Associations between dietary pesticide residue mixture exposure and mortality in a population-based prospective cohort of men and women

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ABSTRACT

Background: There is a concern that pesticide residues, regularly detected in foods, might pose a health risk to the consumer, but epidemiological evidence is limited. We assessed the associations between dietary exposure to a mixture of pesticide residues and mortality.

Methods: Food consumption was assessed in 68,844 participants from the Swedish Mammography Cohort and the Cohort of Swedish Men, 45–83 years at baseline (1997). Concentrations of pesticide residues detected in foods on the Swedish market (1996–1998), mainly fruits and vegetables, were obtained via monitoring programs. To assess mixture effects, we summed per food item the ratios of each single pesticide mean residue concentration divided by its acceptable daily intake to create for each participant a Dietary Pesticide Hazard Index (adjusted for energy intake and expressed per kilogram of body weight). Multivariable-adjusted Cox proportional hazards models were used to estimate hazard ratios (HR) and 95 % confidence intervals (95 %CI).

Results: During 15 years of follow-up (1998–2014), a total of 16,527 deaths occurred, of which 6,238 were caused by cardiovascular disease (CVD) and 5,364 by cancer. Comparing extreme quintiles of Dietary Pesticide Hazard Index, the highest category was inversely associated with CVD mortality HR, 0.82 (95 % CI, 0.75–0.91). In analyses stratified by high/low Dietary Pesticide Hazard Index, similar inverse associations were observed by increasing fruit and vegetable consumption.

Conclusions: We observed no indications that dietary exposure to pesticide residue mixtures was associated with increased mortality, nor any clear indications that the benefits of fruit and vegetable consumption on mortality was compromised. Yet, our results need to be interpreted with caution.

1. Introduction

Pesticides are used worldwide to protect crops from disease and inestations to maintain harvest of high quality and agricultural yields. Being designed to affect living organisms, the global use of pesticides comes at a cost, and direct accidental, occupational or by-stander pesticide poisoning is a problem (Karunarathne et al., 2021; de Graaf et al., 2022), as is the consequences for the planetary health (Jepson et al., 2020; Lykogianni et al., 2021; Singh et al., 2023). Exposure of the general population to pesticides occurs primarily through eating food and, in some areas also via drinking water contaminated with pesticide residues (Jensen et al., 2022; EFSA, 2022). To ensure that the food is safe for consumers, maximum residue levels (MRLs) are established. Currently, the risk assessment of the presence of pesticide residues in food and the establishment of MRLs (highest level of a pesticide residue that is legally tolerated in or on food or feed) are made substance by substance. However, there is a concern regarding the potential health consequences of long-term low-level exposure to a mixture of pesticide residues commonly present in certain foods such as vegetables and fruits. Although the single residues generally are far below MRLs and levels where negative health effects are considered to occur, few studies have, based on the individual estimated exposure, explored the...
associations with the overall development of chronic diseases or mortality (Chiu et al., 2019; Chiu et al., 2018; Wesselink et al., 2020; Sandoval-Insausti et al., 2021; Sandoval-Insausti et al., 2022; Rebouillat et al., 2022; Rebouillat et al., 2021).

The assessment of dietary pesticide exposure and its potential link to human health is complex. Based on data from monitoring programs it is clear that there is a large variation within and between foods in the total number, concentrations as well as the toxicity of specific pesticides detected. Thus, in terms of toxicity, it is not optimal to use a simple sum of the concentrations to estimate the pesticide exposure relevant to human health. Moreover, the dominating source of the exposure to pesticide residues is fruits and vegetables, whose adequate consumption is of great importance in the prevention of major chronic diseases (Lichtenstein et al., 2021; WCRF, 2018; Vaduganathan et al., 2022; GBD Risk Factors Collaborators, 2020). This means that a high consumption of these foods with documented beneficial health effects may mask any detrimental effect of the pesticide residues, and, at the same time, pesticide residues in fruits and vegetables may mitigate the full beneficial effect of these foods.

We aimed at evaluating the associations between dietary exposure to
pesticide residues and all-cause and cause-specific mortality in a large population-based prospective cohort of men and women. For this purpose, we calculated a Dietary Pesticide Hazard Index based on the rationale that this index better mirrors the toxic potency of the mixture of single pesticide residues detected in each food, rather than their presence and actual concentrations. We further explored whether the pesticide residues influenced the observed benefits of fruit and vegetable consumption on mortality.

