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# NeuroToxicology



## Association between pesticide exposure and suicide rates in Brazil



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### ABSTRACT

**Introduction:** The association between pesticide use and an increased suicide risk is a controversial issue. Previous studies have shown higher rates of suicide among agricultural workers and people living in small municipalities, but have not identified the causes of these results.

**Objective:** To investigate the association between pesticide exposure and suicide rates.

**Methods:** Crude suicide rates of a 15-year time series (1996–2010) were examined, followed by an ecological study using age-standardized suicide rates for the period 2006–2010. The unit of analysis was all 558 Brazilian micro-regions. Pesticide exposure was evaluated according to the proportion of farms that used pesticides and had reported cases of pesticide poisonings. The statistics were analysed using Pearson's correlation and multiple linear regression adjusted for socioeconomic, demographic and cultural factors.

**Results:** Among the age group that was analysed, the mean suicide rate was 6.4 cases/100,000 per year in the 2006–2010 period, with a male/female ratio of 4.2. The times series showed that there were higher suicide rates among people aged 35–64 years and among men aged 15–34 years. The ecological analysis showed that the suicide rates were higher in micro-regions with a higher proportion of farms run by 35–64 year olds, female workers and on farms with better economic indicators (higher farming income, level of mechanization and farm area). There was a positive association between the Catholic religion and suicide rates. Micro-regions with a greater use of pesticides, and with a high proportion of pesticide poisoning had the highest suicide rates for all three groups analysed: both genders, men, and women ( $p$  ranging from 0.01 to  $p < 0.001$ ).

**Conclusion:** This study reinforces the hypothesis that pesticide use and pesticide poisoning increase the suicide rates. However, due to the limitations of the study's ecological design, such as ecological fallacy, further appropriately designed studies are needed to confirm the causal relationships.

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### 1. Introduction

The estimated global suicide rate is 16/100,000 inhabitants (WHO/SUPRE, 2013), and therefore suicide is an important public health problem. Although the overall Brazilian rate is relatively low (4.6/100,000 for the entire population in 2005) (Brasil, 2008), it is higher in certain regions, such as the south, which has reported the highest Brazilian suicide rates in recent decades (Brasil, 2008). Studies have shown that suicide rates are higher in small municipalities (<50,000 inhabitants) (Brasil, 2008; Marin-Leon et al., 2012), although there is not much information about the factors that are associated with increased suicides in this context.

In Brazil, studies have found higher rates of suicide and suicide attempts in two areas where pesticides are intensively used: the Dourados region of the state of Mato Grosso do Sul (Pires-a et al., 2005) and the mountainous region (Serrana) of Rio de Janeiro state (Meyer et al., 2010). In Rio Grande do Sul state, one study analysed the temporal trends of suicide rates in the period between 1979 and 1998 and found a higher rate among primary sector workers, especially agricultural workers (Meneghel et al., 2004). However, the association between pesticide exposure and suicide (Faria et al., 2006) could not be verified due to limited data at that time.

Studies among farm workers have shown an association between pesticide poisoning and psychiatric problems, particularly depressive disorders (Stallones and Beseler, 2002; Beseler et al., 2006, 2008; London et al., 2012; Faria et al., 1999; Wesseling et al., 2010; Weisskopf et al., 2013; Beseler and Stallones, 2008; Beard et al., 2011). However, this association is not so clear when analysing pesticide exposure – without poisoning – and the occurrence of psychiatric problems (London et al., 2005, 2012; Freire and Koifman, 2013).

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Several pesticides, especially organophosphates, are neurotoxic and have been associated with increased psychiatric problems, particularly depression (Stallones and Beseler, 2002; Beseler et al., 2006; London et al., 2005, 2012; Wesseling et al., 2010; Beseler and Stallones, 2008; Freire and Koifman, 2013; Lima et al., 2011; Keifer and Firestone, 2007). These problems could contribute to the occurrence of suicide among exposed workers (London et al., 2005, 2012; Stallones, 2006). Furthermore, in several parts of the world intentional pesticide poisoning has been the main method of suicide (London et al., 2005), although this is not the case in Brazil (Brasil, 2008; Marin-Leon et al., 2012).

Parallel to the growing pesticides consumption worldwide, is the increasing concern about their effects on mental health. While the world's pesticide market grew by 93% during the last 10 years, the Brazilian market increased by 190% (ANVISA, 2012) and since 2008 it has been the world's largest pesticide market. Intensive use of these products exposes the majority of the Brazilian population to their effects through food residues, environmental contamination, occupational poisoning or accidental cases. A huge number of Brazilian farm workers are exposed to pesticides at work in a frequent and prolonged manner, often without any protection.

Considering this context of intense pesticide exposure and also the improvement in the quality of secondary data in Brazil, this study examined the association between pesticide exposure and suicide rates in Brazil.

