Original research

Self-reported psychological distress and self-perceived health in residents living near pesticide-treated agricultural land: a cross-sectional study in The Netherlands

Mariana Simoes [1], Anke Huss,[1] Nicole Janssen,[2] Roel Vermeulen [1,3]

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[1]Department of Population Health Sciences, Institute for Risk Assessment Sciences (IRAS), Utrecht University, Utrecht, The Netherlands
[2]Centre for Sustainability, Environment and Health, National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands
[3]Department of Epidemiology, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands

Correspondence to
Mariana Simoes, Department of Population Health Sciences, Institute for Risk Assessment Sciences (IRAS), Utrecht University, Utrecht, The Netherlands; m.simoes@uu.nl

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ABSTRACT

Objectives There is rising concern regarding possible health effects from exposure to pesticides in residents living near agricultural land. Some studies indicated increased risks of reporting symptoms of anxiety and depression among agricultural workers but less is known about the mental and perceived health of rural residents. We aimed to study possible associations between self-reported psychological distress (SPD) and self-perceived health (SPH) in residents near pesticide-treated agricultural land.

Methods Using the Public Health Monitor national survey from 2012, we selected 216 932 participants who lived in rural and semi-urban areas of the Netherlands and changed addresses at most once in the period 2009–2012. Psychological distress (PD) was assessed via the Kessler Psychological Distress scale (K10) and participants were asked to assess their own health. We estimated the area of specific crop groups cultivated within buffers of 50 m, 100 m, 250 m and 500 m around each individual's residence for the period 2009–2012. Association between these exposure proxies and the outcomes was investigated using logistic regression, adjusting for individual, lifestyle and area-level confounders.

Results Overall, results showed statistically non-significant OR across all buffer sizes for both SPD and SPH, except for the association between SPH and 'all crops' (total area of all considered crop groups) with OR (95% CI) ranging from 0.77 (0.63 to 0.93) in 50 m to 1.00 (1.00 to 1.00) in 500 m. We observed that most ORs were below unity for SPH.

Conclusions This study provides no evidence that residential proximity to pesticide treated-crops is associated with PD or poorer perceived health.

Key messages

What is already known about this subject?

- ► Concern about residential exposure to pesticides in people living near agricultural land has increased in the past decade.
- ► Studies have indicated increased risks of reporting symptoms of psychological distress (PD) among agricultural workers but research on residential exposure to pesticides is scarce.

What are the new findings?

- ► We observed overall decreased statistically non-significant ORs of poor self-perceived health in people living near pesticide-treated agricultural land.

How might this impact on policy or clinical practice in the foreseeable future?

- ► This study provides no support to possible associations between residential proximity to pesticide-treated agricultural land and PD and perceived health.

INTRODUCTION

Psychological distress (PD), a mental health disorder usually characterised by depression and anxiety, has been shown to be a leading cause of disability and an important burden to society given its heavy impact on the quality of life, higher risk of premature death and absenteeism costs.[1–4] Some studies indicate increased risks of reporting symptoms of PD among agricultural workers.[5] Literature on residential pesticide exposure and PD is, nevertheless, still scarce.[3] Whereas some studies found indications of increased risks of depression among residents living near agricultural land,[6–8] others were unable to obtain similar results.[9 10] Differences in outcome and exposure assessment and in study design hamper comparability of results. The link between residential exposure to pesticides and PD remains therefore unclear.

Self-perceived health (SPH) is a more extensive measurement of health, constituting an important predictor of morbidity and mortality.[11 12] Encompassing both physical and mental health, it has been shown to be inversely associated with PD.[13 14] Concurrently, while poorer SPH has been reported to be associated with exposure to pesticides in farmers in one study,[15] research on this association among residents is strikingly lacking, given the growing public concern about the possible health effects of residential exposure to pesticides.