2. Methods

2.1. Study population

The present study included participants from the Swedish Mammography Cohort (SMC) and the Cohort of Swedish Men (COSM) (Harris et al., 2013), part of the Swedish Infrastructure for Medical Population-based Life-course and Environmental Research (SIMPLER; https://www.simpler4health.se). In short, all women born 1914 to 1948 in two counties were recruited to SMC in 1987–90 (74 % response rate). In 1997, a detailed questionnaire and food frequency questionnaire (FFQ) (Messerer et al., 2004) was sent to all participants still alive and living in the study area, and 39,227 responded (70 % response rate). At the same time, COSM was initiated, when all men in two counties, born 1918 to 1952, were recruited, 48,850 responded (49 % response rate). The 1997-baseline questionnaire was completed by 84,890 men and women, 45–83 yrs. old. The reproducibility and validity of the 96-item FFQs have been assessed for foods, nutrients, dietary supplements, glycaemic index and glycaemic load by comparison with multiple 24-hour recall interviews and/or diet records as outlined by Harris et al (Harris et al., 2013). From the baseline population, we excluded individuals with a previous diagnosis of cancer, CVD and type 2 diabetes, as well as those with implausible energy intakes and missing information on weight as detailed in Fig. 1. Hence, the final study population involved 32,542 women and 36,302 men (total n = 68,844) (Fig. 1). The study was approved by the Regional Ethical Review Board at Karolinska Institutet (Stockholm, Sweden), and a return of completed questionnaire was considered informed consent.

2.2. Baseline assessment of diet, pesticide residue exposure and covariates

The semi-quantitative FFQ completed at baseline in 1997, in which participants could choose from eight predefined consumption categories (never, 1–3/month, 1–2/week, 3–4/week, 5–6/week, 1/day, 2/day, and 3/day), was used to assess average consumption of foods over the preceding year.

To estimate the dietary exposure to pesticides we created a pesticide residue database. Based on the Swedish Food Agency’s pesticide monitoring program, we collected data on pesticide residues that were measured in food on the Swedish market around the baseline period (1996–98). The monitoring program is risk based and mainly target those food items (EFSA, 2015) that contribute most to the exposure in the population and thus, the foods included were the main fruits, berries, vegetables, and cereals in Swedish diet (in total 9862 samples of 51 food items, and about 400 analytes were covered by the analytical methods). For each single food item, we estimated, in a next step, the mean concentrations of every single pesticide residue detected. If at least one pesticide residue was detected above the limit of quantification (LOQ) for a food item, the corresponding levels < LOQ were then assigned the value of LOQ/2. Concentrations were assumed to be zero if no sample had pesticide residues detected > LOQ for that specific pesticide/commodity combination. For citrus and banana, a general peeling factor of 0.1 was used to get a more realistic estimate for the edible parts.

The calculated mean concentration of each specific pesticide residue was then divided by its respective acceptable daily intake (ADI) (Supplemental Table 1). The ADI, set by the European Commission based on the European Food Safety Authority’s risk assessment (if missing, we used the ADIs set by Joint FAO/WHO Meeting on Pesticide Residues or United States Environmental Protection Agency), is the amount of each pesticide that can be ingested daily over a lifetime without an appreciable health risk. In this way, we obtained a risk index ratio for each single pesticide detected in the included food items (fruits, vegetables and cereals), which was considered to better mirror the potency of toxicological effects than just using the number of pesticides detected or the mean concentrations. All estimated single ratios of individual pesticide residues (up to 40 per single edible food item) were then summed up for each food item to obtain a Pesticide Residue Risk Index Ratio expressed per kg of the specific food and reflecting total toxicity of a mixture of pesticide residues (Supplemental Table 1). The most frequently detected pesticide families contributing to the the Pesticide Residue Risk Index Ratio were organophosphates, carbamates, organochlorines, dithiocarbamates and pyrethroids.

To estimate an individuals exposure to pesticide residues, first we used the participant’s reported food consumption frequency from the FFQ, and age and sex-specific portion sizes (Harris et al., 2013), to estimate the amount of each specific food item consumed. Second, we multiplied the intake of each specific food by its specific Pesticide Residue Risk Index Ratio. Then we summed up all these values and divided by body weight of the participant to create a dietary pesticide residue risk index, which was expressed per kilogram (kg) of body weight and adjusted to the total energy intake (sex-specific) using the residual method (Willett and Stampfer, 1986). The estimated pesticides residue risk index ratio resembles the hazard index (used hereafter and called Dietary Pesticide Hazard Index) (Boobis et al., 2008; Reifstrup et al., 2010) This is a conservative method based on the dose addition model, reflecting exposure to a combined mixture of pesticide residues. It is assumed that when the Hazard Index is < 1, the residue exposure is unlikely to cause adverse health effects. The formula for deriving the Dietary Pesticide Hazard Index is shown in the Supplemental material.

