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Human dietary exposure to chemicals in sub-Saharan Africa: safety assessment through a total diet study



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Summary

Background Human dietary exposure to chemicals can result in a wide range of adverse health effects. Some substances might cause non-communicable diseases, including cancer and coronary heart diseases, and could be nephrotoxic. Food is the main human exposure route for many chemicals. We aimed to assess human dietary exposure to a wide range of food chemicals.

Methods We did a total diet study in Benin, Cameroon, Mali, and Nigeria. We assessed 4020 representative samples of foods, prepared as consumed, which covered more than 90% of the diet of 7291 households from eight study centres. By combining representative dietary surveys of countries with findings for concentrations of 872 chemicals in foods, we characterised human dietary exposure.

Findings Exposure to lead could result in increases in adult blood pressure up to 2.0 mm Hg, whereas children might lose 8.8–13.3 IQ points (95th percentile in Kano, Nigeria). Morbidity factors caused by coexposure to aflatoxin B1 and hepatitis B virus, and sterigmatocystin and fumonisins, suggest several thousands of additional liver cancer cases per year, and a substantial contribution to the burden of chronic malnutrition in childhood. Exposure to 13 polycyclic aromatic hydrocarbons from consumption of smoked fish and edible oils exceeded levels associated with possible carcinogenicity and genotoxicity health concerns in all study centres. Exposure to aluminium, ochratoxin A, and citrinin indicated a public health concern about nephropathies. From 470 pesticides tested across the four countries, only high concentrations of chlorpyrifos in smoked fish (unauthorised practice identified in Mali) could pose a human health risk.

Interpretation Risks characterised by this total diet study underscore specific priorities in terms of food safety management in sub-Saharan Africa. Similar investigations specifically targeting children are crucially needed.

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Introduction

In 2015, UN Member States adopted the Agenda for Sustainable Development,¹ which will be assessed in 2030. However, the Sustainable Development Goals (SDGs) for zero hunger (SDG2), good health and wellbeing (SDG3), decent work and economic growth (SDG8), reduced inequalities (SDG10), and responsible production and consumption (SDG12) will not be met unless food is safe in developing countries.

The public health effect of foodborne diseases globally is unknown.² Assessing long-term effects of chronic exposure to chemicals is a challenge. Studying the adverse effects of chemicals is complex because of the various exposure routes and the multiple causes of health outcomes. Many food chemicals, including heavy metals, mycotoxins, pesticide residues, and industrial contaminants, are associated with a series of non-communicable diseases such as infertility, developmental effects, neurotoxicity, nephrotoxicity, coronary heart disease, and cancer.^{3,4} For instance, aflatoxins,

synergistically with hepatitis B virus, have the potency to increase the incidence of liver cancer.⁵ A much less highlighted, but nonetheless serious, result of exposure to mycotoxins is the possible contribution to child growth impairment and, therefore, to chronic malnutrition.^{6–8} Stunting is now identified as a major global health priority and affects more than 160 million children globally.⁹ Low maternal stature, a result of retarded growth, has been associated in turn with increased fetal growth restriction and child mortality.¹⁰ In addition to developmental neurotoxicity,¹¹ lead exposure can also increase risk of coronary heart disease.¹²

To ascertain the extent to which actual human dietary exposure to food chemicals is likely to harm consumers' health, it is pertinent to assess risks by combining food contamination and food consumption data (dietary exposure) with available toxicological studies.¹³

The total diet study method is a harmonised approach recommended by national and international food safety authorities and agencies for assessing the dietary

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For the French translation see Online for appendix 1

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Research in context

Evidence before this study

We did a systematic literature review to find previous food chemical contamination surveys done in Africa looking at the occurrence of pesticides in raw vegetables, aflatoxins in various raw food commodities, and polycyclic aromatic hydrocarbons in smoked fish. We searched PubMed using the raw food commodities and hazards as keywords, for reports published in English. Available estimates of human dietary exposure to food chemicals in Africa are mainly based on national food balance sheets aggregated at national level with food contamination data generated from targeted analytical plans. Considering the nature of these food consumption and contamination data, the quality of this evidence is too limited, sparse, and generally non-representative of the whole diet or of specific population groups. To address the actual situation in terms of quality and food safety, science-based evidence of human dietary exposure to food chemicals in Africa populations needs to be better recorded through a more refined risk assessment process, so that policy makers can implement corrective actions to ensure a better protection of consumer health.

Added value of this study

We did a systematic, multicentre, total diet study in four countries in sub-Saharan Africa based on foods prepared as

consumed, which covered 90% of typical diets. State-of-the-art analytical techniques based on mass spectrometry screened 872 analytes in foods with the lowest limits of determination currently available. This study is the first to estimate human dietary exposure levels from eight study centres based on harmonised household-based dietary data. The coverage of chemical compounds is also unprecedented in Africa.

Implications of all the available evidence

National food safety authorities from Benin, Cameroon, Mali, and Nigeria, in addition to the Food and Agriculture Organization of the United Nations and WHO international standard setting institution (Codex Alimentarius), gained an evidence-based risk assessment with respect to a wide range of chemicals in African foods. Human dietary exposure levels beyond safe toxicological thresholds mean that implementation of adequate policies, strategies, resources, and targeted risk-mitigation actions are needed. National and international roadmaps to better protect children and adults will be guided by the study results, although additional data might be needed to better and specifically protect the infant and young child in sub-Saharan Africa.

exposure of populations to food chemicals. This methodological approach is cost-effective and more accurately characterises human exposure to food chemicals than do occurrence studies.^{14,15} Specific aspects characterise a total diet study, including the representativeness of the sampling and the preparation of the samples as consumed, so that it represents a pertinent public health risk assessment method, as far as food safety and nutrition are concerned.