## 2. Methods

The crude suicide rates during a 15-year period (1996–2010) were analysed. A time series was plotted to examine the proportion of suicides according to the method of death (direct cause), and suicide rates according to gender and age groups (in groups of 10 years from 15 years to 75 years or over). In addition, an ecological study was carried out, where the unit of analysis was all 558 of the Brazilian geographic micro-regions as defined by the Brazilian Institute of Geography and Statistics (Instituto Brasileiro de Geografia e Estatística – IBGE).

Suicide was defined as death resulting from an intentionally self-inflicted injury/poisoning and registered as the principal cause of death on death certificates. The data on deaths were obtained from the Ministry of Health's Mortality Information System (Sistema de Informações em Mortalidade – SIM/DATASUS-MS) (Estatísticas Vitais, 2010), and the International Classification of Diseases ICD-10 codes X60 to X84 were considered to be deaths from suicide. All suicides were included regardless of the method used. The analyses were restricted to people aged 15 or over because the suicide rate in people younger than 15 accounted for approximately only 1.2% of the total and because of the interest in examining the effects of occupational exposure. Suicides where the age was unknown were also excluded.

The number of suicides for each micro-region was used to build crude suicide rates. Afterwards, suicide rates per micro-region were age-standardized through the direct method, using the World Health Organization standard population (WHO, 2001) as a reference (Ahmed et al., 2000). The standardized rates were calculated according to age groups (15–24; 25–34; 35–44; 45–54; 55–64; 65–74; 75 years or more) per annum, for the entire population (both genders) and stratified according to gender (male suicides and female suicides). The mean standardized rates for a five-year period (2006–2010) were calculated and these results were used in the multivariate analyses.

Multivariate analysis through multiple linear regression was carried out to examine the associations between pesticides (pesticide exposure and pesticide poisonings) and suicide rates (for entire population and stratified by gender). The confounding

factors taken into consideration were demographic and socio-cultural factors (age and schooling of main farm operator, female rural workforce, skin colour, marital status, religion), the Human Development Index – HDI, and economic indicators (farm size, gross income from farming production, level of mechanization, farmworker density). The HDI varies from 0 (worst index) to 1 (best index) and this data was built using information from the Brazilian Demographic Census 2000 (PNUD, 2003).

The main form of exposure was defined by two variables: the proportion of farms using pesticides and the proportion of farms reporting cases of pesticide poisoning. Although they both indicate exposure to pesticides, they reflect a different intensity of exposure. Thus, their effects are not independent and they cannot be included in the same model. Considering the epidemiological controversy about the relationship between pesticide exposure (without poisoning) and rates of suicide, as well as pesticide poisoning as an important indicator of intense exposure, two models were developed, one for each main exposure variable.

All of the above mentioned variables were identified in the official databases that record agricultural work and production, as were the socio-economic and demographic aspects. According to the literature, these aspects might be associated with suicide and were available for the micro-region's aggregation level.

To examine qualitative variables (as religion, skin colour and marital status) and to include them as continuous variable in multiple linear regression, it was necessary a dummy variable, examining if a characteristic was present or not. Only one variable was selected to represent each indicator. Priority was given to the measure with strongest correlation with suicide rates out of all the possible measures for that variable. Therefore, the dummy variable used for religion was '% of Catholics', and the indicator of skin colour was '% of white-skinned people' (Szklo and Nieto, 2012). For marital status, the indicator was 'the rate of divorces and other legal separations/100,000 inhabitants' following the literature (Faria et al., 2006).

For the quantitative variables, several different cut-off points were tested using the Pearson's correlation test and those with strongest correlation were selected. For example, the cut-off point of the farm size (10 ha and over) corresponds to around half of Brazilian farms (47%) and this size had the strongest correlation.

The main exposure was examined in two ways: pesticide exposure and pesticide poisoning (% of farms using pesticides in 2006 and % of farms reporting cases of pesticide poisoning in 2006). The adjustment factors included in the multivariate analysis was: age group (% of farms run by people aged 35–64 years), low schooling (% of farms run by people up to 1 year of schooling), female rural workforce (% of women among people working at farms), skin colour (% of white-skinned people), religion (% of people of Catholic faith), divorce rate (number of people divorced + legally separated/100,000 inhabitants), HDI (mean per micro-region of Human Development Index), farm size (% of farms having an area equal to or greater than 10 ha – around 24.7 acres), farming income (mean value of farming production/farm area in hectare groups), level of mechanization (% of farms with agricultural machinery and implements), farm worker density (number of workers – farmers and farm workers – aged 14 and over, working at each farm).

Data on exposures were obtained from official records: from the Brazilian Institute of Geography and Statistics – IBGE (2006 Agricultural Census (Censo Agropecuário, 2006), the 2000 Demographic Census (Censo Demográfico, 2000), and the 2006 Civil Register (Estatísticas do Registro Civil, 2006)) and from the Brazilian Unified Health System's Database – DATASUS (Estatísticas Vitais, 2010). The HDI was extracted from the 2003 UNDP Atlas (United Nations Development Programme) (PNUD, 2003).