This study aims to contribute to the body of literature on the association between residential pesticide exposure and PD. Using a large nationwide survey of the Dutch adult population, we explored the associations between residential

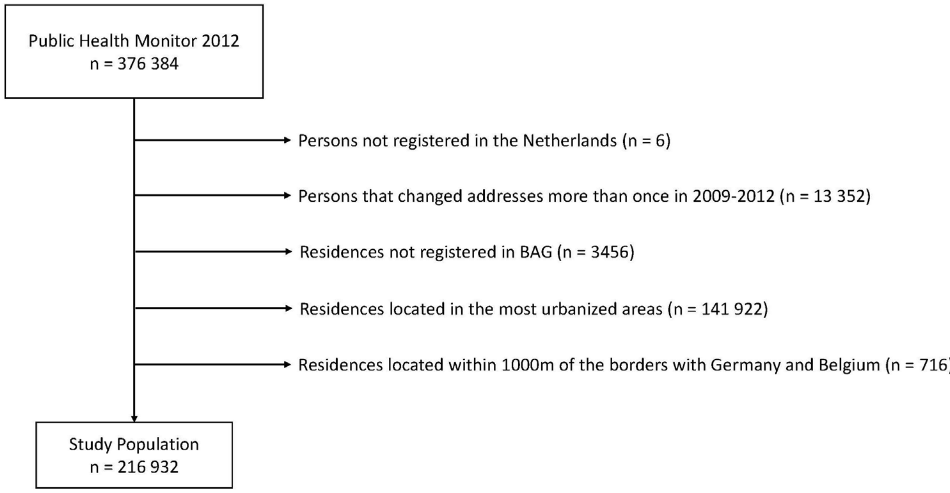

Figure 1 Flowchart of the study population. BAG, Basisregistratie Adressen en Gebouwen, the cadastral dataset containing all addresses in the Netherlands used to compute individual residential exposure proxies.

proximity to crops where pesticides are applied and self-reported psychological distress (SPD) and self-perceived health (SPH).

METHODS

Study population

The Public Health Monitor 2012 (Gezondheidsmonitor) is a national health survey conducted by the 28 regional Public Health Services, Statistics Netherlands (CBS) and the National Institute for Public Health and the Environment (RIVM) that includes information regarding perceived health and lifestyle from citizens aged ≥19 years. Elderly (≥65 years) were over-sampled by design; response rates were 45%–50%.

We excluded persons not registered in the Netherlands; who changed addresses more than once in the period 2009–2012; who lived in the most urbanised areas of The Netherlands (≥1500 addresses/km^2 at neighbourhood level, since urban populations rarely live in proximity to crops and differ in life-style and living environment factors compared with the more rural populations); and who lived within 1000 m from the border (for which we were unable to compute exposure). We included a total of 216 932 participants (figure 1).

Outcomes: phycological distress and perceived health

Outcomes of interest were self-reported phycological distress and self-perceived (general) health. The first was assessed via the Kessler Psychological Distress scale (K10),[16] classifying participants into 'well' and 'low to severe risk of psychological distress', at a cut-off value of >19 of the K10 score. The K10 has been validated for the Dutch population.[17] For the latter, participants were also asked to assess their own health based on a simple question: 'In general, would you say that your health is …'. Participants could answer one of five options that we later dichotomised into 'good to very good' and 'moderate to very poor'.

Exposure: crop area around residences

We used residential proximity to crops as proxy for agricultural pesticide exposure. First, we geocoded all residences using the Basisregistratie Adressen en Gebouwen.[18] Second, for computational reasons we rasterised the annual land use polygon maps from 2009 to 2012 (Basisregistratie Gewaspercelen)[19] and computed area of specific crops around participants' residences, in hectares (ha), using a moving average. This resulted in squared buffers that roughly correspond to radii of 50 m, 100 m, 250 m and 500 m. We assessed 13 crop groups representing 88%–89% of the Netherlands' open field cultivated land, excluding grassland[19]: maize, winter wheat, summer barley, summer wheat, other cereals, potatoes for consumption, potatoes for starch, seed potatoes, beets, ornamental plants and tree nurseries, vegetables, fruit and flower bulbs. Summing the area of all 13 crop groups, we created the group 'all crops'. Third, we averaged the areas across the exposure period (2009–2012) and obtained four land use buffers reflecting the average area (ha) of a specific crop cultivated within 50, 100, 250 and 500 m for each participants residence. We considered that the first two buffer distances to capture direct spray drift of pesticide droplets. This drift is highest within the first few metres of application and has an exponential decrease in concentration with distance, but can be detected up to 100 m away from a field edge (depending on application technique and meteorological conditions).[20 21] The highest environmental exposure to pesticides would therefore occur within these two buffers. Pesticides can however be detected at larger distances due to secondary emission processes such as volatilisation.[21] The two larger buffers are considered to capture this secondary drift. A recent Dutch exposure assessment study observed a high contrast in pesticide concentration in air and house dust between residences within 250 m and beyond 500 m from flower bulb crops and that gradients in concentrations within 250 m distance from fields were weak.[22] We therefore explored OR gradients across 50 m, 100 m, 250 m and 500 m buffers, using the area (in ha) of (specific) crop within a buffer and adjusting the model for the remaining area of that crop up to 500 m (buffers and complementary donuts were thus used continuous variables in the analyses). Our referent ('unexposed') group consisted of participants with zero hectares of (specific) crop within 500 m of their residences.