We aimed to do a multicentre total diet study in sub-Saharan Africa to assess exposure levels to toxic substances resulting from the consumption of food. By comparing human dietary exposure levels with health-based guidance values or toxicological endpoints established by international scientific expert advisory bodies, the risk assessment to foods chemicals of public health concern in sub-Saharan Africa was characterised. We share our conclusions for consideration by policy makers with a mandate in terms of consumer health protection.

Methods

Food consumption data and concentration levels of chemicals

The total diet study method has been described elsewhere.¹⁶ In brief, food consumption data were estimated as the daily amount of food (consumed in g per adult male equivalent per day) derived from previously existing household budget surveys generated by national statistics

authorities in Benin, Cameroon, Mali, and Nigeria from 72 979 households. In total, 4020 food samples, representing at least 90% of each national total diet by weight, were obtained from a core list of 84 subgroups.¹⁶ A food composite approach was taken, pooling 12 samples of the same core food to form 335 pooled samples.¹⁶ Collection was done during a rainy season (October, 2017) and a dry season (November, 2018). Pooling of 12 sub-samples is a cost-effective approach to estimate mean concentration levels, with limited effect on the CI.¹⁷ Both the statistical basis for selection of the number of pooled samples and the principle of using mean concentration levels for estimating human chronic dietary exposure have been previously published.^{13–18} Analytical performance, limit of detection (LOD), and limit of quantification (LOQ) typically become limiting factors for risk assessors. To avoid, as much as possible, uncertainties in estimates of human dietary exposure that could result from inclusion of censored data, testing laboratories with the lowest analytical limits were selected. Composites of foods prepared as consumed were tested by four accredited official laboratories (Laberca-Oniris, Inovalys, and Anses in France; and Boku in Austria) for 872 food chemicals that include 470 pesticides, 295 mycotoxins and other secondary metabolites, 30 metals and trace elements, 20 polycyclic aromatic hydrocarbons, and 57 persistent organic pollutants, including polychlorinated dibenzo dioxins and furans, polychlorinated biphenyls, brominated flame

retardants, perfluoro alkyl substances, and chlorinated flame retardants. The mean concentration levels of chemicals (exceeding 40 000 analytical results) in foods that we generated in the framework of this study were published elsewhere.^{19–23}

Human dietary exposure

The number of households considered at each of the eight study centres (Littoral, Benin; Borgou, Benin; Duala, Cameroon; North Region, Cameroon; Bamako, Mali; Sikasso, Mali; Lagos, Nigeria; and Kano, Nigeria) depended on available data from household budget surveys. Only households with energy intakes equivalent per day were considered (Littoral, 1490 households; Borgou, 1004; Duala, 890; North Region, 508; Bamako, 1318; Sikasso, 1015; Lagos, 301; and Kano, 765).¹⁶ Estimated consumption of 84 core foods from each of the 7291 normal reporting households, expressed in units per kg of bodyweight, was multiplied by the mean occurrence of food chemical concentration levels with corresponding foods reported to be consumed by individuals at each study centre, using SAS software, version 9.4. When a laboratory test did not detect a chemical, the chemical concentration in the sample could have any value between zero and the LOD. Uncertainty attributable to non-detected and non-quantified analytes was taken into consideration and reported in the human dietary exposure results by using zero for concentrations below the LOD and LOQ (lower-bound scenario) and the LOQ for concentrations over the LOD and below the LOQ in the maximalist approach (upper-bound scenario).¹³ The contribution of main core foods to the human dietary exposure was calculated as the proportion of the sum of household exposures and was assessed for each study centre. Estimates of the contribution of core foods to the sum of a household's dietary exposure was completed for each study centre and is, therefore, geographically specific.

Risk characterisation

Human dietary exposure levels were compared with the chemical hazard characterisation established by Joint Food and Agriculture Organization of the United Nations (FAO) and WHO Expert Committees, when available. Since 1956, the Joint FAO and WHO Expert Committee on Food Additives (JECFA) and the Joint FAO and WHO Meeting on Pesticide Residues (JMPR) have assessed and generated a series of health-based guidance values and benchmark dose limits, which are commonly used by food safety authorities as toxicological references for food risk-assessment. A situation at risk is generally considered to be of public health concern when human dietary exposure exceeds a health-based guidance value, or when a margin of exposure (ie, the ratio between a benchmark dose limit and an actual human dietary exposure level) is below a threshold of concern of 10 000.^{13–15} In the case of aflatoxin B1 and lead, the

quantitative risk assessment approach based on human epidemiological evidence as proposed by JECFA was applied.²⁴

Statistical analysis

We calculated the dispersion of human dietary exposure quartiles for each study centre (upper-bound approach) and presented these data as boxplots. Taking into consideration the variability of dietary exposure levels among study centres, and to facilitate comparison of diagrams, we excluded outliers from box-and-whisker representations. We calculated the distribution of human dietary exposure levels for mean and high-exposure levels (95th percentile) and health outcomes with a lower-bound and upper-bound approach. The minimum difference between the lower-bound and upper-bound scenarios can be explained by low analytical limits, or by the sensitivity of our analytical methods. This low difference justified the use (by default) of upper-bound exposure in boxplots, which is both conservative and unlikely to significantly overestimate the exposure. We present upper-bound data here, and lower-bound data are presented in appendix 2 (pp 1–8). We summarised chemical hazards for which the degree of health concern could not be ruled out.

Role of the funding source

The funder had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The first author and the corresponding author had full access to all data in the study and had final responsibility for the decision to submit for publication.

Results

From systematic screening of 872 substances in foods from eight study centres, 305 food chemicals were detected or quantified above the analytical limits (LOD or LOQ). For each of the eight study centres, we assessed the risk associated with dietary exposures to 68 detected chemicals, including aluminium, arsenic, cadmium, mercury, lead, 11 mycotoxins, 13 polycyclic aromatic hydrocarbons, and 39 pesticides. These assessments were based on the availability of a toxicological reference and the priorities expressed by national stakeholders. Health-based guidance values or toxicological endpoints used for the risk assessment of the 24 chemical compounds, which might represent a public health concern in one or more study centre, are shown in table 1.