**Table 1**  
Description of the variables used.

Variables	Mean	SD	Range
<b>Main exposure</b>			
% of farms <sup>a</sup> using pesticides (2006)	26.4%	21.5	0.05–90.7
% of farms reporting cases of pesticide poisoning (2006)	0.4%	0.6	0.0–6.0
<b>Factors adjusted: demographics, cultural and socioeconomics</b>			
(1) % of farms run by people aged 35 and over (2006)	86.7%	5.3	61.4–96.5
(2) % of farms run by people who are illiterate or with very low schooling (2006)	32.6%	21.3	1.8–77.0
(3) Female rural workforce: % of women among rural workers (2006)	28.5%	7.1	5.5–51.3
(4) % of white-skinned population (2000)	50.6%	23.0	6.5–96.0
(5) % of Catholic population (2000)	79.2%	10.5	41.1–97.1
(6) Rate of divorce and other separations: no. of cases among people aged 15 or over/per 100,000 inhabitants (2006)	189.9	116.8	0–567.1
(7) Mean of HDI <sup>b</sup> per micro-region (2000)	0.70	0.08	0.53–0.86
(8) % farms with area greater than 10 ha (2006)	52.2%	23.9	2.4–99.1
(9) Farming income: value of farm production/farm area (2006)	193.9	272.3	0.1–2057.5
(10) Mechanization level: % farms with agricultural machinery and implements (2006)	21.2%	16.1	0.05–74.3
(11) Farm jobs density: mean of agricultural workers/farm (2006)	3.2	1.0	1.9–15.2

<sup>a</sup> The term “farm” is used here as a synonym for “agricultural establishment”.

<sup>b</sup> HDI: Human Development Index.

The frequency of each indicator was described according to mean values and standard deviation, considering its distribution in the 558 micro-regions (unit of analysis): the percentage of farms/micro-region, the percentage of agricultural workers per farms/micro-region, the percentage of people (according to colour or religion)/micro-region and the rate of divorce and separation/micro-region (Table 1).

Associations between the demographic, socio-economic and occupational variables and the standardized suicide rates were examined using the Pearson’s correlation test. A multivariate analysis was carried out using multiple linear regression (backward method) and variables with  $p \leq 0.10$  were kept in the model. In view of possible data limitations in the northern region (the Amazon region), a second analysis was carried out that excluded 64 northern micro-regions. Because this study used secondary data that are available on-line in official databases, it was not submitted to a research ethics committee.

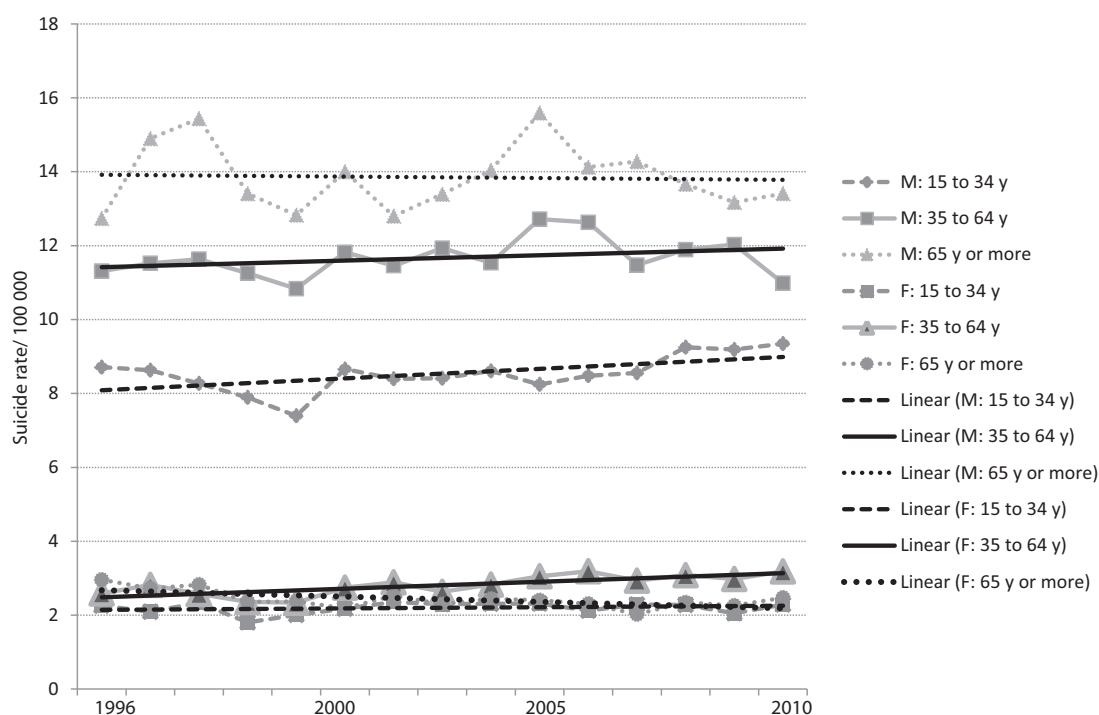
### 3. Results

#### 3.1. Time series analysis

Between 1996 and 2010 there were 117,469 suicides among people aged 15 or over, of which approximately 45,000 occurred between 2006 and 2010. In the times series period, the crude suicide rates slightly increased with 6.4 cases/100,000 at the end of this period.

