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RESEARCH ARTICLE

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Meeting nutritional adequacy in the Brazilian population increases pesticide intake without exceeding chronic safe levels

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ABSTRACT

Achieving nutritional adequacy requires an increase in fresh foods consumption, which may increase pesticide intakes. This study aimed to identify required dietary modifications to achieve nutritional adequacy without exceeding the acceptable daily intake (ADI) for pesticides. Data from the National Dietary Survey 2017–2018 were linked to the pesticide database from the Program on Pesticide Residue Analysis in Food. We performed linear programming models to design nutritionally adequate diets constrained by food preferences for different constraints on pesticide intake at the least cost increment. Nutritional adequacy led to an increase in pesticide intakes without exceeding their ADI. Modifications in diets varied according to the model, but, in general, consisted in an increase in fruits and vegetables, dairy, and seafood, and a reduction in rice, red meat, and sugar-sweetened beverages quantities. In conclusion, meeting nutritional adequacy increases pesticide intake compared to the observed diets, without representing a health concern to consumers.

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Linear programming; nutritional adequacy; diet planning; pesticides

Introduction

The Brazilian dietary pattern has been characterised by a high prevalence of nutrient intake inadequacy, regardless of age or socioeconomic status. In the last two National Dietary Surveys (2008–2009 and 2017–2018), the prevalence of inadequacy was higher than 80% for vitamins A, D, and E, and calcium and between 30% and 70% for magnesium, phosphorus, thiamine, riboflavin, pyridoxine, and vitamin C (Verly-Jr et al. 2021; IBGE 2020). In general, a higher consumption of fresh or minimally processed foods (e.g., fruits and vegetables, legumes, and whole grains) is required for an adequate nutrient intake. However, these modifications in diets can be challenging for countries with high income inequalities such as Brazil, once increasing the consumption of fresh or minimally processed foods could represent an important cost increase in the household food budget (Verly-Jr, Darmon, et al. 2020; Verly-Jr, Pereira, et al. 2020).

Fresh and minimally processed foods are the most important vehicles of pesticide residues in foods (ANVISA 2019) and consequently the highest contributors to pesticide intakes in populations (IPCS 2020). Pesticides are biologically active compounds used in agriculture for crop protection against pests, and some may cause adverse effects on human health (IPCS 2019; IARC 2019; FAO 2018). Data from the two recent Brazilian monitoring programs conducted from 2013 to 2019 showed that about 50% of the 16,667 food samples contained at least one pesticide residue and only 5% were above the maximum residue level (ANVISA 2016, 2019). Nonetheless, previous studies assessing dietary pesticide exposure using a nationwide food consumption survey concluded that both acute and chronic pesticide intakes are not of health concern (Jardim, Mello, et al. 2018; Jardim, Brito, et al. 2018), which is in accordance with studies from different countries (Jensen et al. 2015; Quijano et al. 2016; Sieke et al. 2018; De Rop et al. 2019; Eslami et al. 2021). Those studies were based on the current food consumption in Brazil, in which fruits and vegetables consumption is far below the needed amount to achieve nutrient adequacy. It emerges an important

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question for public health and policy, that is, which is the impact on pesticide intakes when achieving nutritional adequacy in a population?

Nutritional adequacy might be achieved by many combinations of foods, however, in real life, it depends on the affordability and cultural acceptability of these foods. In practice, food choices for distinct subgroups would be based on their budget and eating preference, which may result in a substantial variation in pesticide dietary intakes across the country. Thus, when designing nutritionally adequate diets, these aspects should be accounted for, especially in a large and highly heterogeneous country such as Brazil. To our best knowledge, only one study assessed how diet modifications to achieve nutritional adequacy impact on pesticide intake (Barré et al. 2016). Using linear programming, the authors found that achieving nutritional adequacy might increase dietary pesticide exposure, but within safe levels of chronic pesticide intake by the French population.

Diet modelling with linear programming (LP) is a powerful tool for diet planning as it finds the best mathematical solution for a problem involving multiple constraints (e.g., the highest nutrient content at the lowest cost) (Gazan et al. 2018). It has been successfully applied to design optimised diets that are affordable, nutritionally adequate, and locally acceptable in developed (Darmon et al. 2002; Maillot et al. 2017) and developing countries (Verly-Jr et al. 2020, 2019). In this study, in addition to nutritional requirements and food preferences, dietary pesticide intakes were constrained in the LP models to find the optimum diet modifications. Thus, the objective of this study was to assess the impact of diet modifications to achieve nutritional adequacy without exceeding the acceptable daily intake for pesticide intake. Also, we identified dietary changes needed to achieve nutritional adequacy without increasing current pesticide intakes considering regional food prices and eating preferences.

Methods

Study population

We used data from the National Dietary Survey (NDS) and the Household Budget Survey (HBS), conducted by the Brazilian Institute of Geography and Statistics (IBGE) between July 2017 and July 2018, in a representative sample of Brazilian households. The detailed sampling procedures employed in this survey have been described elsewhere (IBGE 2020). Briefly, HBS adopted a two-stage cluster sampling, with primary sampling units ($n = 5{,}504$ census tracts) grouped into 575 sampling strata with geographical and socio-economic homogeneity and secondary sampling units equivalent to 57,920 households. The NDS comprised a random sub-sample (34.7%) of the HBS households, totalling 20,112 households and 46,164 individuals 10 years or older. Census tracts were selected through systematic sampling with probability proportional to the number of households in each stratum, while households were chosen by simple random selection without replacement in each census tract. Household visits in each stratum were uniformly distributed throughout the 12 months of data collection to account for seasonal effects on food consumption, purchase, and price.

Dietary data collected by short-term instruments such as the 24-hour recall (24 hr) does not accurately describe individual usual food consumption, but the population means are well estimated (Carriquiry 2003). Thus, due to the large heterogeneity in dietary food patterns and prices throughout Brazil, optimised diets were designed for several subpopulations within geographical areas delimited by income level in each Brazilian federal unit. The 575 household strata from NDS were grouped into 27 Brazilian federal units, and further into four levels of household *per capita* income: (1) $\leq$ 0.5 official minimum wage (MW); (2) $>$0.5 and $\leq$ 1.5 MW; (3) $>$1.5 and $\leq$ 3 MW; and (4) $>$ 3 MW (minimum wage: R$954.00 Brazilian Reais; equivalent to US$298.52 United States Dollars in January 15th, 2018); totalling 108 new strata, referred here as "Geographic-Economic Strata" (GES). This procedure was adopted to improve the precision of the estimates by increasing the number of households in each unit of analysis.

