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Cancer incidence and death rates in Argentine rural towns surrounded by pesticide-treated agricultural land

Damián Verzeñassi [a,c], Alejandro Vallini [a,b], Facundo Fernández [a,b], Lisandro Ferrazini [a,b], Marianela Lasagna [a], Anahí J. Sosa [a,b], Guillermo E. Hough [d,*]

[a] Instituto de Salud Socioambiental, Facultad de Ciencias Médicas de la Universidad Nacional de Rosario (UNR), Santa Fe, Argentina
[b] Clínica Ambiental Sede Argentina de la Plataforma de Estudios Ambientales y Sostenibilidad (PEAS) del Centro de Estudios Interdisciplinares (CEI) de la UNR, Argentina
[c] Carrera de Medicina de la Universidad del Chaco Austral (UNCAus), Resistencia, Chaco, Argentina
[d] ConCiencia Agroecológica, Comisión de Investigaciones Científicas de la Provincia de Buenos Aires, 9 de Julio, Buenos Aires, Argentina

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ABSTRACT

Background: A number of published reports have linked agricultural pesticides (AP) to different illnesses, one of which is cancer. Our objectives were to estimate cancer incidence and death rates in small Argentine rural towns affected by AP; and to compare these estimations with indexes from Argentina's general population.
Methodology: An epidemiologic house-to-house health survey conducted by last-year medical students was implemented in 8 small rural towns of the Province of Santa Fe- Argentina (8 T), each surrounded by fields sprayed with AP. The survey covered 27,644 people, accounting for 68% of the total 8 T population.
Results: Odd-ratio between cancer incidence rate in 8 T and the general population was 1.37 (P<5%). For the 15–44 year age-group, odd-ratios between cancer death rates per 100 thousand inhabitants in 8 T and the general population were 2.48 and 2.77 for female and male genders, respectively. Proportion of cancer-deaths in relation to other causes of death varied by age-group and gender, 8 T values were higher than for the general population for all combinations.
Conclusions: Our findings suggest that living in small rural towns affected by nearby AP applications has a negative health impact, namely in cancer outcomes. These results contribute to the need for pesticide-reduction policies, especially in the surroundings of small urban populations.

1. Introduction

In Argentina the central provinces of Buenos Aires, Entre Ríos, East of La Pampa and South of Santa Fe and Córdoba are especially suited for agriculture; this region is known as the Pampas and it produces 85% of Argentine's main crops: corn, wheat and soy.[1] For the 2020–2021 crop season there were 6.1, 14.3 and 6.1 million hectares of the Pampas sown with corn, soy and wheat; respectively. In Argentina agricultural pesticides (AP) use was estimated to be 7.1, 5.4 and 2.8 kg. Hectare^{-1}. Year^{-1} for corn, soy and wheat; respectively.[2] This means that approximately 138 million kg of AP are sprayed over this region yearly.

The average total use of AP in Europe in 2017 was 0.62 kg ha^{-1}.[3] For soy in the USA this number was 2.3 kg-hectare^{-1}.[4] UNEARTHED[5] published that on average 27% of AP used in high-income countries are in the category of highly hazardous, while the percentage increases to 45% for low- and middle-income countries such as Argentina. Thus in Argentina the quantities per hectare are far greater than those used in Europe or the USA, and a greater proportion of them are highly hazardous.

Due to drifts not all AP reach their target, may the target be weeds, fungus or insects. The off-target presence of pesticides has been detected in a number of studies. Some of these performed in the Pampas were: urban or peri urban rain and soil[6]; rural schools[7]; small town environment[8]; and shallow lakes.[9] From these studies it is clear that pesticides can drift through different mechanisms beyond their target and thus reach urban populations of small rural towns. These drifts are aggravated by the large pesticide quantities used in the Pampas as detailed above. Legislation on pesticide use in Argentina is generally lax, and even where it exists, control is weak.[10] This is another factor which increases drifts into rural towns.

