort showing that farmers would be in healthier condition than the general population.

**Keywords** Agriculture · Neoplasms · Enrollment · Mortality

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## Introduction

Even if the proportion of individuals involved in farming has decreased regularly in populations worldwide in the last decades (from 50 % in 1980 to 40 % in 2010), their absolute number rose from 1 billion to 1.3 billion over the same period. However, in high-income countries, the proportion and number of individuals working in agriculture dramatically decreased from 13 % (71 million) in 1980 to 4 % (26 million) in 2010. In France, these proportions were 8.3 and 2 %, respectively, and the number of people involved in farming decreased from 1.9 million to 0.6 million (Food and Agriculture Organization of the United Nations 2011). The active agricultural population is not well characterized, and health studies are often limited to male farm owners (mainly white ones). Besides farm owners, agricultural activities involved farm workers (full-time work or seasonal or migrant), spouses (working full time or partly in farms and/or only living on the farm) (Gladen et al. 1998; Kirrane et al. 2004), other farm family members (often before or at the beginning of their working life), retired farm owners (still working on their farm after retirement). Farm activities induce a large range of occupational exposures (dust, ultraviolet, solvents, diesel exhaust, detergents, viruses, nitrates, etc.). However, most epidemiological studies, especially those on cancer, have focused on pesticide exposure. Agriculture is the leading professional sector for pesticide use in the world with a turnover of about 40 billion US dollars in 2010. Western Europe remains the leading market in the world for pesticide use (28 %), and France is the main user in the European Union with a turnover of 1.8 billion euros. With around 60,000 tons used for agricultural purposes in 2010, France is the fifth pesticide user in the world after the USA, Brazil, Japan and China (Union des Industries de la Protection des Plantes 2011).

It is now widely accepted that agricultural populations present lower rates of mortality globally and for the main causes of death (cardiovascular diseases, cancer overall) (Blair et al. 1992; Acquavella et al. 1998; Blair and Beane Freeman 2009). This can be largely explained by specificities in farmers' life habits: Their lower prevalence of smoking decreases the risk of contracting cardiovascular diseases and some cancers (lung, bladder, pancreas), as their level of physical activity reduces the risk of some other cancers (colon and rectum). On the other hand, farming and occupational exposure to pesticides in farm-related activities have been regularly associated with an increased risk of developing some chronic diseases such as cancers of the prostate, hematological and brain cancers, neurological diseases and reproductive disorders (Blair et al. 1992; Acquavella et al. 1998; Alavanja et al. 2004; Dreiherr and Kordysh 2006). Many epidemiological studies

to date have been retrospective and/or have lacked sufficient statistical power to detect the effect of farm-related exposures (Blair and Beane Freeman 2009). To increase significantly the statistical power especially for cancers with low incidence rates and the quality of pesticide exposure assessment, a large prospective cohort study, the Agricultural Health Study (AHS), has been conducted in the USA since the beginning of the 1990s (Alavanja et al. 1996). It has enrolled around 90 000 individuals including more than 50 000 active farm owners using pesticides in two states where agriculture is mainly devoted to open field and livestock (Lynch et al. 2005). This large prospective North American cohort is part of a newly established International Consortium for Agricultural Cohorts (AGRICOH) coordinated by the National Cancer Institute and the International Agency for Research on Cancer (Leon et al. 2011). The consortium now includes 26 prospective cohorts from 12 countries. We present here the enrollment step of the AGRiculture and CANcer (AGRICAN) study, a large cohort initiated in France in 2005, included in AGRICOH, and the first results on mortality from enrollment until December 31, 2009.

## Methods

### Population

The eligible population included all individuals working in agriculture, currently or in the past, and living in any of the 13 French areas covered by a population-based cancer registry in 2004. The *Calvados* and *Hérault* areas were later excluded because a cohort of farmers had already been set up by the authors in *Calvados* since 1995 and because of a refusal for participation in the *Hérault* area. The 567,157 individuals were identified through the local and central organizations specialized in health insurance for agriculture [*Mutualité Sociale Agricole (MSA)*]. This insurance agency concerns farm owners, farm workers and individuals working for companies or organizations related to agriculture such as private insurance companies, some banks, extension agents, foresters and gardeners. This study was approved by the national ethics committee (*Comité Consultatif sur le Traitement de l'Information en matière de Recherche dans le domaine de la Santé* #01.148 and *Commission Nationale Informatique et Libertés* #05.1292, France), and all participants of the study provided their informed consent by sending back their enrollment questionnaire. Eligible individuals had to (1) be older than 18 years old on January 1, 2004, (2) have been insured by the *MSA* for more than 3 years and (3) live, at the time of selection, in one of the 11 geographical areas covered by the study (*Côte-d'Or, Doubs, Gironde, Isère, Loire-Atlantique,*

