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Health of greenspace workers: morbidity and mortality data from the AGRICAN cohort.

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ABSTRACT

Introduction: Knowledge on the health of greenspace workers is scarce, even though they are exposed to many occupational hazards. The aim of this study was to analyze mortality by cause, prevalence of some non-cancer diseases, and incidence of the main cancers among greenspace workers. **Methods:** A sub-cohort of greenspace workers was formed within the AGRICAN cohort. Demographic information, health characteristics and self-reported diseases at enrollment were described separately in terms of frequencies (%), median and Interquartile Range (IQR) for greenspace workers, farmers, and other non-agricultural workers. Causes of death and cancer incidence were identified through linkage with cancer registries from enrollment (2005-2007) to 2015. Hazard ratio (HR) and 95% Confidence Intervals [95% CI] were estimated using Cox proportional hazard regression with age as the underlying timescale. **Results:** The sub-cohort included 6,247 greenspace workers who were higher proportion men, younger and more frequently smokers than farmers and non-agricultural workers. Male and female greenspace workers reported more history of allergic diseases; and males, more history of depression. Compared to other workers male greenspace workers showed a non-significant higher mortality from ischemic cardiological diseases (HR=1.14 [0.81-1.60]). Incidence was higher in male greenspace workers than farmers for overall cancer (HR=1.15 [1.04-1.27]), cancer of the prostate (HR=1.21 [1.02-1.44]), thyroid (HR=2.84 [1.26-6.41]), testis (HR=3.98 [1.50-10.58]) and skin melanoma (HR=2.15 [1.33-3.47]). Non-significant increased risks were also found for sarcomas, larynx and breast. In women, risk of breast cancer was higher in greenspace workers than in farmers (HR=1.71 [1.17-2.50]). **Conclusions:** Whereas greenspace workers have often been included with other pesticide applicators in epidemiological studies, our analyses highlighted the differences between these two populations. They demonstrate the need to study them separately and to investigate more thoroughly the role of specific occupational exposures such as pesticides as well as the effect on women.

Keywords: occupational epidemiology, greenspace workers, non-agricultural workers, pesticides, cancer, mortality

1. INTRODUCTION

The greenspace industry includes a wide variety of occupations: gardeners and landscapers, municipal workers, maintenance operators of roadsides, railways and other public facilities, employees of golf courses and other sports facilities, horticultural or floricultural workers, plant and tree nursery workers, etc. These workers are exposed to many physical, biological and chemical occupational hazards, including pesticides. Occupational exposure to pesticides has been studied mainly among agricultural workers, and associations with increased risks of some specific cancers have been demonstrated (prostate (1,2), lung, ovarian, rectal, testicular, skin and breast (1), Non-Hodgkin Lymphoma (NHL), multiple myelomas (MM) and leukaemia (1,3)); neurological diseases (Parkinson's disease (4), Alzheimer's disease and amyotrophic lateral sclerosis) and reproduction disorders (spontaneous abortions, stillbirths and sperm quality) have also been associated with pesticide exposure (1). Studies on occupational exposure to pesticides among greenspace workers are scarce and have frequently combined them with farmers or other pesticide applicators. Few studies have focused exclusively on greenspace workers' health and they have indicated higher risks of soft-tissue sarcoma, leukemia, multiple myeloma, Non-Hodgkin's lymphoma and cancer of the skin, central nervous system, prostate, and pancreas (5). Parkinson's disease has also been studied among gardeners, but only non-significant increases in risks were found (5). Adverse effects for reproduction have been investigated in floricultural workers operating in greenhouses, and have shown elevated time to pregnancy (6–12), spontaneous abortions (13,14) and malformations (14–16). Only two prospective cohorts conducted in greenspace workers have been identified: one Danish cohort including ~ 4,000 gardeners (17–19) and the other in Finland with ~ 2,000 herbicide applicators on railroad tracks, highways, electric lines and forests (20,21). Four historical cohorts have been found: two conducted among herbicide applicators along railroad tracks (one Dutch and one Swedish (22–25)), one performed on more than 18,000 pesticide applicators on lawns (26) and another on 686 golf-course superintendents (27).

The French AGRiculture and CANcer prospective cohort (AGRICAN cohort) enrolled not only farmers but also greenspace workers, and offered the opportunity to describe their health. Our main objective was to analyze the morbidity and mortality profiles of greenspace workers, with specific attention to the main cancers within the AGRICAN cohort.

2. MATERIAL AND METHODS

2.1. Cohort

The AGRICAN prospective cohort in France has previously been described in detail (28). Briefly, in 2005, in 11 French areas covered by a population-based cancer registry, questionnaires were sent to the source population: all individuals aged 18 years and over and affiliated for 3 years or more to the health insurance for agriculture (*Mutualité Sociale Agricole*, MSA). In total, 181,842 agreed to participate and sent back their questionnaire. The enrolled population consisted of farm owners and farm workers, but also included workers in companies or organizations related to agriculture, such as foresters, gardeners, employees of cooperatives, office workers in agricultural bodies, etc. The self-administered questionnaire included a complete job calendar with a lifetime history of agricultural activities, demographic characteristics (gender, age, education level, place of birth, etc.), lifestyle habits such as tobacco and alcohol consumption, dietary information and health data (self-reported diseases, height, weight and reproductive history in women). A follow-up questionnaire was sent out from 2015 to 2018 to collect more precise data on occupational history: work on a farm (recording additional details on types of crops and livestock) and work in other sectors (agricultural cooperative, greenspaces, forestry, agricultural contractors, administrative work and others).

2.2. Cohort follow-up

Participants were followed from baseline (date of questionnaire reception) to the date of death, moving house outside the study zone, or end of the follow-up (Dec 31st, 2015), whichever occurred first. Incident and prevalent cancers were identified through crossing-linkage with the population-based cancer registries of the 11 geographic areas of the study. Cancers were coded according to the International Classification of Diseases for Oncology (29) and date of diagnosis and histological types were collected. Vital status was checked annually by crossing the database with the MSA file and the National Death Index (*Répertoire National pour l'Identification des Personnes Physiques*). For each identified death, cause was obtained from the national death registry (*Centre d'épidémiologie sur les causes médicales de décès*, CepiDC). Causes of death were coded according to the International Classification of Diseases 10th edition (30). Place of residence and

affiliation to MSA were checked annually in the MSA files, French National Postal Service (La Poste) and the French National Death Index.