The mycotoxin aflatoxin B1, the most potent aflatoxin, was assessed individually (figure 1A). JECFA estimated that a morbidity factor could be derived from aflatoxin B1 dietary exposure expressed in ng/kg bodyweight per day, multiplied by 0.3 for hepatitis B virus antigen bearers (HBAG-positive) and 0.01 for non-bearers (HBAG-negative).²⁴ Application of these criteria to the national prevalence of HBAG²⁵ led to an estimated morbidity factor within a range from 0.2 (Duala) to

See Online for appendix 2

	Health-based guidance value or toxicological endpoint	Toxicological adverse effect	Animal species	Scientific expert body (report no)	Evaluation year
Aflatoxin B1	Morbidity factor of 0.3 ng/kg bodyweight per day (HBAG-positive) and 0.01 ng/kg bodyweight per day (HBAG-negative)	Liver cancer	Humans	JECFA (83)	2016
Sterigmatocystin	BMDL ₁₀ of 0.16 mg/kg bodyweight per day	Liver cancer	Rodents	JECFA (83)	2016
Fumonisin (sum of B1, B2, and B3)	Group PMTDI of 2 µg/kg bodyweight per day	Nephrotoxicity and aflatoxin synergist	Rodents	JECFA (83)	2016
Ochratoxin A	PTWI of 112 ng/kg bodyweight per week	Nephrotoxicity	Pigs	JECFA (68)	2007
Citrinin	Level of no concern of 0.2 µg/kg bodyweight per day	Nephrotoxicity	Rodents	EFSA (10)	2012
Lead	0.6 µg/kg bodyweight per day loss of 1 IQ point (children)	Neurodevelopment	Humans	JECFA (73)	2010
Lead	1.3 µg/kg bodyweight per day for 1 mm Hg increase in blood pressure (adults)	Cardiovascular	Humans	JECFA (73)	2011
Aluminium	PTWI of 2 mg/kg bodyweight per week	Nephrotoxicity	Rodents	JECFA (74)	2011
Polycyclic aromatic hydrocarbons (sum of 13 carcinogens and genotoxic compounds)	BMDL ₁₀ of 100 µg/kg bodyweight per day	Forestomach squamous cell papillomas and carcinomas and alveolar and bronchiolar adenomas and carcinomas	Rodents	JECFA (64)	2006
Chlorpyrifos	ADI of 0.01 mg/kg bodyweight per day	Neurotoxicity	Humans and rodents	JMPR (178)	2004
Chlorpyrifos	ADI of 0.001 mg/kg bodyweight per day	Neurotoxicity	Rodents	EFSA (12)	2014

HBAG=hepatitis B virus antigen. FAO=Food and Agriculture Organization of the UN. JECFA=Joint FAO and WHO expert committee on food additives. BMDL₁₀=benchmark dose lower confidence limit with increase in adverse response of 10%. PMTDI=provisional maximum tolerable daily intake. PTWI=provisional tolerable weekly intake. EFSA=European Food Safety Authority. IQ=intelligence quotient. ADI=acceptable daily intake. JMPR=Joint FAO and WHO Meeting on Pesticide Residues.

Table 1: Health-based guidance values or toxicological endpoints used for risk assessment of 24 chemical compounds of concern

23.9 (North Region) additional liver cancer cases per 100 000 inhabitants (table 2).²⁴ The main food contributors to aflatoxin B1 exposure were maize followed by peanut and peanut oil.

Sterigmatocystin is an aflatoxin B1 precursor regarded as an emerging mycotoxin, which also presents genotoxic carcinogenic potency. Current knowledge does not enable estimation of the burden of liver cancer attributable to sterigmatocystin exposure. Because it is impossible to establish a toxicity threshold for genotoxic carcinogens, JECFA proposed the margin of exposure approach for assessing the safety of this type of chemical.²⁴ In the case of sterigmatocystin, a ratio between a benchmark dose limit with 10% increase in adverse response (BMDL₁₀) of 0.16 mg/kg bodyweight per day and an exposure level of highly exposed individuals (95th percentile) below 10 000 means that a human health risk cannot be ruled out.²⁴ Margins of exposure below 10 000 were identified in households from several areas (table 2). The main contributors to sterigmatocystin dietary exposure were maize, cotton seed oil, millet, sorghum, and rice. There are currently no Codex Alimentarius standards for sterigmatocystin.

For the fumonisin group of mycotoxins, JECFA proposed a provisional tolerable daily intake²⁴ of 2 µg/kg bodyweight per day for the sum of fumonisins B1, B2, and B3 (figure 1B). Fumonisin B1, B2, B3, and B4 (FUM_{total}) were quantified to provide the exposure assessment and risk characterisation (table 2). This approach is conservative,

but the fact that fumonisin B4, on average, only represented 6% of FUM_{total} means that the risk was not extensively overestimated when compared with the JECFA health-based guidance value. The current Codex Alimentarius FUM_{total} maximum limit of 2 mg/kg was never exceeded in maize samples,²⁰ including in centres where exposure exceeded the provisional tolerable daily intake, which raises the question of whether protection is sufficient at the level of the standard. Maize contributed almost exclusively to the household's FUM_{total} dietary exposure.

Toxicological data for the nephropathy-inducing mycotoxin ochratoxin A were assessed by JECFA, which retained a provisional tolerable weekly intake of 112 ng/kg bodyweight per week (figure 1C).²⁴ In several centres, ochratoxin A exposure exceeded the provisional tolerable weekly intake for more than 20% of households (table 2). Main contributors to dietary exposure were maize, sorghum, rice, red palm oil, and peanut oil, for which no Codex Alimentarius standards applicable to ochratoxin A currently exist.