Dietary data

Food consumption

Food consumption was obtained from a 24 hr answered by all household members aged 10 years or older using the Automated Multiple-Pass Method (Moshfegh et al. 2008). The food consumption data contains detailed information on portion size, amount consumed, cooking method, and time and place of consumption. A total of 1,591 food items were reported in the NDS (coffee, tea, and alcoholic beverage were not considered). Food subtypes, such as different types of the same food, different cooking methods, or different meat cuts were grouped into a single food (e.g., different types of bread into "breads", different beef cuts into "beef", etc.). The final list comprised 100 foods, which varied from 49 to 96 according to the GES (Supplementary Material, Table S1).

Determination of the mean observed diet

The mean observed food consumption was calculated for each GES, considering each GES weight, which was calculated as the sum of its household sampling weights. The mean intakes of each food were used as a starting point in each GES LP model as described below.

Nutritional composition

The nutritional composition of foods was obtained from the Brazilian Table of Food Composition (FoRC 2020). The nutritional composition of each food was calculated as the mean composition of the food subtypes weighted by their frequency of reporting in the NDS.

Food prices

Food prices were obtained from the HBS database, where household members registered every purchase and expenditure amount of food products for home consumption over a seven-day period. Food subtypes were grouped into single foods as done with dietary consumption, also resulting in a list of 100 foods. The price per kilogram of each food was calculated as the mean price of the food subtypes weighted by their frequency of reporting in the HBS (e.g., the average price of "beef" corresponded to the mean price over all beef subtypes weighted by their reporting frequency) within each GES. Therefore, price variations over strata were preserved. The food prices were converted into price per kilogram of edible portion and deflated to the same reference date (January 15, 2018) using official inflation rates to account for food price variation throughout the collection period.

Determination of pesticide intake

Pesticide residues

The pesticide residues concentrations of 228 chemical compounds in 30 foods were obtained from the Program on Pesticide Residue Analysis in Food (PARA) 2013–2018, coordinated by the Brazilian Health Regulatory Agency (ANVISA), and from the Laboratory of Toxicology of the University of Brasília (LabTox). The PARA database included 16,667 food samples randomly sampled in food markets across Brazilian capitals and analysed by private or governmental laboratories that comply with ISO-IEC 17025 (ANVISA 2016, 2019).

Data from the LabTox, which also complies with ISO-IEC 17025, included 110 samples of cashew ($n = 43$) and khaki ($n = 67$) randomly sampled from food stores in the Federal District from 2010 to 2012 (Jardim et al. 2014). Pesticide residues in foods not monitored by PARA or evaluated by LabTox were assumed to be the same as similar foods for which information was available (Supplementary Material, Table S2). For example, pesticide residues for lemons were assumed to be equal to oranges. We also assumed that 5% of the meat-based dishes weight (in grams) referred to garlic as part of their composition and 50% of the wheat-based product's weight (e.g., bread, cakes, cookies, and pasta) referred to wheat flour as part of their composition.

A total of 16,777 food samples were analysed for the presence of 284 pesticides by PARA and LabTox, of which 36% contained at least one of the 146 pesticides detected. The highest percentage of detection was for apple and strawberry (93%), papaya (82%), and tomato (63%), while the lowest percentage was for garlic (5%), sweet potatoes (4%), manioc, and chayote (3%) (Supplementary Material, Table S4).

The pesticide residues concentration in foods used in the models were calculated as the average values obtained from the measurements of the same food collected across the country. Not-detected pesticide residue values were replaced by the limit of detection (LOD) of each pesticide (i.e., the minimum amount in which an active substance can be identified), and non-quantified pesticide residue values were replaced by the limit of quantification (LOQ) (i.e., the minimum amount in which an active substance can be quantified), as described in the EFSA report as "pessimistic approach" (EFSA 2012). We used the LOD and LOQ databases compiled by PARA (ANVISA 2016, 2019).

Because pesticides were evaluated in raw foods, the pesticide residues concentrations in foods were corrected by cooking and correction factors when applied (Bognár 2002). This procedure was applied to link food consumption and pesticide residues data as follows: (1) raw foods may increase or decrease their volume by gaining or losing water during food preparation, which may increase or decrease pesticides concentrations in foods; and (2) raw foods carry pesticide residues in their non-edible parts, which could overestimate total pesticide concentrations in edible parts. Additionally, pesticide residues tend to dissipate when washed or exposed to heat (Kaushik et al. 2009; Bajwa and Sandhu 2014). Therefore, the lowest pesticide reduction found in the literature was used in this study: (1) 17% reduction during cooking for all pesticides in rice, beans, vegetables, and tubers when applied (Kaushik et al. 2009); (2) 4% reduction during a short boiling period for all pesticides in pasta (Bajwa and Sandhu 2014); (3) and 30% reduction during baking for cakes, breads, and cookies (Kaushik et al. 2009; Bajwa and Sandhu 2014).

Food safety assessment

The chronic dietary risk assessment was performed in two ways: (1) by comparing the intake of each compound with its corresponding Acceptable Daily Intake (ADI), performed for the 228 residues, and (2) by comparing the cumulative intake of a set of compounds with the same mechanism of action with the ADI of the Index Compound (IC) of the cumulative group, performed for triazoles and dithiocarbamates (DT) fungicides. The cumulative intake was estimated by normalising the residues of each compound present in foods to equivalent residues of the group IC, which assumes a dose-addition effect between group compounds (USEPA 2002; Boobis et al. 2008). In this approach, the Relative Potency Factor (RPF) of each compound was calculated as the ratio of the No Observed Adverse Effect Level (NOAEL) of the group IC by the compound's NOAEL. The cumulative (normalized) residues for each group/food combination were calculated by summing each residue value multiplied by its RPF, expressed as the IC.

