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Tracking pesticide residues and risk levels in individual samples—insights and applications

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Abstract

Background: A method is now available to quantify the number of pesticide residues and relative pesticide dietary risks in individual servings of food. The Dietary Risk Index (DRI) system combines the results of United States and United Kingdom pesticide residue testing programs with data on food serving sizes and each pesticide's chronic Reference Dose or Acceptable Daily Intake. Chronic DRI values are a ratio: the amount of residue in a serving of food relative to the maximum amount allowed by regulators.

Results: The DRI system generates individual sample tables reporting the number of residues detected and individual pesticide and aggregate-pesticide DRI values in specific, individual samples of food. It is the first such system to do so worldwide. Output tables produce accurate estimates of real-world dietary risks based on current toxicology data and exposure benchmarks set by regulators. System outputs allow assessment of the distribution of pesticide-dietary risks across foods and pesticides and demonstrate that dietary risk levels are highly skewed. A large number of samples pose moderate, low, or very-low risks, and relatively few samples pose high or very-high risks.

Conclusions: The DRI system provides the food industry, regulators and analysts with a simple, accessible online tool to assess pesticide dietary-risk levels by food, by pesticide, as a function of country of origin, and on food grown on conventional versus organic farms. DRI system output tables show that the number of residues in a sample of food is a consistently poor indicator of dietary risk levels. By identifying the relatively small number of high-risk samples, efforts to mitigate pesticide dietary risks can be targeted where the most worrisome risks are.

Keywords: Dietary risk, Pesticide regulation, Residues, Risk assessment, Dietary risk index

Background

Human health risks arising from pesticides in food, water, and beverages are the primary focus of pesticide regulatory agencies worldwide. In the US this focus is driven by clear statutory provisions in the primary federal law governing pesticide use and regulation, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).

FIFRA directs the EPA to apply a risk/benefit balancing standard in deciding whether to approve registration of a new food-use pesticide. The same standard governs the reregistration of an already-approved pesticide, and the cancelation of existing registrations. According to the US Environmental Protection Agency's Office of Pesticide Programs (OPP):

"Before EPA may register a pesticide under FIFRA, the applicant must show, among other things, that using the pesticide according to specifications [on the label] 'will not generally cause unreasonable adverse effects on the environment.' FIFRA defines the term 'unreasonable adverse effects on the environment' to mean: '[1] any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide, or [2] *a human*

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dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with the standard under Sect. 408 of the Federal Food, Drug, and Cosmetic Act."' [Emphasis added] [1].

Accordingly, federal law directs EPA to focus on the dietary risks to consumers arising from legal uses of pesticides covered by established tolerances. This clear mandate is why the tolerance-setting process is the primary hurdle any new food-use pesticide must overcome. Risks to the environment, applicators, and people living near places where pesticides are applied are almost always addressed via combinations of exposure-reduction measures and place-specific or application-method specific requirements or recommendations.

The tolerance process begins with submission by a pesticide manufacturer of a petition requesting approval of a specific set of tolerances. These petitions are accompanied by large data packages including residue chemistry, metabolism, and toxicology studies. These studies are used by EPA to carry out detailed analyses to determine whether the submitted studies "support" approval of the requested tolerances. The data "support" approval of tolerances for pesticide$_x$, and the issuance or continuation of registrations, when the EPA concludes that there is a "reasonable certainty of no harm" to consumers ingesting food containing levels of pesticide$_x$ below the applicable tolerance. Pesticide food-uses that meet this core health-based standard are determined by EPA to be "safe" and hence, eligible for approval, sale, and use.

Before EPA carries out the necessary assessment of human-health risks from pesticide dietary exposure, the Agency requires applicants for new tolerances to submit between 21 and 27 toxicology studies. Twenty-five of the 27 studies are done with technical active ingredients (e.g. imidacloprid, glyphosate). Registrants are allowed to choose between testing active ingredients and formulated end-use products (e.g. Admire [imidacloprid], Roundup [glyphosate]) in the case of dermal penetration and companion-animal toxicity. In nearly all cases registrants have conducted dermal penetration studies using pure active ingredients.

New formulations must also be tested using a "six-pack" of acute toxicity, eye, and skin irritation studies. These "six-pack" studies are relied on by manufacturers and EPA to select the appropriate signal world that must be prominently placed on pesticide product labels (Danger, Caution, Warning, no signal word required).

Data required to conduct a pesticide dietary risk assessment

Pesticide dietary risk assessment requires substantial data. Accuracy and relevance depend on data completeness and quality. The core toxicology studies are used to establish the maximum amount of an active ingredient that a person can be exposed to in a day without exceeding EPA's "level of concern." The key exposure threshold used in nearly all EPA pesticide dietary-risk assessments is the chronic Reference Dose (cRfD), a metric measured in milligrams of a pesticide's active ingredient ingested per kilogram of a person's bodyweight per day.

The presumption and hope is that dietary exposures less than what would be allowed by a pesticide's cRfD, registered uses, and tolerances will be "safe." This is true, of course, only in cases where the toxicology studies submitted by registrants to the EPA lead to a cRfD level low enough to protect people from all possible adverse health impacts, not just those adverse impacts identified in the 21–27 toxicology studies submitted to regulators.

Quantifying pesticide dietary risk arising from a given food-crop application requires two other key data elements: how much of food$_x$ a person ingests in a day, and the expected level of pesticide$_y$ in food$_x$ on any given day. EPA and other regulatory authorities use these two data points to estimate daily cumulative exposures across all foods a pesticide is registered for use on. The goal is to assure estimated, aggregate dietary exposures remain below the pesticide's cRfD.

Despite heavy investments by the EPA, USDA, and industry in generating the data supporting dietary risk assessments, very few independent analyses have been undertaken of the levels and distributions of dietary risks across foods, pesticides, the source of food (domestically grown or imported), and farm production systems (e.g. conventional, organic). The way EPA conducts pesticide dietary-risk assessments and reports results does not allow analyses of overall pesticide risk levels from dietary exposures or relative risks across foods and pesticides, nor changes over time.

Critically, EPA dietary risk assessments also do not support assessments of the distribution of risk levels associated with pesticide$_y$ in food$_x$ based on the distribution of levels of pesticide$_y$ in individual servings of food$_x$. This gap in pesticide dietary risk-assessment capability is a serious one for reasons made clear in this paper.

Across essentially all food-pesticide combinations, dietary risk levels are highly variable. As evident in the Results section, the vast majority of pesticide applications result in no or very low-risk residues, but a small number pose significant risks. Identifying the sources of the relatively few samples of foods containing worrisome residues will benefit farmers, the food industry, pesticide manufacturers, and regulators by targeting high-risk uses for intensified research, promotion of biointensive Integrated Pest Management (bio-IPM), mitigation via pesticide-product label changes, or phase outs.

Tracking pesticide dietary risk levels across foods and pesticides

The Dietary Risk Index (DRI) system was developed to support analyses of relative pesticide-dietary risk levels across foods, pesticides, country of origin, and production systems. DRI data sources and methodologies were described previously [2]. The DRI currently computes pesticide dietary-risk levels in most of the foods moving in international channels of trade. The system generates several hundred thousand unique tables and is freely accessible online [3].

In this paper, an extension of the DRI system is presented that supports analyses of the residues and risk levels in individual samples of food, based on the residues quantified and reported by the U.S. Department of Agriculture's Pesticide Data Program (PDP) [4] and the U.K. Food Standard Agency's residue testing program [5]. The US-PDP has tested over 310,000 samples of 126 commodities, foods, and water over the last 30 years [6]. Multiple food forms are tested for many fruits, vegetables and grains. For example, the PDP has tested fresh apples, applesauce, and apple juice, and tomatoes, tomato sauce and paste, and ketchup. As directed by statute and annual Congressional appropriations, the sampling protocol targets foods that make up a significant share of the diets of pregnant women, infants, and children.

To the extent possible, foods are tested "as eaten" (e.g. skins, shells and seeds removed; fish and animal products as sold to consumers). Domestically grown and imported foods are sampled roughly in accord to market share, as are samples of organic and conventionally grown foods. Over 30 years of PDP testing, 7984 samples of organic food have been tested, or 2.6% of the total. The number of organic samples tested has grown significantly in recent years.