During the study period, the suicide rates remained consistently higher among men than women, with a mean ratio of four male cases (4.2) to one female case. This ratio remained relatively stable throughout the period.

Analysis of the times series revealed an increase of the suicide rates in the 35–64 age groups among men and women. There was an increase in the rates of suicide in the youngest group (15–35 years) among men but among women in this age group the rates remained



**Fig. 1.** Suicide rates according to age and sex: male (M) and female(F); 1996–2010.

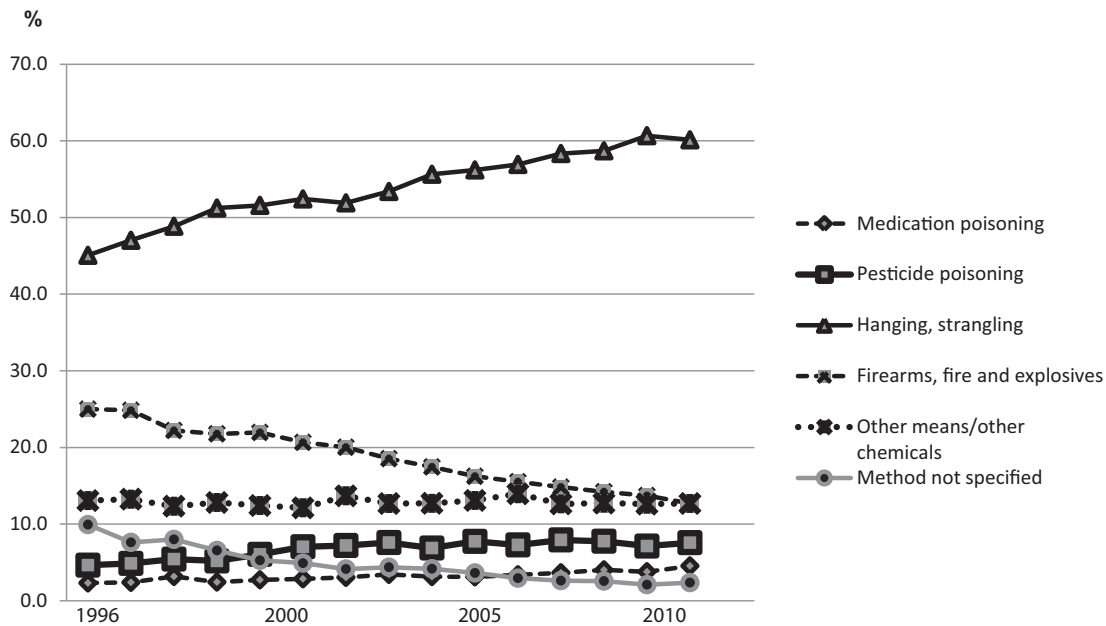


Fig. 2. % of suicides by method, Brazil, 1996–2010.

stable. Although rates are higher among older people (65 and over) and had higher coefficients (for both genders and for men alone), there was a slight decrease over the period. This was seen especially in the analysis relating to male and overall suicides (Fig. 1).

The majority of suicides were by hanging (which presented an increase during the study period), followed by shooting with firearms, which decreased in the same period. The proportion of suicides due to pesticide poisoning was the third main cause of suicide and this increased by 65% in 15 years: from 4.6% in 1996 to 7.6% in 2010 (Fig. 2).

### 3.2. Ecological study (2006–2010)

After exploratory analysis, 11 indicators of exposure correlated to the occurrence of suicide were selected (Table 1). In 2006, in the micro-regions assessed, almost 30% (sd = 22.3) of rural establishments (farms) reported pesticide use and 0.4% (sd = 0.6) reported cases of pesticide poisoning.

There was a positive correlation between suicide rates and a higher proportion of farms run by those aged 35–64 years and between suicide rates and a higher proportion of women among the agricultural workers. Suicide rates were inversely correlated to the proportion of people running farms with little or no formal schooling. Moreover, the correlation test showed that suicide rates were higher in micro-regions with better socioeconomic indicators, such as a better HDI, a higher production value and a higher level of mechanization (Table 2).