For triazoles, the IC for chronic hepatotoxic effects is flusilazole (EFSA 2009). NOAELs were obtained primarily from EFSA (2009), but also from JMPR toxicological evaluations (JMPR 2018) and the USA Environmental Protection Agency (USEPA 2006). For DT, the analytical methods performed by PARA and LabTox (i.e., DT measured as CS2 by either spectrophotometry or gas chromatography coupled to FPD or MS after isooctane extraction or headspace) do not allow the identification of the specific DT compound applied to the crop. Thus, to prevent under (assuming that the detected CS2 was generated from the DT with the lowest toxicity) or overestimation (assuming that residues were generated from the most toxic DT), the approach performed by Caldas et al. (2006) and Jardim, Mello, et al. (2018) was applied to estimate the source of CS2 using DT use and market information in Brazil. Mancozeb is registered for 38 food crops and represents about 78% of the DT commercialised volume in the country for foliar application; metiram is registered in 19 crops, representing about 15% of the market; and propineb is registered in 8 crops, representing about 7% of the market (ANVISA, 2019; IBAMA, 2018; Pires 2013). Thus, it was assumed that 93% ($78 + 15\%$) of the CS2 found in the samples was originated from the use of the EBDCs (mancozeb or metiram), and 7% from the use of propineb.

A RPF for propineb related to EBDC of 1.92 (thyroid effects) was estimated based on the NOAELs of 2.5 and 4.8 mg/kg bodyweight (bw) of propineb and mancozeb, respectively, for effects on the thyroid (JMPR, 1994). Thus, we applied these parameters (93% of EBDC and 7% of propineb, and a RPF of 1.92) to estimate the total DT pesticides residues on foods, as CS2, according to the following equation:

$$\mathrm{DT} = (\mathrm{EBDC} \times 0.93) + (\mathrm{propineb} \times 0.07 \times 1.92).$$

Finally, the total pesticide intake (mg/kg bw/day) of each compound or group in the observed and optimised diets were estimated as the sum of each compound/group (mg/g) concentration per food multiplied by each food average daily consumption (grams/day), divided by the average body weight (in kg) in each GES. The total pesticide intake was considered safe when the total intake was below the ADI (for each compound or the IC of the cumulative group). ADIs were obtained from ANVISA (ANVISA 2016, 2019) reports, and the European Commission database (European Commission 2021).

Modelling

An optimisation model is characterised by an objective function of multiple decision variables (e.g., food consumption) to be optimised (i.e., minimised or maximized) over a set of constraints (e.g., nutrient needs and diet cost). The decision variables were the reported foods (in grams). Nutritional, cultural, and toxicological constraints, as described below, were introduced into the model to identify optimised diets that are nutritionally adequate, safe, and acceptable by consumers across the country. The model was considered feasible when a solution was reached, and the constraints were met. We performed three different models for each 108 GES, totalling 324 (3×108) optimisation models. All models aimed to find combinations of foods and their quantities at the lowest total diet cost while respecting nutritional and acceptability constraints. The models differed according to the set

Table 1. Nutritional constraints imposed into the models.

Nutrient	Unit	Lower constraint	Upper constraint
Calorie	kcal	Observed[a]	EER[b]
Carbohydrate[c]	%kcal	55	75
Protein[c]	%kcal	10	30
Total fats[c]	%kcal	15	30
Polyunsaturated fats[c]	%kcal	6	10
Saturated fats[c]	%kcal	–	10
Trans fats[c]	%kcal	–	1
Fiber[d]	g	30	–
Calcium[d]	mg	868	–
Iron[d]	mg	6.8	–
Magnesium[d]	mg	303	–
Sodium[c]	mg	–	2300
Sodium/Potassium[c]	mg	–	1
Zinc[d]	mg	8	–
Phosphorous[d]	mg	649	–
Copper[d]	mg	0.7	–
Selenium[d]	µg	44.34	–
Folate*,[d]	µg	322	–
Niacin**,[d]	mg	11.5	–
Vitamin A***,[d]	µg	560	–
Vitamin B1[d]	mg	0.9	–
Vitamin B12[d]	µg	2	–
Vitamin B2[d]	mg	1	–
Vitamin B6[d]	mg	1.1	–
Vitamin C[d]	mg	66.1	–

*Dietary Folate Equivalent (DFE).
**Preformed niacin.
***Retinol Activity Equivalent (RAE).
[a]Observed energy level per GES.
[b]Estimated Energy Requirement per GES.
[c]World Health Organisation.
[d]Derived from the Estimated Average Requirement.

of toxicological constraints introduced, described as follow:

Model 1: acceptability and nutritional constraints

Model 2: model 1 + toxicological constraints (Acceptable Daily Intake - ADI)

Model 3: model 1 + toxicological constraints (current level of pesticide intake)

Model constraints

Food acceptability constraints: Upper and lower boundaries refer to the highest and lowest amounts, in grams, from which optimised foods could deviate from observed mean consumption. These constraints prevent optimised diets from being culturally unacceptable. The boundaries were calculated for each food according to the country region (North, Northeast, South, Southeast, and Center-west) to account for the variability in food preferences. The mean food consumption was obtained for each stratum (from the 575 in the HBS sample), and the region-specific distribution of each mean food consumption over the strata was estimated (excluding strata in which the food of interest had not been reported) (Verly-Jr et al. 2019). From this distribution, we obtained the 10th percentile, used as the lower boundary constraint in each GES-LP model within the corresponding region. The upper boundaries were the mean observed consumption calculated among consumers of a specific food (i.e., those who reported consumption greater than zero) in each Brazilian region. In addition, to reduce the distance between the observed and optimised diets, foods were progressively allowed to deviate by 5 g at a time until a feasible solution was reached but censored by each food acceptability constraint.

Food group acceptability constraints: These additional boundaries constrained food groups ($n = 18$, except for fruits and vegetables) consumption not to be higher than each food group average daily consumption between consumers per GES (Supplementary Material, Table S3). This procedure has been previously applied in studies of the same population (Verly-Jr et al. 2020, 2019).