2.3. Identification of the greenspace workers in the AGRICAN cohort

As mentioned above, MSA affiliation concerns not only farmers, but also agricultural workers outside farming, such as greenspace workers. Greenspace workers, regardless of their farming status, were identified in a first step through the job calendar from the enrollment questionnaire (available at https://www.agrican.fr/pdf/questionnaires/questionnaire_AGRICAN_Inclusion_en.pdf). The greenspace sector covers a wide range of occupations. In this study, we selected individuals that mentioned one occupation or more that can be coded as 6113 (*“Gardeners; Horticultural and Nursery Growers”*) or 9214 (*“Garden and Horticultural Labourers”*) in the International Standard Classification of Occupations (ISCO 2008) (31). It included gardeners, landscapers, lawn mowers, tree trimmers, horticulturists, floriculturists, nursery workers, greenkeepers, municipal workers and road and railroad track maintenance workers. Each individual mentioning one occupation or more in this industry was initially selected, regardless of the work duration. In a second stage, the follow-up questionnaire (not available in English) enabled us to identify additional individuals whose initial information was incomplete. Participants who answered positively to the question *“Have you ever worked in a landscaping company or as a gardener?”* were selected; as were those who mentioned any flower or ornamental production under the *“other crops”* item. In a final step, all the individuals selected from enrollment and follow-up were checked individually for consistency in the information. Among the selected individuals, three subgroups were formed according to their main occupation (the one they had performed longest when that information was available, if not the first mentioned): gardeners/landscapers, horticultural workers and plant and tree nursery workers.

2.4. Identification of farmers and non-agricultural workers in the AGRICAN cohort

In the enrollment questionnaire, all participants who mentioned having worked on a farm (working with livestock or crops) and not in the greenspace sector were classified as farmers (n=132,402), others – who had worked in neither sector but were also affiliated to the health insurance system for agriculture (such as

salaried workers of cooperatives, employees in rural craft-making businesses, fishing and forest wardens, employees in the agricultural mutual funds and credit funds, employees of chambers of agriculture etc.) – were defined as non-agricultural workers (n=18,044).

These two groups were considered in our analyses as comparison groups for greenspace workers.

2.5. Exposure assessment

Regardless of having worked on a farm, the question of occupational use of pesticides was asked as follows: “*Have you ever used fungicides or insecticides or herbicides at work?*” (no/yes). In addition, they were asked at enrollment and follow-up whether pesticides had been used for each type of crop and livestock and for weed control in the courtyard or embankments. The following questions: “*In your occupational history, have you ever performed major repairs on pesticide sprayers?*” (yes/no), “*have you ever performed the maintenance of pesticide sprayers?*” (yes/no), “*Have you ever been poisoned by a pesticide?*” (never/once/several times), “*Following this (these) poisoning(s): Did you consult a doctor? Were you admitted to hospital?*” were used to assess their history of pesticide poisoning.

2.6. Statistical analysis

Demographic and health characteristics were described separately in terms of frequencies (%) and median and interquartile range (IQR) for greenspace workers, farmers and other non-agricultural workers.

Self-reported diseases in greenspace workers at enrollment were compared with farmers and with non-agricultural workers using χ^2 test and logistic regression models with adjustment on age (supplementary materials).

Hazard Ratios (HR) were calculated for all causes of death and incident cancers and presented for all causes with more than 3 observed deaths, and separately for females and males and for greenspace workers, farmers and non-agricultural workers (used as two separate references). HRs and their 95% CI were estimated using Cox proportional hazard regression with age as the underlying timescale. Left truncation (i.e. delayed entry data) was considered using age at enrollment. For each cause of death or incident cancer, potential confounders were tested by comparing HR without and with the covariable. Potential confounders that were tested systematically were history of tobacco smoking, alcohol

consumption and Body Mass Index (BMI). In addition, for cancer of the uterus and ovary, the use of oral contraceptives and hormone replacement therapy were tested as well. Only HR adjusted on age and stratified on gender were presented since no substantial change (>20%) was observed after adjustments on other confounders.

The proportional hazards assumption was tested for all analyses by modeling a linear interaction between the timescale and each independent variable ($p < 0.05$). When a variable did not verify this assumption, we performed stratification on it. All statistical analyses were performed using R software (version 1.2.1578) (32).

Among greenspace workers, we described health issues separately in gardeners, horticultural workers and plant nursery workers. In addition, sensitivity analyses were performed and consisted of the following: i) restricting to greenspace workers who had never worked on a farm; ii) comparing greenspace workers who declared using pesticides *vs* non-users; iii) comparing greenspace workers to farmers working only with livestock or only crops; and iv) stratifying on “never smokers (supplementary materials).

3. RESULTS

3.1. Cohort characteristics

3.1.1. Greenspace workers

On the basis of the enrollment questionnaire, 4,847 individuals were identified as greenspace workers. Thanks to the follow-up questionnaire, an additional 1,631 were found, which made a total of 6,478 workers. Finally, the selection process retained 6,247 individuals (3.4% of the total cohort), as 231 persons were excluded because they did not mention any occupation related to the greenspace sector in the job calendar

(Figure 1).

Among them, 82.2% were men and they were younger than the two other groups, with a median age of 52 years at enrollment (Table 1). Only 21.7% were retired at enrollment. They also had a higher educational level than farmers. They were more frequently current or former smokers, regardless of gender, than individuals from the other two groups, and the proportion of regular alcohol consumers (39.2%) appeared lower. Most greenspace workers (55.3% and 45.8% respectively in women and men) had a normal weight

(BMI=18.5-25 kg/m²), whereas male farmers and non-agricultural workers were more frequently overweight or obese (BMI>25 kg/m²) (48.9% and 47.3% respectively). Regarding female reproductive characteristics, female greenspace workers declared higher use of contraceptive pill than farmers (63.2% *vs* 28.3%).

3.1.2. Farmers

Among the 181,842 participants in the AGRICAN cohort, 132,402 individuals answered that they had worked on one or several crops or types of livestock and they were classified in the farmer group. More than half of them were males (55.6%) and 60.9% were farm-owners. Their median age at enrollment was 68 years and half of them were retired at enrollment (53.3%) (Table 1).

3.1.3. Non-agricultural workers

The group of non-agricultural workers included 18,044 workers, half of whom were women (51.7%), and the median age was 57 years (Table 1). Most of them were employees (73.7%), still active at enrollment (75%), and had worked in the tertiary sector (59.2%, of whom 77.5% outside the agricultural work environment). A quarter of them (25.9%) worked neither in agriculture nor in the tertiary sector (artisans, merchants, etc.) and 9.9% were in agriculture but not in livestock or crops (employees of cooperatives (55.0%), workers in the wood industry (11.2%) or in agricultural machinery (12.2%), etc.).