Regarding the area of farms, there was a positive correlation between the proportion of properties that were 10 ha or larger and suicide rates (Pearson correlation related to suicide rate for both genders = 0.22) (Table 2). However, the strongest correlation was in the 10–50 ha group (Pearson correlation for both genders = 0.33). In the group of farms bigger than 50 ha, the correlations were weaker (Pearson correlation less than 0.14). The suicide rates were directly correlated to a higher proportion of white people, the Catholic religion and the occurrence of divorce

Table 2

Pearson correlations (*p* value) between evaluated indicators and suicide rates (both genders, male and female).

	Standardized suicide rates, Brazil, 2006–2010		
	Both genders	Male	Female
<b>Main exposure</b>			
% of farms using pesticides (2006)	0.46 <sup>***</sup>	0.46 <sup>***</sup>	0.37 <sup>***</sup>
% of farms reporting cases of pesticide poisoning (2006)	0.42 <sup>***</sup>	0.41 <sup>***</sup>	0.36 <sup>***</sup>
<b>Other indicators: demographics, cultural and socioeconomics</b>			
(1) % of farms run by people aged 35 and over (2006)	0.29 <sup>***</sup>	0.30 <sup>***</sup>	0.25 <sup>***</sup>
(2) % of farms run by people who are illiterate or with very low schooling (2006)	−0.30 <sup>***</sup>	−0.30 <sup>***</sup>	−0.21 <sup>***</sup>
(3) % of women among rural workers (2006)	0.29 <sup>***</sup>	0.28 <sup>***</sup>	0.22 <sup>***</sup>
(4) % of white-skinned population (2000)	0.44 <sup>***</sup>	0.46 <sup>***</sup>	0.32 <sup>***</sup>
(5) % of Catholic population (2000)	0.20 <sup>***</sup>	0.19 <sup>***</sup>	0.20 <sup>***</sup>
(6) Rate of divorce and other separations: no. of cases among people aged 15 or over/per 100,000 inhabitants (2006)	0.11 <sup>**</sup>	0.11 <sup>**</sup>	0.10 <sup>*</sup>
(7) Mean of micro-region HDI <sup>a</sup>	0.30 <sup>***</sup>	0.31 <sup>***</sup>	0.20 <sup>***</sup>
(8) % farms with area greater than 10 ha (2006)	0.22 <sup>***</sup>	0.20 <sup>***</sup>	0.18 <sup>***</sup>
(9) Value of farm production/farm area (2006)	0.31 <sup>***</sup>	0.32 <sup>***</sup>	0.21 <sup>***</sup>
(10) % farms with agricultural machinery and implements (2006)	0.46 <sup>***</sup>	0.47 <sup>***</sup>	0.33 <sup>***</sup>
(11) Farm job density: mean of agricultural workers/farm (2006),	−0.12 <sup>**</sup>	−0.13 <sup>**</sup>	−0.09 <sup>*</sup>

<sup>a</sup> Human Development Index.

\* *p* < 0.05.

\*\* *p* < 0.01.

\*\*\* *p* < 0.001.

**Table 3**

Multivariate analysis (global): crude and adjusted coefficients of linear regression (B), confidence interval (CI) and *p* value. Outcome: age-standardized suicide rates. Exposure: % of establishments using pesticides in 2006.

Variables	Crude both genders – B (CI)	Adjusted both genders – B (CI)	Adjusted male suicide – B (CI)	Adjusted female suicide – B (CI)
Main exposure: using pesticides	0.12(0.10–0.14)***	0.05(0.02–0.07)***	0.07(0.03–0.11)**	0.03(0.02–0.04)***
Factors adjusted				
(1) Main farm operator aged 35–64 years	0.30(0.22–0.38)***	0.10(0.004–0.19)*	0.15(0.003–0.31)*	0.08(0.04–0.13)***
(2) Low schooling of main farm operator	–0.08(–0.10 to –0.06)***	–0.003(–0.06 to 0.05)	–0.03(–0.06 to 0.11)	–0.01(–0.03 to 0.003)
(3) Female rural workforce	0.22(0.16–0.28)***	0.21(0.15–0.27)***	0.34(0.24–0.44)***	0.08(0.05–0.12)***
(4) White skin	0.11(0.09–0.12)***	0.02(–0.01 to 0.05)	0.03(–0.04 to 0.09)	–0.0003(–0.02 to 0.02)
(5) Catholic religion	0.11(0.06–0.15)***	0.09(0.05–0.12)***	0.13(0.07–0.19)***	0.04(0.03–0.06)***
(6) No. divorce + separations/pop ≥ 15 years	0.005(0.001–0.009)**	–0.002(–0.006 to 0.002)	–0.003(–0.01 to 0.004)	–0.0002(–0.002 to 0.002)
(7) HDI/micro-region	21.31(15.67–26.95)***	4.14 (–6.33 to 14.62)	9.39 (–5.87 to 24.66)	–3.64(–11.41 to 4.13)
(8) Farm area ≥ 10 ha	0.05(0.03–0.07)***	0.04(0.03–0.06)***	0.05(0.03–0.08)***	0.02(0.01–0.03)***
(9) Farming production value/area	0.006(0.005–0.008)***	0.002(0.0001–0.003)*	0.003(0.001–0.006)**	–0.0001(–0.001 to 0.001)
(10) Farms with agricultural machinery and implements	0.16(0.13–0.18)***	0.08(0.04–0.11)***	0.16(0.10–0.21)***	0.007(–0.02 to 0.03)
(11) Mean of workers in farms ≥ 14 years	–0.66(–1.09 to –0.22)**	–0.37(–0.75 to 0.02) <sup>o</sup>	–0.69(–1.33 to –0.04)*	–0.11(–0.31 to 0.10)