Statistical analyses

Imputation

The data set comprised 147 886 (68%) complete cases, with missing values in both outcome and potential confounders variables (table 1) in a non-monotone pattern. We used multiple imputation by chained equations to impute missing values in

Table 1 Population characteristics (before imputation)

	Study population (n=216 932)
Outcomes	
Self-perceived health	
Good to very good (n (%))	158 458 (73.05)
Moderate to very poor (n (%))	55 535 (25.60)
NA (n (%))	2939 (1.35)
Risk of psychological distress	
None (''well'') (n (%))	134 976 (62.22)
Low to severe (n (%))	75 534 (34.82)
NA (n (%))	6422 (2.96)
Individual covariates	
Sex	
Men (n (%))	99 926 (46.06)
Women (n (%))	117 006 (53.94)
Age*	
19–24 (n (%))	9666 (4.46)
25–29 (n (%))	6423 (2.96)
30–34 (n (%))	8291 (3.82)
35–39 (n (%))	10 003 (4.61)
40–44 (n (%))	14 934 (6.88)
45–49 (n (%))	17 045 (7.86)
50–54 (n (%))	17 822 (8.22)
55–59 (n (%))	18 247 (8.41)
60–64 (n (%))	19 313 (8.90)
65–69 (n (%))	33 709 (15.54)
70–74 (n (%))	23 608 (10.88)
75–79 (n (%))	19 441 (8.96)
80–84 (n (%))	11 791 (5.44)
85–89 (n (%))	5095 (2.35)
90–94 (n (%))	1367 (0.63)
95+ (n (%))	177 (0.08)
Marital status	
Married/living together (n (%))	161 735 (74.56)
Single (n (%))	18 887 (8.71)
Divorced (n (%))	10 225 (4.71)
Widowed (n (%))	22 737 (10.48)
NA (n (%))	3348 (1.54)
Country of origin†	
Dutch (n (%))	197 462 (91.02)
Non-Dutch, western (n (%))	3535 (1.63)
Non-western (n (%))	15 935 (7.35)
Education level	
Low (n (%))	19 386 (8.94)
Middle 1 (n (%))	77 343 (35.65)
Middle 2 (n (%))	60 481 (27.88)
High (n (%))	52 610 (24.25)
NA (n (%))	7112 (3.28)
Physical activity‡	
Complies with none of exercise norms (n (%))	66 663 (30.73)
Complies with at least one of exercise norms (n (%))	132 689 (61.17)
NA (n (%))	17 580 (8.10)
Chronic disease	
No chronic diseases (n (%))	61 124 (28.18)
At least one chronic disease (n (%))	130 973 (60.38)
NA (n (%))	24 835 (11.45)
Alcohol use	
Never (n (%))	22 440 (10.34)
Former (n (%))	12 043 (5.55)
Current (n (%))	176 613 (81.41)
NA (n (%))	5836 (2.69)
Smoking	
Never (n (%))	82 553 (38.05)
Former (n (%))	84 064 (38.75)
Current (n (%))	36 124 (16.65)
NA (n (%))	14 191 (6.54)
Body mass index§	
Underweight (n (%))	2326 (1.07)
Normal (n (%))	95 240 (43.90)
Pre-obesity (n (%))	2326 (1.07)
Obesity I (n (%))	22 127 (10.20)
Obesity II (n (%))	4644 (2.14)
Obesity III (n (%))	1134 (0.52)
NA (n (%))	8600 (3.96)
Children	
No children (n (%))	139 605 (64.35)
Lives with children <18 years old (n (%))	45 439 (20.95)
Lives with children ≥18 years old (n (%))	16 092 (7.42)
NA (n (%))	15 796 (7.28)
Country level covariates	
Greenspace (NDVI) in 500 m buffer (mean (SD))¶	0.58 (0.09)
Neighbourhood socioeconomic status score (mean (SD))**	0.38 (1.01)