3.2. Exposure characteristics

Among greenspace workers, most were gardeners and landscapers – including municipal workers – (n=4,508, 77.8%), ahead of horticultural workers (n=1,170, 13.7%) and plant nursery workers (n=569, 8.5%). The median duration working in greenspaces was 10 years (IQR 5-21 years). Fifty-nine percent of greenspace workers had also worked on a farm (among whom 94.8% on crops and 48.3% with livestock). About 68% of greenspace workers reported using pesticides at work (*vs* 51.6% in farmers and 4.6% in non-agricultural workers), a difference explained by a greater proportion of men among users, regardless of the group. Among pesticide users, personal protective equipment was reported by 73.4% of greenspace

workers (*vs* 55.7% in farmers and 61.3% in non-agricultural workers). Major repairs and maintenance of sprayers were performed by more farmers than greenspace workers (Table 2).

3.3. Chronic diseases reported at enrollment

3.3.1. Men

Two health conditions were reported more frequently in male greenspace workers than in the two other groups: depression in 8.7% of them and allergic diseases (asthma, eczema, allergic rhinitis) in 8.6 to 11.9% of them (Figure 2). On the other hand, they reported cardiovascular conditions (hypertension 19.2%, arrhythmias 10.3% and myocardial infarction 5.1%) and diabetes (6.3%) less frequently. The frequency of chronic bronchitis in greenspace workers (9.0%) was higher than non-agricultural workers (7.4%) but lower than farmers (12.2%). Two conditions were not frequent in males, and even lower in greenspace workers: retinal disease (1.9%) and thyroid disease (2.1%). Taking differences in age between the three groups into account (OR adjusted on age), the patterns remained similar for allergic conditions and depression, with an increased risk in male greenspace workers. Bronchitis, arrhythmia, thyroid and retinal diseases also appeared elevated in this group compared to others, while hypertension appeared lower (Supplementary Figure 1).

In sensitivity analyses stratified on working only with livestock, overall risk for allergic diseases was significantly higher in greenspace workers than in farmers working only with livestock (OR=1.37 [1.19-1.59]). The risk of allergic rhinitis was also significantly higher in greenspace workers (OR=2.01 [1.58-2.58]). Regarding eczema, greenspace workers were at higher risk, whatever the group of comparison. However, the association was greater when they were compared to farmers working only with livestock (OR=1.70 [1.30-2.26]). No difference between the original analyses and those presented here was found for asthma (Supplementary Table 1).

3.3.2. Women

In women, allergic diseases also appeared more frequently in greenspace workers and even more frequently than in men, as 13.8% of women reported allergic rhinitis, 12.5% eczema and 9.9% asthma (Figure 2). Conversely, thyroid disease, a condition that is much more common in women than in men, appeared less frequently in greenspace workers (10.6%) than in the other groups. For other diseases,

female greenspace workers were generally in an intermediate situation between farmers and non-agricultural workers, as well as for cardiovascular diseases (23.6% for hypertension), depression (14%), diabetes (5%), retinal diseases (2.5%) or chronic bronchitis (6.0%) (Figure 2). Taking differences in age between the three groups into account, patterns remained similar for allergic conditions, with an increased risk in female greenspace workers and a lower risk for thyroid diseases. Arrhythmia also appeared elevated in this group (Supplementary Figure 2).

In sensitivity analyses stratified on working only with livestock, overall risk for allergic diseases in women was also significantly higher in greenspace workers, whatever the group of comparison, but the association was greater and statistically significant when compared to farmers working only with livestock (OR=1.55 [1.33-1.81]). In addition to allergic rhinitis and eczema, the risk of asthma and bronchitis was significantly higher in greenspace workers when we used farmers working only with livestock as comparison (respectively OR=1.59 [1.24-2.02] and OR=1.49 [1.10-2.00]) (Supplementary Table 2).

3.4. Mortality and Causes of Death

In the greenspace sub-cohort, 465 individuals (7.4%) died between enrollment and 2015: 388 men (7.6%) and 47 women (4.2%). Average age at death was 81 years (range 36-106 years) in men and 87 years (range 41-103 years) in women. Causes of death were available for 424 individuals (380 men and 44 women). In men, the most common cause of death was cancers (134 cases, 35.3%), followed by circulatory system diseases (106 cases, 27.9%) (Figure 3). In women, death by circulatory system diseases and other causes were the most frequent (equally 14 cases, 31.8%), followed by cancer (8 cases, 18.2%) (Figure 4).

3.4.1. Men

Overall mortality (adjusted on age) was not statistically different between greenspace workers and farmers (380 cases, HR=1.01 [0.91-1.12]) or non-agricultural workers (HR=0.96 [0.85-1.08]), nor were any of the major causes of mortality (Figure 3). In comparison with farmers, a slightly higher (but not statistically significant) figure was observed in ischemic cardiopathy mortality among greenspace workers (34 cases, HR=1.14 [0.81-1.60]) and a not statistically significant lower trend in deaths caused by nervous system and mental disorders (21 cases, HR=0.84 [0.55-1.30]) and external causes of death (26 cases, HR=0.77 [0.52-

1.14]). Only two greenspace workers died from cerebrovascular diseases, which did not allow their risk to be estimated. When compared with non-agricultural workers, slightly lower (but not statistically significant) figures were observed in deaths from cancers (134 cases, HR=0.86 [0.71-1.05]), respiratory diseases (22 cases, HR=0.88 [0.54-1.42]) and external causes of death (26 cases, HR=0.83 [0.53-1.32]). Regarding external causes of death in greenspace workers, 9 were suicides (34.6%), 5 were caused by accidents (19.2%) and 4 were caused by falls (15.4%).

3.4.2. Women

For all causes, mortality tended to be lower (but not statistically significant) in female greenspace workers in comparison with farmers (44 cases, HR=0.83 [0.62-1.12]) and non-agricultural workers (HR=0.76 [0.56-1.04]) (Figure 4). The same applies for mortality due to cancer (8 cases, respectively HR=0.63 [0.32-1.27] and HR=0.51 [0.25-1]) and for the circulatory system (14 cases, respectively HR=0.77 [0.45-1.30] and 0.80 [0.46-1.39]). For ischemic heart diseases, cerebrovascular diseases, respiratory diseases and external causes of death, but the number of cases was not sufficient to calculate stable hazard ratios.

3.5. Cancer incidence

3.5.1. Men

Among greenspace workers, 388 men (7.6%) developed an incident cancer between enrollment and 2015 (Table 3). The overall risk of cancer in greenspace workers was significantly increased compared to farmers (HR=1.15 [1.04-1.27]), but not in comparison with non-agricultural workers (HR=0.93 [0.83-1.05]).