While over 70% of the land area in the United Kingdom (UK) is agricultural, the UK imports roughly 60% of its food supply [7]. As a result, the UK-FSA residue testing program focuses on a wide range of foods, food ingredients, beverages, and multi-ingredient foods imported into the UK. Results of UK-FSA testing are reported in four quarterly reports each year. In 2020, 2,460 samples of 33 different foods were tested. The goal of the UK-FSA residue testing program is to detect and facilitate the removal of high-risk foods containing residues exceeding applicable Maximum Residue Limits (the international equivalent of EPA tolerances).

Over 56% of food samples tested by the UK-FSA in 2020 contained no detectable residues. The number of pesticide analytes the program was capable of detecting that year varied from 371 in fruits and vegetables and 367–368 in grains, starchy foods, and baby food, to 110 in animal products. Four samples with high-risk residues were referred to the Food Standards Agency to assess potential risks and two samples were reported to the Rapid Alert System for Food and Feed to assist efforts to keep the food from reaching consumers [8]. Over the last 18 years (2003–2020) the UK-FSA has sampled around 64,722 samples of 724 foods/sub-foods. Imported samples account for about 51% of total samples. Like the US-PDP, the UK-FSA selects and tests samples of organic food. Over the 18 years, 4,212 samples of organic food have been tested, 6.5% of the total.

A list and description of DRI system output tables can be found in Benbrook and Davis (2021) [2]. By combining US-PDP and UK-FSA residue data in the DRI, the system provides the first opportunity to track differences in pesticide dietary-risk levels in much of the global food supply. The DRI draws primarily on the toxicology data and risk assessments conducted by the EPA; the UK-FSA is the source of toxicology data and food-serving sizes for a few pesticides and foods not regulated by the US EPA nor tested by the US PDP.

This paper introduces the methodologies supporting individual sample tables and provides examples of various options to assess the distribution of pesticide residues and dietary risks. Individual sample tables are presented from recent residue testing carried out by the USDA's PDP (2020 sampling) and by the UK-FSA in the first and second quarters of 2021 (hereafter Q1 and Q2).

Methods

The DRI value for a given food-pesticide combination is the ratio of the level of pesticide$_x$ in food$_y$ divided by the maximum acceptable level of pesticide$_x$ that can be in a serving of food$_y$ without exceeding the allowed daily intake of pesticide$_x$ as determined by the EPA. DRI values across foods are based on single-serving sizes in grams as reported in the USDA's Reference Amounts Customarily Consumed per eating occasion (RACCs) [9]. See Benbrook and Davis, 2020 for methodological details [2].

DRI values can be calculated for a person of any weight. The DRI currently generates tables applicable to a child weighing 16-kg (35.3 lb), corresponding to a child around 4-years-old, based on the 50th percentile in growth charts (average of boys and girls) [10]. Serving sizes applicable to children in the DRI system are estimated as 2/3 of the RACCs for the general population.

By age four, children are consuming a mix of foods similar to adults, yet remain substantially more vulnerable per unit of exposure. This is because they consume more food per kg of bodyweight than adults to support their growth, their bodies are less efficient in breaking down and excreting ingested pesticides, and neural development continues through about age 16 [11].

Individual sample tables

Results tables in this paper focus on the residues and risks arising from the pesticides found in individual food samples. Most tolerances are set to encompass residues of the parent compound/active ingredient, as well as one or more breakdown product or moiety. DRI values for breakdown products and moieties are based on the parent compound's cRfD, unless EPA has set breakdown-product-specific cRfDs.

One of the technical challenges in developing the DRI system entailed dealing with changes over time in how the USDA-PDP and UK-FSA have reported residue findings for a particular pesticide. For example, over time multiple combinations of various analytes detected from an application of the insecticide permethrin have been reported. The three forms of permethrin residues detected and reported by the PDP in 2020, the total number of samples, and number of positives include:

- Total permethrin: 4086 samples tested and 63 positives,
- Permethrin cis: 5514 samples, 101 positives,
- Permethrin trans: 5514 samples, 93 positives.

Methods to aggregate DRI values from parent compounds and their breakdown products are incorporated in the DRI system and are referred to as "Risk Groups." This allows assessments and comparisons of the total estimated dietary risks from one pesticide compared to others, taking into account all the forms of a given pesticide detected in food. The DRI avoids double counting residues in cases where values are reported for "Total Permethrin" or "Total Pesticide$_x$", as well as metabolites and moieties as previously described [2].

Individual sample results are reported at two levels of aggregation:

> Detailed tables: all pesticides found in individual samples listed separately along with corresponding DRI values.
>
> Summary tables: aggregate DRI values across all pesticides reported in a sample and number of residues detected (but no details on the individual pesticides in the sample).

A detailed individual sample report for food$_x$ in year$_y$ typically contains the following data points:

- Sample ID
- Pesticide/analyte detected
- Residue level (ppm)
- DRI value
- Market claim (conventional or organic)
- Origin (domestic or imported), and
- State (if domestic), or country of origin (if imported).

The pesticides/analytes in detailed individual sample report are ranked by each pesticide's DRI value from highest to lowest.

The pesticide dietary risk continuum

In any given year for a specific food, or across all foods, pesticide dietary risk levels can be thought of as lying along a continuum from no or very low-risk, to sizable risks. To provide perspective on relative dietary risk levels across individual samples in a selected food, or across all foods, three relative risk thresholds are set along the continuum:

- Very low-risk individual samples have aggregate DRI values < 0.01
- Low-risk sample DRIs are < 0.1 and at or above 0.01
- Moderate-risk samples fall between 0.1 and 0.999
- High-risk samples range from 1.0 to 9.99
- Very high-risk samples have DRI values of 10 or higher.

Relative-risk zones along the dietary-risk continuum can be determined based on a number of criteria. In DRI applications and for this paper, risk thresholds are typically set based on acceptable levels of exposure to different pesticides as determined by EPA. Any single sample with a DRI value of 1 or higher for a specific pesticide reflects exposures at or above EPA's "level of concern" for a typical 4-year-old. DRI values of 1.0 or higher warrant risk-mitigation efforts to comply with contemporary EPA risk thresholds, toxicology data, and acceptable-risk standards embedded in federal law.

The low-risk threshold of 0.1 is set based on the assumption that any residue associated with a DRI value of 0.1 or lower poses presumptively low-risks. DRI values above 0.1 are of concern and warrant monitoring because most pesticides are applied on dozens of foods and residues may appear in many crops/foods. However, relatively few pesticides pose DRI risk levels at or above 0.1 in 10 or more foods in a given year, hence the selection of 0.1 as the DRI index threshold above which efforts are warranted to track, and possibly reduce risks.

A DRI value below 0.01 is the threshold dividing "low-risk" samples from "very low-risk" samples. "Very low-risk" samples can generally be regarded as posing *deminimus* risks for two reasons: extremely modest contribution to overall risks, and very low-risks relative to the dietary-exposure thresholds established by EPA. However, some "very-low risk" samples may actually pose higher risks than currently known via mechanisms not studied or encompassed in existing toxicology data (e.g. by triggering microbiome dysbiosis or heritable epigenetic increases in adult-onset disease).

The "high" to "very high" risk threshold is a DRI value of 10 or higher. "Very high-risk" samples exceed EPA's maximum allowed exposures by tenfold or more and eliminate at least one of the two tenfold safety factors routinely incorporated in EPA-set chronic Reference Doses.

Results

Figure 1a displays the number of samples in the very low and low-risk zones (n = 5783) across the 19 foods tested by the USDA-PDP in 2020. Figure 1b encompasses individual samples falling within the moderate risk, high and very high-risk zones for the same 19 foods (n = 981). The figures drive home the point that the majority of the samples tested are low-risk. Tangerines had the highest number of positive samples, with 670, while only 6 samples of frozen blueberries contained one or more residues. Sweet bell pepper individual samples accounted for the highest number of samples falling within the moderate and high-risk zones.