**Table 1** Characteristics of individuals eligible or enrolled in the AGRICAN cohort

	Eligible (n = 567,157)						Enrolled (n = 180,060)					
	Farm owners <sup>a</sup> (n = 295,887)		Agricultural workers <sup>b</sup> (n = 271,270)		All (n = 567,157)		Farm owners <sup>a</sup> (n = 97,969)		Agricultural workers <sup>b</sup> (n = 82,091)		All (n = 180,060)	
	Males N (%)	Females N (%)	Males N (%)	Females N (%)	Males N (%)	Females N (%)	Males N (%)	Females N (%)	Males N (%)	Females N (%)	Males N (%)	Females N (%)
Age (years) <sup>c</sup>												
<30	2,372 (1.3)	263 (0.2)	7,924 (5.8)	2,189 (1.6)	10,296 (3.2)	2,452 (1.0)	730 (1.3)	109 (0.3)	1,828 (4.7)	770 (1.8)	2,558 (2.6)	879 (1.0)
30–39	14,393 (7.9)	3,942 (3.5)	19,385 (14.0)	10,315 (7.8)	33,778 (10.5)	14,257 (5.8)	4,563 (7.8)	1,483 (3.8)	4,490 (11.5)	3,616 (8.4)	9,053 (9.3)	5,099 (6.2)
40–49	26,072 (14.2)	12,368 (11.0)	20,393 (14.8)	12,904 (9.7)	46,465 (14.5)	25,272 (10.3)	8,423 (14.3)	4,437 (11.3)	4,947 (12.7)	4,377 (10.2)	13,370 (13.7)	8,814 (10.7)
50–59	29,770 (16.3)	19,700 (17.5)	22,415 (16.2)	12,734 (9.6)	52,185 (16.3)	32,434 (13.2)	10,184 (17.3)	7,455 (19.1)	6,947 (17.8)	4,848 (11.3)	17,131 (17.5)	12,303 (15.0)
60–69	35,514 (19.4)	26,209 (23.2)	23,951 (17.3)	16,902 (12.7)	59,465 (18.5)	43,111 (17.5)	12,358 (21.0)	10,435 (26.7)	7,535 (19.3)	6,507 (15.1)	19,893 (20.3)	16,942 (20.6)
70–79	49,637 (27.1)	28,167 (24.9)	29,019 (21.0)	42,479 (31.9)	78,656 (24.5)	70,646 (28.7)	15,964 (27.1)	9,704 (24.8)	9,392 (24.1)	14,539 (33.7)	25,356 (25.9)	24,243 (29.5)
80–89	22,957 (12.6)	18,355 (16.2)	13,164 (9.5)	29,100 (21.9)	36,121 (11.2)	47,455 (19.3)	6,198 (10.5)	4,796 (12.2)	3,553 (9.1)	7,337 (17.0)	9,751 (10.0)	12,133 (14.8)
≥90	2,251 (1.2)	3,917 (3.5)	1,953 (1.4)	6,443 (4.8)	4,204 (1.3)	10,360 (4.2)	411 (0.7)	719 (1.8)	310 (0.8)	1,095 (2.5)	721 (0.7)	1,814 (2.2)
Mean age (range)	63 (21–103)	66 (21–105)	58 (19–105)	68 (20–105)	61 (19–105)	67 (20–105)	62 (22–103)	65 (21–105)	59 (20–103)	66 (20–105)	61 (20–103)	65 (20–105)
Retired (%) <sup>d</sup>	50	52	39	67	45	60	47	47	42	63	45	55
Duration												
Retired												
4–10	27,490 (30.1)	15,519 (26.4)	14,755 (27.5)	18,446 (20.8)	42,245 (29.2)	33,965 (23.0)	6,415 (23.1)	3,885 (21.2)	3,605 (22.0)	4,546 (16.8)	10,020 (22.7)	8,431 (18.5)
11–30	21,965 (24.1)	16,934 (28.8)	11,901 (22.2)	25,983 (29.3)	33,866 (23.4)	42,917 (29.1)	5,502 (19.8)	4,941 (26.9)	2,965 (18.1)	7,489 (27.6)	8,467 (19.1)	12,430 (27.3)
31–40	22,825 (25.0)	12,935 (22.0)	19,532 (36.4)	27,032 (30.5)	42,357 (29.2)	39,967 (27.1)	8,923 (32.1)	4,732 (25.8)	7,442 (45.3)	9,394 (34.6)	16,365 (37.0)	14,126 (31.1)
≥41	18,917 (20.8)	13,395 (22.8)	7,435 (13.9)	17,221 (19.4)	26,352 (18.2)	30,616 (20.8)	6,966 (25.0)	4,788 (26.1)	2,402 (14.6)	5,690 (21.0)	9,368 (21.2)	10,478 (23.1)
Mean (SD)	25 (16)	26 (16)	25 (15)	27 (14)	25 (16)	27 (15)	28 (16)	28 (15)	28 (14)	29 (14)	28 (15)	28 (15)
Active												
4–7	11,511 (12.5)	8,619 (15.9)	33,348 (39.4)	17,716 (39.9)	44,859 (25.4)	26,335 (26.7)	3,065 (9.9)	2,641 (12.7)	6,814 (30.2)	5,090 (31.9)	9,879 (18.4)	7,731 (21.0)
8–15	19,806 (21.6)	11,946 (22.1)	24,731 (29.2)	13,960 (31.5)	44,537 (25.3)	25,906 (26.3)	5,690 (18.3)	4,089 (19.7)	6,105 (27.0)	4,950 (31.0)	11,795 (22.0)	9,039 (24.6)
16–25	25,950 (28.3)	12,761 (23.6)	14,693 (17.4)	7,155 (16.1)	40,643 (23.0)	19,916 (20.2)	8,585 (27.7)	4,825 (23.2)	4,687 (20.7)	3,126 (19.6)	13,272 (24.8)	7,951 (21.6)
≥26	34,502 (37.6)	20,812 (38.4)	11,809 (14.0)	5,553 (12.5)	46,311 (26.3)	26,365 (26.8)	13,685 (44.1)	9,237 (44.4)	4,982 (22.1)	2,804 (17.5)	18,667 (34.8)	12,041 (32.8)
Mean (SD)	21 (11)	21 (11)	13 (10)	13 (9)	17 (11)	17 (11)	23 (11)	22 (11)	16 (11)	15 (10)	20 (11)	19 (11)
Place of birth												
France (%) <sup>e</sup>	96.8	97.4	94.1	96.2	95.6	96.7	97.7	98.0	95.2	96.8	96.7	97.4
Other country (%)	3.2	2.6	5.9	3.8	4.4	3.3	2.3	2.0	4.8	3.2	3.3	2.6

<sup>a</sup> Includes only individuals who worked all or at least part of their working life as farm owners  
<sup>b</sup> Includes individuals working on farms but also those working for companies or organizations associated with agriculture (bank insurances...)  
<sup>c</sup> Age in 2005  
<sup>d</sup> Individuals who were retired at the time of enrollment  
<sup>e</sup> France includes both metropolitan and overseas areas; 26 individuals with missing information

*Manche, Bas-Rhin, Haut-Rhin, Somme, Tarn and Vendée*). The selected areas were representative of agriculture in France. The proportion of the main agricultural activities are similar among these 11 areas and France (open field: 17.6 vs. 20.5 %, vineyard: 18 vs. 14 %, fruit growing: 1.6 vs. 3.9 %, horticulture: 2.0 vs. 1.3 %, cattle: 26 vs. 25 %, poultry: 1.8 vs. 2.0 % other livestock: 10.8 vs. 10.6 %, for the 11 areas and France, respectively). “The sample size of the eligible population was different in each area ranging from 26,807 (Haut Rhin area) to 92,143 individuals (Gironde area).” The use of the files compiling information on occupational history in agriculture enabled us to identify not only individuals still working in agriculture but also all retired individuals and active people no longer working in agriculture at the time of enrollment.