Nutritional constraints: These constraints were set to establish nutritional targets that optimised diets should achieve. The nutritional constraints are shown in Table 1: (1) observed energy intake and Estimated Energy Requirement (EER) (IoM 2005) as lower and upper boundaries for energy content, respectively; (2) Estimated Average Requirements (EAR) for calcium, copper, folate, iron, magnesium, niacin, zinc, selenium, phosphorus, and vitamins A, B1, B12, B2, B6, and C (IoM 2000), and Adequate Intake (AI) for fiber as lower boundaries for nutrient contents; (3) Chronic Disease Risk Reduction (CDRR) for sodium (IoM 2019); and (4) WHO recommendation for noncommunicable chronic diseases (NCD) prevention for macronutrients, sodium-potassium ratio, polyunsaturated, saturated and trans-fat (WHO 2003). Once the EARs differ by age-sex groups, the EAR-constraint for each nutrient corresponded to the mean EAR over the age-sex groups weighted by their corresponding frequency of participants in the sample.

Toxicological constraints: Two sets of constraints were used: (i) each compound/group ADI multiplied by the average body weight estimated in each GES (model 2); and (ii) current level of pesticide intake in the observed diets (model 3). Toxicological constraints were not included in model 1.

Objective function

The modelling process was conducted in two steps. First, we ran the models with objective function 1, as described below. When one or more nutrient constraints cannot be attained within these food acceptability constraints in a given GES, this nutrient is called a "limiting" constraint, and the model does not return a feasible solution (infeasible model). In the case of model infeasibility, a built-in algorithm in the PROC OPTMODEL (SAS software) was used to identify the nutrient constraints that caused unfeasibility. The occurrence of model unfeasibility led to step two, in which the constraints on the limiting nutrients were removed and an additional term was added in the objective function 2, in addition to the total diet cost minimisation of objective function 1. This term minimises the "undesirable deviation," that is, the difference between the nutrient intake target and the optimised content of a limiting nutrient. For example, for a nutrient constrained at $\geq$100 mg, a negative undesirable deviation of 10 mg refers to an optimised diet with 90 mg instead of 100 mg. The two objective functions minimise the diet cost as described below.

$$O[minimize] = \left[\sum_{i=1}^{i=n}(Q_{f \cdot g}^{opt} * P_{f \cdot g})\right], \text{(Objective Function 1)}$$

$$O[minimize] = \left[\sum_{i=1}^{i=n}(Q_{f \cdot g}^{opt} * P_{f \cdot g})\right] + \left[\sum_{x=1}^{n} D_x\right] \text{(Objective function 2)}$$

where (O) represents the objective function to be minimised; i is the food reported in a set of n consumed foods; $Q_{f \cdot g}^{opt}$ and $P_{f \cdot g}$ are the optimised food quantity and price of food f in GES g, respectively; and (D) is the undesirable deviation amount of the nutrient x.

Uncertainty analysis

To deal with the uncertainties in pesticide residue measurements, we performed a probabilistic assessment with 1,000 bootstrap replications. Uncertainty in mean residues was quantified by resampling the residue data: in each resampling, for each food, the number of measurements of each pesticide residue, equal to the number of its measurements in the observed data, is drawn at random with replacement from the observed data. The residue means were calculated for each resampling, for which a food safety assessment was performed. The estimates from the 1,000 replications generated a distribution of the intake for each pesticide residue and GES, from which we obtained the lower (2.5 percentile) and upper (97.5 percentile) limits (95% confidence interval) per intake percentile.

Descriptive analysis

Results are presented as the overall mean and 25th–75th percentile food group and nutrient contents for the observed and optimised diets over 108 GES. The 100 foods quantities in the observed and optimised diets were aggregated into 19 food groups (Supplementary Material, Table S1), as follows: beans (beans and other legumes); rice (white and whole rice); fruits and vegetables (FV) (all fruits and vegetables excluding tubers), tubers, oilseeds, dairy (whole and non-fat milk, cheese, yogurt, and other dairy products); red meats (including processed meats); chicken; eggs; fish and seafood; breads; pasta; sugar-sweetened beverages (SSB); fast foods (hamburgers, snacks, pizza, salt pastries), sweets, cookies, cakes, margarine, and olive oil.

Pesticide intakes (for each compound or cumulative group) were expressed as the percentage relative to their respective ADIs. In addition, we identified the foods that contributed the most to the highest increases in pesticide intake.

Results

Model feasibility

In the model 1, where only nutritional and cultural acceptability constraints were imposed, feasible solutions were found for all GES using the objective function #1, meaning that all constraints were met. Diet changes using the model 1 led to an increase in pesticide intakes, but below their ADI in all GES. Thus, there was no need to perform the model 2. In the model 3, where pesticide intakes were constrained at their current intake level, it was not possible to simultaneously meet all toxicological, nutritional, and acceptability constraints in 89 out of 108 GES. Depending on the GES, calcium, potassium, magnesium, fiber, total fats, carbohydrates, vitamins A, B6, and C were limiting constraints in the optimizations when model 3 was used with objective function #1 (first round). Therefore, optimisation using the model 3 with objective function #2 was run in a second-round to minimise the undesirable deviation of those nutrients when they were not met in the first round for a given GES.

Pesticide intakes in diets

In the model 1, diet modifications to reach the nutritional recommendations led to an average overall increase in pesticide intakes (Figure 1), mainly for heptachlor (66% of ADI in diets optimised with model 1 vs. 45% in the observed diets), aldrin (64% vs. 45%), benfuracarb (63% vs. 52%), endrin (57% vs. 40%), terbufos (42% vs. 33%), carbofuran (41% vs. 27%), fipronil (33% vs. 22%), and chlorthiophos (32% vs. 22%). The