With no risk assessment for the mycotoxin citrinin from JECFA, the sub-Saharan Africa total diet study exposure data were compared with the European Food Safety Authority (EFSA)²⁶ opinion on the safety of citrinin, which takes nephrotoxicity of this chemical into consideration. EFSA estimated that dietary exposure below 0.2 µg/kg bodyweight per day was of no health concern. In several centres, citrinin exposure exceeded the EFSA level of no concern for more than 30% of

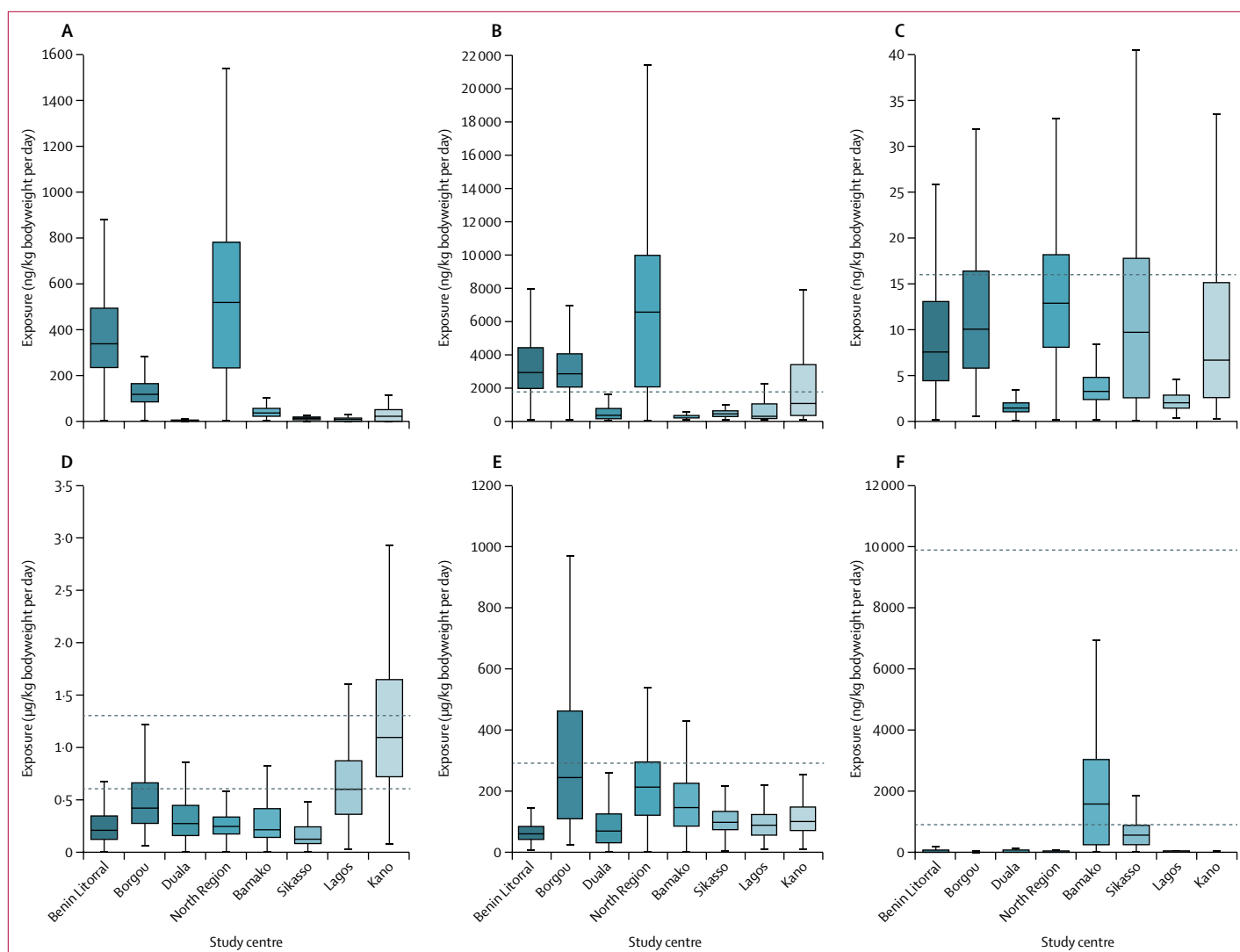


Figure 1: Dispersion of human dietary exposure to chemicals

Graphs show dispersion of human dietary exposure to aflatoxin B1 (A), fumonisins (B), ochratoxin A (C), lead (D), aluminium (E), and chlorpyrifos (F). Boxes represent the IQR, solid horizontal line the median, and whiskers represent 1.5 IQR. For fumonisins (B), JECFA provisional maximum tolerable daily intake is 2 µg/kg bodyweight per day (dotted line). For ochratoxin A (C), JECFA provisional tolerable weekly intake is 112 ng/kg bodyweight per week, corresponding to 16 ng/kg bodyweight per day (dotted line). For lead (D), JECFA estimate 1.3 µg/kg bodyweight per day for 1 mm Hg increase in blood pressure in adults (upper dotted line), and 0.6 µg/kg bodyweight per day for 1 IQ point loss in children (lower dotted line). For aluminium (E), JECFA provisional tolerable weekly intake is 2 mg/kg bodyweight per week, corresponding to 286 µg/kg bodyweight per day (dotted line). For chlorpyrifos (F), Joint FAO and WHO Meeting on Pesticide Residues acceptable daily intake is 0.010 mg/kg bodyweight per day (upper dotted line); European Food Safety Authority acceptable daily intake was 0.001 mg/kg bodyweight per day (lower dotted line; revoked in 2019). FAO=Food and Agriculture Organization of the UN. JECFA=Joint FAO and WHO Expert Committee on Food Additives. IQ=intelligence quotient.

households (table 2). The main citrinin dietary exposure contributor was maize. There is currently no Codex Alimentarius standard for citrinin.