The main characteristics of the eligible population are described in Table 1. Men were more represented than women (57 vs. 43 %) and farm owners slightly more than agricultural workers (52 vs. 48 %). The mean age was 61 years in men (range 19–105), 58 years for agricultural workers and 63 years for farm owners. Average age was 67 years in women (range 20–105), 68 years in agricultural workers and 66 years in farm owners. A larger proportion of women (60 %) were retired at enrollment, while a majority of men were still professionally active (55 %). At enrollment, duration of work in agriculture averaged 25–27 years in retired people, 21 years in active farm owners and 13 years in agricultural workers. Most of the eligible individuals were born in France, in a proportion slightly lower in men than in women (95.6 vs. 96.7 %) and in agricultural workers than in farm owners (95.1 vs. 97.0 %).

#### Data collection and enrollment

The postal enrollment questionnaire was sent twice, the first time between November 2005 and March 2006 and a second time for initial non-responders between January and June 2007. The eight-page self-administered questionnaire (available on request) mainly concerned (1) demographic characteristics (sex, age, educational level, place of birth...), (2) personal life habits: history of smoking, some information on diet and alcohol consumption, (3) health data: height and weight, self-report of 15 health conditions and reproductive history (age at menarche, number of pregnancies and children), (4) a complete job calendar with a lifetime history of agricultural activities including details on 13 crops (grassland, vineyard, wheat or barley, corn, field peas, potatoes, tobacco, beet, sunflower, rape, fruit-growing, greenhouse and field-grown vegetable crops) and 5 livestock (cattle, horses, sheep and goats, hogs and poultry). For all crops and livestock, information on dates of beginning and end, minimum and maximum surface areas concerned by the task (or minimum and maximum

number of animals), history of pesticide treatments and other tasks in contact with crops (or animals) was sought. When the subject had been involved in pesticide treatment tasks, the history of spraying equipment and practice (type and tank volume of sprayer, number of days of use per year) and the history of using personal protective equipment were also sought.

#### Cohort follow-up

Place of residence and affiliation to the health insurance scheme are checked annually in the *MSA* files to prevent cohort members being lost to follow-up. Vital status of all eligible individuals is also checked annually by crossing the database with the *MSA* files and, for cohort members only, with the National Death Index (*Répertoire National pour l'Identification des Personnes Physiques*). Matching with National Death Index is based on last name, first names, date and place of birth and gender. For each identified death among cohort members, cause of death is subsequently obtained from the national death registry (*Centre d'épidémiologie sur les causes médicales de décès, Ce-*pi*DC*). Person-year accumulation began in the cohort from the date of enrollment (date of reception of the questionnaire) in the study (November 1, 2005–December 31, 2007) and ended on December 31, 2009, or on the date of death or on the date the study participant was lost to follow-up.

#### Statistical analysis

##### *Mortality data*

Standardized mortality ratios (SMR) were calculated for 81 categories of the International Classification of Diseases 10th edition (World Health Organization 1992) and causes of deaths and presented for all those with more than 5 observed deaths and separately for females and males and for farm owners and agricultural workers. For comparison with the general population, area-specific rates were stratified by gender and 5-year age and calendar time period (2005–2008). Ninety-five percent confidence intervals for the SMR were calculated as recommended by Breslow and Day (1987). All statistical analyses were performed using SAS version 9.2 (SAS Institute, Inc., Cary, NC) and STATA version 7 (Stata Corporation).

## Results

### Enrollment

The enrollment questionnaire was completed by 112,932 individuals at first sending and by 67,128 more subjects at

second sending, leading to a total of 180,060 participants included in the cohort. Table 1 presents the general characteristics of eligible and enrolled individuals obtained from the MSA databases, separately for men and women and for farm owners and agricultural workers. For the latter group, most of them worked on farms but also some work in other professional sectors such as extension services, forestry but also in bank or insurance companies. Global participation rate at enrollment was 32 %, ranging from 27 to 42 % according to the study area, with 10 out of 11 areas having very close participation rates: 27–33 %. Participation was associated with gender and age. Women globally participated more than men (33 vs. 30 %), but their participation declined in the oldest (35 % before 80 years and 24 % after). The effect of age was not as clear in men: The lowest participation rate was observed before 50 years (28 %) and after 80 years (26 %) and the highest between 50 and 80 years. Mean age of enrolled and non-participants males were similar: 62 versus 63 years for farm owners and 59 versus 58 years for agricultural workers. In the same way, mean age of enrolled females was similar between enrolled and non-participants for both farm owners (65 vs. 67 years) and agricultural workers (66 vs. 68 years), leading to a slightly lower proportion of retired females in the cohort (55 vs. 60 %, Table 1). The mean duration of work in agricultural was almost the same between enrolled and non-participants for both retired (25–27 vs. 28 years) and individuals still at work (17 years among eligible subjects and 19–20 years for enrolled females and males, respectively). Overall, the cohort comprised 32 % male farm owners (mean age 62 years, 47 % retired), 22 % male agricultural workers (mean age 59 years, 42 % retired), 22 % female farm owners (mean age 65 years, 47 % retired) and 24 % female agricultural workers (mean age 66 years, 63 % retired).