The frequency and average number of residues found in the individual samples of foods tested by the PDP in 2020 are shown in Table 1. A total 6764 samples across 19 foods contained one or more residues (70%) and no residues were found in 30%.

The average number of residues per sample ranged from lows of 1.3 in kiwi fruit and 1.4 in cauliflower to 7.5 in frozen blueberries. Despite the highest average number of residues per sample, frozen blueberries posed relatively low DRI risks (0.106). Green bean individual samples posed the highest average aggregate DRI in 2020 (0.620), and have done so in other years as a result of organophosphate (OP) residues (typically acephate and methamidophos). The average DRI value in green beans is nearly 3-X the next highest average (0.225 in sweet bell peppers).

Seven of the 19 foods pose possibly worrisome risks based on average aggregate average DRI values above 0.1. Three of the foods (orange juice, cauliflower, tomato paste) pose average individual sample risk below 0.01 and fall in the "very low-risk" zone of the dietary-risk continuum. The average DRI value across the top-three foods in Table 1 exceeds the average of the bottom three foods by almost 63-fold.

As often the case, there is no clear relationship between the average number of residues per sample and average aggregate DRI values. This is because in the majority of samples, one or two analytes account for 90% or more of aggregate sample DRI values.

The summary data by food in Table 1 sheds no light on the distributions of residue levels and aggregate DRI values across individual samples of each food tested. To gain such perspective, a table was generated displaying the number of residues and aggregate DRI values in all 6764 individual samples tested by the USDA in 2020 that contained one or more residues (see Additional file 1: Table S1).

Results by quartile

Table 2 extracts results from Additional file 1: Table S1 for the top 5 samples in each quartile ranked by aggregate individual sample DRI. Each quartile contains 1691 samples. Individual sample DRI values among the top 5 samples in each quartile provide insight into the distribution of individual sample DRI values across the 6764 samples containing one or more residues.

A green bean sample grown in Florida contained 9 residues and an aggregate DRI of 39.1, the highest of any of the 9600 samples of food tested by PDP in 2020. Residues in two more samples were associated with DRI values over 30 (green collard, another green bean). The average aggregate DRI across the top-five samples in quartile 1 is 25.0, and three of the five samples are clearly in the "very high-risk" zone of the dietary risk continuum. In contrast, the top five samples in the 2nd Quartile had an average DRI of only 0.0304, or 822-times lower than the average DRI across the top-five samples in Quartile 1.

Results reported by the UK-FSA residue testing program for samples tested in the 1st and 2nd quarters of 2021 can be used to construct comparable tables. Table 3 describes the foods sampled by the UK-FSA in the first half of 2021, ranked by number of samples. A total of 934 samples were tested of 42 foods. The UK-FSA tests many more foods per year than the PDP, but far fewer samples of each food (between 1 and 79 samples, compared to 400–650 in the PDP). In Table 3, nine foods for which the UK-FSA tested 4 or fewer samples are combined and results are reported as "Other Foods."

As the case with PDP results in 2020, green beans were the food with the highest average aggregate DRI value (2.17) based on UK-FSA testing. The green beans tested by the UK-FSA in the first half of 2021 contained residues leading to an average, aggregate DRI about 3.5-times higher than the green beans tested by PDP in 2020. A single green bean sample from Pakistan tested by the UK-FSA had an aggregate DRI of 58.3.

The frequency of residues, average number of residues per sample, and average aggregate DRI varies greatly across foods and food groups in both UK-FSA and US-PDP testing. Of the 42 foods tested by the UK-FSA, the average aggregate DRI was over 0.1 for 13 foods (31%), and below 0.01 in the case of 9 foods (21%).

Table 4 covers the top-five individual samples ranked by aggregate DRI among all samples tested by the UK-FSA

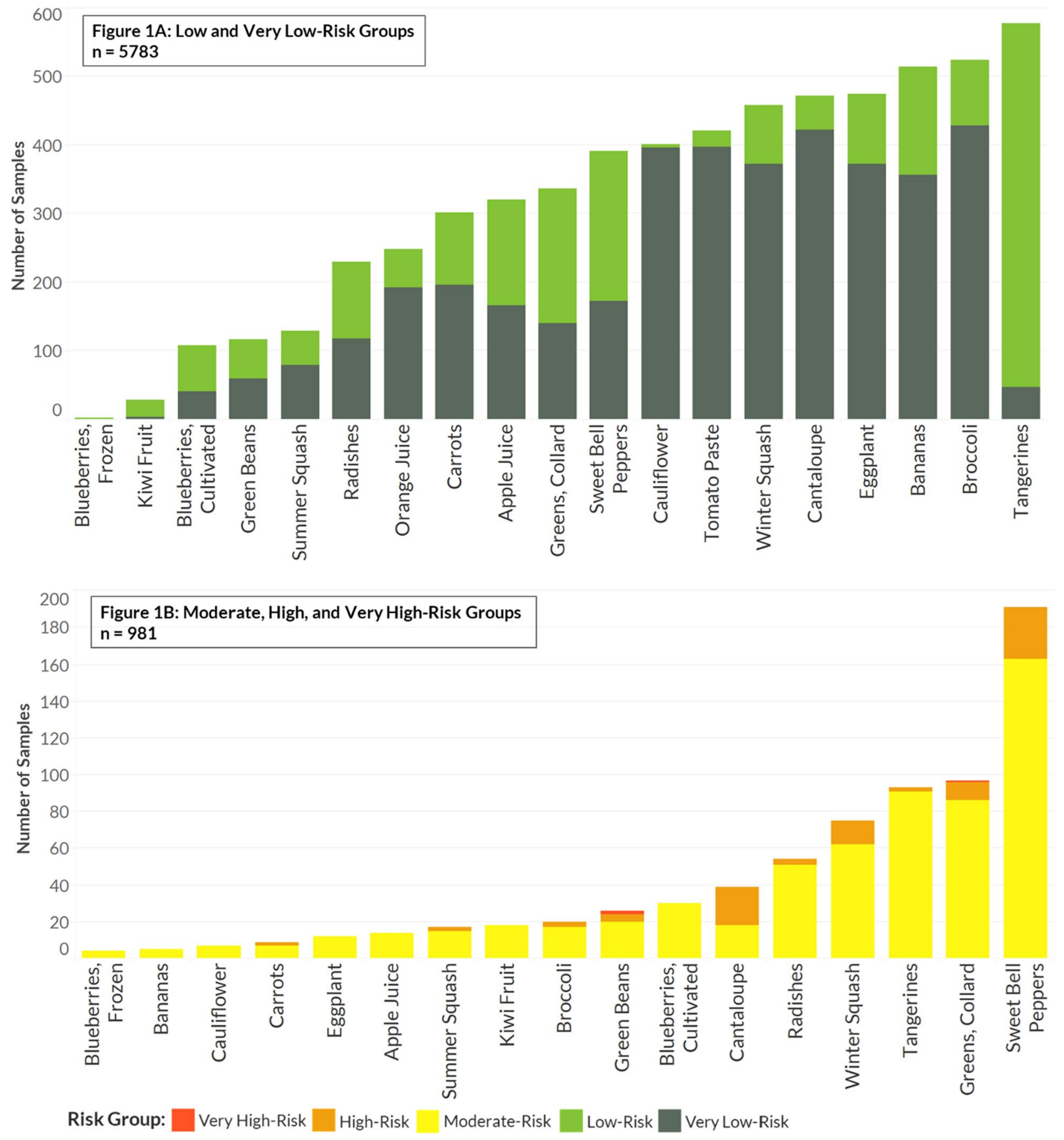

Fig. 1 US-PDP Individual samples tested in 2020: number of positive samples by food, risk group

in the first half of 2021. Like Table 2, the top-five individual samples are shown in each of the four quartiles, along with averages across the five samples. The "very high-risk" green bean sample from Pakistan is the highest-risk sample across all samples tested in this time period by the UK-FSA. It poses a DRI value 4.2-fold higher than the second riskiest sample (an aubergine [eggplant] sample from Uganda). It is noteworthy that all five of the highest risk samples were associated with foods imported into the UK (3 green bean samples and 2 eggplant samples).