*Age was categorised into 5-year categories for <65 years old and into 10-year categories for ≥65 years old.
†Origin was defined as the country of birth of the mother (or that of the father if information on the mother was unavailable). Countries were grouped into western and non-western, except for the Netherlands which constitutes a separate category.
‡Nederlandse Norm Gezond Bewegen (NNGB) and Fitnorm are two Dutch common standards for healthy exercise that take into account the amount of time, frequency and intensity of physical activity. Participants were classified into two categories depending on whether they complied with 0='none' or 1='at least one' of these norms.
§Body mass index (BMI) categories were defined according to the WHO nutritional status, where underweight≤18.5, normal weight=18.5–24.9, pre-obesity=25.0–29.9, obesity class I=30.0–34.9, obesity class II=35.0–39.9 and obesity class III≥40.
¶The NDVI (Normalised Difference Vegetation Index) describes the amount of green vegetation using reflectance measured by satellites. Here, we used the average NDVI within 500 m of the participant's residence (values: 0–1) as calculated by Klompmaker *et al.*
**We used socioeconomic position as defined by the SCP (Sociaal en Cultureel Planbureau); it is a social status score taking into account average income, percentage of people with a low income, percentage of people with a low education and percentage of unemployed people in a postal code area.

20 datasets with 10 iterations. For the imputation models, we considered all variables included in the statistical models for the analyses (outcomes, potential confounders and total crop area in 500 m) and data on prescription of antidepressants, anxiolytics and hypnotic-sedative drugs in 2012, paid work and urbanisation degree, which were predictive of some of the imputed variables but were not included in the statistical models. Collinearity between predictors was measured by variance inflation factors using a cut-off of 3. Binary variables were imputed using

Table 2 ORs of self-reporting low to severe psychological distress and of self-reporting moderate to very poor health per increase in 1 hectare of area of (specific) treated-crop and their 95% CIs (full models)