#### Characteristics of enrolled individuals

Tables 2 and 3 present general agricultural characteristics of enrolled individuals ( $n = 180,060$ ) separately between farm owners and agricultural workers. Most of the men were married at the time of enrollment (74.9 %), and 11.5 % were single (10.0 % among farm owners and 13.7 % among agricultural workers). The proportion of widows was higher among females than widowers among males (27.7 vs. 6.1 %). A comparable proportion of men had attained middle (40.5 %) or secondary (42.6 %) level of education, while only 10.4 % had reached university level, a proportion slightly higher among agricultural workers (13.0 %) than among farm owners (8.6 %). The level of education was lower among females than among males with 53.1 % having completed only middle school (40.5 % among males) and 7.7 % (10.4 % among males)

having attained some university level (9.8 % among agricultural workers and 5.3 % among farm owners). Very few women reported that they were current (4.8 %) or former (9.1 %) smokers, but the proportion of women with a history of smoking was higher in workers than in farm owners (16.4 vs. 11.2 %). Smoking frequency was higher in men than among females (12.4 % current smokers and 39.3 % former smokers), and the global proportion of smokers was also higher in male workers than in farm owners (56.0 vs. 48.9 %). Few males reported no alcohol consumption (9.6 % among farm owners and 11.5 % among agricultural workers), and 69.2 % were regular alcohol consumers (at least once a week). Almost one-third of females reported no alcohol consumption, and one-third was regular consumers. Half of the men were overweight (42.1 %) or obese (13.6 %), a proportion lower in women (27.2 % overweight and 11.3 % obese).

#### Main agricultural characteristics

Eighty-three percent of cohort members reported having been a farm owner or farm worker at some time in their life. Table 3 presents the main characteristics of their agricultural activities including tasks with direct or indirect exposure to pesticides.

Cattle was the most frequent livestock, whatever the occupational status or gender (ranging from 61.0 to 73.5 %). For these individuals, the most frequent task was milking, whatever the gender or job title. Around half of the males had used insecticides on cattle (55.4 % in farm owners and 40.5 % in farm workers) versus 16.3 % of females. Almost half of the female agricultural workers had been involved in poultry farming versus 37.7 % of female farm owners, 24.8 % of male agricultural workers and 22.7 % of male farm owners. However, males were two times more frequently exposed to insecticide use on poultry than females. Female farm workers were more frequently involved in hog farming than farm owners (33.1 vs. 23.3 %). Males were more frequently involved with horses than females (23.3 vs. 13.0 %), and around 10 % of males and females were involved with sheep or goats. Insecticide use on animals was more frequent among males than females (29.7 vs. 13.1 % for workers and 46.0 vs. 19.4 % for farm owners, respectively).

Eighty-three percent of males (65.3 % of females) had been involved with at least one of the 13 main crops. The most frequent crop grown was grass, whatever the gender or job title (from 44.1 to 69.8 % in their lifetime). The absolute frequencies of individuals working on each specific crop and the ranking of crops (i.e., exposure associated with these crops like type of pesticides) were different according to gender and job title. For female farm workers, vine was the second most prevalent crop (37.9 %),

followed by potato (32.2 %), wheat or barley (29.6 %), fruit (18.5 %), beet (17.7 %) and corn (13.7 %). For female farm owners, vine was also the second most prevalent crop (27.7 %), followed by wheat or barley (21.2 %), potato (20.4 %), fruit (16.6 %), corn (13.1 %) and beet (12.4 %). For male agricultural workers, wheat or barley was the second most prevalent crop (49.4 %), followed by vine (42.4 %), corn (33.1 %), potato (28.4 %), beet (22.3 %) and fruit (20.1 %). Lastly, for male farm owners, wheat or barley was the second most prevalent crop (61.4 %), followed by corn (48.4 %), vine (32.7 %), potato (23.5 %), beet (20.8 %) and fruit (17.4 %). Pesticide use was always much higher among males than females whatever the crops, between 33.0 and 74.4 % for males and around 10 % for females. Moreover, male farm owners were more frequently pesticide users than male agricultural workers, especially for open field crops. Harvesting tasks concerned 60–80 % of the individuals whatever the crop and independently of gender and status (workers or owners). Females were more numerous than men only for fruit harvesting. Reentry tasks (i.e., indirect exposure to pesticides) in vineyards were more frequent among males than females, especially for agricultural workers (72.8 vs. 56.5 %). The frequencies of individuals involved in harvesting were similar among the four gender/job title categories for most other crops. However, females had a higher frequency of exposure to this task in fruit growing for both job titles, and males had a higher frequency of corn harvesting for farm owners.

#### Global mortality data

Between enrollment and December 31, 2009, 11,450 individuals (6.4 %) died and less than 0.3 % of the cohort was lost to follow-up ( $N = 600$ ). There were 6,741 deaths in men with an average age at death of 79 years (range 27–105 years) and 4,709 deaths in women with an average age at death of 84 years (range 33–107 years). Compared with the general population of the 11 geographical areas (Table 4), enrolled individuals had significantly lower death rates (SMR = 0.68, 95 % CI 0.67–0.70 for males and SMR = 0.71, 95 % CI 0.69–0.73 for females).

#### Mortality for non-cancerous diseases

There were no increased SMRs that were statistically significant. Three causes of non-cancer deaths were nonsignificantly increased in the cohort: rheumatoid arthritis and arthrosis (SMR = 1.06, 95 % CI 0.61–1.72 for females and SMR = 1.10, 95 % CI 0.44–2.27 for males), death from suicide for females (SMR = 1.12, 95 % CI 0.81–1.50) and death from event of undetermined intent for males (SMR = 1.25, 95 % CI 0.50–2.58). For all other

non-cancer causes of death, we observed deficits of deaths. For cardiovascular diseases, the figure was almost the same between males and females, even if SMRs were slightly higher among females, especially for ischemic cardiopathies (SMR = 0.78, 95 % CI 0.71–0.87 for females and SMR = 0.65, 95 % CI 0.60–0.70 for males).

#### Cancer mortality

No statistically significant excess was observed for any specific cancer. Among males, the number of deaths from all cancers ( $n = 2,218$  observed deaths, Table 5) was significantly lower than expected (SMR = 0.67, 95 % CI 0.65–0.70), especially from cancers highly related to smoking like larynx, trachea and lung cancers (SMR = 0.49, 95 % CI 0.44–0.54), bladder cancers (SMR = 0.59, 95 % CI 0.46–0.73), esophagus cancers (SMR = 0.61, 95 % CI 0.47–0.77) and pancreatic cancers (SMR = 0.78, 95 % CI 0.65–0.94) but also for cancers of the buccal cavity, stomach, colon, prostate and lymphatic and hematopoietic cells. The number of deaths was slightly increased only for one of the 14 cancer localizations studied, i.e., breast cancers (SMR = 1.24, 95 % CI 0.56–2.35). The same analyses conducted separately for farm owners and agricultural workers showed a higher but nonsignificant risk of death from rectal cancers (SMR = 1.26, 95 % CI 0.87–1.65), skin melanoma (SMR = 1.07, 95 % CI 0.55–1.87) and breast cancers (SMR = 1.86, 95 % CI 0.60–4.35) for agricultural workers.