Exposure to the mycotoxins zearalenone, deoxynivalenol, and nivalenol were also assessed and did not raise any public safety concern, according to risk characterisation data. Human dietary exposure did not exceed JECFA health-based guidance values.²⁷

Looking at metals and trace elements, JECFA estimated that a lead dose of 0.6 µg/kg bodyweight per day was associated with a decrease of one intelligence quotient (IQ) point for children (figure 1D). In the case

of adults, a lead dose of 1.3 µg/kg bodyweight per day could result in a blood pressure increase of 1 mm Hg.²⁴ Linear extrapolation of dietary exposure of households in Kano with JECFA toxicological endpoints suggested a mean loss of 2.4 (SD 1.4) and 4.4 IQ points for children exposed at the mean and 95th percentile exposures, respectively (table 2). Because the sub-Saharan Africa total diet study was not designed to specifically assess exposure for children, and JECFA estimates that children tend to have two to three times higher intake per bodyweight ratio than do adults, these results must be interpreted cautiously. Applying a correction factor of

	Benin		Cameroon		Mali		Nigeria	
	Littoral	Borgou	Duala	North Region	Bamako	Sikasso	Lagos	Kano
Aflatoxin B1, ng/kg bodyweight per day	394 (234; 847)	134 (70; 261)	4 (3; 10)	526 (360; 1117)	41 (28; 89)	12 (6; 23)	10 (10; 32)	37 (40; 125)
Sterigmatocystin, ng/kg bodyweight per day	6.4 (3.6; 13.4)	4.1 (2.8; 9.6)	1.3 (1.0; 3.5)	11.3 (6.9; 23.2)	9.9 (9.2; 29.8)	10.1 (6.9; 24.3)	5.5 (3.8; 12.3)	4.0 (3.1; 10.0)
Fumonisin (sum of B1, B2, B3, B4), ng/kg bodyweight per day	3450 (2209; 7615)	3222 (1670; 6260)	566 (719; 1764)	6826 (5287; 16169)	286 (127; 522)	460 (218; 878)	855 (1323; 3658)	2352 (2888; 8656)
Ochratoxin A, ng/kg bodyweight per week	71.1 (58.1; 185.8)	88.0 (71.8; 228.0)	11.2 (6.3; 23.8)	93.5 (57.0; 190.0)	27.2 (16.5; 62.0)	83.3 (73.3; 226.6)	15.5 (7.4; 29.3)	78.0 (82.6; 243.5)
Citrinin, ng/kg bodyweight per day	2341 (1532; 5228)	2767 (1469; 5499)	180 (297; 655)	263 (196; 615)	23 (10; 41)	67 (46; 160)	71 (78; 225)	169 (173; 544)
Lead, µg/kg bodyweight per day	0.27 (0.24; 0.72)	0.53 (0.38; 1.22)	0.34 (0.26; 0.88)	0.27 (0.18; 0.53)	0.37 (0.42; 1.22)	0.20 (0.19; 0.60)	0.68 (0.39; 1.43)	1.24 (0.75; 2.65)
Aluminium, µg/kg bodyweight per week	457 (271; 905)	2358 (2109; 6688)	643 (637; 1915)	1480 (837; 2879)	1167 (801; 2703)	734 (330; 1331)	650 (362; 1316)	787 (403; 1613)
Polycyclic aromatic hydrocarbons (sum of the 13 carcinogens and genotoxic compounds), ng/kg bodyweight per day	14 (10; 34)	40 (72; 169)	9 (9; 27)	14 (18; 50)	26 (23; 70)	26 (16; 56)	10 (8; 24)	9 (10; 27)
Chlorpyrifos, ng/kg bodyweight per day	71 (57; 177)	8 (4; 16)	56 (35; 123)	37 (25; 78)	2161 (2316; 6970)	631 (495; 1595)	34 (27; 75)	28 (32; 91)

Data are mean (SD; 95th percentile).

Table 2: Human dietary exposure levels

three, the IQ loss would be 6.3 (SD 4.2) at the mean and would be 13.3 at the 95th percentile. The main contributors to lead dietary exposure were sorghum, millet, and cassava.

The provisional tolerable weekly intake of aluminium proposed by JECFA is 2 mg/kg bodyweight per week, corresponding to 286 µg/kg bodyweight per day in adults (figure 1E).²⁴ In several centres, mean aluminium dietary exposure exceeded the JECFA provisional tolerable weekly intake for more than 10% of households (table 2). Main contributors to aluminium dietary exposure were maize, sorghum, and millet cassava.

According to the sub-Saharan Africa total diet study data, total arsenic, cadmium, and mercury exposures did not pose any major public health issue based on the comparison of dietary exposures with JECFA health-based guidance values.

Benzo[a]pyrene, benzo[a]anthracene, benzo[b]fluoranthene, and chrysene, and nine other polycyclic aromatic hydrocarbons are genotoxic carcinogens that were detected in sub-Saharan Africa total diet study samples.²⁰ Because of scarcity of specific toxicological studies for each polycyclic aromatic hydrocarbon congener, JECFA recommended using the surrogate approach, with BMDL₁₀ of 100 µg/kg bodyweight per day for the sum of 13 genotoxic polycyclic aromatic hydrocarbons.²⁴ The margin of exposure (95th percentile) in all geographical areas was less than 10 000 (table 2), which meant that risk was ubiquitous throughout the eight study centres. The main contributors to polycyclic aromatic hydrocarbon exposure were smoked fish and various edible oils, including red palm oil and peanut oil. The

Codex Alimentarius does not currently regulate the concentration of polycyclic aromatic hydrocarbons in foods.