* Corresponding author. Frondizi 1226, 6500, 9 de Julio, Buenos Aires, Argentina.
E-mail address: guillermohough@yahoo.com (G.E. Hough).

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Health risks related to AP exposure are well documented. The IARC classified glyphosate as "probably carcinogenic to humans (Group 2 A)". In a recent review Weisenburger[11] provided evidence that glyphosate and glyphosate-based- formulations are a cause of Non-Hodgkin lymphomas in humans. Other AP have also been related to cancer.[12] Evidence of cancer and/or genotoxicity increases in rural workers or communities living close to sprayed fields has been found in different countries and settings.[13,14,15] In the Pampas increased genotoxicity was found in children living close to sprayed fields[16]; and cancer incidence rates were high in a small town where pesticides were present in deposits, machines and fields.[8]

Schinasi and Leon[15] pointed out the lack of investigations on pesticide use and Non-Hodgin Lymphoma in low- and middle-income countries, despite producing a large portion of the world's agriculture. A similar observation was made by Arancibia et al.[10] who stated that in Argentina there is a lack of published epidemiological studies on tumor incidences, although exposure to pesticides is much higher than in Europe or North America where such associations have been shown.

The hypothesis of our work was that living in small rural towns affected by nearby AP applications has a negative health impact, manifested in cancer indexes.

2. Methods

2.1. Survey

The final exam for students of the Faculty of Medicine of the Rosario National University- Argentina, from 2010 to 2019, was to participate in a health workshop (HW) in a small town of <10,000 inhabitants. Students were trained during 3 months on the activities they had to perform. One of these was a house-to-house health survey. As the HW was part of the Faculty's approved curricula, the survey had Institutional approval (Faculty Resolution 2086/2010). The town area was divided by the number of students in order to obtain a survey as complete as possible. Each student had to identify all the housing units in their area to thus survey them. Permanent community living quarters such as care-homes for the elderly were not considered. At each housing unit an individual 18-years or over answered the questionnaire for all household members. If no one answered, the student returned a maximum of three times. Previous to answering the questionnaire respondents signed a consent form. The full questionnaire can be accessed in the Supplemental Material. It covered demographics; housing facilities; health ailments and related issues; and perception of health and contamination problems in the town. The specific questions corresponding to the health issues addressed in this work are presented below. Each student-respondent interview lasted between 15 and 45 min. On returning from the field work in the corresponding town, students passed the data from the paper questionnaires to an Excel file under the supervision of teaching staff. After this, teaching staff controlled the transcription of each questionnaire. Paper questionnaires have all been scanned as backups and Excel data files also have their backups.

2.2. Towns and population

Eight towns (8 T) were chosen from the Province of Santa Fe covering an agriculturally intensive region of the Pampas. Since the introduction of glyphosate-resistant soy in 1996, husbandry has been uniform in this region as in most of the Pampas. Demographics are in Table 1.

The white Caucasian ethnicity is uniform over the 8 T. 87% of those between 15 and 44 years and 95% of those 45 or older had lived in their respective towns for at least 5 years; sufficient time for environmental exposures to have possible effects.

The total population of each town was unknown as the last census' published data in Argentina correspond to 2001 and 2010. The yearly change since 2010 was considered equal to the yearly change between the last census'. This was used to estimate the surveyed population in relation to the total population of each town. The survey covered a total of 27,644 people; approximately 68% of the total 8 T population.

The MAGP[17] agricultural data base was consulted to estimate the land occupied by corn + soy + wheat. The median for the 8 T was 80% (range 49%–87%). People in 8 T live at a distance of 0–400 m from sprayed fields. Other than surrounded by cultivated land, none of the 8 T had an economic activity likely to affect inhabitant's health.