HDI – Human Development Index (UNDP).

<sup>o</sup> *p* < 0.10.

\*\* *p* ≤ 0.05.

\*\*\* *p* ≤ 0.01.

\*\*\*\* *p* ≤ 0.001.

**Table 4**

Multivariate analysis (global): crude and adjusted coefficients of linear regression (B), confidence interval (CI) and *p* value. Outcome: age-standardized suicide coefficients. Exposure: % of establishments with cases of pesticide poisoning in 2006.

Variables	Crude both genders – B (CI)	Adjusted both genders – B (CI)	Adjusted male suicide – B (CI)	Adjusted female suicide – B (CI)
Main exposure: pesticide poisoning	4.03(3.31–4.75)***	1.86(1.14–2.58)***	2.70(1.50–3.89)***	1.10(0.73–1.47)***
Factors adjusted				
(1) Main farm operator aged 35–64 years	0.30(0.22–0.38)***	0.14(0.05–0.23)**	0.21(0.05–0.36)**	0.09(0.04–0.13)***
(2) Low schooling of main farm operator	–0.08(–0.10 to –0.06)***	–0.007(–0.05 to 0.05)	0.02(–0.07 to 0.11)	–0.02(–0.03 to –0.005)**
(3) Female rural workforce	0.22(0.16–0.28)***	0.20(0.15–0.26)***	0.31(0.21–0.41)***	0.07(0.04–0.10)***
(4) White skin	0.11(0.09–0.12)***	0.02(–0.006 to 0.05)	0.04(–0.01 to 0.09)	0.003(–0.02 to 0.02)
(5) Catholic religion	0.11(0.06–0.15)***	0.08(0.05–0.12)**	0.12(0.06–0.18)***	0.06(0.04–0.08)***
(6) No. divorce + separations/pop ≥ 15 years	0.005(0.001–0.009)**	–0.002(–0.006 to 0.002)	–0.003(–0.01 to 0.004)	–0.0003(–0.003 to 0.002)
(7) HDI/micro-region	21.31(15.67–26.95)***	4.48(–5.84 to 14.80)	8.13(–9.08 to 25.34)	–3.69(–11.35 to 3.98)
(8) Farm area ≥ 10 ha	0.05(0.03–0.07)***	0.04 (0.02–0.06)***	0.05(0.02–0.08)***	0.02(0.007–0.03)***
(9) Farming production value/area	0.006(0.005–0.008)***	0.003(0.001–0.004)**	0.005(0.002–0.007)***	0.0003(–0.0005 to 0.001)
(10) Farms with agricultural machinery and implements	0.16(0.13–0.18)***	0.08(0.05–0.11)***	0.16(0.11–0.21)***	0.007(–0.01 to 0.03)
(11) Mean of workers in farms ≥ 14 years	–0.66(–1.09 to –0.22)**	–0.22(–0.61 to 0.16)	–0.54(–1.17 to 0.10) <sup>o</sup>	–0.06(–0.26 to 0.15)

HDI – Human Development Index (UNDP).

<sup>o</sup> *p* < 0.10.

\*\* *p* ≤ 0.01.

\*\*\* *p* ≤ 0.001.

and legal separation, but negatively correlated to the number of people working at the farms (Table 2).

After adjustment for confounding factors, pesticide exposure continued to be associated with age-standardized suicide rates in both genders, in female suicide and, above all, in male suicide (Table 3). Likewise, multivariate analysis showed a similar association and a more pronounced effect between pesticide poisoning and suicide rates for both genders, in female suicide and especially in male suicide (Table 4).

The analysis that excluded the northern region presented the same pattern, with a significant association between pesticide exposure and suicide rates, as well as a stronger association between pesticide poisoning and suicide. With regard to the other independent variables, the main difference was the direct association between the HDI and suicide rates for both genders and for male suicide.

As for the other factors relating to the rural work process, regression analysis identified those that were associated independently with suicide rates. In all the analysis models, suicide rates were higher in micro-regions with a greater proportion of women working on farms and where the farm area was equal to or greater

than 10 ha. The proportion of farms run by people aged 35–64 years was associated with suicide rates in the analysis related to all 558 micro-regions, but this association did not exist when the northern region was removed from the model.