From systematic screening of 470 pesticides in total diet study food samples from sub-Saharan Africa, 39 pesticides were detected,²¹ mainly organophosphate pesticides and pyrethroids. The 95th percentile dietary exposures to detected pesticides never exceeded 70% of JMPR acceptable daily intake, with the maximalist upper-bound hypothesis.²⁷ Exposure to chlorpyrifos in four households (in Bamako) exceeded the 2004 JMPR acceptable daily intake of 0.010 mg/kg bodyweight per day (figure 1F) because of the massive contribution of smoked fish, in which chlorpyrifos is not permitted by the Codex Alimentarius. The household with the most exposure had 27% of the JMPR acute reference dose of 0.100 mg/kg bodyweight per day (table 2). Toxicological evidence, which was not available at the time of the JMPR assessment, led the EFSA to establish (in 2014) an acceptable daily intake of 0.001 mg/kg bodyweight per day.²⁸ Dietary exposure to chlorpyrifos (the EFSA acceptable daily intake) was, thus, exceeded by 62% of households in Bamako and by 22% of households in Sikasso. Since our evaluation and in view of peer-review done by the EFSA that raises uncertainties about genotoxic concerns, the European Commission voted for the withdrawal of chlorpyrifos from the EU market for 2020.²⁹ No household was exposed to chlorpyrifos in excess of the JMPR or EFSA acceptable daily intakes in Benin, Cameroon, and Nigeria.

Other food chemicals, including dioxins, polychlorinated biphenyls, brominated flame retardants, and

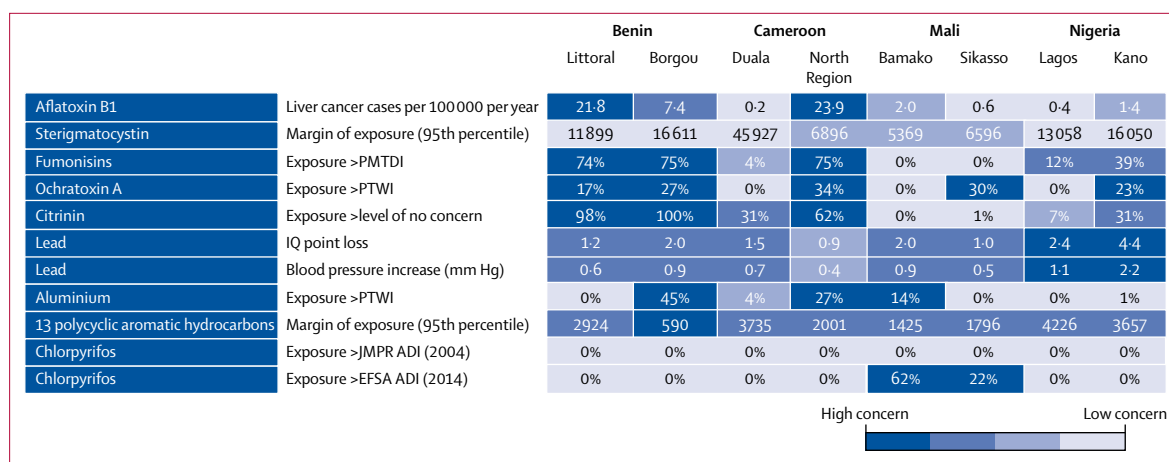


Figure 2: Risk characterisation scorecard

Scorecard summarises the chemical hazards for which health concern could not be ruled out. PMTDI=provisional maximum tolerable daily intake. PTWI=provisional tolerable weekly intake. IQ=intelligence quotient. FAO=Food and Agriculture Organization of the UN. JMPR=Joint FAO and WHO Meeting on Pesticide Residues. ADI=acceptable daily intake. EFSA=European Food Safety Authority.

perfluorinated compounds, were detected at low concentrations.²⁴ Human dietary exposure to these chemicals is not presented here.

Figure 2 shows the risk characterisation scorecard, summarising the chemical hazards for which degree of health concern could not be ruled out.

Discussion

The generation of data for the occurrence of chemicals in food in sub-Saharan Africa is not, as such, a new finding; our previous work has described chemical concentration patterns in food.^{19–23} However, use of dietary data representing, by weight, more than 90% of foods prepared as consumed by households in eight study centres, the precise analytical results attributable to various applications of mass spectrometry, and the wide range of analytes covered by this study are unprecedented in Africa.

For many of the chemicals analysed in this study, human dietary exposures were below levels of toxicological concern thought to present risk of adverse effects. This finding is instrumental in focusing efforts towards the chemicals for which a risk cannot be ruled out.

High exposure to several mycotoxins, polycyclic aromatic hydrocarbons, lead, and aluminium were identified in several study centres. In the case of Mali, regardless of the choice of using the JMPR or the EFSA acceptable daily intake as reference, the magnitude of exposure attributable to use of chlorpyrifos in smoked fish might indicate potential acute toxicity incidents. Although the total diet study method is not adequate for completion of acute exposure assessments, we can assume (based on the fact that consumers can eat in a day all the quantity of fish reported over a 15-day period) that some household exposures might have exceeded the JMPR daily acute reference dose of 0.100 mg/kg bodyweight per day for chlorpyrifos.

Potential adverse health effects to people caused by chemicals in food in Africa need addressing. Reducing exposure to mycotoxins can generally be achieved by field controls and by improving postharvest handling of food commodities, including application of basic good hygiene practices and adequate drying and storage conditions. Reduction of polycyclic aromatic hydrocarbons in smoked fish and edible oils can be achieved by using adequate food preparation processes, including choice of combustion sources and moderate heating temperature and time. The intentional use of a pesticide in smoked fish should, theoretically, be easy to mitigate. However, with respect to mycotoxins, polycyclic aromatic hydrocarbons, and chlorpyrifos, it is essential to understand the important part played by insufficient education, poverty, fear of food loss, and the associated potential loss of income from changing current practices. Although achieving SDG2, SDG3, SDG8, SDG10, and SDG12¹ will be necessary to address the issue of high food chemical exposure, additional efforts will still be needed. Therefore, although technically possible, addressing the safety issues caused by these food chemicals remains challenging.