2.3. Cancer incidence rate

The survey asked: "Has anyone in the household had some type of tumor or cancer in the last 15 years? (*Regardless of whether they died or not*)". The question included details such as year of diagnosis, age at diagnosis and type of cancer. As the incidence rate had to be corrected by the population's age distribution and we only had the present age distribution obtained from the survey for each town, only tumors or cancers which had been diagnosed in the last complete year previous to the survey for each one of the towns were considered (See Table 1); counting both diagnosed-living and diagnosed-deceased. Cancer incidence rate for the 8-T was estimated based on diagnosed tumors falling under the international classification of diseases[18] (ICD-10) of C00–C99 and D00-D09. Age distribution correction was performed following the PAHO guidelines.[19]

2.4. Cancer deaths

Deaths by cancer were estimated from the following question: "Has any member of the household died in the last 15 years?" The answers included gender, age, year and cause of death. As for cancer incidence rate, cancer deaths were classified under the ICD-10[18] classification. As they can be the first or second death cause, circulatory system deaths were also estimated as those coming under ICD-10[18] I00–I99.

Classifying deaths by age and gender was of interest. Age classification was: Child: 0–14 years; Young: 15–44 years; Old: over 45.

For Child, there were 5 cancer deaths over the 15 years for the 8 T, too few to meaningfully compare to the Argentine general population (GP). For Young, death numbers over the 8 T for year 15 (last year)

Table 1
Surveyed towns and basic demographics. % of total population was estimated from 2001 to 2010 census'. % female and % age distribution are based on surveyed population. The TOTAL row summarizes information from the 8 towns.

Town	Surveyed population	Survey date	% of total population	% Female	% less 14 years	% 15–44 years	% 45 and over
Acebal	3514	Mar 14	63	51.8	19.2	42.6	38.2
Arteaga	2278	Dec 18	64	50.7	18.7	38.8	42.4
Chabás	5594	Dec 14	78	51.8	20.3	40.5	39.2
Luis Palacios	911	Mar 16	93	48.5	27.7	42.0	30.3
San Genaro	5910	Jun 15	64	52.5	21.3	42.4	36.3
Sastre	3645	Mar 17	62	53.3	20.6	39.7	39.8
Timbúes	3725	Dec 16	73	50.4	28.9	46.9	24.2
Villa Eloisa	2067	Set 18	69	52.4	18.3	37.4	44.3
TOTAL	27,644		68	51.8	21.5	41.6	36.9

amounted to 6, also too few to compare to the GP. To consider more meaningful numbers, we aggregated deaths over years both common to the 8 T (see Table 1) and common to official National Death data availability[20]; this left 9 years from 2005 to 2013, over which deaths were aggregated.

Considering the Old age category, if a house was approached with the question "Has any member of the household died in the last 15 years?" the following situations could have arisen.

(a) A respondent could answer for the death of a relative, with relative accuracy regarding age and calendar-year of death.
(b) A respondent would not report the death of their aged relatives having occurred in a Care Home, these locations were not covered in the survey. These deaths would be recorded by National entities by death certificates.
(c) In Argentina approximately 21% and 31% of the population live alone or in a single-generation household, respectively.[23] Thus if an aged individual or individuals should die within the 15-year period, the house would become unoccupied or be occupied by a person who would not consider the deceased as their own household members; even if the person who died was related.

Situation (a) could lead to inaccurate reporting; and situations (b) and (c) could lead to number of deaths per 100 thousand inhabitants to be under estimated for 8 T. Even considering these limitations, the question would still provide an adequate sample of old-age deaths and their causes, to thus estimate cancer deaths as a proportion of overall causes of death, and compare them to the GP.

Argentina's death rates were taken from official health statistics data base,[20] which covers years starting 2005. The data bases included province, gender, age and cause of death classified by ICD-10.[18] However, they did not detail deaths in individual towns within each province, such as the 8 T of the present study.