Among females, the same pattern was observed even if the SMR for all cancers was higher than among males (SMR = 0.76, 95 % CI 0.71–0.80) and was nonsignificantly lower for cancers of the esophagus and pancreas. Contrary to what is observed in men, there was no excess risk of death from breast cancer. In fact, the risk of death from breast cancer for all women was significantly lower (SMR = 0.70, 95 % CI 0.60–0.81). When we analyzed data for females separately for farm owners and agricultural workers, farm owners had a slightly increased risk of skin melanoma (SMR = 1.17, 95 % CI 0.52–2.22).

#### Mortality in non-participants

Among non-participating males ( $n = 513,224$  person-years), 17,278 deaths were observed leading to a significant excess for all causes of deaths (SMR = 1.06, 95 % CI 1.04–1.07) compared with the significant deficit among enrolled males (SMR = 0.68, 95 % CI 0.67–0.70 for 6,741 deaths). Among females ( $n = 375,045$  person-years), 13,312 deaths were observed leading also to a significant excess of death (SMR = 1.03, 95 % CI 1.01–1.04) compared with the significantly decreased risk among enrolled

**Table 2** Baseline demographic characteristics (%) for enrolled individuals in the AGRICAN cohort 2005–2007

	Farm owners <sup>a</sup> (54.4)		Agricultural workers (45.6)		All (n = 180,060)	
	Males (60.1)	Females (39.9)	Males (47.5)	Females (52.5)	Males (54.4)	Females (45.6)
<b>Marital status</b>						
Single	10.0	4.2	13.7	6.5	11.5	5.4
Divorced or separated	3.7	3.0	4.6	4.5	4.1	3.8
Married or living together	76.5	64.3	72.5	55.5	74.9	59.7
Widow(er)	6.3	25.0	5.7	30.1	6.1	27.7
Missing	3.5	3.4	3.5	3.5	3.5	3.5
<b>Highest grade completed</b>						
Middle school or less	39.9	52.5	41.3	53.7	40.5	53.1
High school	44.7	34.2	39.3	27.6	42.6	30.7
High school or more	8.6	5.3	13.0	9.8	10.4	7.7
Missing	6.7	8.0	6.4	8.8	6.6	8.5
<b>Smoking status</b>						
Never	44.8	78.7	38.1	72.6	42.2	75.5
Former	38.9	8.0	40.0	10.1	39.3	9.1
Current	10.0	3.2	16.0	6.3	12.4	4.8
Missing	6.3	10.2	5.9	11.0	6.1	10.6
<b>Alcohol consumption</b>						
Never	9.6	29.0	11.5	31.4	10.3	30.3
Rarely (monthly)	12.1	23.4	13.3	21.8	12.6	22.6
Regular (daily/weekly)	70.5	36.1	67.2	34.0	69.2	35.0
Missing	7.8	11.5	8.0	12.8	7.9	12.2
<b>Body mass index (kg/m<sup>2</sup>)</b>						
<18.5	0.4	1.9	0.6	2.4	0.5	2.2
18.5–25	30.5	39.6	32.6	40.4	31.3	40.1
25–30	43.1	28.2	40.6	26.2	42.1	27.2
>30	13.8	11.7	13.4	11.0	13.6	11.3
Missing	12.1	18.5	12.8	20.0	12.4	19.3

<sup>a</sup> Includes only individuals who worked all or at least part of their working life as farm owners

females (SMR = 0.71, 95 % CI 0.69–0.73 for 4,709 deaths).

## Discussion

The AGRICAN cohort provides new data concerning mortality by cancer and other causes in a very large sample of the agricultural population, including both men and women, active and retired farm owners, and farm workers. For the latter, data are scarce on the health effects of their occupational exposures. In European agriculture where fungicide use is high especially in open fields, vineyards and fruit farms, both fungicides and herbicides are more widely used than in North America.

To minimize the healthy worker effect, we intend to enroll not only active farm owners and agricultural workers but also all individuals (retired or not) having worked at least 3 years in agriculture in the areas of concern. The overall SMR (i.e., including both enrolled and non-enrolled individuals) of around 0.92 could mean that there is no strong healthy worker effect. However, the mortality rates were higher than expected among non-enrolled individuals (both for males and females), suggesting a participation bias related to the health status at the time of enrollment and/or a higher prevalence of deleterious habits like smoking among non-enrolled individuals.

Despite the two consecutive mailings of the enrollment questionnaire, the participation rate did not exceed 34 %. However, this rate is consistent with that obtained in

**Table 3** Lifetime agricultural activities (livestock, crops and various tasks) for enrolled individuals (%) in the AGRICAN cohort 2005–2007