Treated-crop	Buffer size (m)	Number of participants: Unexposed (0 hectares of crop)	Number of participants: Exposed (>0 hectares of crop)	OR (95% CI)*: Self-reported psychological distress	OR (95% CI)*: Self-perceived health
Maize	50	204 959 (94.5%)	11 973 (5.5%)	0.79 (0.59 to 1.05)	0.68 (0.49 to 0.96)
	100	190 279 (87.7%)	26 653 (12.3%)	0.94 (0.89 to 1.00)	0.90 (0.84 to 0.97)
	250	140 671 (64.8%)	76 261 (35.2%)	0.99 (0.98 to 1.00)	0.99 (0.98 to 1.00)
	500	75 816 (34.9%)	141 116 (65.1%)	1.00 (1.00 to 1.00)	1.00 (1.00 to 1.01)
Winter wheat	50	211 278 (97.4%)	5654 (2.6%)	1.06 (0.57 to 1.98)	0.53 (0.25 to 1.12)
	100	204 186 (94.1%)	12 746 (5.9%)	1.09 (0.96 to 1.23)	0.90 (0.77 to 1.05)
	250	178 060 (82.1%)	38 872 (17.9%)	1.02 (1.00 to 1.04)	0.99 (0.97 to 1.02)
	500	139 146 (64.1%)	77 786 (35.9%)	0.99 (0.99 to 0.99)	1.00 (0.99 to 1.00)
Summer barley	50	215 507 (99.3%)	1425 (0.7%)	0.94 (0.17 to 5.37)	0.15 (0.02 to 1.41)
	100	213 407 (98.4%)	3525 (1.6%)	0.92 (0.64 to 1.33)	0.79 (0.50 to 1.23)
	250	202 898 (93.5%)	14 034 (6.5%)	0.97 (0.91 to 1.03)	0.99 (0.92 to 1.06)
	500	176 862 (81.5%)	40 070 (18.5%)	0.97 (0.96 to 0.98)	0.99 (0.97 to 1.00)
Summer wheat	50	215 323 (99.3%)	1609 (0.7%)	0.57 (0.09 to 3.54)	0.41 (0.04 to 3.79)
	100	213 107 (98.2%)	3825 (1.8%)	0.85 (0.58 to 1.24)	0.70 (0.44 to 1.10)
	250	202 053 (93.1%)	14 879 (6.9%)	0.96 (0.91 to 1.02)	0.95 (0.88 to 1.02)
	500	174 236 (80.3%)	42 696 (19.7%)	0.98 (0.97 to 0.99)	0.99 (0.97 to 1.00)
Other cereals	50	215 758 (99.5%)	1174 (0.5%)	0.75 (0.10 to 5.37)	0.92 (0.10 to 8.78)
	100	213 659 (98.5%)	3273 (1.5%)	1.02 (0.68 to 1.51)	0.90 (0.56 to 1.44)
	250	202 758 (93.5%)	14 174 (6.5%)	1.03 (0.97 to 1.10)	0.94 (0.87 to 1.01)
	500	177 844 (82.0%)	39 088 (18.0%)	1.00 (0.99 to 1.02)	1.02 (1.00 to 1.03)
Potatoes for consumption	50	211 606 (97.5%)	5326 (2.5%)	1.16 (0.43 to 3.13)	0.82 (0.25 to 2.68)
	100	204 719 (94.4%)	12 213 (5.6%)	1.11 (0.91 to 1.35)	1.02 (0.81 to 1.29)
	250	178 343 (82.2%)	38 589 (17.8%)	1.00 (0.97 to 1.03)	1.00 (0.96 to 1.04)
	500	136 573 (63.0%)	80 359 (37.0%)	0.99 (0.99 to 1.00)	1.00 (0.99 to 1.00)
Potatoes for starch	50	216 525 (99.8%)	407 (0.2%)	0.06 (0.00 to 1.04)	1.93 (0.09 to 42.32)
	100	216 107 (99.6%)	825 (0.4%)	0.61 (0.35 to 1.06)	0.95 (0.49 to 1.83)
	250	214 709 (99.0%)	2223 (1.0%)	0.98 (0.89 to 1.08)	0.99 (0.88 to 1.11)
	500	211 675 (97.6%)	5257 (2.4%)	0.99 (0.98 to 1.01)	1.00 (0.99 to 1.01)
Seed potatoes	50	215 616 (99.4%)	1316 (0.6%)	1.03 (0.14 to 7.46)	0.39 (0.03 to 4.62)
	100	214 192 (98.7%)	2740 (1.3%)	1.02 (0.70 to 1.49)	0.80 (0.50 to 1.28)
	250	208 320 (96.0%)	8612 (4.0%)	1.00 (0.94 to 1.06)	0.95 (0.88 to 1.02)
	500	196 123 (90.4%)	20 809 (9.6%)	0.99 (0.98 to 1.00)	0.98 (0.97 to 0.99)
Beets	50	212 462 (97.9%)	4470 (2.1%)	1.31 (0.42 to 4.12)	0.35 (0.09 to 1.40)
	100	206 307 (95.1%)	10 625 (4.9%)	1.04 (0.83 to 1.31)	0.73 (0.55 to 0.96)
	250	181 942 (83.9%)	34 990 (16.1%)	0.98 (0.95 to 1.02)	0.95 (0.91 to 0.99)
	500	141 899 (65.4%)	75 033 (34.6%)	0.99 (0.98 to 0.99)	1.00 (1.00 to 1.01)
Ornamental plants and tree nurseries	50	215 257 (99.2%)	1675 (0.8%)	1.90 (0.90 to 4.01)	0.76 (0.32 to 1.81)
	100	212 927 (98.2%)	4005 (1.8%)	1.06 (0.90 to 1.25)	0.90 (0.74 to 1.08)
	250	202 567 (93.4%)	14 365 (6.6%)	1.00 (0.97 to 1.03)	1.00 (0.97 to 1.03)
	500	177 835 (82.0%)	39 097 (18.0%)	1.00 (0.99 to 1.00)	1.01 (1.00 to 1.01)
Vegetables	50	214 255 (98.8%)	2677 (1.2%)	0.76 (0.34 to 1.72)	0.78 (0.31 to 2.00)
	100	210 653 (97.1%)	6279 (2.9%)	0.95 (0.81 to 1.12)	0.87 (0.72 to 1.05)
	250	194 848 (89.8%)	22 084 (10.2%)	0.99 (0.97 to 1.02)	0.97 (0.94 to 1.00)
	500	162 344 (74.8%)	54 588 (25.2%)	1.00 (0.99 to 1.00)	1.01 (1.00 to 1.01)
Fruit	50	214 867 (99.0%)	2065 (1.0%)	0.96 (0.55 to 1.67)	0.84 (0.45 to 1.60)
	100	211 778 (97.6%)	5154 (2.4%)	1.00 (0.88 to 1.13)	0.91 (0.79 to 1.06)
	250	200 303 (92.3%)	16 629 (7.7%)	0.99 (0.97 to 1.01)	1.00 (0.98 to 1.02)
	500	180 137 (83.0%)	36 795 (17.0%)	0.99 (0.99 to 1.00)	1.00 (1.00 to 1.01)
Flower bulbs	50	215 774 (99.5%)	1158 (0.5%)	1.59 (0.49 to 5.16)	1.95 (0.52 to 7.29)
	100	214 311 (98.8%)	2621 (1.2%)	1.22 (0.95 to 1.57)	1.28 (0.96 to 1.71)
	250	208 613 (96.2%)	8319 (3.8%)	1.01 (0.97 to 1.06)	1.04 (0.99 to 1.09)
	500	196 249 (90.5%)	20 683 (9.5%)	0.99 (0.99 to 1.00)	0.99 (0.99 to 1.00)

