SCIENTIFIC REPORTS

natureresearch

Check for updates

OPEN

# Probabilistic risk assessment of dietary exposure to aflatoxin $B_1$ in Guangzhou, China

Weiwei Zhang[1], Yufei Liu[1], Boheng Liang[1], Yuhua Zhang[1], Xianwu Zhong[1], Xiaoyan Luo[1], Jie Huang[1], Yanyan Wang[1], Weibin Cheng[2] & Kuncai Chen[1]✉

**Aflatoxin $B_1$ ($AFB_1$) contamination in foods is an important health challenge for low-and middle-income countries in subtropical regions. $AFB_1$ has been detected in a variety of foodsin Guangzhou, while the risk of dietary exposure is unknown. This study aimed to assess the probabilistic risk of dietary exposure to $AFB_1$ contamination in food stuffs in Guangzhou by using margin of exposure (MOE) and quantitative liver cancer risk approaches. A total of1854 $AFB_1$-contaminated foodstuffs were sampled in supermarkets, agricultural markets, retail shops, and family workshops from 11 districts of Guangzhou, and $AFB_1$ content was determined by HPLC-fluorescence detector. In total, 9.9% (184/1854) of the test samples had $AFB_1$ concentrations above the limit of detection. Home-made peanut oil had the highest $AFB_1$ concentration, with a mean value of $38.74 \pm 47.45\,\mu g\,kg^{-1}$. The average MOE levels of Guangzhou residents ranged from 100 to 1000. The risk of liver cancer was 0.0264 cancers (100,000 population year)$^{-1}$. The health risks of suburban people were higher than those of urban people, and home-made peanut oil was the main contributorto dietary exposure to $AFB_1$ among suburban residents in Guangzhou. The production of home-made peanut oil should be supervised to reduce the risk of $AFB_1$ exposure.**

Aflatoxins (AFs) are mycotoxins produced by the common fungi *Aspergillus flavus*and *Aspergillus parasiticus*[1] and have been found in a wide range of crops such as maize, peanut, and walnut and their derived products[2]. There are four major aflatoxins ($AFB_1$, AFB2, AFG1, and AFG2) produced by the two fungi that commonly found in contaminated crops[3–5]. $AFB_1$ and $AFB_2$ can be produced by *A. flavus* (both S and L strains) and *A. parasiticus*, while$AFG_1$ and $AFG_2$ can be produced by *A. flavus* S strains and *A. parasiticus*[5,6]. $AFB_1$ is considered the most toxic carcinogenwhich is classified as Group 1 human carcinogen by the International Agency for Research on Cancer (IARC)that induces mainly liver cancer[7–9] and to a lesser degree rectal cancer[10].

$AFB_1$ is commonly found in cereals and nuts[11], and it has attracted concern in lessdeveloped tropical regions[12–15]. Previous studies showed that AFs were found in 5%-30%of raw peanuts and peanut products in major peanut-producing regions in China[16]. Since some crops susceptible to AFs contamination, such as peanuts, are commonly consumed, it is hard to achieve zero exposure to AFs. Therefore, it is important to reduce the exposure to total AFsby establishing regulatory limits to AFs.The Codex Alimentarius Commission, the Joint Food and Agriculture Organization (FAO), and the World Health Organization (WHO) Food Standards Program jointly adopted a maximum level of $15\,\mu g\,kg{-}1$ for total AFsin unprocessed peanuts[17]. The European Commission regulation (EC) No. 1881/2006 set a maximum limit for $AFB_1$ of $2\,\mu g\,kg^{-1}$ for peanuts and cereals that are intended for direct consumption[18]. In China, the National Food Safety Standard set the limit of $20\,\mu g\,kg^{-1}$ for $AFB_1$ in peanut and its products and in maize and its products[19]. In addition to setting regulatory limits for $AFB_1$,it is also necessary to conduct dietary exposure risk assessments in the population. A low-dose extrapolation approach introducedby the Joint FAO/WHO Expert Committee on Food Additives(JECFA)[20] in 1997 and the margin of exposure (MOE) method proposed at the 64$^{th}$ JECFAmeeting in 2005[21] were both recommended and have been widely used worldwide[14,22,23] to assess the risk of dietary exposure to$AFB_1$.

JECFAperformed adietary exposure risk assessment for AFs as early as 1997. However, the data used were not considered representativebecause of the bias for the highest contamination level in food sampling[24]. In view of this scenario, national or regional AFhealth risk exposure assessments have beenundertakensince then,especially in tropical and subtropical regions[12–15]. In general, economically developed countries have a lower risk of

[1]Guangzhou Center for Disease Control and Prevention, Guangzhou, 510440, China. [2]Guangdong Second Provincial General Hospital, Guangzhou, 510000, China. ✉e-mail: ckc@gzcdc.org.cn

health hazard assessment than developing or less developed countries. Dietary exposureto AFsestimated by the European Union ranged from 0.93 to 2.45 ng $kg^{-1}$ bw $day^{-1}$ for the lower bound to the upper bound[25]. In the United States, exposure was estimatedat 2.7 $ngkg^{-1}$ bw $day^{-1}$ [26] In Asia, the population of Japan[27], with anintake ranging from 0.003 to 0.004 $ngkg^{-1}$ bw $day^{-1}$, hasa lower riskthan those of Indonesia[13] (from 0.02 to 427.8 $ngkg^{-1}$ bw $day^{-1}$) and Vietnam[23] (from 35.0 to 43.7 $ngkg^{-1}$ bw $day^{-1}$).