	Farm owners <sup>a</sup> (60.8)		Agricultural workers (39.2)		All (n = 149,450)	
	Males (62.5)	Females (37.5)	Males (48.0)	Females (52.0)	Males (56.8)	Females (43.2)
Livestock						
Cattle	73.5	70.3	61.0	65.8	69.4	68.2
Milking <sup>b</sup>	72.3	85.9	70.7	84.9	71.8	85.4
Insecticide use <sup>b</sup>	55.4	20.3	40.5	11.5	51.1	16.3
Building disinfection <sup>b</sup>	50.0	20.4	42.5	15.0	47.9	18.0
Milking equipment disinfection <sup>b</sup>	45.4	41.1	36.7	32.3	42.9	37.1
Sheep or goat	12.3	11.1	11.7	11.9	12.1	11.5
Insecticide use <sup>b</sup>	34.3	16.3	28.1	12.3	32.3	14.3
Hogs	21.3	23.3	24.1	33.1	22.2	27.9
Insecticide use <sup>b</sup>	27.3	11.2	23.3	9.7	25.9	10.4
Horses	21.8	10.9	26.3	15.3	23.3	13.0
Insecticide use <sup>b</sup>	17.7	12.9	16.1	11.6	17.1	12.2
Poultry	22.7	37.7	24.8	45.8	23.4	41.5
Insecticide use <sup>b</sup>	34.0	16.7	26.2	14.1	31.3	15.4
Building disinfection <sup>b</sup>	50.4	29.3	42.9	24.9	47.8	27.0
Insecticide use on livestock <sup>c</sup>	46.0	19.4	29.7	13.1	40.6	16.4
Grasslands	69.8	44.2	56.5	44.1	65.4	44.2
Herbicide use <sup>b</sup>	41.2	10.2	30.7	10.9	38.2	10.5
Hay <sup>b</sup>	92.5	91.9	89.5	89.1	91.7	90.6
Vineyard	32.7	27.7	42.4	37.9	35.9	32.5
Reentry tasks <sup>b</sup>	77.3	65.8	72.8	56.5	75.5	60.7
Grape harvesting <sup>b</sup>	85.1	83.6	82.1	84.1	84.0	83.9
Pesticide use <sup>b</sup>	64.5	9.7	53.5	9.4	60.2	9.5
Corn	48.4	13.1	33.1	13.7	43.4	13.4
Pesticide use <sup>b</sup>	74.4	13.9	54.9	10.1	69.4	12.0
Seeding treatment <sup>b</sup>	21.5	13.6	26.3	16.2	22.7	14.8
Harvesting <sup>b</sup>	77.1	71.7	78.2	74.4	77.4	73.0
Wheat or barley	61.4	21.2	49.4	29.6	57.4	25.1
Pesticide use <sup>b</sup>	67.1	9.7	50.0	8.1	62.3	8.8
Seeding treatment <sup>b</sup>	47.1	17.6	43.9	17.2	46.2	17.4
Harvesting <sup>c</sup>	82.2	79.7	81.9	79.0	82.1	79.3
Beet	20.8	12.4	22.3	17.7	21.3	14.9
Pesticide use <sup>b</sup>	40.9	6.0	33.0	4.9	38.2	5.4
Fruit growing	17.4	16.6	20.1	18.5	18.3	17.5
Cutting <sup>b</sup>	51.9	14.7	54.4	16.0	52.8	15.3
Harvesting <sup>b</sup>	69.4	76.2	67.0	76.5	68.5	76.3
Pesticide use <sup>b</sup>	36.9	7.3	35.3	7.2	36.3	7.3
Potatoes	23.5	20.4	28.4	32.2	25.1	25.9
Pesticide use <sup>b</sup>	39.6	7.3	33.4	7.3	37.3	7.3
Harvesting <sup>b</sup>	58.6	58.9	55.8	53.3	57.5	55.6
Seeding treatment <sup>b</sup>	13.7	4.6	11.7	5.1	13.0	4.9
Pesticide use on crops <sup>d</sup>	66.1	11.3	51.9	12.5	61.4	11.8

<sup>a</sup> Includes only individuals who worked all or at least part of their working life as farm owners

<sup>b</sup> Percentage of individuals having performed specific tasks among those who have worked on the specific crop/livestock

<sup>c</sup> Insecticide use on animals whatever the animal

<sup>d</sup> Pesticide use on crops whatever the crop



another large prospective study in France with mailed self-administered questionnaires (Clavel-Chapelon et al. 1997). However, studies with a low participation rate are prone to selection bias. As we collected some data for all eligible individuals, we were able to check the characteristics of non-participants. Even if enrolled individuals were more likely to be women, slightly younger (especially for women) and to have worked longer in agriculture, they were globally comparable to non-participants. Moreover, the participation rate was very close in each of the 11 geographical areas despite the very different agricultural activities conducted in them. If a selection bias is involved, it is probably conservative because individuals the most likely to be occupationally exposed seemed to participate more, i.e., people having worked longer in agriculture. Finally, even if a selection bias occurred in the enrollment phase of this cohort, association between cancer incidence of specific cancers and agricultural activities will be analyzed by internal comparisons less or not-prone to this type of bias.

Lower overall mortality rates than in the general populations of the 11 geographical areas were observed among both males and females enrolled in the AGRICAN cohort. These results are consistent with those obtained in retrospective agricultural cohorts studied in several states of the USA, including Iowa (Burmeister 1981; Cerhan et al. 1998), North Carolina (Delzell and Grufferman 1985), Wisconsin (Saftlas et al. 1987), Florida (Fleming et al. 1999) and 23 different States (Blair et al. 1993), in Canada (Howe and Lindsay 1983) and Australia (Fragar et al. 2011) but also in European countries such as Iceland (Rafnsson and Gunnarsdottir 1989), Italy (Alberghini et al. 1991; Torchio et al. 1994; Nanni et al. 2005), Sweden (Thelin et al. 2009), the UK (Frost et al. 2011) and for all Nordic countries (Pukkala et al. 2009). The same pattern was observed in the largest prospective agricultural cohort to date conducted among farmers with the same duration of follow-up as in our study (Blair et al. 2005) but also with a period of more than 13 years of follow-up (Waggoner et al. 2011). In the present study, significant decreased risks were detected for most non-cancer causes of death. However, a slightly increased risk was observed for death from rheumatoid arthritis and arthrosis in both genders. Non-significant decreased risks were observed for these causes of deaths among private applicators (SMR = 0.50)

and among their spouses (SMR = 0.73) in the AHS (Waggoner et al. 2011). A nested case–control study of rheumatoid arthritis was conducted among women enrolled in the AHS, but no significant excess risk was associated with pesticide exposure, even if some non-significant excesses were observed with some pesticides such as the insecticide lindane (De Roos et al. 2005). In a case control study conducted in Sweden, an increased risk of rheumatoid arthritis was observed only among males exposed to farm animals and also to those exposed to molds (Reckner Olsson et al. 2001). Overall, cancer mortality was significantly decreased for both genders, especially for cancers strongly associated with smoking. The pattern of deficit for these cancers was very close to that observed in the AHS for a longer period of follow-up. For example, for lung cancer deaths, the ratio was 0.49 for males in our study (0.60 for females) versus 0.43 for private farmers in the AHS (0.38 for spouses).