The risk of cancer was significantly increased among greenspace workers compared to farmers for several cancers: prostate (HR=1.21 [1.02-1.44]), skin melanoma (HR=2.15 [1.33-3.47]), thyroid (HR=2.84 [1.26-6.41]) and testis (HR=3.98 [1.50-10.58]). A non-statistically significant increased risk was also observed for sarcomas (HR=1.64 [0.65-4.10]), larynx (HR=2.17 [0.85-5.52]) and breast (HR=3.22 [0.95-11.00]), but with limited numbers of cases (3 to 5 cases). Except for testis, these increases were also seen when the reference group was non-agricultural workers, although non-significant. For cancers of the lung, liver and pancreas, buccal cavity and pharynx and kidney, the risk in greenspace workers appeared lower than in the

two reference groups, reaching significance for lung cancer *versus* non-agricultural workers (HR=0.62 [0.41-0.95]).

For other cancer sites, male greenspace workers were in an intermediate situation, with a non-statistically significant higher risk than farmers but lower than non-agricultural workers for colorectal cancers, bladder, and leukemia, and for the central nervous system a non-statistically significant lower risk than farmers but higher than non-agricultural workers (but with a limited number of cases (N=4)).

3.5.2. Women

Among female greenspace workers, 58 (5.2%) developed a cancer between enrollment and 2015. Breast cancer was the most common (28 cases, 48.3% of total cancer), followed by colon cancer (7 cases, 12.1%) (Table 4). As in men, although not statistically significant, incidence of cancer overall tended to be higher than in farmers (HR=1.16 [0.89-1.51]) but lower than in non-agricultural workers (HR=0.82 [0.62-1.07]). For breast cancer, the incidence was significantly higher in greenspace workers than in farmers (HR=1.71 [1.17-2.50]). For other cancers, the numbers were limited, but tendency towards a non-statistically significant increased risk was observed for skin melanoma compared to farmers and non-agricultural workers (respectively HR=1.91 [0.70-5.18]) and HR=1.19 [0.42-3.40]). Conversely, a trend towards a decreased risk was observed for cancer of the uterus and ovary *versus* the two reference groups but was not statistically significant and with a limited number of cases (N=4).

3.5.3. Sensitivity analysis

In analyses conducted on male greenspace workers who had never worked on a farm, similar associations and significance were reached for colorectal cancer and sarcoma. Moreover, non-significant increased risks were observed for lung cancer and non-Hodgkin's lymphoma (Supplementary Table 3). In women, similar associations were also found (Supplementary Table 4).

In analyses comparing male pesticide users *vs* non-users, the overall risk of cancer was not different. However, we observed elevated risks for cancers of the colon, rectum and anus, larynx, prostate, thyroid, skin melanoma, non-Hodgkin's lymphomas and leukemia, but none of these associations were statistically significant (Supplementary Table 5). In female greenspace workers, the overall risk of cancer was higher in

pesticide users and was close to being statistically significant. An elevated risk for breast cancer was also found but was not statistically significant (Supplementary Table 6).

When stratifying on the variable “working with livestock”, no major differences with our main analysis were found and associations were most of the time in the same direction (except for bladder), whatever the type of farmers. However, slight variations were observed in men (no change in women) (Supplementary Table 7 and 8): i) in greenspace workers, the risk of colorectal cancer was higher than in farmers working only with livestock (although it remained not statistically significant); ii) For lung cancer, they remained at lower risk whatever the group of comparison, but they had a lower (and statistically significant) risk than farmers growing only crops; iii) For skin melanoma, they remained at higher risk whatever the group of comparison, but the hazard ratio was higher than in farmers working only with livestock; and iv) for cancer of the thyroid, greenspace workers were at higher risk, but especially when compared to farmers growing only crops.

In analyses restricted to “never smokers”, overall risk of cancer was roughly unchanged whatever the group of comparison. However, we observed slight variations from our primary analyses (Supplementary Table 9): i) in men, when compared to farmers, we observed an increased risk for cancer of the esophagus and stomach, testis, thyroid, non-Hodgkin’s lymphoma and leukemia. On the other hand, we no longer found elevated risks for colorectal and prostate cancer. When compared to non-agricultural workers, we observed a slight increase for cancers of the esophagus and stomach, testis and thyroid; ii) in women, breast cancer remained statistically higher in greenspace workers than in farmers (Supplementary Table 10).

3.5.4. Occupational groups among greenspace workers

Cancers for which an increased risk was observed among greenspace workers were studied within subgroups (Table 5). Taking non-agricultural workers as the reference, the risk of cancer overall in gardeners and in horticultural workers was comparable (respectively HR=0.99 [0.87-1.13] and HR=1.07 [0.82-1.42]), while a non-statistically significant slight decrease was observed in plant-nursery workers (HR=0.80 [0.58-1.11]). Using farmers as the reference, risks in general were slightly increased, so the overall risk of cancer appeared increased in gardeners (HR=1.17 [1.04-1.31]) and in plant-nursery workers

(HR=1.28 [0.93-1.74]). The risk of skin melanoma was quadrupled in horticulturists (HR=3.99 [1.61-9.88] with non-farmers as the reference and HR=4.30 [1.90-9.74] with farmers as the reference) and also increased in gardeners (HR=1.22 [0.61-2.42] with non-farmers as the reference), significantly when farmers were considered as the reference (HR=1.83 [1.02-3.30]). No case was observed in plant-nursery workers. [...] Using farmers as reference, the risk of breast cancer was higher in the three subgroups and reached statistical significance in plant-nursery workers (HR=2.82 [1.26-6.29]).

Regarding female cancers, compared to non-agricultural workers, horticulturists, gardeners and plant-nursery workers had a non-significant lower incidence for cancer overall (respectively HR=0.78 [0.54-1.15], 0.93 [0.62-1.40] and 0.63 [0.28-1.40]) (Table 6). Regarding breast cancer, gardeners seemed to have a non-significant lower risk than non-agricultural workers (HR=0.81 [0.44-1.49]), whereas the risk was higher, but not statistically significant, for plant-nursery workers (HR=1.61 [0.71-3.62]). Using farmers as reference, the risk of breast cancer was higher in the three subgroups and reached statistical significance in plant-nursery workers (HR=2.82 [1.26-6.29]).

4. DISCUSSION

4.1. Main results

Within AGRICAN, a sub-cohort of greenspace workers was constituted and specific patterns were observed. In comparison with farmers and non-agricultural workers, differences were found in the prevalence of some health conditions at enrollment and in mortality, and in cancer incidence over a 10-year period. Male and female greenspace workers reported more allergic-related diseases and depression than farmers and non-agricultural workers at enrollment. Overall mortality was globally comparable with the other two groups, even if mortality of greenspace workers appeared not significantly higher for ischemic heart diseases (*vs* farmers) and not significantly higher lower for cancer, respiratory diseases and external causes (*vs* non-agricultural workers). Comparing cancer incidence in greenspace workers to that of farmers, the main results were an excess risk in males, overall and for prostate, testis, thyroid and skin melanoma, and an excess risk in females, for breast cancer. Results were roughly overall unchanged in sensitivity analyses.