Table 5 provides insights on the magnitude of differences in the average number of residues and average

Table 1 Individual samples tested by US-PDP in 2020: frequency, average number of residues, average aggregate DRI

Foods containing residues	Samples tested			Averages per sample	
	Number	Number of positives[a]	Percent positive (%)	Number of residues	Aggregate DRI
Green beans	177	143	81	3.76	0.620
Sweet bell peppers	675	582	86	4.72	0.225
Greens, collard	514	433	84	4.89	0.206
Cantaloupe	694	511	74	1.99	0.147
Winter squash	677	533	79	2.99	0.138
Kiwi fruit	177	47	27	1.26	0.137
Blueberries, frozen	7	6	86	7.50	0.106
Summer squash	176	146	83	3.42	0.0780
Radishes	689	284	41	1.95	0.0718
Tangerines	687	670	98	2.72	0.0648
Blueberries, cultivated	168	138	82	4.09	0.0589
Broccoli	675	544	81	2.44	0.0259
Apple juice	724	334	46	2.60	0.0226
Carrots	499	311	62	1.89	0.0223
Eggplant	661	486	74	2.95	0.0151
Bananas	703	519	74	1.82	0.0105
Orange juice	499	248	50	1.61	0.00836
Cauliflower	692	408	59	1.42	0.00552
Tomato paste	506	421	83	4.70	0.00285
Totals	9600	6764			

[a] Number of samples with one or more analytes detected

aggregate DRI values by quartile in US-PDP testing in 2020 and UK-FSA testing in the first half of 2021. The steep decline in average aggregate DRI values across the top-five samples in each quartile is evident in Table 5. In the case of US-PDP testing, the average DRI across the top-five samples in quartile 1 compared to quartile 2 falls 822-fold (from 25 to 0.0304). The reduction grows to 4389-fold in quartile 3 compared to quartile 1, and 22,727-fold in quartile 4.

In the case of the top-five samples by quartile in UK-FSA testing, the drop in average aggregate DRI across the quartiles is less dramatic than in the case of the US-PDP results. Note that the average number of residues per sample declines only when comparing quartile 1 to quartile 4 in the case of samples tested by the US-PDP, and actually increases from quartile 2 to 3 in the UK-FSA samples. This is clear evidence that the number of residues detected in individual samples is a poor indicator of relative dietary risks.

Individual sample results in high-risk and low-risk foods

Results in Table 1 and 3 provide a basis to select foods posing relatively high, average dietary risks versus those posing much lower risks. Tables 6–9 report the residues found in one high-risk (sweet bell peppers) and one low-risk food (tomato paste) tested by the US-PDP (2020), and in grapefruit (high-risk) and red raspberries (low-risk) samples tested by the UK-FSA (Q1 and Q2 2021).

The highest DRI value across the 675 sweet bell pepper samples tested in 2020 by the US-PDP was 6.4 in a conventionally grown pepper from Mexico that contained 11 residues; the second highest-risk pepper came from Maryland and posed comparable risks (Aggregate DRI = 5.7), but contained only 2 residues (see Table 6).

The average aggregate DRI values across the top-five samples by quartile decline dramatically from 4.8 in quartile 1 to 0.17, 0.034, and 0.0068 in quartiles 2, 3, and 4. In the case of peppers from California and Mexico, there is a sizable spread in aggregate DRI values, with some conventionally grown samples posing up to 954-fold higher risks than other conventionally-grown, low-risk samples.

Table 7 displays the levels and distribution of aggregate DRI values in individual samples of tomato paste tested by the PDP in 2020. All the tomato paste samples in Table 7 were domestically grown and none were labeled organic. Even the highest-risk sample, #8758 from Illinois, poses minimal risk (Aggregate DRI = 0.0239). All samples in quartiles 2, 3 and 4 fall in the *deminimus* zone along the dietary risk continuum

Table 2 Top five individual samples tested by PDP in 2020: by quartile, ranked by aggregate DRI[a]

Sample ID	Food	Number of residues	Aggregate DRI	State or country of origin	Market claim
Quartile 1					
4865	Green beans	9	39.1	Florida	Conventional
5006	Greens, collard	4	37.7	California	Conventional
4941	Green beans	6	31.0	Unknown	Conventional
3048	Cantaloupe	2	9.34	California	Conventional
9036	Winter squash	5	7.72	California	Conventional
Averages		5.20	25.0		
Quartile 2					
126	Apple juice	5	0.0305	Texas	Conventional
6186	Orange juice	2	0.0305	California	Conventional
7932	Tangerines	2	0.0305	California	Conventional
8409	Tangerines	2	0.0305	Peru	Conventional
1421	Bananas	2	0.0303	Guatemala	Conventional
Averages		2.60	0.0304		
Quartile 3					
3182	Cantaloupe	2	0.00572	Guatemala	Conventional
3497	Cantaloupe	2	0.00571	California	Conventional
3268	Cantaloupe	4	0.00571	Guatemala	Conventional
243	Apple juice	3	0.00571	Florida	Conventional
908	Bananas	2	0.00570	Ecuador	Conventional
Averages		2.60	0.00571		
Quartile 4					
2725	Cauliflower	2	0.00108	California	Conventional
4272	Eggplant	1	0.00108	California	Conventional
3046	Cantaloupe	1	0.00108	California	Conventional
3576	Cantaloupe	1	0.00108	California	Conventional
3334	Cantaloupe	1	0.00108	Mexico	Conventional
Averages		1.20	0.00108		

PDP tested 19 foods and reported a total of 6,764 positive samples in 2020

by virtue of two or more zeros in aggregate DRI values. Unlike the big reduction in average DRI values in the top-five samples by quartile in the case of sweet bell peppers and most other relatively high-risk foods, there is only a 29-fold difference between quartile 1 and 4 in Table 7. The decline in the number of residues per sample across the quartiles is modest (8.6 to 4) and similar to the decline in most high-risk foods.

Grapefruit (Table 8) was among the high-risk foods tested by the UK-FSA in 2021. All 41 samples of grapefruit tested in the first half of 2021 were conventionally grown, imported, and contained residues. The majority of samples came from South Africa [14], Israel [9], Spain [7], and Turkey [6] (see Additional file 1: Table S2). While the average number of residues per sample across the quartiles is comparable to many other high and low-risk foods, the differences in average aggregate DRI values are much smaller than in the case of other foods. There is only a 5.5-fold difference between the average DRI across the top-five samples of grapefruit in quartile 1 compared to quartile 4.

But note that the average grapefruit DRI in the lowest-risk quartile is 0.269, well above the 0.1 moderate dietary risk threshold. Accordingly, the majority of grapefruit imported into the UK in the first half of 2021 posed risks possibly of concern, but none of the samples contained residues leading to a DRI score over 10.

The DRI values associated with over three-quarters of the individual samples of red raspberries tested by the UK-FSA in the first half of 2021 pose low or very low-risks (see Table 9). All the samples were conventionally grown and 20 out of the 25 were imported. Three of the five highest-risk samples came from Spain and five of the 10 riskiest samples were domestic samples grown in the UK. The top five, low-risk samples in the fourth quartile were grown in Morocco and the UK. The average DRI in the quartile 1 samples exceeded the DRI in the 4th quartile by 50-fold.