With regard to male suicide and suicide for both genders, a positive association was found between a higher value of farming production and a higher level of mechanization and increased suicide rates. This pattern occurred in the model relating to pesticide exposure and also in the model that examined pesticide poisoning.

The proportion of people of Catholic faith was directly associated with all suicide rates, in particular male suicide. This association was consistent for all the models, including the analyses that excluded the northern region.

#### 4. Discussion

All of the analyses in this study showed that there was an association between pesticide exposure and suicide rates. In line with international publications, there was an even stronger association between pesticide poisoning and suicide rates. Several



epidemiological studies have shown there is a greater risk of psychiatric problems, mainly depression, in people exposed to pesticides – especially those who have suffered from pesticide poisoning – in different countries such as the USA (Stallones and Beseler, 2002; Beseler et al., 2008; Beseler and Stallones, 2008), France (Weisskopf et al., 2013), Costa Rica (Wesseling et al., 2010), Brazil (Meyer et al., 2010; Faria et al., 1999) and South Africa (London et al., 2012).

The results are consistent with case–control studies in the USA, which found higher suicide rates in occupations where there is a likelihood of pesticide exposure (Stallones, 2006; van Wijngaarden, 2003). In Brazil, a study conducted in Rio de Janeiro state found higher rates of hospitalization for mood disorders and suicide attempts as well as deaths due to suicide in regions with intense pesticide exposure when compared with other regions (Meyer et al., 2010). Similarly, an ecological study carried out in Spain documented a significant increase in hospital admissions for affective disorders and suicide attempts in regions with more intense pesticide exposure (Parron et al., 2011).

The American Agricultural Health Study (AHS) assessed pesticide applicators and their spouses and found diverse results in relation to pesticides and suicide: an analysis of 110 suicide cases did not find a significant association between prior pesticide use and suicide (Beard et al., 2011). Another analysis, from the same study, found a positive association between exposure to the organophosphate chlorpyrifos and suicide rates in groups with greater cumulative exposure and more intense exposure (Lee et al., 2007).

The biological plausibility of these results was not completely established yet and the mechanism of toxicity of pesticides can vary depending on the type of chemicals used. The nervous system represents a prime target for acute and chronic effects of many pesticides (Keifer and Firestone, 2007). The neurotoxic effects of organophosphates (OP), one of the most widely used pesticides, are well established (London et al., 2005, 2012; Lima et al., 2011; Keifer and Firestone, 2007). OP neurotoxicity can include psychological and neurobehavioral effects, which can be related to depression and/or high impulsiveness (London et al., 2005, 2012; Wesseling et al., 2010). A study among banana plantation workers in Costa Rica found that organophosphate poisonings (OP) were related to the occurrence of mood disorders (depression) and suicidal ideation (Wesseling et al., 2010). In an extensive review, London et al. (2005) stated that OP are not only a suicide agent (method) but may be part of the causal pathway. Studies using animals showed that prolonged exposure to organophosphate pesticides interferes with serotonergic systems, producing behavioural alterations similar to depressive disorders (London et al., 2005; Lima et al., 2009, 2011; Chen et al., 2011).

The positive association between better conditions of farming production – micro–regions with larger farms, greater productivity (higher production value/area) and higher mechanization level – could be markers of intensive pesticide use justifying their positive association with suicide rates (especially male suicide) in this kind of farms. Besides that, this result also may be related to greater threat of insolvency faced by farmers who have more to lose if farming fails. Farming fails could cause psychological distress not only in farmers but also in all micro–region population.

The absence of an association with HDI in the majority of models is consistent with the results of the previous study on suicides in the state of Rio Grande do Sul (Faria et al., 2006) and may be due to the adjustment for other socioeconomic variables.

Farms that have a higher proportion of female workers as well as a smaller number of workers are associated with higher suicide rates, and might reflect a scenario of intense work. A higher proportion of female rural workers might indicate a situation where all people available are involved in farming activities, while

a smaller number of workers might reflect selective male migration to urban regions, which occurs in periods when there are crises in agricultural production.

The evaluation of the times series of suicide over 15 years (1996–2010) showed that there was a reduction in suicide using firearms (preceding the Brazilian policy on disarmament, in 2003) and an increase in suicide through hanging. Suicide by pesticide ingestion has become the third most common method in Brazil. Self-poisoning with pesticides has been the predominant cause of suicides in several regions of the world, such as India, China, Sri Lanka and others (London et al., 2005; Freire and Koifman, 2013). Because of the increase in the use of this method, and the sharp growth in pesticide consumption in Brazil, policies must be established to restrict access to more toxic and lethal products, and health services must be prepared to recognize and manage pesticide poisonings (Bertolote et al., 2006).