The smoking prevalence we observed in AGRICAN (around 50 % current or ex-smokers in men aged 26–75 years) was lower than that found in the French population of the same age (60–70 %) (Institut National de Prévention et d'Éducation Pour la Santé 2007). This lower smoking prevalence was even more pronounced among females (10–40 % current or ex-smokers versus 30–60 % in the general population, according to the age category). In spite of a larger differences of smoking prevalence between cohort members and the general population among females than among males, the decreased risks estimated with SMR for lung cancer for example were similar between males and females (SMR = 0.43 for males farm owners and SMR = 0.47 for females). These similarities could be explained by (1) remaining of age confounding, (2) different frequencies of exposure to some risk factors between males and females, (3) different lethality between males and females or (4) higher misclassification of smoking among females since the frequency of missing data for smoking was higher among females (10.6 %) than among males (6.1 %). Yet the frequencies of smoking remained higher than in the AHS study where 47 % private farmers and 22 % spouses ever smoked (Waggoner et al. 2011). Besides this lower prevalence of smoking among the rural population, it is often suggested that the lower mortality rates for cancer and cardiovascular diseases could be explained by a healthier diet and a higher level of physical

**Table 4** Standardized mortality ratios for non-cancer causes of deaths in the AGRICAN cohort 2005–2009

Causes of deaths (ICD10)	Males (329,085 PY)				Females (276,871 PY)			
	Observed	Expected	SMR	95 % CI	Observed	Expected	SMR	95 % CI
All causes	6,741	9,889	0.68*	0.67–0.70	4,709	6,667	0.71*	0.69–0.73
Infectious diseases (A00–B99)	133	172	0.77*	0.65–0.91	82	127	0.65*	0.51–0.80
Tuberculosis (A15–A19 B90)	6	13	0.45*	0.16–0.97	2	9		
Human immunodeficiency virus (B22–B24)	4	5			0	1		
Blood and blood forming organs diseases (D50–D89)	31	40	0.78	0.53–1.11	20	29	0.70	0.43–1.08
Endocrine nutritional and metabolic diseases (E00–E90)	214	310	0.69*	0.60–0.79	191	277	0.70*	0.60–0.80
Diabetes mellitus (E10–E14)	120	200	0.60*	0.50–0.72	94	150	0.63*	0.51–0.77
Digestive system diseases (K00–K93)	258	427	0.60*	0.53–0.68	151	267	0.57*	0.48–0.66
Ulcers (K25–K28)	6	16	0.38*	0.14–0.83	4	10		
Cirrhosis and other liver diseases (K70 K73–K74)	70	140	0.50*	0.39–0.63	15	40	0.38*	0.21–0.62
Mental and psychological disorders (F00–F99)	110	259	0.42*	0.35–0.51	113	258	0.44*	0.36–0.53
Alcoholism (F10)	18	45	0.40*	0.24–0.63	3	8		
Nervous system disorders (G00–H95)	279	461	0.61*	0.54–0.68	272	447	0.61*	0.54–0.68
Circulatory system (I00–I99)	1,998	2,936	0.68*	0.65–0.71	1,653	2,249	0.73*	0.70–0.77
Ischemic cardiopathy (I20–I25)	598	922	0.65*	0.60–0.70	391	499	0.78*	0.71–0.87
Other cardiopathy (I30–I33 I39–I52)	528	802	0.66*	0.60–0.72	507	693	0.73*	0.67–0.80
Cerebrovascular diseases (I60–I69)	432	606	0.71*	0.65–0.78	370	551	0.67*	0.60–0.74
Respiratory system diseases (J00–J99)	420	696	0.60*	0.55–0.66	262	422	0.62*	0.55–0.70
Pneumonia (J12–J18)	105	196	0.54*	0.44–0.65	104	155	0.67*	0.55–0.81
Chronic lower respiratory diseases (J40–J47)	143	233	0.62*	0.52–0.72	52	92	0.57*	0.42–0.75
Asthma (J45–J46)	10	12	0.85	0.41–1.57	9	17	0.54	0.24–1.02
Skin and subcutaneous tissue diseases (L00–L99)	21	25	0.83	0.51–1.27	20	34	0.59*	0.36–0.90
Musculoskeletal and connective system diseases (M00–M99)	46	52	0.89	0.65–1.18	43	64	0.67*	0.49–0.90
Rheumatoid arthritis and arthrosis (M05–M06 M15–M19)	7	6	1.10	0.44–2.27	16	15	1.06	0.61–1.72
Genitourinary system diseases (N00–N99)	113	177	0.64*	0.53–0.77	63	121	0.52*	0.40–0.67
Chronic and unspecified nephritis renal failure (N00–N29)	85	138	0.62*	0.49–0.76	46	94	0.49*	0.36–0.65
External causes of death (V01–Y89)	423	561	0.75*	0.68–0.83	233	334	0.70*	0.61–0.79
Injuries (V01–X59)	252	368	0.68*	0.60–0.77	179	272	0.66*	0.57–0.76
Transportation injuries (V01–V99)	26	45	0.57*	0.37–0.84	10	14	0.69	0.33–1.28
Falls (W00–W19)	66	102	0.65*	0.50–0.82	54	77	0.70*	0.52–0.91
Accidental poisoning (X40–X49)	6	12	0.51	0.19–1.12	10	11	0.94	0.45–1.73
Other injuries (V01–X59)	154	209	0.74*	0.62–0.86	105	169	0.62*	0.51–0.75
Suicides (X60–X84)	144	153	0.94	0.79–1.10	44	39	1.12	0.81–1.50
Event of undetermined intent (Y10–Y34)	7	6	1.25	0.50–2.58	1	1		
Other external causes of death (V01–Y89)	20	31	0.65	0.40–1.00	8	21	0.38*	0.17–0.76
Other and unspecified causes (R00–R99)	336	478	0.70*	0.63–0.78	341	462	0.74*	0.66–0.82

\*  $p < 0.05$ 

activities. However, we observed more overweight or obese individuals in AGRICAN than in the general French population (Charles et al. 2008).