Table 3 Positive individual samples tested by UK-FSA in 2021: residues, frequency, and aggregate DRI values

Food	Sub-food	Samples tested			Averages per sample	
		Number	number positives[a]	Percent positive (%)	Number of residues	Aggregate DRI
Beef	Not specified	79	1	1	1.00	0.00236
Potatoes	Not specified	64	33	52	1.18	0.197
Sweet peppers	Not specified	54	40	74	2.53	0.0304
Grapes	Not specified	53	52	98	3.81	0.138
Aubergines	Not specified	52	38	73	2.29	0.591
Cooking oils	Olive oil	48	13	27	1.54	0.00497
Beans with pods	Green beans	47	34	72	2.53	2.17
Grapefruit	Not specified	41	41	100	5.29	0.563
Wheat flour	Wholemeal	41	29	71	1.69	0.158
Broccoli	Fresh	41	25	61	2.24	0.0813
Bananas	Not specified	41	31	76	3.35	0.0709
Berries	Raspberries (fresh)	36	21	58	2.24	0.0743
Mushrooms	Button	32	10	31	1.80	0.0506
Berries	Raspberries (frozen)	30	30	100	4.47	0.0458
Asparagus	Not specified	30	5	17	1.20	0.00905
Berries	Blueberries (fresh)	26	15	58	2.27	0.0594
Mushrooms	Chestnut	24	12	50	1.50	0.0248
Rice	Basmati	21	10	48	4.40	0.641
Specialty vegetables	Kale	21	8	38	1.88	0.0700
Specialty vegetables	Spring greens	18	10	56	1.70	0.0134
Melons	Honeydew	14	14	100	1.93	0.235
Melons	Watermelon (prepared)	14	4	29	1.75	0.0277
Fish	Cod	14	1	7	1.00	0.00425
Melons	Watermelon	9	9	100	1.56	0.191
Melons	Cantaloupe	9	8	89	2.63	0.0518
Broccoli	Frozen	7	5	71	2.00	0.298
Berries	Blackberries (fresh)	7	5	71	4.60	0.174
Melons	Galia	7	7	100	2.57	0.158
Cheese	Mozzarella	7	2	29	1.00	0.0768
Plantain	Plantain	7	7	100	1.86	0.0463
Rice	Other	6	4	67	2.50	0.0214
Cheese	Ricotta	5	3	60	1.00	0.0709
Berries	Blueberries (frozen)	5	5	100	3.40	0.0248
Other foods	Not specified	24	19	79	1.54	0.221
Totals		934	551			6.60

1. Number of samples with one or more analytes detected. 2. Nine foods with fewer than 5 samples tested were omitted from table; data for these nine foods are grouped together and reported as "Other Foods"

Tables 10 and 11 are examples of two different ways to assess the distribution of the number of residues and aggregate DRI values in samples of a given food. Both tables cover data from the 479 individual samples of apples found to contain residues in US-PDP testing in 2016. Table 10 ranks samples by aggregate DRI and reports results for the samples with the highest (100th/Max) and lowest (First/Min) DRI, as well as samples landing at the 99.5th, 75th, 50th, and 25th percentile of the distribution of DRI values.

Over one-half of the apple samples in Table 10 contained residues associated with aggregate DRI values of 0.11 or higher. All such samples pose risks of possible concern. Less than one-quarter of all samples fall in the low-risk zone along the dietary risk continuum ($DRI < 0.1$).

Table 4 Top five UK-FSA tested individual samples Q1, Q2 2021: by quartile, ranked by aggregate DRI[a]

Sample ID	Food	Sub-food	Number of residues	Aggregate DRI	Country of origin	Market claim
Quartile 1						
3869/2021	Beans with pods	Green beans	2	58.3	Pakistan	Conventional
3916/2021	Aubergines	Not specified	3	13.7	Uganda	Conventional
0093/2021	Aubergines	Not specified	1	5.47	Netherlands	Conventional
3810/2021	Beans with pods	Green beans	5	4.75	India	Conventional
3829/2021	Beans with pods	Green beans	5	4.18	India	Conventional
Averages			3.20	17.3		
Quartile 2						
3573/2021	Berries	Blueberries (fresh)	2	0.124	Morocco	Conventional
0209/2021	Mushrooms	Button	3	0.120	Ireland	Conventional
0130/2021	Cheese	Ricotta	1	0.118	Italy	Conventional
1245/2021	Berries	Blueberries (fresh)	4	0.116	Chile	Conventional
3831/2021	Broccoli	Fresh	2	0.114	Spain	Conventional
Averages			2.40	0.118		
Quartile 3						
0084/2021	Rice	Other	2	0.0277	UK	Conventional
3983/2021	Aubergines	Not specified	3	0.0273	Spain	Conventional
1064/2021	Rice	Basmati	1	0.0264	Netherlands	Conventional
3659/2021	Berries	Blueberries (fresh)	5	0.0258	Morocco	Conventional
3699/2021	Bananas	Not specified	3	0.0257	Costa Rica	Conventional
Averages			2.80	0.0266		
Quartile 4						
3292/2021	Wheat flour	Wholemeal	2	0.00517	UK	Conventional
0965/2021	Berries	Blueberries (fresh)	1	0.00514	Spain	Conventional
2475/2021	Wheat flour	Wholemeal	2	0.00513	UK	Conventional
4000/2021	Grapes	Not specified	3	0.00508	South Africa	Conventional
3382/2021	Wheat flour	Wholemeal	1	0.00500	UK	Conventional
Averages			1.80	0.00510		

Table 11 provides another perspective on the distribution of residues and aggregate DRI values among the 479 samples of apples found to contain residues in 2016.

Table 5 Individual samples tested by US-PDP/UK-FSA: relationship of average residues and aggregate DRI, By Quartile

Metric	Quartile ratios		
	One to two	One to three	One to four
US-PDP 2020			
Number of residues	2.00	2.00	4.33
Aggregate DRI	821	4378	23,148
UK-FSA Q-1&2 2021			
Number of residues	1.33	1.14	1.78
Aggregate DRI	14	650	3392

The distribution of samples is broken into deciles and average values calculated within the deciles. Accordingly, the top decile included 47 samples with an average DRI value of 0.592; the lowest-risk decile was associated with an average DRI of 0.0048, a level clearly in the "very low-risk" zone. The 47 samples in the high-risk decile posed risks 124-fold greater than the 48 samples in the low-risk decile. Table 11 shows that almost 60% of the 479 apple samples contained aggregate DRI values over 0.1.

Figure 2 provides an additional way to graphically portray the distribution of DRI aggregate values across individual samples. The 6764 samples with one or more residue in 2020 US-PDP testing are arrayed along the five risk zones in the dietary risk continuum. Sample number governs the placement of samples within each zone along the horizontal axis; the vertical height of each bar reflects the aggregate DRI of each sample.

Table 6 US-PDP selected individual sweet bell pepper samples 2020: number of residues and aggregate DRI values

Sample ID	Number of residues	Aggregate DRI	Country of origin	Market claim
Top samples 1st quartile				
6337	11	6.415	Mexico	Conventional
6443	2	5.686	Maryland	Conventional
6728	8	4.020	Unknown	Conventional
6246	8	3.947	California	Conventional
6545	7	3.900	Dominican Republic	Conventional
Averages	7.20	4.79		
Top samples 2nd quartile				
6738	5	0.174	Mexico	Conventional
6505	4	0.172	Georgia	Conventional
6417	10	0.169	Florida	Conventional
6418	8	0.166	Florida	Conventional
6477	12	0.163	Mexico	Conventional
Averages	7.80	0.169		
Top samples 3rd quartile				
6802	4	0.0348	Mexico	Conventional
6729	5	0.0347	Mexico	Conventional
6553	2	0.0345	Mexico	Conventional
6813	8	0.0342	Mexico	Conventional
6474	7	0.0340	Mexico	Conventional
Averages	5.20	0.0344		
Top samples 4th quartile				
6803	3	0.00683	Mexico	Conventional
6376	3	0.00683	Unknown	Conventional
6248	4	0.00680	California	Conventional
6446	3	0.00675	Texas	Conventional
6759	2	0.00673	Unknown	Conventional
Averages	3.00	0.00679		

Discussion

The USDA's Pesticide Data Program tested 9,600 samples of 18 foods in 2020. In the case of blueberries, the PDP tested two food forms (fresh/cultivated and frozen) for a total of 19 foods [12]. The US-PDP is targeted by statute toward those foods that account for a significant share of the diet of pregnant women, infants, and children. This sampling strategy was motivated by the realization in the early 1990s that infants and children are not just "little adults" because they are uniquely vulnerable to pesticide exposures [11]. In this way, US law and policy strives to assure a "reasonable certainty of no harm" to the most vulnerable population cohorts, accepting that this strategy often overprotects healthy adults.