In the case of high lead and aluminium dietary exposures, both identification of their sources and remedial policies remain challenging. First, it is necessary to identify through additional research whether a geological, environmental, or a particular food process is the main reason for the high level of exposure to lead in Nigeria and to aluminium in Benin and Cameroon. To investigate these issues, soil and other environmental samples and raw food commodities (before and after various processing stages, including drying and milling) will need to be tested. Moreover, some artisanal kitchen utensils made from recycled aluminium are likely to increase the lead and aluminium content of foods, particularly when preparing acidic foods such as tomato.²²

Some existing Codex Alimentarius food standards (eg, for aflatoxins and chlorpyrifos) have not been met, according to our total diet study results. This finding highlights that adequate action needs to be taken to improve and monitor the application of available codes of practice and good postharvest practices. Additionally, the absence of Codex Alimentarius standards applicable to some major exposure contributors is noted. Food standards and regulations indicating the maximum chemical concentrations in food commodities are necessary to enable issues related to food contamination to be tackled. Our total diet study findings have highlighted that new standards are needed for aflatoxin B1 in maize, for ochratoxin A in edible oils, rice, and sorghum, for sterigmatocystin in maize, millet, and sorghum, for citrinin in maize, and for polycyclic aromatic hydrocarbons in smoked fish and oils. Exposure to fumonisins exceeded the health-based guidance value, although the concentration of fumonisins in maize (the main contributor) was below the Codex Alimentarius maximum limit; these findings imply that the protective level of this standard is insufficient in the African context and needs to be addressed at the appropriate level.

Our study has several limitations. First, the number of study centres was low (two per country), which limits robust interpretation of the national situation. Second, for the aflatoxin B1 quantitative risk assessment, we considered only one value for the prevalence of HBAg-positive per country, which was from the same source (a worldwide systematic review).²⁵ We acknowledge that other data sources exist and that intracountry variation of hepatitis B prevalence was not captured in our assessment. Third, use of household-based dietary data, without individual food consumption data, means insufficient specificity in assessing children's dietary exposure. Moreover, toxicology is an evolving science, so the hazard characterisation, including thresholds of toxicological concerns, are likely to vary, to the rhythm of research outcomes. In particular, the study of additive, synergistic, or antagonistic effects of combined exposures to chemicals is only currently at its dawn. This study nonetheless provides useful data until additional toxicological data are available.

On June 7, 2019, the UN celebrated the first ever World Food Safety Day, conveying as a key message that food safety is everybody's business.³⁰ Food safety is a cross-cutting aspect of health and development, which can be affected by multiple direct and underlying causes. The first ever multicentre total diet study done in sub-Saharan Africa, a powerful and yet cost-effective method, has highlighted several potential health concerns associated with 24 food chemicals, with different magnitudes in the various geographical areas under study.

Although this total diet study can serve to identify areas of concern to public health, remediation will depend on the willingness and ability of all stakeholders to leverage these results into actions at a national and international

level, to improve public health in sub-Saharan Africa and beyond. Such efforts need to be coordinated and engage the international community, as well as national, regional, and local decision makers, to establish and enforce suitable food safety standards.

First, a strong commitment is urgently needed from all members of the Codex Alimentarius commission, which is the FAO and WHO institution in charge of setting international food standards, and to establish or revise those standards or codes of practice that have been identified as missing in this study. Among others, the Codex Alimentarius might consider lowering maximum limits for fumonisins in maize, regard edible oils as contributors to mycotoxins and polycyclic aromatic hydrocarbons, and request that JECFA assess citrinin toxicological data and propose a health-based guidance value. According to EFSA conclusions addressing uncertainty about genotoxicity (leading to the withdrawal of chlorpyrifos from the EU market in 2020), the Codex Alimentarius committee on pesticide residues might also consider the opportunity to request that JMPR assess toxicological data and establish if an update of the current toxicological status of chlorpyrifos is necessary.

Second, national food safety authorities, in conjunction with national and international partners from the health, agriculture, and trade sectors, are invited to draft national roadmaps, including a selection of risk-mitigation options, and to extensively communicate their conclusions to national leaders. Multisectoral roadmaps provide the feasibility and legitimacy to mobilise resources through consensual support of national stakeholders and development partners. Roadmaps, among other things, can incorporate production and dissemination of adequate educational materials for promotion of good agricultural and hygiene practices and access to laboratory facilities for food contamination monitoring and surveillance.

Third, it is primarily the role of governments to regulate and enforce national food standards to improve the safety of the food supply and to act to protect the health of consumers in sub-Saharan Africa. Food safety is, however, a collective responsibility.³⁰

Contributors

LI contributed to study design, project operational coordination, and writing of the report, and was part of the scientific committee secretariat. PV contributed to the project technical proposal, study design, and writing of the report, and was part of the scientific committee secretariat. M-MG contributed to the project technical proposal. AA, SEH, and AZK coordinated the collection and preparation of food samples in Nigeria, Benin, and Mali, respectively. EJ, ADD, SBA, JO, SD, and ZJD processed raw data from national household budget surveys to generate food consumption data. PJ, LL-P, MS, PM, TG, RH, and RK generated food contamination data. SE supervised study coordination in Cameroon. CM contributed to the project technical proposal. JK, BO, ML, and RC supervised project implementation and contributed to writing of the report. BLB coordinated the generation of food contamination data. J-CL was the Food and Agriculture Organization of the UN lead technical officer for the total diet study programme, coordinated study design and implementation, contributed to writing of the report, and was part of the scientific committee secretariat. All authors approved the final manuscript as submitted.

Declaration of interests

We declare no competing interests.