Cancer-death estimations are often expressed per 100 thousand inhabitants. 8 T and National populations at the midpoint of the 9-year cancer-death period were considered for these estimations, that is year 2009, midpoint between 2005 and 2013. As explained above, 8 T 2009 surveyed population was estimated based on 2001 and 2010 census'. The Argentine population estimate for 2009 was taken from DatosMacro.[21]

3. Results

3.1. Cancer incidence rate

In Table 2 are the number of reported cancer cases in 8 T considering the last year previous to each town's survey, and the gross and age-distribution corrected incidence rates. Argentina's corrected rates for year 2018 are also presented.[22]

Odd-ratios and 95% confidence intervals are also in Table 2. The odd-ratio for the total population was significant (lower interval >1), but this was due to the female population, whose odd-ratio was 1.66. Thus for the female population of the 8 T there was a 66% higher probability of acquiring cancer over the last year in comparison to the GP.

Fig. 1 shows incidence rates for cancer types in the 8 T with rates >10. Corresponding rates for Argentina[22] are also shown. Except for prostate cancer, all other odd-ratios were >1. Confidence intervals were wide due to small number of cases in the 8 T, thus significance ($P < 0.05$) could not be shown, except for uterus and larynx with lower confidence intervals >1. These two cases could be a spurious effect as $P < 0.05$ means 1 in 20 can be by chance.

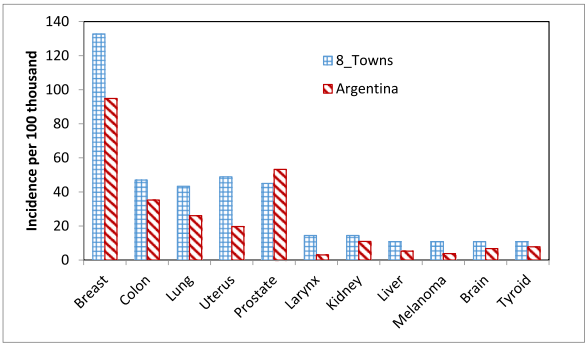

Fig. 1. Cancer incidence rates per 100 thousand inhabitants for the cancer types in the 8 T with rates >10; and corresponding rates for Argentina.

3.2. Cancer deaths in relation to total live population

For the Young age-group, yearly overall death rates in 8 T and Argentina were similar over the 9-year period, with mean rates of 60 and 56, respectively; and did not show trends over time.

For the Old age-group the mean yearly death rate over the 9-year period was 684 deaths/100-thousand for Argentina (range: 664–714). For 8 T the estimated mean yearly death rate was 439 (range: 310–544); significantly lower than for Argentina. The 8 T death rates were clearly underestimated, especially for the initial years. As mentioned in Section 2.4, and discussed below, this was a consequence of how the survey collected the death data by asking: "Has any member of the household died in the last 15 years?" Due to this under estimation, cancer deaths in relation to the total population for the Old age-group were not considered.

Table 3 shows cancer deaths over the 14-year period in relation to living population for the young age-group, discriminated by location (8 T and Argentina) and gender. As commented above, Child and Old age-groups were not considered for these estimations. For both genders odd ratios showed a higher probability of dying of cancer if living in the 8 T than for the GP. The probability of dying of cancer per 100 thousand young inhabitants was 2.48 and 2.77 times more likely if living in 8 T,

Table 3
Number of cancer deaths in 8 T and Argentina over a 9-year period by gender for the young age-group (15–44 years). Yearly cancer deaths were estimated over 100 thousand young age-group inhabitants. Odd ratios are the quotient (yearly cancer deaths 8 T)/(yearly cancer deaths Argentina). 95% confidence intervals (CI) are included.

	Female		Male	
	8 Towns	Argentina	8 Towns	Argentina
Cancer deaths	25	16,442	21	12,460
Yearly deaths/100 thousand	49.2	19.9	42.5	15.3
Odd ratios (95% CI)	2.48 (1.68–3.67)		2.77 (1.81–4.25)	

Table 2
Number of cancer cases and corresponding incidence rates per 100 thousand inhabitants for the 8 towns (8 T), both gross and age-distribution corrected; and age-distribution corrected incidence for Argentina. Odd-ratios and 95% confidence intervals.