As a measure of healthy eating habits, we used the FFQ to construct a modified Mediterranean diet score based on intake of eight food groups (fruits and vegetables, legumes and nuts, whole grain/fibre-rich foods, fermented dairy foods, fish, red and processed meat (as a negative component), and olive/rapeseed oil) and alcohol in moderation (10–30 g/day for men and 5–15 g/day for women), as previously described in more detail (Tektonidis et al., 2015; Tektonidis et al., 2016). For this paper, however, we excluded the two food groups fruit and vegetables, and whole grain since these are the major sources of pesticides, ending up with six food groups and the corresponding scores ranging from 0 to 6. Via the self-administered baseline questionnaire, we obtained information about education, family history of myocardial infarction in parents or siblings before the age of 60 years, presence of hypertension, presence of hypercholesterolemia, daily walking/cycling, leisure time inactivity, smoking status and waist circumference.

2.3. Case ascertainment

Information on death and causes of death was ascertained through linkage of the two cohorts to the Swedish Cause of Death Register at the National Board of Health and Welfare considered almost complete. Using the International Classification of Diseases, 10th Revision (ICD-10) we applied the codes I00-I78 for CVD-specific mortality and C00-C97 for cancer-specific mortality.

2.4. Statistical analyses

We categorized the participants into cohort-specific (i.e. by sex) quintiles of Dietary Pesticide Hazard Index at baseline in the main analyses. Participants were followed from January 1st, 1998 until the date of death or end of follow-up (throughout 2014), whichever came first. Associations of Dietary Pesticide Hazard Index with total and CVD- and cancer-specific mortality were assessed using Cox proportional hazards regression models, with attained age (1-year units) as the underlying
timescale, estimating hazard ratios (HR) with 95 % confidence intervals (CI). We additionally examined the association between fruit and vegetables intake and mortality risk stratifying by low (< median) and high (≥ median) Dietary Pesticide Hazard Index, to explore any indications of whether a high Index compromised the health benefits of fruit and vegetable consumption.

Summarized HR for men and women were obtained using the ‘strata’ command option in Stata. Multivariable-adjusted models included the following baseline potential confounders: attained age (years), education level (<12 or >12 y), self-reported family history of myocardial infarction (yes/no), hypertension (yes/no), hypercholesterolemia (yes/no), daily walking/cycling (<40 min/day or >40 min/day), leisure-time inactivity (<2 h/day or >2 h per day), smoking status (current, former, never), waist circumference (94 cm, 94–102, >102 cm), modified Mediterranean diet score (3 categories low (0–2), medium (3–4), high (5–6)), dietary fibre intake (quintiles, g/day) and energy intake (quintiles, kcal/day).

In additional analyses, we stratified the cohort by below and above the median of the Dietary Pesticide Hazard Index to assess the associations between fixed number of servings of fruit and vegetables and mortality. As expected, in this analysis the cutoff for the reference group, representing the lowest number of daily servings of fruit and vegetables, could not be set at the same frequency of consumption in both strata (i.e., few participants had a high Dietary Pesticide Hazard Index and at the same time a low consumption of fruit and vegetables). Consequently, the cutoffs for the number of daily servings in the reference groups were ≤ 1 at low Dietary Pesticide Hazard Index, while it was set to ≤ 2 at Dietary Pesticide Hazard Index.

Missing information on components of the modified Mediterranean diet score were treated as no consumption, while we fitted the multivariable-adjusted models including other missing values in a separate category. Missing information was generally low, except for waist circumference (17 %), daily walking/cycling (16 %) and family history of myocardial infarction (23 %). The adequacy of proportional hazards assumption was checked by using Schoenfeld residuals and no evidence of departure from this assumption was observed for the main exposures. All analyses were run in Stata version 14.0 (StataCorp LP), with statistical significance set at the two-sided 0.05 level.