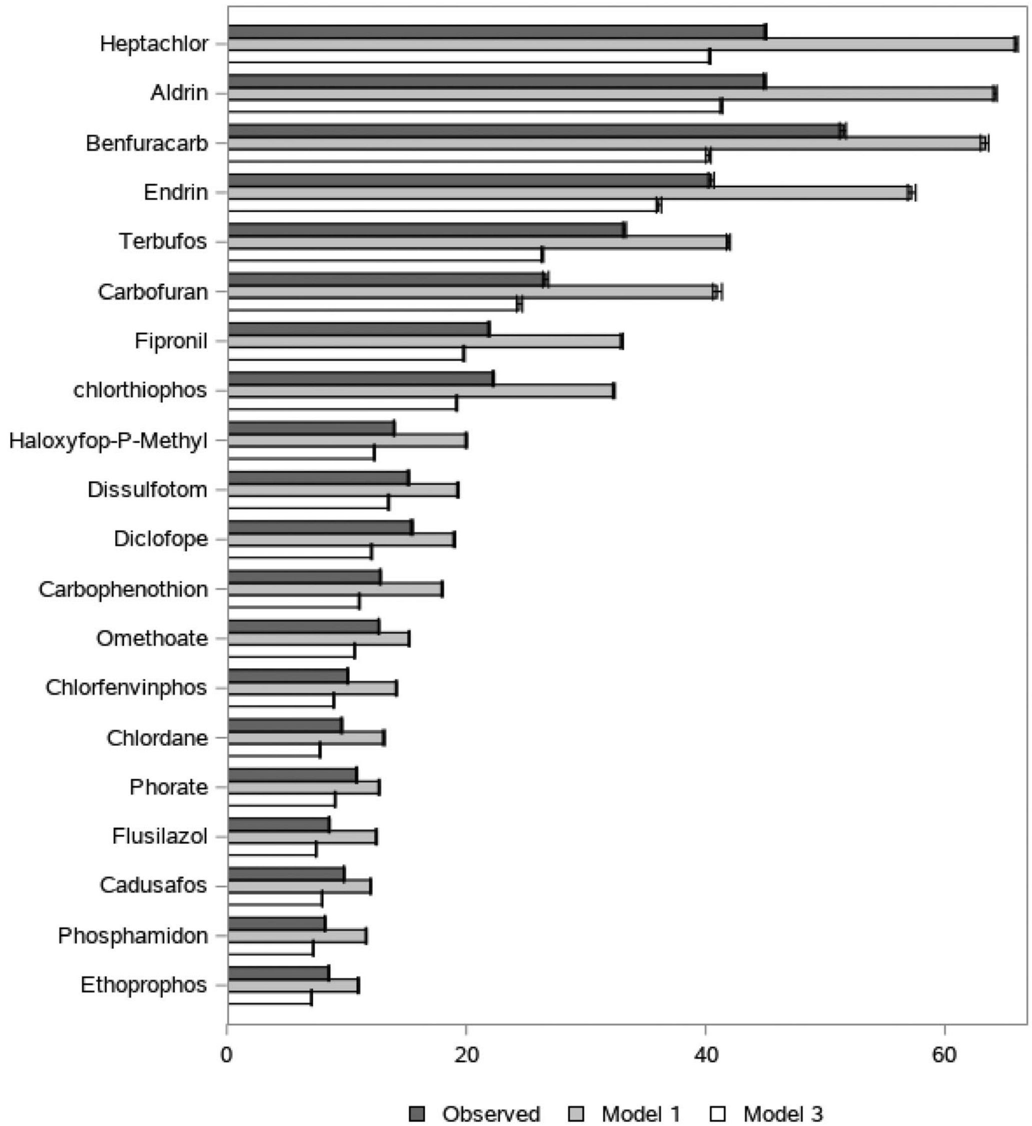

Figure 1. Mean percentage of the ADI[a] over the GES[b] ($n = 108$) of pesticide intake levels in the observed and optimised diets, according to the model[c].
[a]Acceptable Daily Intake.
[b]Geographic-Economic Strata.
[c]Model 1: acceptability and nutritional constraints; Model 3: model 1 + toxicological constraints (current level of pesticide intake).
The 95% confidence intervals were estimated by uncertainty analysis.

differences between the intakes in the observed and optimised diets for the remaining pesticides were below 6% (data not shown). Among the 228 pesticides, only four (glyphosate, trifloxysulfuron, and phenoxycarb) had their intake reduced (>1% of the ADI) (data not shown). Six pesticides had their intake increased by more than 50% of their corresponding ADI: benfuracarb (in 104 GES), heptachlor (in 108 GES), aldrin (in 108 GES), endrin (in 100 GES), terbufos (in 17 GES), and carbofuran (in 20 GES); an increase higher than 90% of the ADI was observed for heptachlor (in 2 GES) and benfuracarb (in 12 GES) (data not shown).

Foods that most contributed to pesticide intake (among those higher than 50% of the ADI in the optimised diets) were beans, rice, orange, papaya, banana, and manioc flour (Table 2). In the model 3, all pesticide intake in the optimised diets were below or equal to the current intake (Figure 1). For example, benfuracarb was, on average, 52% of the ADI in the observed diets (5.3×10^{-3} mg/kg bw/day) and 40% in the model 3 (4.2×10^{-3} mg/kg bw/day); and heptachlor was 45% of ADI (3.1×10^{-3} mg/kg bw/day) in the observed diets, and 40% (2.7×10^{-3} mg/kg bw/day) in the model 3 (data not shown).

Table 2. Contribution (%) of foods[a] to pesticide intake[b] in the optimised diets (only model 1[c]).

Food	Benfuracarb	Heptaclor	Aldrin	Endrin	Terbufos	Carbofuran
Modeled diet						
Beans (%)	3	16	13	11	22	11
Rice (%)	33	10	13	16	10	11
Orange (%)	21	10	7	10	20	9
Papaya (%)	0	5	3	3	9	0
Banana (%)	0	9	10	5	0	10
Manioc (%)	0	5	7	4	3	5
Observed diet						
Beans (%)	4	19	15	13	27	14
Rice (%)	42	12	17	19	13	13
Orange (%)	16	7	6	8	15	7
Papaya (%)	0	1	1	1	2	1
Banana (%)	0	3	3	2	0	3
Manioc (%)	0	1	2	1	1	1

[a]Foods that most contributed to pesticide residues intakes higher than 50% of ADI
[b]Pesticide residues intakes higher than 50% of ADI
[c]Model 1: acceptability and nutritional constraints

Food and nutrient contents in diets

In the model 1, nutritional constraints were met in all GES. The average energy content increased from 1732 kcal in the observed to 1936 kcal in the optimised diets to meet nutritional targets within food acceptability constraints (Table 3). The main changes in the diets were characterised by an increase of 407 g in FV quantities (641 g in the optimised vs. 234 g in observed diets), 68 g in dairy products (166 g vs. 98 g), 26 g in tubers (68 g vs. 42 g), 19 g in fish and seafood (38 g vs. 19 g), 15 g in oilseeds (15 g vs. 0.3 g), and 25 g in breads (83 g vs. 58 g) and a decrease of 28 g in rice quantities (122 g vs. 150 g), 45 g in red meat (54 g vs. 99 g), and 25 g in SSBs (56 g vs. 81 g) (Figure 2).