4.2. Study strengths and limitations

The AGRICAN cohort provided the opportunity to study a large sample of greenspace workers, larger than the two previous prospective cohorts dedicated to them (17,33). However, numbers of cases remained limited at this stage of the cohort for the less frequent health issues, when considering women or specific subgroups separately within greenspace workers. Constituting the sub-cohort of greenspace workers was challenging because AGRICAN was not initially designed for studying these workers specifically, but we succeeded by a thorough review of the complete occupational calendars and follow-up questionnaires. Thanks to this thorough review, we were able to define the jobs precisely and to create subgroups within our sub-cohort (gardeners, horticulturists, nursery workers), while in many previous studies the definition of greenspace workers remained unclear and could lead to misclassifications.

The healthy worker effect was limited in AGRICAN overall and in our sub-cohort, because we enrolled all adults affiliated to the MSA in the study area for 3 years, even if they had left their job at some point in their career – including for medical reasons. However, it is noteworthy that not all greenspace workers are affiliated to the MSA in France. Indeed, some municipal workers and maintenance operators of railways or other public facilities, for instance, are affiliated to other health insurance systems. We hypothesize that greenspace workers affiliated to the MSA are more closely related to agriculture and do not represent all French greenspace workers.

In addition, we took advantage of multiple health data collected in the cohort, making it possible to address morbidity and mortality in this group with validated sources (death certificates and cancer registries) that are known to approach completeness. Concerning the health issues reported at enrollment, although the questionnaire mentioned that they had to be diagnosed by a doctor, we cannot rule out errors or memory bias. Even if the collection of cancer data was based on validated sources that are population-based cancer registries, access to health care might differ between the 11 geographic areas and between the urban or rural environment. Therefore, we cannot rule out the possibility that the differences, in terms of cancer incidence, observed between occupational groups could be explained by different levels of access to health care depending on the area of living.

Because AGRICAN was originally designed for farmers, only one question allowed us to determine whether greenspace workers used pesticides (yes/no) at work, and no detailed information was collected

at enrollment on tasks, types of pesticides or equipment. At this step we therefore cannot provide results for specific tasks and hazards like pesticides.

In the present analysis, we did not explore specific hypotheses that could explain the difference; however, the reference group is of importance regarding possible unknown confounding factors. This is why greenspace workers were compared with two groups of workers within the cohort: farmers on one hand and non-agricultural workers on the other. However, as in many other studies of these workers, more than half of greenspace workers had also worked on a farm for a period in their occupational life. We therefore checked that our results did not change when restricting our analysis to greenspace workers who had never worked on a farm. Within the cohort, we had a group of workers (non-agricultural workers) less likely to share occupational exposures (such as pesticides) with greenspace workers, which was used as a reference considered as relatively comparable to the general population. However, because they were affiliated to the health insurance scheme for agriculture, we cannot exclude that they had some links or similarities with workers in agriculture or in greenspaces. Their number was also relatively limited, but the power proved to be sufficient to observe statistically significant results.

4.3. External validity

Our results underlined some specificities of greenspace workers, such as their sociodemographic characteristics, life habits (such as smoking), pesticide use and personal protective equipment in comparison with farmers or non-agricultural workers.

The higher prevalence of allergic conditions observed among greenspace workers (8.6%) is in line with previous studies. In a study conducted in Denmark, Spain, Switzerland and Germany, the prevalence of asthma was found to be 7.7%, and higher in greenhouse flower and ornamental plant growers than in other crop growers (34). Asthma could be explained by sensitization to flower allergens and/or mold present as contaminants in the air of greenhouses, a hypothesis confirmed by allergological tests for sensitization to ornamental plants (skin prick test), that were found to be positive more frequently in flower growers (52%) than in other groups of the population (35). Eczema was also found to be reported more frequently (19%) in a study conducted in Danish gardeners and greenhouse workers (36). In sensitivity analyses stratified on working only with livestock or crops, greenspace workers were still at

higher risk of allergic diseases. This association was even stronger when compared to farmers working only with livestock, suggesting that exposure to livestock could be protective against allergic rhinitis and eczema in men but also against asthma and bronchitis in women. These results are in line with previous studies conducted in AGRICAN where asthma was more prevalent in farmers exposed to several crops (fruit-growing, vineyards, greenhouses and grassland farming) but not in farmers working only with livestock (37). Living on a farm in early childhood was also found to be protective against allergic asthma. However, we did not find this association in greenspace workers.

Our study also found a higher prevalence of depression in male greenspace workers than in farmers and non-agricultural workers. To our knowledge, although many studies on mental health have been conducted in farmers, very few have been carried out in greenspace workers. Two case-control studies have analyzed the risk of suicide among greenspace workers pooled with other pesticide applicators (38,39). Only one of these studies found a decreased risk in gardeners, horticulturists and nurserymen (38).

Regarding mortality (overall and for cardiovascular diseases), we did not find differences in greenspace workers compared to farmers or non-agricultural workers. Other studies found non-significant lower overall mortality and cardiovascular diseases in greenspace workers (21–23,26,33,40,41), but one study conducted in golf-course employees found results comparable to ours (27). Our result of lower mortality for respiratory diseases and cancer in greenspace workers corresponds to results found in other studies (22,23,26,40,41).

The higher proportion of smokers in greenspace workers should presumably increase the risk of tobacco-related diseases, but it is not the case in our study. The impact of physical activity, which is supposedly greater in greenspace workers than in the other occupation groups, might have acted as a protective effect on cardiovascular and respiratory diseases. Further research is needed to determine which factors might influence the association.

Our results on cancer are in line with other studies that demonstrated increased risks in skin melanoma (23,40,42–44), cancers of the prostate (27,41,45), colon, rectum and anus (46) and testis (45) and sarcomas (17,18,47) among male greenspace workers, in comparison with the general population. However, to our knowledge, this study is the first to indicate higher risk for these cancers in greenspace workers in comparison with farmers.