3. Results

In total 225 pesticides were detected in at least one food sample of fruits, vegetables and cereals sampled at baseline in 1996–1998. As shown in Supplemental table 1, the food items with the highest Pesticide Residue Risk Index Ratio (mean pesticide residue levels/ADI) were grapes and bell peppers followed by pears, apples, and cucumber. For cereals, the Pesticide Residue Risk Index Ratio was considerably lower (rice = 44; wheat and rye = 14) than for fruits and vegetables (e.g., grapes = 657; pear and apple ~ 450; sweet pepper = 487; cucumber = 409). In Supplemental table 2, the 20 pesticides with the highest contribution to the total Residue Risk Index Ratio per kilogram of foods are listed. Higher Pesticide Residue Risk Index Ratios, were due to higher pesticide concentrations or a lower ADI value.

Within our study population of 68,844 men and women, when consumption data were included in the calculation, the median Dietary Pesticide Hazard Index was 0.9 (5–95 percentiles 0.3–2.2). The main contributors to Dietary Pesticide Hazard Index were apples/pears, which bring on the 30 % of the Index, followed by tomatoes, a mixture of fruits (including grapes), berries and lettuce, which all together are the source of another 30 % of the Dietary Pesticide Hazard Index (Fig. 2). Those in the highest quintile of Dietary Pesticide Hazard Index (mean 1.9 ± 0.6) consumed on average 7 fruits and vegetables per day, as compared to the 2 servings consumed in the lowest quintile. As expected, the Dietary Pesticide Hazard Index correlated with the modified Mediterranean diet score: the greater adherence to the diet the greater exposure to pesticides. There were no other major differences in age-standardized personal characteristics across quintiles of the Dietary Pesticide Hazard Index, but those in the highest quintile had a higher education, were slightly more physically active, less often smokers and had a smaller waist than those in the lowest quintile (Table 1).

A total of 16,527 deaths occurred during an average of 15 years of follow-up (1,064,062 person-years), of which 6,238 were caused by CVD and 5,364 by cancer. In multivariable-adjusted models, the Dietary Pesticide Hazard Index was inversely associated with all-cause mortality (HR 0.86, 95 % CI 0.81–0.90), with CVD mortality (HR 0.82, 95 % CI 0.75–0.90) and with cancer mortality (HR 0.82, 95 % CI 0.75–0.91), comparing the highest quintile of the Dietary Pesticide Hazard Index with the lowest (Table 2). No appreciable difference in the results were observed after either excluding from the baseline population those with self-reported hypertension and high cholesterol (n = 14,438), or by excluding from the model the corresponding covariates (Supplemental Tables 3a–b).

We further stratified the cohort by the median Dietary Pesticide Hazard Index and assessed the associations between fixed servings of fruit and vegetables and mortality (Table 3). Clear inverse associations were observed at low Dietary Pesticide Hazard Index for total and cardiovascular mortality, while the inverse associations observed at high Dietary Pesticide Hazard Index (with a higher consumption in reference group) were not statistically significant. No associations were observed for cancer mortality in either strata.

4. Discussion

In this large population-based cohort with a long follow-up, we estimated the combined toxic potential of the exposure to pesticide mixture via food. We observed no indications that the Dietary Pesticide Residue Index exposure via plant-based food was associated with increased mortality, rather the opposite. This could indicate that the estimated combined exposure might be low enough to not affect the population health, as well as due to the well-established beneficial effects on health of fruit and vegetable consumption. Although there was no clear indication that the pesticide exposure compromised the health effects of fruit and vegetable consumption, we must be cautious in the interpretation of our findings, giving the complexity of the exposure assessment of pesticides residues in food.