continued

Table 2 continued

Treated-crop	Buffer size (m)	Number of participants		OR (95% CI)*	
		Unexposed (0 hectares of crop)	Exposed (>0 hectares of crop)	Self-reported psychological distress	Self-perceived health
'All crops'	50	195 784 (90.3%)	21 148 (9.7%)	0.97 (0.82 to 1.15)	0.77 (0.63 to 0.93)
	100	173 195 (79.8%)	43 737 (20.2%)	1.00 (0.96 to 1.03)	0.93 (0.89 to 0.97)
	250	110 810 (51.1%)	106 122 (48.9%)	1.00 (0.99 to 1.00)	0.99 (0.98 to 1.00)
	500	168 088 (77.5%)	48 844 (22.5%)	1.00 (1.00 to 1.00)	1.00 (1.00 to 1.00)

The referent ('unexposed') group in all models was participants with zero hectares of (specific) crop within 500 m of their residences.
*Models were adjusted for: adjusted for the area of the considered crop that remained until 500 m ('complementary donut'), age, sex, body mass index (BMI), country of origin, marital status, educational level, living with children, having a chronic condition, presence of other crops within 500 m of the participant's residence (except for when 'all crops' was the exposure), physical activity, alcohol status, smoking status, neighbourhood socioeconomic position and Normalised Difference Vegetation Index within 500 m of the participant's residence.

logistic regression and continuous and categorical variables were imputed using predictive mean matching.

Main analysis

We applied logistic regression, building four models with increasing covariate adjustment for each crop-specific land use buffer and outcome combination:

- *Basic model*, adjusted for the area of the considered crop that remained until 500 m ('complementary donut'), age and sex.
- *Individual confounders model*, consisting of basic model and body mass index, country of origin, marital status, educational level, living with children, having a chronic condition and the presence (yes/no) of other crops within 500 m of the participant's residence (except for when 'all crops' was the exposure).
- *Lifestyle confounders model*, extending the individual model with physical activity,[23] alcohol status and smoking status.
- *Full model*, adding neighbourhood socioeconomic position[24] and Normalised Difference Vegetation Index, a measure of green space[25] within 500 m of the participant's residence to lifestyle models (see table 1 for confounder categories).

Sensitivity and additional analyses

We performed four sensitivity analyses on full models. First, we restricted analysis to participants living in a rural setting (<1000 addresses/km^2 at neighbourhood level) to assess potential bias from a semi-urban environment. Second, since changes in address may be related to physical or mental health problems, we excluded participants that changed address during 2009–2012. Third, we restricted the analysis to complete cases to assess the impact of using imputed datasets. Fourth, in order to exclude a possible influence of occupational exposure, we linked microdata on employment and self-employment available from CBS to identify and exclude people that worked for at least 1 year in agriculture in the period 2009–2012. Furthermore, because the epidemiology of PD differs between women and men, we conducted a stratified analysis by sex.[26] Finally, since the elderly were oversampled in the survey we conducted an analysis stratified by age (<65 vs 65+ years old).

For completeness we also conducted additional analyses using different exposure metrics. We calculated the area of cultivated crops around the residence as 'donuts with holes' (<100 m, 100–250 m and 250–500 m) that we used as continuous and as binary ('presence'/'absence' of crop) variables in the analyses. We also computed the average distances to nearest crop (categorised into <50 m, 50–100 m, 100–250 m, 250–500 m, ≥500 m) in 2009–2012.

Statistical analyses were performed in R V.3.4.1 (2017-06-30).