In the model 3, in which the pesticide intakes were not allowed to exceed their current intake level, the main dietary changes were characterised by an increase of 107 g in FV quantities (341 g in optimised vs. 234 g in observed diets), 67 g in dairy products (165 g vs. 98 g), 50 g in fish and seafood (69 g vs. 19 g), 16 g in oilseeds (16 g vs. 0.3 g), and 3 g in breads (61 g vs. 58 g), and a decrease of 38 g in rice quantities (112 g vs. 150 g), 34 g in red meat (65 g vs. 99 g), and 12 g in SSBs (69 g vs. 81 g). A higher quantity of fish and seafood (69 g in model 3 vs. 38 g in model 1), and a lower quantity of FV (341 vs. 641 g), tubers (38 g vs. 68 g), and rice (112 g vs. 122 g) were needed when compared to the model 1 (Figure 2).

Diets cost

The estimated average cost over the 108 GES in the observed and optimised diets (model 1) were US$2.82 (standard error: 0.09) and US$3.89 (0.11) per person/day, respectively (an increase in the average diet cost by US$1.07 (0.08)). The average cost of the diets optimised with the model 3 (pesticide intakes constrained at their current intake) was US$3.70 (0.1), which is slightly lower than the average cost of the diets optimised with the model 1 (US$3.89). However, in the model 3, some nutritional constraints (as described above) were not met in several GES (optimisation with objective function #2).

Discussion

This study assessed the compatibility between nutritional adequacy, food acceptability, and safety levels for chronic pesticide residue intake in optimised diets at the lowest cost for the Brazilian population. The results showed that it is possible to meet nutritional recommendations without exceeding pesticide intake above their corresponding chronic safe intake (ADI). The main implication of these results is that, in light of what is known so far concerning the effects of pesticide intake on health, an increase in fresh foods needed to meet nutritional recommendations does not seem to be a health concern for the Brazilian population. Dietary changes needed to meet nutritional adequacy mainly included increases in fruits, vegetables, and dairy products and decreases in red meat and SSBs, similar to what was found in previous studies in Brazil (Verly-Jr et al. 2019; Dos Santos et al. 2018) as well as in other countries (Maillot et al. 2010, 2017). The intake of many pesticides increased when moving from the observed to nutritionally adequate diets. Nonetheless, pesticide intakes in the optimised diets were below their corresponding ADIs. For example, the highest increase was observed for heptachlor (3.1×10^{-3} mg/kg bw/day in the observed and 4.8×10^{-3} mg/kg bw/day in the optimised diets), which represents 69% of the ADI (1×10^{-4} mg/kg bw/day). A similar result was also observed in an optimisation study in the French population, where the

Table 3. Mean nutrient contents in the observed diets and optimised diets and its 25th and 75th percentile intervals.

Nutrient	Unit	Observed diets	Model 1 diets	Model 3 diets
Calories	kcal	1732 (1710–1754)	1936 (1787–2046)	1839 (1741–1923)
Carbohydrate	%kcal	53.9 (51.9–55.6)	59.9 (59.7–59.9)	52.5 (52.4–53.4)
Protein	%kcal	18.4 (17.7–18.6)	16.5 (16.5–16.5)	19.2 (18.6–19.1)
Total fats	%kcal	30.3 (29.2–31.8)	27.2 (27.0–26.9)	31.4 (29.9–32.5)
Polyunsaturated fats	%kcal	7.9 (7.6–8.3)	6.3 (6.1–6.4)	7.0 (6.7–7.3)
Saturated fats	%kcal	9.5 (9.1–10.0)	8.8 (8.6–8.8)	10.4 (9.7–11.2)
Trans fats	%kcal	0.7 (0.6–0.7)	0.6 (0.6–0.6)	0.7 (0.6–0.7)
Monounsaturated fats	%kcal	9.9 (9.1–10.6)	8.5 (8.3–8.3)	9.9 (9.2–10.3)
Fiber	g	22.8 (22.0–23.5)	34.2 (33.1–35.3)	28.8 (27.6–30.0)
Calcium	mg	432 (408–456)	868 (868–868)	865 (862–868)
Iron	mg	10.9 (10.8–11.1)	12.9 (12.6–13.2)	12.4 (11.8–13.0)
Magnesium	mg	269 (262–275)	352 (343–361)	312 (303–316)
Sodium	mg	2486 (2443–2530)	2300 (2300–2300)	2299 (2298–2301)
Potassium	mg	2224 (2178–2270)	2959 (2737–3173)	2666 (2595–2737)
Sodium/potassium	mg	1.1 (1.1–1.1)	0.8 (0.7–0.8)	0.9 (0.8–0.9)
Zinc	mg	10.9 (10.6–11.1)	10.6 (10.3–10.9)	10.8 (10.5–11.1)
Phosphorous	mg	985 (972–998)	1201 (1137–1236)	1249 (1211–1287)
Copper	mg	1.4 (1.4–1.5)	1.8 (1.7–1.8)	1.5 (1.3–1.6)
Selenium	µg	39.3 (36.9–41.6)	71.4 (59.4–84.4)	86.0 (71.0–101.0)
Folate *	µg	415 (404–426)	542 (531–553)	487 (468–507)
Niacin **	mg	15.2 (14.8–15.7)	13.3 (12.7–13.8)	13.7 (13.1–14.3)
Vitamin A ***	µg	419 (386–453)	850 (665–876)	717 (611–823)
Vitamin B1	mg	1.0 (1.0–1.0)	1.1 (1.0–1.1)	1.0 (0.9–1.0)
Vitamin B12	µg	4.2 (3.9–4.4)	4.7 (4.1–5.2)	6.0 (5.2–6.8)
Vitamin B2	mg	1.1 (1.0–1.1)	1.4 (1.3–1.4)	1.3 (1.3–1.4)
Vitamin B6	mg	0.6 (0.6–0.7)	1.1 (1.1–1.1)	0.9 (0.6–1.1)
Vitamin C	mg	120 (113–127)	354 (233–344)	129 (121–138)
Vitamin D	µg	1.5 (1.4–1.5)	2.3 (2.1–2.5)	2.6 (2.3–3.0)
Vitamin E****	mg	6.6 (6.3–7.0)	9.8 (9.1–10.6)	8.4 (7.9–8.8)