A few prospective cohort studies have estimated the exposure to pesticide residues from food in relation to health outcomes in the general population. Chiu et al, 2018 observed higher consumption of fruit and vegetables.
and vegetables with a high-pesticide residue score to be associated with lower probabilities of pregnancy and live birth following infertility treatment (Chiu et al., 2018). In this study, they created a Pesticide Residue Burden Score based on the sum of the tertiles of each of three measures of contamination: (1) the percentage of samples tested with any detectable pesticides, (2) the percentage of samples tested with pesticides exceeding the tolerance level, and (3) the percentage of samples with 3 or more individual detectable pesticides (the US Department of Agriculture Pesticide Data Program 2006–2015). A Pesticide Residue Burden Score of 4 or greater (on a scale of 0 to 6) was classified as high pesticide residue exposure and subsequently assigned to 14 fruit and vegetables. This Pesticide Residue Burden Score has been validated against urinary biomarkers (Hu et al., 2016; Chiu et al., 2018) and also used to assess incidence of coronary heart disease (Chiu et al., 2019), cancer (Sandoval-Insausti et al., 2021) and mortality (Sandoval-Insausti et al., 2022), showing no overall associations. Common was however, that high consumption of fruits and vegetables with low Pesticide Residue Burden Score was inversely associated with coronary heart disease and mortality (Chiu et al., 2019; Sandoval-Insausti et al., 2022) but not with cancer (Sandoval-Insausti et al., 2021), while those fruit and vegetables with a high Pesticide Residue Burden Score was not associated with these outcomes. Potentially this indicates a more beneficial effect from fruit and vegetables with lower content of pesticide residues for some of the outcomes studied, in accordance with the well-documented health benefits of these foods (Lichtenstein et al., 2021; WCRF, 2018; Vadgama et al., 2022; GBD Risk Factors Collaborators, 2020). This is in line with our results for all-cause and CVD mortality at a low Dietary Pesticide Residue Index, while at a high Dietary Pesticide Residue Index (with a higher consumption in the reference category), the inverse associations were slightly attenuated in our study, because of different regulatory framework and approaches to pesticide regulation in the US as compared to the European Union (EU).
Table 3
Hazard ratios (HR) for total- and cause-specific mortality according to fixed servings of fruit and vegetables consumption, stratified by low and high Dietary Pesticide Hazard Index in the Swedish Mammography Cohort and the Cohort of Swedish Men (N = 68,844).

<table>
<thead>
<tr>
<th>Fruits and vegetables consumption (servings/day)</th>
<th>Low dietary pesticide hazard index</th>
<th>High dietary pesticide hazard index</th>
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<tr>
<td>Categories of fruit and vegetables intake</td>
<td>Low dietary pesticide hazard index</td>
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<td>Categories of fruit and vegetables intake</td>
<td>Low dietary pesticide hazard index</td>
<td>High dietary pesticide hazard index</td>
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1 Energy-adjusted expressed per kg body weight.
2 The reference group was increased from <1 to ≤ 2 daily servings of fruit and vegetables. 3 Stratified by cohort and adjusted for attained age (years), education level (<12 or > 12 y), family history of myocardial infarction before the age of 60 years (yes/no), hypertension (yes/no), hypercholesterolemia (yes/no), daily walking/cycling (<40 min/day or > 40 min/day), daily leisure-time inactivity (<2 h/day or > 2 h per day), smoking status (current, former, never), waist circumference (<80, 80-87, >87 cm; <94, 94-102, >102 cm), dietary fiber intake (quintiles), energy intake (quintiles, kcal/day), modified Mediterranean diet without fruit and vegetables and non-refined high fibre grains, as scored items (0-6 categorized into low, medium or high adherence).

EU/Sweden.

Based on data from a study in a French population, Rebouillat et al., used Non-negative Matrix Factorization to assess the association between pesticide exposure and incidence of postmenopausal breast cancer (Rebouillat et al., 2021) and diabetes type 2 (Rebouillat et al., 2022). One of the factor components (reflecting exposure to chlorpyrifos, imazalil, malathion, thiabendazole) was associated with increased cancer risk among overweight women and borderline increased risk of type 2 diabetes, while another factor component (reflecting low pesticides mixtures with cancer and CVD mortality does not preclude associations of specific pesticides with specific cancers or certain pathologies such as infertility, or in vulnerable subjects such as pregnant women or the fetus. Moreover, although it does not allow for a definitive statement, the consumption of an organic diet (i.e., less likely to contain pesticide residues) in comparison to its conventional counterpart, a reduction in the incidence of e.g. non-Hodgkin lymphoma has been suggested. (Baudry et al., 2018; Kesse-Guyot et al., 2022; Bradbury et al., 2014).

The references of the study include its prospective population-based design, a large sample size of both men and women and the computerized linkage to the Cause of Death Register, providing ample statistical power and complete follow-up of participants, minimizing differential loss to follow-up. Moreover, the detailed questionnaire included both a validated FFQ, enquiring food consumption over the last year and questions on a wide variety of risk factors, which allowed us to capture the main dietary sources of pesticides as well as to adjust for relevant potential confounders. Additional strengths, is the comprehensive estimation of the combined toxic potential of each single pesticide detected in fruit, vegetables and cereals, proposed to better mirror the actual potency of toxicological effects as compared to just adverse effects, there has been a successive banning of the more toxic and persistent pesticides (including the chlorinated pesticides) over the last several decades. If successful, no adverse effects should be expected, as further evidenced by our present study as well as by some previous studies using a different approach. (Chiu et al., 2019; Sandoval-Insausti et al., 2021; Sandoval-Insausti et al., 2022). Nevertheless, the evidence is still scant related to human health outcomes as some recent studies may indicate health concern (Rebouillat et al., 2022; Rebouillat et al., 2021; Sagiv et al., 2023), and importantly, our observed inverse associations of pesticides mixtures with cancer and CVD mortality does not preclude associations of specific pesticides with specific cancers or certain pathologies such as infertility, or in vulnerable subjects such as pregnant women or the fetus. Moreover, although it does not allow for a definitive statement, the consumption of an organic diet (i.e., less likely to contain pesticide residues) in comparison to its conventional counterpart, a reduction in the incidence of e.g. non-Hodgkin lymphoma has been suggested. (Baudry et al., 2018; Kesse-Guyot et al., 2022; Bradbury et al., 2014).
using the number of pesticides detected or their mean concentrations.