RESULTS

Table 1 describes the study population's demographic characteristics. We included 216 932 participants (46% men, median age 61); 78 355–78 522 (36.12%–36.20%) participants had low to severe risk of PD and 56 615–56 688 (26.10%–26.13%) had moderate to very poor SPH, depending on the imputed data set. There were 21 148 (9.75%), 43 737 (20.16%), 106 122 (48.92%) and 168 088 (77.48%) people exposed to at least one type of treated-crop in the 50, 100, 250 and 500 m buffer, respectively. We observed mostly low (Pearson correlation <0.39) correlations between the buffer areas of crops, except for the moderate correlations between winter wheat, potatoes for consumption and beets (Pearson correlations ranging from 0.56 to 0.61), which are grown in a rotation scheme.

Table 2 shows the number of unexposed and exposed participants per buffer size and type of crop. For some of the less prevalent crops, such as potatoes for starch and other cereals, the number of exposed people in the smaller buffers was very low, resulting in wide confidence intervals of the estimates. This table also displays the OR per increase in 1 hectare of area of (specific) crop and their 95% CIs for the full models. We found no clear evidence of associations between presence of specific crops and SPD and SPH. We observed overall patterns of OR below unity for SPH, with increasing gradient of effect sizes from the smaller to the largest buffers. Nevertheless, none of these associations showed statistically significant results consistently among the four buffers. Solely the association between 'all crops' and SPH showed statistically significant results in the 50, 100 and 250 m buffers, with OR ranging from 0.77 (0.63 to 0.93) in the 50 m buffer to 0.99 (0.98 to 1.00) in the 250 m buffer. Increasing covariate adjustment in the 50 m and 100 m buffer models resulted in effect estimates that were, in general, closer to unity and, in rare cases, change in direction of effect (online supplemental tables S1 and S2). Furthermore, higher levels of adjustment resulted in loss of statistical significance across all buffer models. Neither sensitivity (online supplemental table S3 and S4) nor stratified (online supplemental table S5 and S6) analyses showed material changes in effect estimates. Results using the donuts and distance exposure metrics, shown in online supplemental table S7 and S8, did not change our interpretation of the findings.

DISCUSSION

We used a cross-sectional national survey to study the association between presence of crops near residences and SPD and SPH. Analyses did not indicate that living close to treated-crops was associated with increased risks of SPD or poorer SPH. In fact, we observed overall negative non-significant associations.

The use of the national Public Health Monitor survey allowed us to include a large population of over 200 000 participants, making it one of the largest studies on SPD and residential pesticide exposure. It also enabled for adjustment of a range of relevant lifestyle aspects, although possibly some bias might have been introduced due to self-reporting and average response rate of 47%. We were also able to adjust for the presence of green space in the living environment, which previously has been associated with better mental and physical health in the Public Health Monitor 2012.[25 27 28] Furthermore, although we did not have exposure data based on measurements, we were able to estimate proxies of exposure at individual level that represented the specific pesticide mixtures and farming methods used in these crops.

Although pesticide exposure was not measured, it was assessed at individual level based on the area of crops around residences. This has been shown previously to be suitable in estimating pesticide levels in residences located near crops,[29] but entail important assumptions and limitations that could have resulted in exposure misclassification. First, we did not consider participants' time-activity patterns, their presence at the residence during spraying events (which may influence exposure levels) or other relevant locations for exposure, such as the workplace. Of all, workplace is probably the most important alternative source of exposure and our sensitivity analysis excluding agricultural workers did not show substantial differences in effect estimates from the main analysis. Domestic use of pesticides or nutritional exposure were not considered but are unlikely to differ substantially within the short distances from treated agricultural fields considered in this study, abating residual confounding. We also did not account for wind speed and direction, which affect spread of pesticides applied in fields. In the Netherlands, prevailing wind is West to South West, but Eastern winds are generally associated with lower wind speed and therefore also important for stable lower spread of pesticides at short distances. In this study we used symmetric (squared) buffers around residences since the best non-symmetrical buffer is difficult to determine. Finally, since no information was available, we were unable to differentiate between conventional and organic crops, but the latter comprised only 1.8% of the total area of investigated crops the Netherlands in 2015.[30]