One or more residues were found in 6764 US-PDP samples, or 70%. The percent of samples containing one or more residues is highly variable across the 19 foods. Across all PDP years, the percentage of positive samples tends to be high, and sometimes well over 90% in the case of fresh fruits and vegetables, lower for grain-based foods and processed foods, and with one exception, very low for most animal products. The exception is residues of legacy, persistent pesticides (e.g. organochlorines) in fish and animal products. There are, as well, a few unusual food-pesticide combinations, such as the fungicide diphenylamine often detected in milk, but typically as a result of industrial uses of diphenylamine in rubber tubing and gaskets on dairy farms and in milk processing plants.

The UK imports roughly 60% of its food supply from abroad. For this reason, imported samples are a primary focus in sample selection. The UK-FSA sampling protocol adapts year-to-year based on the frequency and level of risk associated with residues across foods in previous program years [8]. Typically the UK-FSA selects about one kilogram of food for testing (about 10 apples); while the PDP selects 5-pounds of apples.

Glyphosate is by far the most heavily used pesticide worldwide [13]. The UK-FSA has tested for glyphosate in food for several years and in 2020 testing, it found

Table 7 US-PDP tomato paste selected individual samples tested in 2020: number of residues, aggregate DRI values

Sample ID	Number of residues	Aggregate DRI	State grown
Top samples 1st quartile			
8758	8	0.0239	Illinois
8878	9	0.0197	Illinois
8648	10	0.0195	Illinois
8874	8	0.0186	Texas
8675	8	0.0160	Illinois
Averages	8.60	0.0196	
Top samples 2nd quartile			
8432	9	0.00331	Illinois
8578	3	0.00330	Illinois
8637	5	0.00330	California
8836	4	0.00323	Arkansas
8748	6	0.00311	Illinois
Averages	5.40	0.00325	
Top samples 3rd quartile			
8447	4	0.00150	Illinois
8832	6	0.00149	Ohio
8877	7	0.00149	California
8421	4	0.00149	Idaho
8847	6	0.00148	Illinois
Averages	5.40	0.00149	
Top samples 4th quartile			
8532	2	0.000693	California
8672	6	0.000684	North Carolina
8699	6	0.000682	California
8567	2	0.000679	Maryland
8488	4	0.000678	Indiana
Averages	4.00	0.000683	

Table 8 UK-FSA grapefruit individual samples in Q1/Q2 2021: number of residues and aggregate DRI values

Sample ID	Number of residues	Aggregate DRI	Country of origin
Top samples 1st quartile			
3569/2021	6	2.48	Morocco
3517/2021	7	1.45	Turkey
3511/2021	9	1.35	Turkey
3925/2021	8	1.16	Cyprus
3091/2021	4	0.962	Israel
Averages	6.80	1.48	
Top samples 2nd quartile			
1542/2021	4	0.663	South Africa
2368/2021	6	0.637	South Africa
1555/2021	3	0.632	Spain
3262/2021	5	0.604	Israel
3048/2021	5	0.574	Israel
Averages	4.60	0.622	
Top samples 3rd quartile			
0785/2021	6	0.467	South Africa
3118/2021	4	0.428	South Africa
3606/2021	9	0.427	Turkey
3669/2021	9	0.427	Cyprus
3892/2021	4	0.417	Israel
Averages	6.40	0.433	
Top samples 4th quartile			
3818/2021	4	0.286	Spain
3104/2021	5	0.278	Spain
0867/2021	5	0.276	South Africa
3533/2021	3	0.265	South Africa
3503/2021	4	0.240	Spain
Averages	4.20	0.269	

glyphosate in 36% of bread samples and all 96 samples of rye. The illegal glyphosate residues found by the UK-FSA in 2020 included three samples of dry mung beans with over-tolerance residues (2 from South Africa, 1 from France). There is no comparable data from the US since the US-PDP has never tested food for residues of glyphosate.

In both programs, the average number of pesticides/analytes found in individual samples varies greatly across foods and food groups. Aggregate DRI levels are highly skewed within foods and across foods. A small percentage of samples account for most of the aggregate dietary risk across all foods. The majority of samples pose risks far lower than high-risk samples.

A small number of pesticide active ingredients, and roughly the same set year to year, are associated with most of the high-risk samples. Figure 1 drives home this point by displaying the distribution by risk group of DRI values for the 6764 individual samples tested by the US-PDP in 2020 that contained one or more residues. Placement along the horizontal axis is determined by sample number and accounts for where each vertical sample bar lies.

Interpreting aggregate DRI values

Proper interpretation of DRI system output tables requires understanding what a DRI value for a given food-pesticide combination reflects, as well as what aggregate DRI values represent. In the case of pesticide$_x$ in food$_y$, the DRI value is the share of the maximum amount of pesticide$_x$ that a four-year old child can ingest in a day without exceeding EPA's "level of concern."

Aggregate DRI values reflect cumulative risks in an individual sample of food, or across all samples tested of a food, taking into account all the analytes detected in the food. The calculation of aggregate risks across multiple

Table 9 UK-FSA red raspberry samples tested in Q1/Q2 2021: residues and aggregate DRI values

Sample ID	Number of residues	Aggregate DRI	Country of origin
Top samples 1st quartile			
4751/2021	2	0.617	Spain
1619/2021	5	0.451	Spain
0051/2021	5	0.219	UK
3289/2021	5	0.171	Serbia
0169/2021	3	0.138	Spain
Averages	4.00	0.319	
Top samples 2nd quartile			
0013/2021	5	0.0511	Serbia
1101/2021	5	0.0499	Serbia
1012/2021	7	0.0481	UK
1219/2021	6	0.0447	Spain
0812/2021	5	0.0445	Serbia
Averages	5.60	0.0477	
Top samples 3rd quartile			
3264/2021	6	0.0257	Serbia
0135/2021	4	0.0255	UK
2317/2021	2	0.0253	Morocco
1154/2021	1	0.0241	Morocco
0073/2021	2	0.0227	Serbia
Averages	3.00	0.0247	
Top samples 4th quartile			
0828/2021	1	0.00904	Morocco
2268/2021	3	0.00832	UK
2488/2021	1	0.00617	Morocco
1139/2021	3	0.00441	UK
1505/2021	1	0.00412	Morocco
Averages	1.80	0.00641	

Table 10 US-PDP samples of domestic, conventional apples tested in 2016: selected samples, DRI results and percentiles

Sample ID	Number of positives	Aggregate sample DRI	Ranking	Percentile
211	7	2.03	1	100th/Max
313	6	2.01	2	99.5th
243	6	0.208	120	75th
600	2	0.112	240	50th
705	3	0.0448	360	25th
400	1	0.000313	479	First/Min
Total positive samples:	479			

Table 11 US-PDP samples of domestic, conventional apples tested in 2016: number and aggregate DRI by Decile

Decile group number	Number of samples	Average number of positives	Average aggregate DRI
1	47	6.36	0.592
2	48	5.48	0.278
3	48	4.54	0.210
4	48	5.06	0.167
5	48	4.48	0.129
6	48	3.90	0.0979
7	48	5.19	0.0723
8	48	3.90	0.0456
9	48	4.10	0.0215
10	48	2.73	0.00479

residues in a given sample of food assumes that multiple DRI values are additive.

This assumption both overestimates and understates actual aggregate risks when a sample of food contains two or more pesticide residues. It overstates risk since each individual-pesticide DRI value represents a portion of an EPA-set maximum acceptable intake. That acceptable intake level is, in turn, based on the risk endpoint used to set the cRfD for that pesticide. For example, one pesticide in an individual sample might be associated with 1/10 of the maximum allowed dietary intake based on an adverse impact on the immune system, while other pesticides might represent 1/3 or 1/40th of maximum allowed levels of exposure based on adverse reproductive or neurological effects. Such portions of allowable risk are not simply additive, nor are they generally equivalent.