As always, the observational design cannot exclude residual con-
 founding by unknown or unmeasured factors. Limitations also include
 the single exposure assessment at baseline, assuming the dietary habits
 and pesticide residue exposure to remain the same over the entire
 period. Dietary variations over time, any misreporting of dietary intake
 as well as a higher historical exposure to pesticides would contribute to
 exposure misclassification. Moreover, we cannot exclude selection of
 foods in the pesticide monitoring programs and that the pesticides
 detected in the foods not fully reflect the levels in the foods consumed by
 the participants, nor do we have information on to what extent organic
 foods were consumed. On the other hand, the exposure may have been
 overestimated. In many cases a specific pesticide was only detected in
 less than one percent of all the samples from a crop commodity. Since
 the limit of quantification of the analytical methods used in the late 90’s
 was rather high at the time that the residue levels were estimated, the
 non-detects (samples with residues below LOQ that were counted as
 levels at ½ LOQ) contributed to the estimated exposure. Storage,
 transport, washing, cleaning, and cooking of foods may also affect the
 pesticide residues, contributing to exposure misclassification. The lack
 of any validation of the exposure using biomarkers is an apparent
 weakness of our study. On the other hand, because the majorities of
 the pesticides currently used are short-lived in the body, using biomarkers
 for the assessment of pesticide residue exposure, would most likely
 contribute little to answering the question on mixture effects of long-
term low-level residue exposure. It should also be emphasized that
 ADIs may not accurately account for all potential mixture effects, and
 the factors used to extrapolate the thresholds from experimental studies
 to humans are arbitrary. Another issue of importance is that the use of
 some pesticides that substantially contributed to the Dietary Pesticides
 Hazard Index at baseline in the present study, has decreased or even
 been banned (e.g., carbofuran, chlorfenvinphos, dichlorvos, dicofol,
diazinon, parathion-methyl, prothiophos) during the follow-up period of
 this study. Based on Swedish monitoring data, the estimated exposure to
 organophosphates pesticides declined during 2005–2011 (Widenfalk
 and Fohgelberg); while corresponding exposure to pyrethroids was
 stable at low levels (Mårtensson). Nevertheless, for accuracy we
 assigned the actual exposure at the time of the completion of the FFQ,
 based on pesticide monitoring data present at baseline of the present
 study (in total 9862 samples) to prevent the underestimation of any
 potential effect of long-term exposure to pesticides residues on chronic
 disease development. It is, however, important with extensive pesticide
 monitoring programs to allow for as realistic estimates of dietary pes-
ticide exposure as possible, and to increase the knowledge of the effects
 of different procedures in affecting the residue levels.

In summary, although we cannot preclude that dietary pesticide
 residue exposure could be linked to specific adverse effects or diseases
 outside the scope of this study and the validity of the exposure in rela-
tion to biomarkers is unknown, the inverse associations observed be-
tween the residue exposure and mortality herein, and the later banned
 use of some of the more toxic pesticides, support current advice to
 consume several servings of fruit and vegetables daily. Yet, the use of
 pesticides should be in a sustainable manner for human and planetary
 health.

CRediT authorship contribution statement

Agnete Åkesson: Data curation, Formal analysis, Methodology, Writing – original draft. Carolina Donat-Vargas: Formal analysis, Methodology, Writing &ndash; review & editing. Elinor Hallström: Methodology. Ulf Sonesson: Funding acquisition, Methodology. Anneli Widenfalk: Conceptualization, Data curation, Methodology, Writing &ndash; review & editing. Alicja Wolk: Conceptualization, Data curation, Funding acquisition, Methodology, Writing &ndash; review & editing.
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