*Dietary Folate Equivalent (DFE).
**Preformed niacin.
***Retinol Activity Equivalent (RAE).
****Total alpha-tocopherol.
Intervals were estimated as the 25th and 75th percentiles of the distribution of the mean quantities over the GES.

highest intake was observed for hexachlorobenzene, reaching 63% of the ADI (Barré et al. 2016). Similar to our study, Barré et al. applied the pessimistic scenario approach, which potentially leads to an overestimation of pesticide intake in the optimised diets.

A possible solution to achieve nutritional adequacy without increasing pesticide intake in Brazil would be the promotion of food policies destined to increase organic food consumption. There is promising evidence suggesting that organic dietary interventions reduce pesticide residues urinary levels (Lu et al. 2006; Bradman et al. 2015; Hyland et al. 2019). Additionally, once organic food prices are generally higher than those from conventional agriculture (Islam and Colonescu 2019), the affordability is a key aspect to be considered, mainly for low-income families with restricted budget destined to food supplies.

The approach performed in this study probably overestimates the dietary exposure to several pesticide residues. Many pesticide residues were not detected or quantified in many food samples; that is, they were below either the LOD or LOQ. About 64% of the samples considered in this study had no detected residues. To deal with non-quantified or non-detected values, we adopted the pessimistic scenario approach, which assumes the non-detected residues as the LOD value and non-quantified residues as the LOQ value. As a consequence, the four pesticides in which the intakes were above 60% of the ADI (i.e., heptachlor, benfuracarb, aldrin, and endrin) in the model 1 were those that had not been detected in the monitoring program. Furthermore, the pessimistic approach was adopted for all pesticides evaluated in all foods, even when they were not expected to be found in a specific food crop. For example, benfuracarb (the third highest %ADI found in this study) is only registered in Brazil for cotton and sugarcane crops. Heptachlor, aldrin, and endrin were banned from Brazil over 30 years ago but are still under surveillance once they are persistent organic pollutants. In addition, we assumed a very conservative percentage of pesticide dissipation (i.e., the minimum observed per cooking method) for foods that were somehow cooked, which is likely to be much higher for some pesticides depending on several food preparation procedures (Bajwa and Sandhu 2014). Therefore, the decisions above probably led to an overestimation of pesticide intake.

As part of the pessimistic approach, foods not included in the PARA or LabTox (i.e., food with no pesticide residue information) were assumed to have