The predominance of male suicide rates has been verified in most of the world, especially in western countries (WHO/SUPRE, 2013; London et al., 2005) and is consistent with previous Brazilian publications (Brasil, 2008; Meyer et al., 2010; Faria et al., 2006). Considering the predominance of male workers in high-risk agricultural activities (such as operating machines and applying pesticides) this result may reflect the association between pesticide exposure and suicide rates, as well as the relationship between high intensity work and suicide. Gender differences, related to how to deal with work-related problems or economic failures, may also have contributed to this result.

The times series showed there were high suicide rates in the more productive age groups: the middle age group (35–64 years) for both genders and in the youngest male group (15–34 years). Although rates of suicide are higher among the elderly (65 or more), this age group had slightly decreasing suicide rates. In addition, in the ecological analysis, micro–regions with a higher proportion of farms run by people aged 35–64 years, had increased rates of suicides. Considering that suicide rates are higher in small communities (Brasil, 2008; Marin-Leon et al., 2012; Faria et al., 2006), which have a lower frequency of urban problems such as chemical dependence and violence, this result seems to be related to occupational factors in farming production, such as pesticide exposure.

Micro–regions with a higher percentage of Catholics had higher suicide rates in all of the analyses. In the bivariate analysis other religions also had significant correlations with increased suicide rates, such as evangelical religions, especially the Lutheran church. However, considering the important presence of the Catholic religion in all of the country's regions, this religion indicator was selected for the multivariate analysis. The impact of religion on suicide rates was first examined in an ecological analysis by Durkheim, which found increased suicide rates in Protestant regions (Durkheim, 2003). A longitudinal study suggested that religion could present a protective effect among young people, but that this effect declined during adulthood (Nkansah-Amankra et al., 2012).

The result of this current study is consistent with another Brazilian ecological study in a metropolitan area, which also found an association between the Catholic religion and suicide rates. However, associations between aggregated data are subject to ecological fallacy, thus these results should be evaluated with caution. Considering the complexity of this relationship, one must assess not only the individual faith but also the degree of religiosity in order to understand the influence of religion on suicide rates (Gearing and Lizardi, 2009).

This study's main limitation was its ecological design, mainly the ecological fallacy that restricts causal inferences at the individual level. On the other hand, there are also benefits of looking at group level determinants in order to reveal an increased risk in some groups such as: the middle-age group, regions with a high proportion of women taking part in farming work and areas

with intense agricultural production. Using official data from the Agricultural Census for the ecological analysis enabled us to identify the rising suicide rates in regions with an intensive use of pesticides and a higher proportion of pesticide poisonings. However, the secondary data did not enable the identification of exposure intensity, cumulative exposure or the examination of the data according to chemical type.

The study was limited to those cases in which the intention to commit suicide was reported on the death certificate. However, cultural taboos regarding suicide lead to under-reporting (Faria et al., 2006). As such, cases of suicide may have occurred in the group of deaths where intention was not confirmed. This group was larger than the suicide group for the study period.

Among the farms using pesticides, 1.8% reported cases of pesticide poisoning in 2006 (around 25,000 cases). This percentage is lower than that found in population-based epidemiological studies but is much higher than the official data (Faria et al., 2007). Data regarding the proportion of divorce and legal separation do not include informal separation, which is frequent.

On the other hand, systematic under-reporting differences are not expected for exposure or for the outcomes in the different micro-regions and, therefore, the main conclusions of this study are unlikely to be affected by these limitations (Faria et al., 2006).

The study processed recent official data for the entire nation and replicated methods previously used in other studies (Faria et al., 2006; Parron et al., 2011; Bando et al., 2012). The characterization of exposure up to 2006 and of suicides from then onwards reduced the temporal ambiguity of the association. The choice of micro-regions as the unit of analysis meant that we could avoid oscillations in the rates of smaller municipalities and problems of population definition regarding the creation of new municipalities during the study period (Faria et al., 2006).

The association between pesticide exposure and increased suicide rates was verified in the multivariate analysis for all suicides and in the gender stratified analysis and it became stronger when the northern region data (possibly of poorer quality) were excluded. The most pronounced effect of this association was found with the intense pesticide exposure indicator (pesticide poisonings), particularly in the male suicide analysis. This result is consistent with many studies (Meyer et al., 2010; London et al., 2005; Stallones, 2006; van Wijngaarden, 2003; Lee et al., 2007) and reinforces the possible relationship with occupational pesticide exposure.

Owing to the limitations of the ecological design, more studies are recommended to confirm the association between pesticide exposure and poisoning and suicide and to deepen the knowledge about the mechanisms of these associations. Nevertheless, the results of this and other studies are sufficient to recommend that actions must take place to widely reduce pesticide exposure and prevent pesticide poisonings in rural populations and/or small municipalities.

### Conflict of interest statement

The authors declare that there are no conflict of interest.

### Transparency document

The Transparency document associated with this article can be found in the online version.

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