Aggregate DRI values represent the sum of partial risks across multiple, adverse outcomes. It is important to note that regulatory authorities worldwide strive to regulate pesticides equitably, yet set key exposure thresholds on the basis of different adverse-effect endpoints. These endpoints vary significantly in terms of severity, impacts across population cohorts, treatability, and reversibility. Accordingly, two pesticides with the same chronic Reference Dose often do not pose comparable risks. Also, some pesticides pose different risks through more than one mechanism (e.g. organophosphates can impair health through developmental neurotoxicity and cholinesterase inhibition), while other pesticides can increase the risk of multiple adverse health outcomes via a single mechanism of action (e.g. oxidative stress). The way cRfDs are

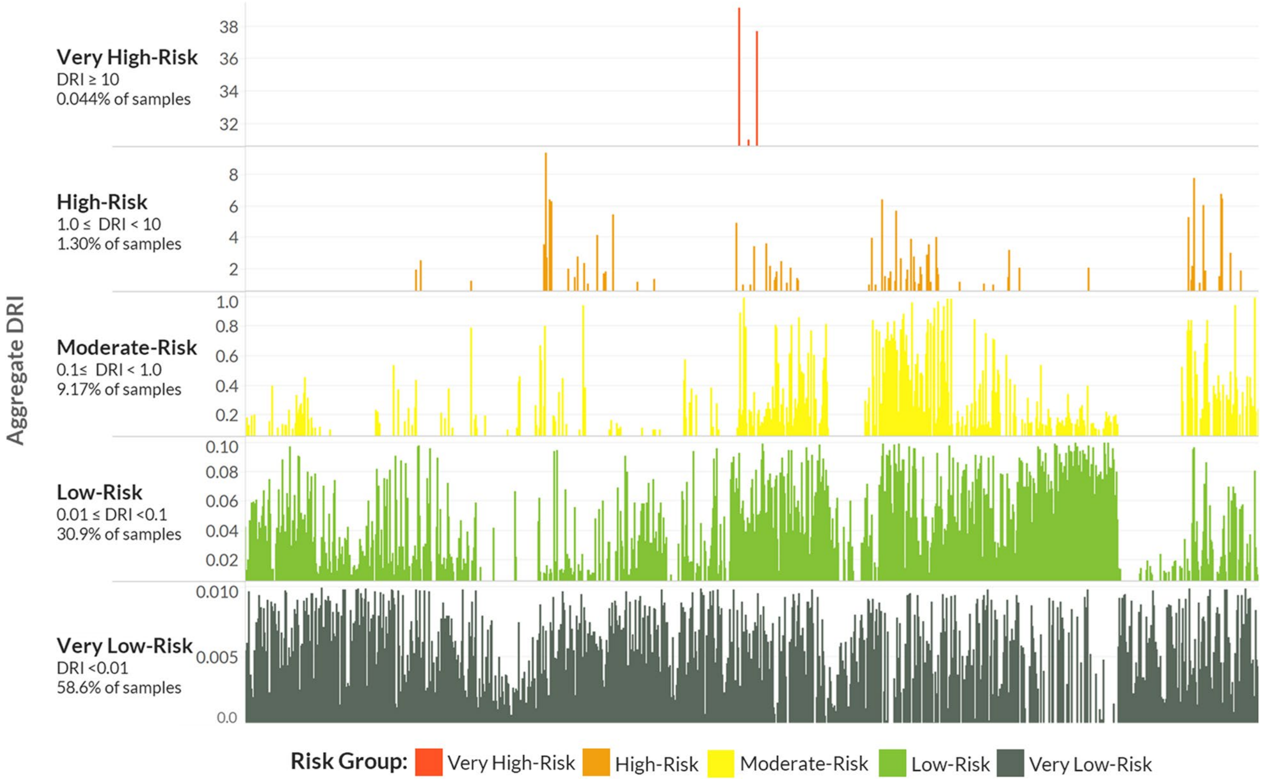

Fig. 2 US-PDP Individual samples tested in 2020: aggregate DRI by risk group of 6764 positive samples

set and most dietary risk assessments conducted do not take these differences into account.

The DRI also underestimates risks in four ways: (a) synergistic effects may be triggered as a result of dietary exposures to two or more pesticides in a given serving of food and/or other xenobiotics in food or a person's environment, (b) existing cRfDs may be too high because pesticides have not been tested for certain adverse outcomes that might be triggered at lower doses (e.g. microbiome dysbiosis), (c) virtually all toxicology studies used to set cRfDs are done on parent compounds, not formulations, and some co-formulants alter a pesticide's ADME (Absorption, Distribution, Metabolism, Excretion) in ways that increase risk levels, and (d) flawed or inappropriately analyzed toxicology studies sometimes lead to inappropriately high cRfDs [14, 15].

Tracking high-risk food-pesticide combinations

Regardless of the methods used to quantify pesticide dietary risks, the number of low-risk samples vastly exceed the number of high-risk samples in most crops/foods. Identifying high-risk samples supports more effective targeting of research and regulatory efforts. It can also help reduce focus on consistently low-risk foods and pesticides, freeing up resources to target known risk-drivers.

The DRI value for a given food-pesticide combination is an index that reflects the degree to which the residues in a single serving of food fills the applicable "risk cup" for that pesticide in a given food. The pesticide dietary "risk cup" concept was developed and used by EPA in the process of implementing the Food Quality Protection Act (FQPA) [16]. A "risk cup" for pesticide$_x$ reflects the maximum amount of pesticide$_x$ that can be in all foods ingested in a day without exceeding the EPA's "level of concern." The risk-cup concept and the DRI index are two ways to analyze the same thing—actual or projected pesticide dietary exposures relative to maximum, allowed and presumably "safe" exposures. Both rely on essentially the same data and are grounded in EPA dietary risk-assessment policies and procedures.

Because all DRI values are calculated based on to the most recent EPA assessment of pesticide chronic toxicity, DRI system output is useful and relevant in assessing the degree to which pesticide product labels are keeping pesticide-residue levels in food below EPA's contemporary "level of concern" (i.e. cumulative exposures are below a pesticide's cRfD). Any DRI value over one presumptively exceeds EPA's level of concern.

The provisions in the FQPA and EPA dietary risk-assessment policy call for the setting of tolerances and pesticide label provisions such that total expected, or "cumulative" dietary exposures from all food-crop uses of a pesticide do not overfill the pesticide's "risk cup." Hence, current law and policy mandate consideration of aggregate dietary exposures and risk across all crops a pesticide is registered for use on.

As evident in tables and figures throughout this paper, pesticide dietary risks are highly skewed, with most of the risk in a given food accounted for by a very few relatively high-level residues. Does this mean pesticide law and policy are mostly achieving their stated objectives?

The US-PDP typically selects several hundred samples of a given food in a given year. Samples are collected across states and by country of origin roughly proportional to their contribution to the overall supply of the food. Hence, the distribution of residues in PDP samples can be used to approximate the residues and risk levels likely present in the total US supply of each food in the program.

Table 12 provides examples of the calculations required to estimate how many servings of a given food are represented by a single PDP sample. The calculations utilize total annual per capita consumption of each food, the total pounds of the food consumed by the US population, and the share of that total intake represented by a single PDP sample.

For example, nearly 6 billion pounds of apples were consumed in 2016. Considering that one PDP sample of apples is typically derived from a composite 5-pound selection of apples, the total number of 5-pound samples of apples would be ~ 1.2 billion if all apples nation-wide were tested. Based on the typical, child-serving size for apples of 99 g (about 2/3 of a medium size apple), each PDP sample represents around 74,600 daily servings of apples. This calculation overstates the number of servings across the whole population by about 40%, since the typical adult serving size is around 140 g. But clearly, any single high-risk food sample represents many thousand daily servings of most foods.

It is also probable that the highest-risk sample of a given food tested by the US-PDP or the UK-FSA in a given year is actually not the highest-risk sample across all the food ingested in a given year.

Insights and implications for pesticide risk assessment and regulation

Combinations of residues of about a dozen pesticide-active ingredients in around 10 foods account for nearly all pesticide dietary risk from year to year [2]. Relatively few pesticides account for most of the risk annually, and 90% or more of the several hundred active ingredients included in US-PDP and UK-FSA testing programs contribute modestly or hardly at all to pesticide dietary risks. The most heavily used type of pesticide—herbicides—contribute modestly or not all to pesticide dietary risks across the food supply.