Like farmers, greenspace workers are very likely to be exposed to various hazardous substances, such as pesticides, solvents, diesel exhausts, fuels, oils, organic and inorganic dusts, and many more. The wide variety of contaminants makes it challenging to determine the intensity and duration for each exposure over the course of life and their health impact. Regarding pesticide exposure and its effects on workers' health, many results have been obtained in farmers and elevated risks for certain types of cancers have been observed repeatedly, such as for prostate cancer (2,48–50), including in the AGRICAN cohort where it was found associated with cattle breeding, grassland, fruit growing, potato and tobacco growing (51). No definitive conclusion has been reached on the pesticides that could explain the increased risk of prostate cancer, however associations between herbicide exposures and prostate cancer have been demonstrated in several studies (52–54). Herbicides are widely used on turfgrass (27,55,56), public facilities (57,58) and sports fields (59). In France, in 2000, they represented 87% of products (in tons) used in gardens and greenspaces (*vs* 33% in agriculture) (60). In our study, horticulturists had the highest risk when compared with non-agricultural workers, which can suggest some specific exposure in this occupation. In comparison with gardeners and landscapers, ornamental horticulturists are more likely to use insecticides and fungicides than herbicides (61). Regarding insecticides, the role of organochlorines in prostate cancer has been suggested in studies (62,63), which could be consistent with their estrogen-like effects and could explain their implication in hormone-related cancers (63).

Despite limited numbers, the excess risk of testis cancers found in our analysis is also in line with previous studies (64,65). Regarding skin melanoma, our study found higher risk for greenspace workers than farmers, and horticulturists were the most at risk. Elevated risks have already been suggested in exposure of workers to pesticides (66), and more notably when exposed to herbicides (glyphosate) and fungicides (67). This association was even greater when combined with occupational sun exposure (67). Major risk factors for skin melanoma are the phenotype, high number of nevi, family history of skin cancer, sun sensitivity and UV radiation. However, chronic sun exposure was found to reduce the risk of skin melanoma in outdoor workers, which suggests a difference in the effects of chronic and intermittent sun exposure (68). Elevated risks have already been suggested in workers exposed to pesticides, and more notably to herbicides and insecticides. These associations were even greater when combined with occupational sun exposure(68). Dermal exposure is the primary route of occupational exposure to

pesticides and sun exposure might increase the temperature of the skin, thereby increasing blood flow and sweating and facilitating the transcutaneous absorption of pesticides.

To our knowledge, this is the first time that an increased risk of thyroid cancer has been observed in greenspace workers. However, thyroid cancer was found in excess in relation with pesticide exposure in farmers (69,70), and more specifically with herbicide exposure (71). While an elevated risk of laryngeal cancer was found in our study, it was based on a very limited number of cases (only five) and was not statistically significant. As greenspace workers have a higher rate of smoking, its implication in the incidence of laryngeal cancer must be considered. However, in our analysis, adjusting on tobacco did not substantially modify the association (data not shown). Adjustment on alcohol consumption, another well-known risk factor (72), was also tested and did not change the association either. Other occupational exposures, such as asbestos, polycyclic aromatic hydrocarbons and engine exhaust (73), are suspected of causing laryngeal cancer. Exposure assessments on greenspace workers are needed. Regarding central nervous system tumors, we did not find associations, although previous studies found elevated risks for golf-course superintendents (27) and in greenspace workers (74). The latter study observed an elevated risk for workers directly exposed and those exposed for more than 10 years (74).

Although the sample size for female greenspace workers was limited, a significant increased risk for breast cancer was observed, which was more pronounced in plant-nursery workers, a result that was not found in a previous study (75). In analyses restricted to non-smokers, breast cancer remained statistically higher in greenspace workers than in farmers, which ruled out tobacco as a potential cofounder.

The type of pesticide used differed between farming and the greenspace sector and within the greenspace sector (5). In the greenspace sector, 50% of the active ingredients used are herbicides, followed by insecticides (40%) and fungicides (10%), whereas in agriculture, 48% of the most active ingredients used are herbicides, followed by fumigants (20%), fungicides (16%) and insecticides (5%) (76). In floriculture, 47% of the active ingredients applied are growth regulators, animal repellents and disinfectants, 22% are fungicides, 17% insecticides and 13% herbicides (58). On turfgrass, sport fields and public facilities, herbicides such as glyphosate and 2,4-D are widely used. On golf courses, fungicides such as chlorothalonil are the most used. In terms of quantities, it has been suggested that per surface treated, more product is used on greenspaces than on agricultural lands (77). Moreover, pesticide use is greater on

floriculture than on other types of crops (78). In terms of spraying equipment, it has been suggested that equipment used in the greenspace sector might lead to more exposure (79). When farmers often use tractors with a cabin, greenspace workers are more likely to use knapsack sprayers, watering cans and hand sprayers, which might lead to a higher exposure (risk of leakage, distance between the operator and the sprayer reduced etc.). In addition, the work environment might play a major role in the exposure: nursery work and floriculture are mostly conducted inside greenhouses where the lack of ventilation, the high temperature and humidity and the air containment are known to increase the level of exposure (80). The use of protective equipment might also differ as greenspace workers, and especially gardeners, often work on different sites and are less likely to have a place dedicated to their protective equipment (81). Finally, because they perform a wide range of manual tasks, greenspace workers are more prone to indirect exposure through frequent contact with treated plants (80).

These first analysis on greenspace workers within the AGRICAN cohort highlighted specificities of this group and encouraged further analysis to explain the differences in morbidity and mortality in comparison with other workers i.e., farmers and other non-agricultural workers. Because many tasks performed in the greenspace industry consist in weeding, the implication of herbicide exposure should be investigated with thorough exposure assessment, but we cannot rule out the role of other pesticides. With larger numbers - expected to be available in the follow-up of the cohort - it will be possible to further analyze risks in specific subgroups within the greenspace sector. Types of pesticides used, equipment and work environment need to be further and thoroughly investigated to better understand the differences we observed, especially in the occurrence of some cancers, but also in the prevalence of allergic symptoms and depression. Because greenspace workers such as gardeners or municipal workers might be involved in other activities, such as masonry work, other occupational exposure should also be taken into account. The use of devices with thermal engines should also be taken into account. Additional studies are underway to better characterize their exposure and the information they will provide will be used in next steps of the cohort to further analyze morbidity and mortality data.

5. CONCLUSION

Greenspace workers have often been included with other pesticide applicators such as farmers in epidemiological studies. Yet, this study highlights the difference between these two populations in terms of sociodemographic characteristics, life habits such as tobacco, medical history, mortality and cancer incidence. It demonstrates the need to study them separately from other pesticides applicators to elucidate the role of specific factors like herbicides and other pesticides. Further studies should also focus on female greenspace workers and subgroups of workers within the greenspace industry, as numbers were too limited at this step of the AGRICAN cohort.

KEY POINTS:

- Greenspace workers should be studied separately and not pooled with farmers in epidemiological studies.
- Significantly elevated risks for overall cancer, skin melanoma, and cancer of the prostate, testis and thyroid were found in men, and breast cancer in women.
- Further studies should be conducted with better occupational exposure assessment.