Gender	Number of cases 8 T	Gross incidence 8 T	Age-distribution corrected incidence 8 T	Argentina corrected incidence	Odd- ratios	95% confidence intervals
Female	63	440	347	209	1.66	1.30–2.12
Male	43	323	237	223	1.06	0.79–1.44
Total	106	383	291	212	1.37	1.13–1.66

for females and males, respectively.

3.3. Cancer deaths as a proportion of total deaths

In addition to cancer deaths per 100,000 inhabitants, an index of interest is the proportion in relation to total deaths. In the previous section the Old age-group was excluded due to an under estimation of overall deaths for this group in the 8 T. However, when comparing cancer deaths to total deaths, the number of deaths accounted for by the survey can be considered a representative sample of total deaths for this population. To sustain that this was not a biased sample, %Cancer death over total deaths for each of the 9 years was estimated; both for 8 T and Argentina. There was no tendency over time, neither for 8 T or Argentina. Average %Cancer deaths were 30.0% (range 24.5–34.5) and 19.8% (range 19.1–20.7), for 8 T and Argentina; respectively. 8 T estimations presented higher variability due to lower number of cases compared to the total for Argentina.

Table 4 shows cancer deaths and odd-ratios in the 9-year period discriminated by location (8 T and Argentina), age and gender. As commented in Section 2.4, child age-group was not considered. For both genders and age groups, odd ratios showed a higher probability of dying of cancer than other causes in the 8 T than for the GP. For example, it was 1.95 times more likely for a young-female in 8 T to die of cancer than other causes than a young-female in the GP to die of cancer than other causes.

Considering all age-groups and both genders, in the 8 T over the 9-year period, cancer and coronary related deaths represented 29.2% and 28.7% of total deaths, respectively. The corresponding percentages for the GP were 18.7% and 30.3% for cancer and coronary, respectively. Thus in the 8 T cancer and coronary represented similar percentages over total deaths, while in the GP coronary were clearly higher and cancer lower.

4. Discussion

Three indexes were considered when comparing the presence of cancer in 8 T with the presence of cancer in the GP: incidence rate, deaths per 100 thousand inhabitants for the Young age-group, and percent cancer-deaths in relation to other causes for the Young and Old age-groups. All three indexes showed significantly higher values for 8 T.

A close observation of Table 3 shows that the higher odds-ratio for Young-males in comparison to Young-females (2.77 vs 2.48) was due to either higher female cancer-deaths (CD) in the GP; or higher male CD in 8 T. Looking into the type of cancers that provoked these higher female CD in the GP, they were almost exclusively due to breast- (C50), uterus- (C53–C55) and ovary- (C56) cancers; representing 51% of total CD. In 8 T these same cancers represented 22% of total female CD. In 8 T colon cancer (C18) represented 30% of total male CD; compared to 8% in Argentina.

The IARC[24] presented online data on incidence and cancer-deaths for the year 2020, which can be consulted by gender, age-group and country or region. The population-corrected incidence rate for Argentina was 218, slightly higher than the 2018 value of 212 shown in Table 2. Argentina had a higher value than the average for Latin America and the Caribbean of 187. Argentina death-rates for the year 2020 for the Young age-group were 23 and 14.6 per 100 thousand, for females and males, respectively. These same values for Latin America and the Caribbean as a whole were 21 and 14.6. The IARC[24] death-rate values were thus similar to those estimated and presented in Table 3.

Some cancer types have been linked to specific AP, for example non-Hodgkin's lymphoma to glyphosate[11] or lung cancer to 2-4-D.[25] However, explaining the presence of specific cancer-types in 8 T is difficult due to the wide range of AP active ingredients used close to 8 T. The well-documented data on increased genotoxicity due to chronic AP exposure, both in children[26] and adults,[14,27] can lead to different cancer types depending on each individual's geno- and phenotype. The most likely outcome is that high incidence cancers such as those shown in Fig. 1 are enhanced when genotoxicity is present.