DRI system output tables similar to Table 1 and Table 3 above can be generated for all years and used to identify foods often appearing among the top-ten when ranked by aggregate DRI values. Then, by focusing on the individual sample tables for a given high-risk food, it is possible to identify samples falling in the very high and high-risk zone along the dietary risk continuum. Individual sample tables include where the sample was grown and the production system used.

Table 12 Number of servings represented in one PDP sample for selected high-consumption foods in the U.S

Food (PDP year)	Apples (2016)	Peaches and nectarines (2015)	Strawberries (2016)	Kale (2018)	Sweet peppers (2019)	Tomatoes (2016)
Annual consumption per Capita (lbs)	18.5	2.80	6.80	0.900	10.4	17.3
U.S. population (million)	322.2	321.0	323.3	326.9	328.5	323.2
Total annual U.S. consumption (million lbs)	5961	899	2198	294	3416	5591
PDP sample size (lbs)	5	5	5	3	5	5
Total annual number of 5-pound samples (million)	1192	180	440	98	683	1118
Single serving size (grams)	99.3	100	96	56.7	61.3	96
Number of servings in one 5-pound sample	22.8	22.7	23.6	24.0	37.0	23.6
Number of servings per year represented by one PDP sample	27,230,411	4,076,609	10,387,165	2,353,813	25,277,973	26,415,544
Number of servings per day represented by one PDP sample	74,604	11,169	28,458	6449	69,255	72,371

As new samples are tested by the US-PDP and UK-FSA, they can be run through the DRI, or a similar system, to recognize those samples and residues posing risks of possible concern. Currently, only samples of food containing residues above US EPA-set tolerances or international Maximum Residue Levels (MRLs) are flagged for enforcement scrutiny in the US and UK. Such samples occasionally pose relatively high-risks, but often do not.

The far more worrisome, systemic deficiency in how regulatory authorities around the world now strive to assure pesticide residues in food are "safe" is the fact that many residues below tolerance or MRL levels in individual samples of food pose risks that clearly exceed the dietary-risk thresholds regulators have established to govern presumptively "safe" daily exposures. The reason for this blind-spot in dietary risk assessment and related regulatory decisions is that regulators base decisions on typical, average, or expected residues, and *not on actual high-end residues present in some samples*. This is why focus should now shift to the actual residues and estimated risks in individual samples of food.

Limitations and future research needs

The goal of pesticide regulators and related toxicology and public health research is to prevent exposures that might possibly trigger harm. There are two essential clusters of data needed to quantify and track pesticide-dietary risks. One leads to estimates of dietary exposure to a given pesticide via a given food or several foods, and the second draws on toxicology data to translate estimated exposures into quantifiable risks of adverse health outcomes.

In general for widely consumed foods, and especially fruits and vegetables, the residue data and methods now accessible to estimate daily pesticide intakes via food across the US or UK population are of high quality. There is much greater uncertainty in the accuracy of EPA-set or international chronic Reference Doses for any individual pesticide and across pesticides. However, the cRfDs established for different pesticides are the only science-based threshold available for use by regulators, scientists, and industry.

Many current cRfDs likely do support generally safe food uses of pesticides, especially when coupled with pesticides that rarely result in residues. This is the case for most herbicides. But insecticide and fungicide residues are common on many fruits and vegetables. Indeed, four or more residues are detected in many of the samples of fresh produce.

New methods are needed to set pesticide chronic Reference Doses that more accurately reflect the potential of pesticides to trigger adverse health outcomes [17]. Novel methods need to take into account the full range of adverse impacts observed in animal and other studies, rather than just the single adverse outcome identified in the toxicology study used to set a pesticide's cRfD. For example, adjustments could be made in pesticide cRfDs for the severity of the adverse impact, its reversibility and treatability, the degree to which certain segments of the population might be more vulnerable to a certain type of adverse impact, and the number of different mechanisms through which a given pesticide might trigger adverse health outcomes (e.g. oxidative stress: damage to DNA, reproductive impacts, developmental delays).

The accuracy and reliability of pesticide dietary-risk assessments are typically greatest in the case of fresh foods and single-ingredient foods, yet different food forms and multi-ingredient foods account for two-thirds or more of daily caloric consumption. Better methods and data are needed to accurately estimate dietary exposures from processed and multi-ingredient foods. Currently, various assumptions and default values are used to estimate residue levels in dried, frozen, canned, and cooked foods, as well as in juices, pastes, sauces, dressings, and condiments. The accuracy of these adjustment factors should be tested and improved via expanded testing of residue levels in a greater diversity of foods. Other needed steps to improve the accuracy of pesticide risk assessments are outlined in recent papers [17–19].

Conclusions and policy implications

The calculation of pesticide dietary risks in individual samples of food can support important enhancements in ongoing efforts to curtail the presence of possibly risky residues in food. The highly-skewed distribution of dietary risk levels across individual samples of food points to significant opportunities to drive down dietary risk levels by targeting efforts toward the relatively few food-pesticide combinations that fall in the high and very high-risk zones along the dietary risk continuum.

Likewise, sharper focus on the distribution and levels of individual sample dietary risks will show that most pesticide applications rarely if ever result in worrisome residues. Redirecting some of the resources now allocated to tracking insignificant risks towards tracking high-risk foods can speed progress in reducing overall risks.

It is clear that tracking the average number of residues in different foods, or across individual samples of any given food is an unreliable indicator of actual dietary risk levels. Pesticide dietary risk analytical systems that place heavy weight on the number of residues detected should shift to heightened focus on actual risks per serving based on reported residue levels and current estimates of pesticide toxicity (e.g. cRfDs).

Government and private residue-testing programs can enhance return on investment by running new results through a dietary risk-assessment system like the DRI. Such a system can be programmed to flag possibly worrisome residues. By identifying high-risk samples, government agencies will have a better chance year to year of keeping high-risk foods out of the food supply. Tracking high-risk samples back to the field of origin will incrementally build knowledge regarding the geographic regions, and sometimes even growers most often shipping high-risk foods.

For decades, government pesticide-regulatory authorities and residue testing programs have reassured consumers about pesticide residues in food by reporting the generally low percentage of samples found to contain residues exceeding established tolerances or MRLs. Such assurances of safety are overstated and unreliable. A future paper will report the portion of the supply of different foods that contain residues below applicable tolerances and MRLs that nonetheless lead to risks exceeding regulatory "levels of concern".

The DRI system facilitates identification of such foods and samples so that dietary risk-mitigation efforts can be targeted where the real risks are. Enhanced focus on the distribution of pesticide dietary-risk levels across individual samples and servings of food will provide key new data and insights to support efforts to drive down overall pesticide dietary risks.

Abbreviations

ADME: Absorption, distribution, metabolism, excretion; CDC: Centers for disease control (United States); cRfD: Chronic reference dose; DRI: Dietary risk index; EPA: Environmental protection agency (United States); FIFRA: Federal insecticide, fungicide, and rodenticide act; FQPA: Food quality protection act; ID: Identification; Kg: Kilogram; Lb: Pound; MRL: Maximum residue level; OPP: Office of pesticide programs; PPM: Parts per million; Q1: Quarter 1; Q2: Quarter 2; RACC: Reference amount customarily consumed; UK: United Kingdom; UK-FSA: Food standards agency (United Kingdom); US: United States; USD: United States Department of Agriculture; US-PDP: Pesticide data program (United States).

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12302-022-00636-w.

Additional file 1: Table S1. US-PDP—all samples: individual positive samples, ranked by aggregate sample DRI (Highest - Lowest) for all commodities tested by in 2020. **Table S2.** UK-FSA grapefruit samples tested in Q1/Q2 of 2021.

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Author contributions

CMB developed the DRI system and the individual sample methodology, generated the tables, and wrote the paper. The author read and approved the final manuscript.

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Availability of data and materials

Access the DRI system at https://hygeia-analytics.com/pesticides/dietary-risks/dietary-risk-index/.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The author has served as an expert witness in pesticide litigation in the US. None of these expert witness engagements have focused on pesticide dietary exposures and risk levels.

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