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References

- 1 Waage J, Yap C, Bell S, et al. Governing the UN sustainable development goals: interactions, infrastructures, and institutions. *Lancet Glob Health* 2015; **3**: e251–52.
- 2 Havelaar AH, Cawthorne A, Angulo F, et al. WHO Initiative to Estimate the Global Burden of Foodborne Diseases. *Lancet* 2013; **381** (suppl): S59.
- 3 Grandjean P, Landrigan PJ. Developmental neurotoxicity of industrial chemicals. *Lancet* 2006; **368**: 2167–78.
- 4 Grandjean P, Landrigan PJ. Neurobehavioural effects of developmental toxicity. *Lancet Neurol* 2014; **13**: 330–38.
- 5 Liu Y, Wu F. Global burden of aflatoxin-induced hepatocellular carcinoma: a risk assessment. *Environ Health Perspect* 2010; **118**: 818–24.
- 6 Gong Y, Hounsa A, Egal S, et al. Postweaning exposure to aflatoxin results in impaired child growth: a longitudinal study in Benin, west Africa. *Environ Health Perspect* 2004; **112**: 1334–38.
- 7 Turner PC, Collinson AC, Cheung YB, et al. Aflatoxin exposure in utero causes growth faltering in Gambian infants. *Int J Epidemiol* 2007; **36**: 1119–25.
- 8 Chen C, Mitchell NJ, Gratz J, et al. Exposure to aflatoxin and fumonisin in children at risk for growth impairment in rural Tanzania. *Environ Int* 2018; **115**: 29–37.
- 9 De Onis M, Branca F. Childhood stunting: a global perspective. *Matern Child Nutr* 2016; **12** (suppl 1): 12–26.
- 10 Black RE, Victora CG, Walker SP, et al. Maternal and child undernutrition and overweight in low-income and middle-income countries. *Lancet* 2013; **382**: 427–51.
- 11 Reuben A, Caspi A, Belsky DW, et al. Association of childhood blood lead levels with cognitive function and socioeconomic status at age 38 years and with IQ change and socioeconomic mobility between childhood and adulthood. *JAMA* 2017; **317**: 1244–51.
- 12 Ding N, Wang X, Weisskopf MG, et al. Lead-related genetic loci, cumulative lead exposure and incident coronary heart disease: the Normative Aging Study. *PLoS One* 2016; **11**: e0161472.
- 13 WHO. Principles and methods for the risk assessment of chemicals in food: environmental health criteria 240. Dec 31, 2008. <https://www.who.int/publications-detail/principles-and-methods-for-the-risk-assessment-of-chemicals-in-food> (accessed May 7, 2020).
- 14 European Food Safety Authority, Food and Agriculture Organization of the United Nations, World Health Organization. Towards a harmonised total diet study approach: a guidance document. 2011. https://www.who.int/foodsafety/publications/tds_guidance/en/ (accessed May 7, 2020).
- 15 Moy G, Vannoort R. Total diet studies. New York, NY: Springer-Verlag, 2013.
- 16 Ingenbleek L, Jazet E, Dzossa AD, et al. Methodology design of the regional sub-Saharan Africa total diet study in Benin, Cameroon, Mali and Nigeria. *Food Chem Toxicol* 2017; **109**: 155–69.
- 17 Tsukakoshi Y. Sampling variability and uncertainty in total diet studies. *Analyst* 2011; **136**: 533–39.
- 18 Armaroli E, Bechaux C, Delagrave R, Ingenbleek L, Leblanc JC, Verger P. A method to prioritize the surveillance of chemicals in food commodities to access international market and its application to four countries in sub-Saharan Africa. *Environ Int* 2020; **135**: 105386.
- 19 Ingenbleek L, Sulyok M, Adegboye A, et al. Regional sub-Saharan Africa total diet study in Benin, Cameroon, Mali and Nigeria reveals the presence of 164 mycotoxins and other secondary metabolites in foods. *Toxins* 2019; **11**: 54.
- 20 Ingenbleek L, Veyrand B, Adegboye A, et al. Polycyclic aromatic hydrocarbons (PAHs) in foods from the first regional sub-Saharan Africa total diet study: contamination profile and occurrence data. *Food Control* 2019; **103**: 133–44.
- 21 Ingenbleek L, Lopes-Pereira L, Paineau A, et al. Sub-Saharan Africa total diet study in Benin, Cameroon, Mali and Nigeria: pesticides occurrence in foods. *Food Chem X* 2019; **2**: 100034.
- 22 Jitaru P, Ingenbleek L, Laurent C, et al. Occurrence of 30 trace elements in foods from a multi-centre sub-Saharan Africa total diet study: focus on Al, As, Cd, Hg and Pb. *Environ Int* 2019; **133**: 105197.
- 23 Vaccher V, Ingenbleek L, Veyrand B, et al. Levels of persistent organic pollutants (POPs) in foods from the first regional sub-Saharan Africa total diet study. *Environ Int* 2020; **135**: 105413.
- 24 WHO. Evaluations of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). June, 2019. <http://apps.who.int/food-additives-contaminants-jecfa-database/search.aspx> (accessed May 7, 2020).
- 25 Schweitzer A, Horn J, Mikolajczyk RT, Krause G, Ott JJ. Estimations of worldwide prevalence of chronic hepatitis B virus infection: a systematic review of data published between 1965 and 2013. *Lancet* 2015; **386**: 1546–55.
- 26 European Food Safety Authority. Scientific opinion on the risks for public and animal health related to the presence of citrinin in food and feed. *EFSA J* 2012; **10**: 2605.
- 27 WHO. Inventory of evaluations performed by the Joint Meeting on Pesticide Residues (JMPR). 2018. <http://apps.who.int/pesticide-residues-jmpr-database> (accessed May 7, 2020).
- 28 European Food Safety Authority. Conclusion on the peer review of the pesticide human health risk assessment of the active substance chlorpyrifos. *EFSA J* 2014; **12**: 3640.
- 29 European Commission. Chlorpyrifos & chlorpyrifos-methyl. Feb 18, 2020. https://ec.europa.eu/food/plant/pesticides/approval_active_substances/chlorpyrifos_chlorpyrifos-methyl_en (accessed May 7, 2020).
- 30 UN. World Food Safety Day: June 7. <https://www.un.org/en/observances/food-safety-day> (accessed June 17, 2020).