Because a growing season only lasts for a limited time per year, living at a specific address only for a short period of time increases uncertainty in the exposure estimates. We therefore included people that moved at most once in the period 2009–2012 to minimise uncertainty around exposure that arises from multiple address changes. This resulted in the exclusion of only a minor proportion of the study population (3.5% of the original number of participants in the Public Health Monitor 2012, figure 1). Changes in address may be related to the investigated outcomes, introducing another source of bias in the study. Unfortunately, we were unable to determine the reasons for moving addresses and we recognise that people might move to residences both further away or nearer to more rural areas for health reasons. Still, a sensitivity analysis restricted to people that never moved addresses in 2009–2012 and a sensitivity analysis restricted to people living in rural areas (<1000 addresses per km^2) did not show major changes in estimates. Outcome misclassification could have been aggravated by the cross-sectional design of the study since we were unable to establish the temporality of onset of the outcomes, which might have occurred before exposure.

Oversampling of elderly could have left the study vulnerable to selection bias. Nevertheless, our stratified analyses did not indicate substantial differences in risk estimates between people under and above 65 years of age. Similarly, even though women have higher risks of PD, no major differences were found in the OR obtained for women and men in a stratified analysis by sex.

Our findings show no associations between proximity to pesticide-treated crops and SPD. This is in line with results from longitudinal studies that found no association between cumulative exposure from pesticide usage among farmers' families and depression.[8–10] Nevertheless, exposure and outcome misclassification were important limitations in these studies, mainly because information was collected via self-report. In contrast, the same studies reported increased risks of depression when pesticide exposure was deemed high enough to induce poisoning. The link between exposure to poisoning inducing pesticide concentrations and increased risk of depression was also reported in a cross-sectional study among farmers and their wives.[7] Two other studies reported positive associations between depression and pesticide exposure as well. One suggested that residential proximity to organophosphate application sites was associated with progression of depressive symptoms in a cohort of Parkinson's disease patients.[31] The other, an ecological study, reported higher rates of depression among agricultural workers living in areas with intense pesticide application when compared with city dwellers.[6]

We used SPH as an extension of SPD in this study, since SPH is an important component of mental health. SPH has been suggested to be a mediator of the relationship between physical and mental health and shown to be an important indicator of current health status and predictor of depression and mortality.[32 33] We observed that OR for SPH were more often below unity for study participants living close to treated-crops. One would expect an equal ratio between risk estimates above and below unity if presence of crops had no effect on these outcomes. It is unclear why this 'protective' effect was observed, but it may be an indication of uncontrolled bias. Furthermore, given the limitations described above regarding our exposure proxy, it may be possible that we were unable to detect weak to moderate signals. On the other hand, previous studies have also shown negative associations to environmental exposures among the Dutch rural population, namely lower (non-accidental) mortality rates and respiratory problems.[34 35] We are unable to provide data-driven explanations for the (statistically non-significant) negative associations found. In the Netherlands, socioeconomic position distribution is relatively similar across all areas of urbanisation degree. Tentative explanations could include exposure misclassification, uncontrolled bias and the fact that rural populations in the Netherlands may have a better quality of life (better air quality, lower costs, less stress, perhaps more physical activity). It remains, however, unclear why we see this trend in such a small spatial scale (500 m), that is, among the rural to semi-urban population itself.

In conclusion, this study provides no evidence that residential proximity to pesticide treated-crops is associated with PD or poorer perceived health. In fact, we observed an overall indication of lower risks of poorer SPH. Exposure and outcome misclassification remain important limitations in studies assessing these associations and hamper interpretation of results, including this one.

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Data availability statement The datasets on buildings and addresses (Basisregistratie Adressen en Gebouwen, BAG) on land use (Basisregistratie Gewaspercelen) were derived from the public domain. These geodatabases are available every year at https://data.overheid.nl/dataset/basisregistratie-adressen-en-gebouwen--bag- and http://www.nationaalgeoregister.nl/geonetwork/srv/dut/catalog.search#/metadata/b812a145-b4fe-4331-8dc6-d914327a87ff. Data on participants, including outcome and individual covariates included in the statistical models, cannot be made publicly available due to privacy protection of individuals included the study. The data are accessible via de Microdata services from CBS. https://www.cbs.nl/en-gb/our-services/customised-services-microdata/microdata-conducting-your-own-research. Neighborhood-level covariates were also available within the secure environment of CBS and linkable to individuals via their address.

ORCID iDs
Mariana Simoes http://orcid.org/0000-0002-2555-5366
Roel Vermeulen http://orcid.org/0000-0003-4082-8163

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