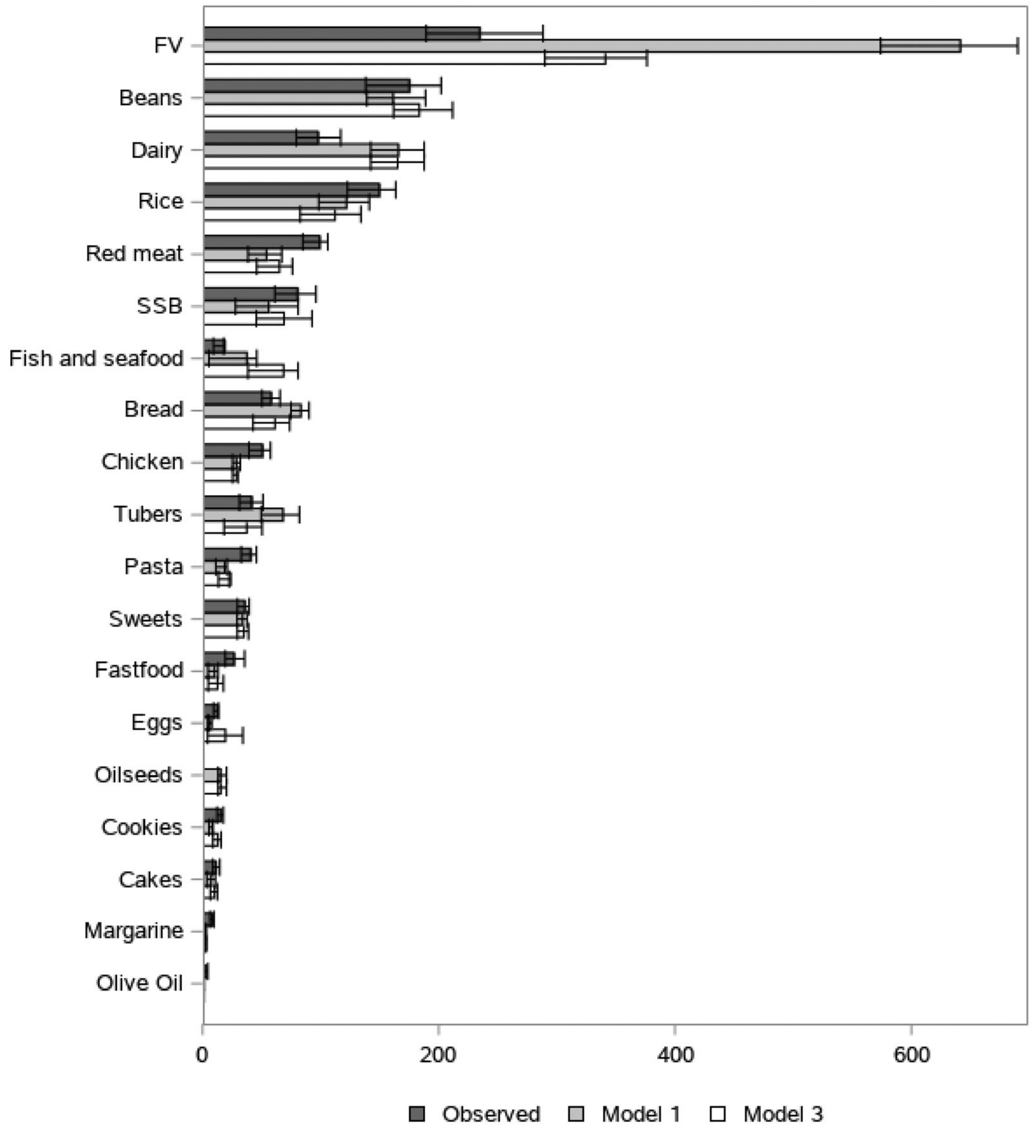

Figure 2. Mean food group contents over the GES[a] ($n = 108$) in the observed and optimised diets, according to the model[b].
[a]Geographic-Economic Strata.
[b]Model 1: acceptability and nutritional constraints; Model 3: model 1 + toxicological constraints (current level of pesticide intake).
Intervals were estimated as the 25th and 75th percentiles of the distribution of the mean quantities over the GES.

the same concentration as similar foods for all pesticides assessed. The direction and magnitude of a potential misestimation of the total pesticide residues in the optimised diets (i.e., if this procedure under or overestimates the residues and how much) is not known. However, in general, the foods analysed in the PARA are the most consumed by the Brazilian population, thus we believe that using a surrogate measurement of pesticides in the non-assessed foods probably did not substantially impact the conclusion of this study.

Although the ADIs are the international parameter for dietary chronic risk assessment, there are some considerations on its use and interpretation that should be addressed. The ADI is derived from the no-observed-adverse-effect level doses of toxicity of a single active substance in animals, corrected by a safety factor that accounts mainly for inter-and-intra-species variability (JMPR 2018). Therefore, not exceeding the ADI does not exclude the possibility of risk. Additionally, there is a growing body of evidence suggesting that pesticide formulations may have toxicological effects beyond their active substances (Mesnage et al. 2013; Defarge et al. 2016, 2018; Vanlaeys et al. 2018), which we did not account for in this study.

The absence of chronic risk in theoretical diets does not redeem the environmental impacts of pesticides. Pesticides contaminate soil, air, surface, and groundwater, directly affecting the biodiversity of non-target vegetation and organisms, such as fish, birds, beneficial soil microorganisms, bees, and humans (Aktar et al. 2009). Increased demand for fresh foods might lead to a higher use of pesticides, assuming that most of the fresh food in Brazil comes from conventional agriculture. It is difficult, however, to predict the overall impact of pesticide use on the environment. Also, acute pesticide poisoning is an ongoing major global public health challenge, particularly on farmers and farmworkers. However, there is lack of evidence for identifying and tracking its chronic effects (Boedeker et al. 2020). Thus, the direct and indirect environmental and health impacts of pesticide use are out of the scope of this study.

Diet modifications identified to meet nutritional needs without exceeding the ADI were delimited by regional food and food group acceptability constraints. These boundaries limit the amount of food and food groups allowed to deviate from observed diets considering regional food preferences. The exception was for FV once the consumption in Brazil is, on average, lower than the 400 g recommendation to prevent chronic diseases. Thus, FV quantities were not constrained at the upper-boundary in the models. Also, the objective function minimised the diet cost, which is an important determinant of food choices (French 2003; Darmon and Drewnowski 2015). Therefore, our optimisation models designed realistic nutritionally adequate diets, from which we can estimate the potential impact of pesticide intakes. The GES-modelling was necessary not only to consider variations in food prices and preferences across the country, but also to estimate the variability in pesticide intakes.

Despite using models that minimised the diet cost, the nutritional adequacy demanded an average increase by 40%, from US$2.82 in observed to US$3.89 in optimised diets. It implies that nutritional adequacy is likely to be restricted in low-income families. This finding is in line with previous studies in the same population (Verly-Jr et al. 2019). The cost increment in the optimised diets was necessary even in the model with no toxicological constraints. Thus, keeping diets safe does not increase the cost beyond that imposed to reach nutritional adequacy.

An important limitation of the study was that the risk assessment was performed by comparing the GES-mean pesticide intakes with the ADI, i.e., it does not consider the within-GES variability in pesticide intakes. It implies that a fraction of people in a given GES could be at risk of excessive pesticide intake, even if the mean GES intake for that pesticide was below the ADI. This limitation was likely to be mitigated once we stratified the analysis over GES, which considers the variability in dietary consumption over many subpopulations across the country. As the GES are supposed to cluster households with territorial and economic homogeneity, the variability over the mean-GES intakes recovers, at least in part, the overall variability in the dietary and pesticide intakes in the country. This approach was developed and applied in previous study once the optimisation modelling is, by definition, a deterministic method (Verly-Jr, Darmon, et al. 2020; Verly-Jr, Pereira, et al. 2020).

Another limitation of this study is that the monitoring program does not assess all the pesticides authorised for agriculture in Brazil. For instance, glyphosate has been the most used pesticide in Brazil for a long time, but it was only recently assessed in rice (out of 72 crops for which the use of glyphosate is permitted) (ANVISA 2019). Additionally, the recent changes in the legislation have authorised an increased number of pesticides in Brazil, of which there is no information yet of their use (MAPA 2021). Therefore, the intakes of all registered pesticides in Brazil are unknown. Accordingly, our conclusion is limited to the pesticides included in the monitoring program. Moreover, the results of this study should be updated as soon as new foods or pesticides are included in the monitoring program. This is the first study in a developing country that addresses the relationship between nutrient adequacy and pesticide intakes. The main strength was the GES-modelling approach, which is innovative and suitable to consider the variation of the study variables across the country.

In conclusion, this study demonstrated that adopting nutritionally adequate diets increases pesticide intakes, but mostly far below the ADI. It also showed that dietary improvement is possible without increasing current pesticide intakes. Reaching diet adequacy demanded increase in FV, dairy, fish and seafood, and oilseed, with consequent increase in diet cost. The method developed in this study may be applied in worldwide studies to identify diet modification to improve the nutritional quality while keeping diets toxicologically safe.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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