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Table 1 : Demographic and health characteristics of workers enrolled in the AGRICAN cohort (N=156,693)

	Greenspace workers* N=6,247 (%)	Farmers N= 132,402 (%)	Nonagricultural workers N= 18,044 (%)
Gender (n=156,693)¹			
Male	5,133 (82.2)	73,647 (55.6)	8,717 (48.3)
Female	1,114 (17.8)	58,755 (44.4)	9,327 (51.7)
Median age (IQR^a) (n=156,693)	52 (39-65)	68 (55-77)	57 (45-67)
Professional status (n=156,693)			
Self-employed	2,761 (44.2)	80,641 (60.9)	4,748 (26.3)
Employee	3,486 (55.8)	51,761 (39.1)	13,296 (73.7)
Retired at enrolment (n=156,693)			
Yes	1,355 (21.7)	70,616 (53.3)	4,512 (25.0)
No	4,892 (78.3)	61,786 (46.7)	13,532 (75.0)
Educational level (n=147,612)			
Elementary	1,707 (28.1)	6,9051 (55.7)	3,207 (18.2)
High school	3,643 (59.9)	46,231 (37.3)	9,773 (55.4)
University	72,8 (12.0)	8,626 (7.0)	4,646 (26.4)
Marital status (n=151,230)			
Single	1,108 (18.2)	11,169 (8.7)	1,377 (7.8)
Divorced or separated	384 (6.3)	4,338 (3.4)	1,236 (6.9)
Married	4,268 (80.1)	90,480 (70.5)	13,787 (77.6)
Widower	330 (5.4)	22,394 (17.4)	1,359 (7.7)
Smoking status (n=147,346)			
Never	2,746 (45.3)	80,555 (65.1)	8,790 (50.0)
Former	2,079 (34.3)	31,893 (25.8)	6,265 (35.6)
Current	1,241 (20.5)	11,239 (9.1)	2,538 (14.4)
Alcohol consumption (n=146,198)^b			
Never	791 (13.1)	24,866 (20.3)	2,559 (14.7)
Rare	1,005 (16.7)	21,407 (17.4)	4,098 (23.5)
Moderate	2,141 (35.6)	33,412 (27.2)	6,053 (34.7)
Regular	2,087 (34.6)	43,030 (35.1)	4,749 (27.2)
Body mass index (kg/m²) (n=136,351)			
< 18.5	61 (1.1)	1,542 (1.4)	341 (2.0)
18.5-25	2,723 (47.5)	45,592 (40.0)	8,288 (49.7)
25-30	2,252 (39.3)	49,338 (43.3)	6,064 (36.4)
> 30	698 (12.2)	17,469 (15.3)	1,983 (11.9)
Female reproductive characteristics²			
Median age at first menstruation (IQR) (n= 63,431)	13 (11-15)	13 (11-15)	13 (11-15)
Having taken a contraceptive pill (n=65,945)	690 (63.2)	15,784 (28.3)	22,685 (67.7)
Median number of pregnancies (IQR) (n=59,995)	2 (1-3)	3 (1-5)	2 (1-3)
Menopausal women (n=68,547)	617 (56.7)	49,964 (85.8)	5,247 (56.9)

* Greenspace workers: any worker in the Agrican cohort who had at least one experience in the greenspace industry. Are included greenspace workers without any farming experience (n=2,614) and greenspace workers with a farming experience (n=3,633).

^a Interquartile Range

^b **rare** = less than 3 times a month; **moderate** = between 3 times a month to 2/3 times a week; **regular** = between 4 and 7 or more times a week.

¹ number of individuals for whom the information was available out of 156,693

² number of individuals for whom the information was available out of 68,536

Table 2: Exposure characteristics self-declared at enrolment in the AGRICAN cohort (N=156,693) and at follow-up in greenspace workers (N=6,247)

Exposure characteristics at <u>enrolment</u>	Men			Women			
	Greenspace workers* N= 5,133 (%)	Agricultural workers N= 73,647 (%)	Non-agricultural workers N= 8,717 (%)	Greenspace workers N= 1,114 (%)	Agricultural workers N= 58,755 (%)	Non-agricultural workers N= 9,327 (%)	
Pesticide use (n=69,351)	Yes	3,310 (75.6)	42,718 (73.0)	521 (8.1)	262 (30.2)	5,988 (16.7)	101 (1.4)
Major repairs on sprayer (n= 66,509)	Yes	364 (8.6)	7,077 (12.8)	209 (2.9)	10 (1.1)	346 (0.9)	51 (0.7)
Median number of years doing repairs (IQR ^a) (n= 5,969)		16 (12)	22 (13)	16 (12)	9 (6)	16(14)	6 (5)
Maintenance of sprayers (n= 70,232)	Yes	1,390 (31.5)	22,097 (37.7)	318 (4.5)	46 (5.1)	803 (2.1)	41 (0.5)
Median number of years doing maintenance (IQR) (n= 19,386)		16 (12)	23 (12)	17 (12)	9 (7.81)	17(13.09)	11(16.12)
Pesticide poisoning (n=79,829)	Yes	336 (6.5)	4,451 (6.0)	85 (1.0)	53 (4.8)	936 (1.6)	40 (0.4)
Frequency of poisoning	Never	4,458 (93.0)	62,423 (93.3)	8,076 (99.0)	988 (94.9)	49301 (98.1)	8785 (99.5)
	Several times	83 (1.7)	1,074 (1.6)	10 (0.1)	18 (1.7)	244 (0.5)	9 (0.1)
	One time	253 (5.3)	3,377 (5.0)	75 (0.9)	35 (3.4)	692 (1.4)	31 (0.4)
Exposure characteristics at <u>follow-up</u> among greenspace workers	Gardeners N= 2,836 (%)	Horticultural workers N= 549 (%)	Plant-nursery workers N= 261 (%)	Gardeners N= 451 (%)	Horticultural workers N= 413 (%)	Plant-nursery workers N= 73 (%)	
Pesticide use in greenspaces	Yes	1,842 (79.3)	226 (82.8)	125 (84.5)	119 (35.7)	40 (49.4)	14 (58.3)

* Greenspace workers: any worker in the Agrican cohort who had at least one experience in the greenspace industry. Are included greenspace workers without any farming experience (n=2,614) and greenspace workers with a farming experience (n=3,633).

^a Interquartile Range

Table 3: Hazard ratios for cancer incidence among men in the AGRICAN cohort (n=87,497).