In the introduction a number of articles were mentioned that have shown the association of AP to cancer risk, for example Weisenburger[11] and Rani et al.[12] 87% and 95% of the Young and Old populations, respectively, had lived in their respective towns for at least 5 years exposed to chronic AP drifts. Thus it is no surprise that the cancer indexes in 8 T were higher than for the GP.

Regarding the association of AP to cancer, an important event developed in Sastre (one of the 8 T, Table 1) where a 2-year old girl who lived next to a sprayed agricultural field developed a lymphoblastic lymphoma. In spite of medical instructions that she could not be exposed to pesticide drifts, spraying continued. The community reacted with a collective lawsuit against the city council.[28] In September 2020, the Judge established an AP restriction of 1000 m surrounding the town. A key witness in the judicial process was given by the director of the health workshops described in Section 2.1, who presented published evidence linking AP to cancer.

Limitations of the present study were.

a) The ecological nature of the study meant that there was no data on the nature and duration of specific AP in each town or on each individual. However, as the crop types and AP used in the region are uniform, it can be assumed that population exposure to AP over time was homogenous.
b) As the surveys in each town were not simultaneous (Table 1), cancer death-rates had to be estimated over a 9-year period covering 2005–2013. AP applications surrounding these towns have changed since then; however, the variety and quantity of AP have increased, mainly due to an increase in herbicide-resistant weeds and in insecticide-resistant insects.[29–32] An improvement in AP health-related issues is highly unlikely.
c) The study was restricted to 8 T of the Province of Santa Fe, a region of the Argentine Pampas. Here again, the crop types in this region were similar to the Pampas overall.
d) Results were based on self-reported data, not on clinical records or medical diagnosis. As interviewers were medical students close to finishing their careers, and had received extensive training on their task, the questionnaire was considered rigorous.

Table 4
Number of cancer deaths in 8 T and Argentina over a 9-year period, by gender and age group. % cancer deaths were the % of cancer deaths in relation to the total number of deaths. Odds ratios are the quotient (% cancer deaths 8 T)/(% cancer deaths Argentina). 95% confidence intervals (CI) are included.

	Female				Male			
	Young (15–45 years)		Old (>45 years)		Young (15–45 years)		Old (>45 years)	
	8 T	Argentina	8 T	Argentina	8 T	Argentina	8 T	Argentina
Number of cancer deaths	25	16,442	140	226,147	21	12,460	212	262,814
% Cancer deaths	49.0	25.1	27.9	18.6	20.0	9.1	31.8	20.8
Odd ratios (CI)	1.95 (1.31–2.90)		1.50 (1.27–1.77)		2.19 (1.43–3.36)		1.53 (1.34–1.75)	

e) Death rates in relation to the living population for the Old population group were under-estimated. This factor has been detected in published research, for example when five methods to estimate mortality were compared, results were biased downwards at the oldest ages.[33] Lankoandé et al.[34] attributed under-estimation to *"recall errors, the dissolution of households following the death of adults and coverage errors"*; these errors were inherent to the present survey question (see Section 2.4). To obtain better estimates of death rates for the old-age population in 8 T, other questionnaire tools such as the sibling survival method could have been used.[35,36] However, the HW question did provide an adequate sample with which to compare cancer deaths to other causes of death.

5. Conclusion

Overall, and in spite of limitations, we were able to confirm the hypothesis that living in small rural towns nearby AP applications has a negative health impact, namely in cancer outcomes. The present work has added epidemiological knowledge relating tumor incidences to AP; knowledge that is scarce in countries such as Argentina where exposure to AP is much higher than in Europe or North America.[10] Due to the wide range of active ingredients and formulants in AP used close to 8 T, molecular level causality between a specific pesticide and a specific illness is difficult to establish. However, this does not overrule the precautionary principle which should lead to pesticide-reduction policies, especially in the surroundings of small urban populations. One such policy was the lawsuit outcome described above for Sastre, one of the 8 T.

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Declaration of competing interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cegh.2023.101239.

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