Overall, the AGRICAN cohort provides data for the first time on causes of deaths in a large population of active and retired farm owners and farm workers in a European

**Table 5** Standardized mortality ratios for deaths from cancers in the AGRICAN cohort 2005–2009

Causes of death (ICD10)	Farm owners <sup>a</sup>				Agricultural Workers				All enrolled					
	Males		Females		Males		Females		Males		Females			
	SMR (95 % CI)	SMR (95 % CI)	SMR (95 % CI)	SMR (95 % CI)	SMR (95 % CI)	SMR (95 % CI)	SMR (95 % CI)	SMR (95 % CI)	Observed	Expected	SMR (95 % CI)	Observed	Expected	SMR (95 % CI)
All cancers (C00–D48)	0.64* (0.60–0.67)	0.73* (0.68–0.81)	0.74* (0.69–0.79)	0.78* (0.72–0.84)	2,218	3,287	1,187	1,569	0.67* (0.65–0.70)	1,187	1,569	0.76* (0.71–0.80)	1,569	0.55 (0.24–1.08)
Lip buccal and pharynx (C00–C14)	0.44* (0.28–0.66)	<5deaths	0.62* (0.37–0.97)	0.66 (0.21–1.54)	42	83	8	15	0.51* (0.37–0.69)	8	15	0.55 (0.24–1.08)	15	0.55 (0.24–1.08)
Esophagus (C15)	0.61* (0.44–0.82)	0.77 (0.28–1.67)	0.61* (0.40–0.90)	0.87 (0.37–1.71)	68	112	14	17	0.61* (0.47–0.77)	14	17	0.82 (0.45–1.38)	17	0.82 (0.45–1.38)
Stomach (C16)	0.84 (0.64–1.07)	1.01 (0.63–1.53)	0.85 (0.59–1.17)	0.88 (0.56–1.31)	98	117	46	49	0.84 (0.68–1.02)	46	49	0.94 (0.69–1.25)	49	0.94 (0.69–1.25)
Colon (C18)	0.67* (0.55–0.81)	0.84 (0.64–1.08)	0.87 (0.70–1.08)	0.83 (0.66–1.04)	193	259	136	163	0.74* (0.64–0.86)	136	163	0.83* (0.70–0.99)	163	0.83* (0.70–0.99)
Rectum (C19–C21)	0.68* (0.48–0.93)	0.52* (0.26–0.93)	1.26 (0.87–1.65)	0.69 (0.42–1.07)	80	91	31	50	0.88 (0.69–1.09)	31	50	0.62* (0.42–0.88)	50	0.62* (0.42–0.88)
Biliary (liver and gallbladder C22)	0.73* (0.59–0.88)	0.56* (0.30–0.96)	0.64* (0.47–0.84)	0.59* (0.35–0.94)	153	221	31	53	0.69* (0.59–0.81)	31	53	0.58* (0.39–0.82)	53	0.58* (0.39–0.82)
Pancreas (C25)	0.78* (0.62–0.99)	0.92 (0.66–1.25)	0.78 (0.56–1.05)	0.92 (0.69–1.19)	116	148	98	107	0.78* (0.65–0.94)	98	107	0.92 (0.75–1.12)	107	0.92 (0.75–1.12)
Larynx trachea bronchus lung (C32–C34)	0.43* (0.38–0.51)	0.47* (0.32–0.69)	0.56* (0.48–0.66)	0.69* (0.52–0.93)	338	694	77	129	0.49* (0.44–0.54)	77	129	0.60* (0.47–0.75)	129	0.60* (0.47–0.75)
Skin melanoma (C43)	0.87 (0.50–1.42)	1.17 (0.52–2.22)	1.07 (0.55–1.87)	0.64 (0.23–1.38)	28	30	15	17	0.95 (0.63–1.37)	15	17	0.88 (0.49–1.44)	17	0.88 (0.49–1.44)
Breast (C50)	0.87 (0.23–2.23)	0.71* (0.56–0.88)	1.86 (0.60–4.35)	0.69* (0.56–0.85)	9	7	173	247	1.24 (0.56–2.35)	173	247	0.70* (0.60–0.81)	247	0.70* (0.60–0.81)
Cervix (C53)		<5 deaths		0.98 (0.39–2.02)			10	13		10	13	0.78 (0.37–1.47)	13	0.78 (0.37–1.47)
Uterus other (C54–C55)		0.84 (0.53–1.28)		0.71 (0.45–1.08)			44	57		44	57	0.77 (0.56–1.04)	57	0.77 (0.56–1.04)
Ovary (C56)		0.80 (0.55–1.12)		0.86 (0.61–1.17)			72	87		72	87	0.83 (0.65–1.04)	87	0.83 (0.65–1.04)
Prostate (C61)	0.78* (0.67–0.89)		0.78* (0.65–0.94)		317	407				317	407	0.78* (0.70–0.87)		
Kidney (C64)	0.79 (0.56–1.08)	0.60 (0.26–1.18)	0.92 (0.61–1.13)	0.67 (0.33–1.19)	66	79	19	30	0.84 (0.65–1.06)	19	30	0.64* (0.38–0.99)	30	0.64* (0.38–0.99)
Bladder (C67)	0.52* (0.38–0.70)	0.48 (0.17–1.04)	0.69* (0.48–0.96)	0.54 (0.26–1.00)	78	133	16	31	0.59* (0.46–0.73)	16	31	0.52* (0.29–0.84)	31	0.52* (0.29–0.84)
Lymphatic and hematopoietic (C81–C96)	0.85 (0.71–1.00)	0.89 (0.68–1.15)	0.80 (0.64–1.00)	0.94 (0.75–1.15)	221	267	145	158	0.83* (0.72–0.95)	145	158	0.92 (0.77–1.08)	158	0.92 (0.77–1.08)
Other malignant	0.54* (0.46–0.63)	0.71* (0.57–0.89)	0.76* (0.64–0.89)	0.75* (0.62–0.91)	321	514	193	262	0.62* (0.56–0.70)	193	262	0.74* (0.64–0.85)	262	0.74* (0.64–0.85)
Other benign	0.70* (0.53–0.91)	0.48* (0.28–0.77)	0.75 (0.52–1.04)	0.85 (0.61–1.15)	90	125	59	85	0.72* (0.58–0.88)	59	85	0.69* (0.53–0.90)	85	0.69* (0.53–0.90)

\*  $p < 0.05$

<sup>a</sup> Includes individuals who worked all or at least part of their agricultural career as farm owners

country where pesticide use has been very intensive for decades. Extended follow-up of mortality data as well as cancer incidence will make it possible to study the effect of occupational agricultural exposures in various agricultural contexts and populations.

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