	Men		
		Greenspace workers vs farmers	Greenspace workers vs non-agricultural workers
	n	HR ^a crude [CI 95%]	HR crude [CI 95%]
Buccal cavity and pharynx (C00-14)	9	0.86 [0.44-1.68]	0.85 [0.39-1.83]
Esophagus and stomach (C15-16)	14	0.92 [0.54-1.57]	1.06 [0.55-2.00]
Colon, rectum and anus (C18-21)	49	1.27 [0.95-1.70]	0.85 [0.61-1.20]
Liver and pancreas (C22-25)	13	0.60 [0.34-1.04]	0.58 [0.31-1.06]
Larynx (C32)	5	2.17[0.85-5.52]	1.51 [0.48-4.78]
Lung (C33-34)	27	0.89 [0.61-1.32]	0.62* [0.41-0.95]
Skin melanoma (C44)	19	2.15* [1.33-3.47]	1.42 [0.70-2.56]
Breast (C50)	3	3.22 [0.95-11.00]	7.21 [0.75-69.3]
Prostate (C61)	140	1.21* [1.02-1.44]	1.12 [0.91-1.37]
Testis (C62)	6	3.98* [1.50-10.58]	0.98 [0.32-2.99]
Bladder (C67)	14	1.30 [0.76-2.23]	0.66 [0.37-1.20]
Kidney (C64-66 & C68)	12	0.82 [0.46-1.47]	0.71 [0.37-1.36]
Central nervous system (C70-72)	4	0.64 [0.24-1.75]	1.30 [0.38-4.46]
Thyroid (C73)	7	2.84* [1.26-6.41]	1.89 [0.65-5.49]
Non-Hodgkin's lymphoma^c	29	1.01 [0.69-1.47]	0.74 [0.48-1.14]
Leukemia (C92)	12	1.07 [0.60-1.91]	0.75 [0.39-1.48]
Sarcomas (C46)	5	1.64 [0.65-4.10]	2.57 [0.68-9.64]
Other cancer	18	1.33 [0.83-2.14]	1.03 [0.58-1.80]
Total^b	388	1.15* [1.04-1.27]	0.93 [0.83-1.05]

^a Hazard Ratio (Confidence Interval 95%) estimated in Cox models with age as underlying timescale. * p value < 0.05

^b Total of cancers among men. Only cancer sites with more than 3 cases are shown.

^c Includes Multiple Myeloma

Table 4 : Hazard ratios for cancer incidence among women in the AGRICAN cohort (n=69,196).

	Women		
	Greenspace workers vs farmers		Greenspace workers vs non-agricultural workers
	n	HR ^a crude [CI 95%]	HR crude [CI 95%]
Colon, rectum and anus (C18-21)	7	1.17 [0.56-2.48]	0.90 [0.41-1.97]
Skin melanoma (C44)	4	1.91 [0.70-5.18]	1.19 [0.42-3.40]
Breast (C50)	28	1.71* [1.17-2.50]	1.00 [0.68-1.48]
Cervix, corpus uterus and ovary (C53-57)	4	0.84 [0.31-2.26]	0.58 [0.21-1.61]
Bladder and kidney (C64-68)	4	2.00 [0.74-5.42]	2.44 [0.78-7.66]
Non-Hodgkin's lymphoma^b	4	1.01 [0.38-2.70]	0.76 [0.27-2.14]
Total^c	58	1.16 [0.89-1.51]	0.82 [0.62-1.07]

^aHazard Ratio (Confidence Interval 95%) estimated in Cox models with age as underlying timescale. *p value <0.05

^bIncludes Multiple Myeloma

^cTotal of cancers among women. Only cancer sites with more than 3 cases are shown.

Table 5 : Hazard ratios for cancer incidence among male greenspace workers (n=5,133), AGRICAN cohort.

	Men								
				vs farmers			vs non-agricultural workers		
	Gardeners		Horticultural workers	Plant-nursery workers		Gardeners	Horticultural workers	Plant-nursery workers	
	n	HR [CI 95%]	n	HR [CI 95%]	n	HR [CI 95%]	HR [CI 95%]	HR [CI 95%]	HR [CI 95%]
Buccal cavity and pharynx (C00-14)	7	0.90 [0.42-1.91]	1	-	1	-	0.88 [0.38-2.07]	-	-
Colon, rectum and anus (C18-21)	39	1.36 [0.98-1.87]	7	1.15 [0.54-2.41]	3	0.80 [0.26-2.49]	0.94 [0.66-1.35]	1.20 [0.56-2.60]	0.35 [0.11-1.12]
Skin melanoma (C44)	12	1.83 [1.02-3.30]	6	4.30 [1.90-9.74]	0	-	1.22 [0.61-2.42]	3.99* [1.61-9.88]	-
Prostate (C61)	101	1.19 [0.97-1.45]	23	1.17 [0.77-1.76]	16	1.50 [0.92-2.46]	1.16 [0.92-1.46]	1.36 [0.88-2.08]	1.18 [0.71-1.97]
Non-Hodgkin's lymphoma	20	0.94 [0.60-1.48]	5	1.04 [0.43-2.54]	4	1.47 [0.55-3.94]	0.77 [0.47-1.26]	0.92 [0.34-2.53]	0.83 [0.30-2.31]
Total	293	1.17 [1.04-1.31]	55	0.99 [0.76-1.29]	40	1.28 [0.93-1.74]	0.99 [0.87-1.13]	1.07 [0.82-1.42]	0.80 [0.58-1.11]

^aHazard Ratio (Confidence Interval 95%) estimated in Cox models with age as underlying timescale. *p value <0.05.

^bIncludes Multiple Myeloma

^cTotal of cancers among men. Only cancer sites with more than 3 cases are shown.

Table 6 : Hazard ratios for cancer incidence among female greenspace workers (n=1,114), AGRICAN cohort.

	Women								
	vs farmers			vs non-agricultural workers					
	Gardeners		Horticultural workers		Plant-nursery workers		Gardeners	Horticultural workers	Plant-nursery workers
	n	HR [CI 95%]	n	HR [CI 95%]	n	HR [CI 95%]	HR [CI 95%]	HR [CI 95%]	HR [CI 95%]
Breast (C50)	11	1.38 [0.76-2.50]	11	1.75 [0.96-3.17]	6	2.82 [1.26-6.29]	0.81 [0.44-1.49]	1.03 [0.56-1.89]	1.61 [0.71-3.62]
Total	28	1.10 [0.76-1.60]	24	1.35 [0.90-2.00]	6	0.90 [0.41-2.02]	0.78 [0.54-1.15]	0.93 [0.62-1.40]	0.63 [0.28-1.40]

^a Hazard Ratio (Confidence Interval 95%) estimated in Cox models with age as underlying timescale. *p value <0.05

^b Total of cancers among women. Only cancer sites with more than 3 cases are shown.