Guangzhou, one of the major metropolitan areas in southern China, is located in Guangdong Province and has more than 14 million people. Due to the subtropical monsoon climate (with a relatively humid environment), Guangzhou,with coexisting urban and rural areas, has been facing the challenge of $AFB_1$contamination in foodstuffs[28–31]. Warm and humid conditions are favourable for *A.flavus* growth in some types of food, such as peanut and maize. A survey of foodstuffs (rice, wheat flour, peanut and peanut oil, corn flour and corn oil, and soybean) that areprone to contamination by AFs found that the overall detection rate of $AFB_1$ was 31.7%, with the highest concentration of 39.3 μg kg−1 found in peanut oil[29]. However, the health risk of $AFB_1$ dietary exposure to local residents was unknown.

In this context, Guangzhou Center for Disease Control and Prevention conducted a surveillance programme for three consecutive years to monitor contamination of foodstuffsby $AFB_1$. We present the probabilistic risk of dietary exposure to $AFB_1$ among Guangzhou residents by using MOE andquantitative liver cancer risk approaches.

## Materials and methods

**Sampling.** From January 2015 to December 2017, typical $AFB_1$-contaminated foodstuffs, includingrice and rice products, wheat and wheat products, maize and maize products, vegetable oil(including home-made peanut oil), nuts, and tea,were bought from household supply retail shops covered in all eleven districts of Guangzhou. These foods were considered theprobable sources of $AFB_1$exposure in Guangzhou[29].

Individual streetswere set as the sampling units. Street information was obtained from local governmental authorities. Three streets (two central streets and one remote street) were randomly selectedand stratified by district and type of streets (central or remote) using computer-generatedrandom digits. A total of 33 streets (22 central streets and 11 remote streets) were selected as food sampling sites. Trained investigators bought foodstuffs fromsupermarkets, agricultural markets, retail shops, and family workshops. Finally, a total of 1854 single-species food samples were included in this study, and alist of sampling sites isshown in Supplementary Table 1.

**Analytical procedure (high-performance liquid chromatography).** In accordance with a previouslyvalidated method, the procedure to determine $AFB_1$in foods was applied with some slight modifications[32–34]. First,for solid samples, the sampling quantity should be more than 1 kg, and the sample should be crushed by a high-speed crusher and then sieved to make particles smaller than 2 mm. The test sieve should be mixed evenly, condensed to 100 g, and then stored in a sample bottle and sealed for storage until detection. The sampled amount of liquid samplesshould be greater than 1 L. For bagged, bottled and other packaged samples, at least 3 packages (the same batch or number) should be collected, all liquid samples should be mixed in a container with a homogenizer, and any 100 g (mL) of the liquid samples can be tested.The prepared samples were stored in a refrigerator at 0~4 °C for no more than 48 hours before analysis. Second,for solid samples, 5 g was weighed (accurate to 0.01 g) into a 50 mL centrifuge tube, 20.0 mL methanol-water solution (70 + 30) was added, and the sample was mixed by vortex, put into an ultrasonic oscillator for 20 min (or a homogenizer for 3 min), and centrifuged at 6000$rmin^{-1}$ for 10 min (or applied to glass-fibre filter paper after homogenization).The supernatant was taken for later use. For vegetable oil, 5 g (accurate to 0.01 g) was placed into a 50 mL centrifuge tube, 20 mL methanol-water solution (70 + 30) was added, and the sample was mixed by vortex, put into ultrasonic oscillator for 20 min, and centrifuged at 6000$rmin^{-1}$ for 10 min.The supernatant was taken for use.Whatman GF/A glass-fibre filter paper was used to filtrate 10 ml extract and to collect the filtrate in the clean container. In addition, 5 ml extract was diluted with 20 ml purified water and filtered before being tested. $AFB_1$ content was determined by an HPLC-fluorescence detector (excitation, 360 nm; emission, 450 nm) (Waters Alliance e2695) by using post-column-photochemical reactor derivatization.

**Quality control.** The limit of detection (LOD)in our study was0.1 μg $kg^{-1}$ and determined from a signal-to-noise ratio equal to 3:1,and the limit of quantification(LOQ) was determined as the point at which this ratio was more than 10:1. Recovery rates in each foodwere ascertained by spiking with $AFB_1$, and the rates rangedfrom 95% to 105%.

**Estimation of daily food consumption.** Food consumption data were derived from a national food consumption survey of urban and rural residents in Guangzhou performed in 2011. Information on dietary intake was based on a three-day consecutive 24-h recall questionnaire in combination with the weighing method for edible cooking oil. Details of the methodology are available in our previously published manuscripts[35,36]. In sum, 2960 residents from 998 households were surveyed in the study. Among the subjects, 1416 were male and 1544 were female. Urban residents accounted for 63.8% (1888) of the total, and suburban residents accounted for 36.2% (1072). The age ranged from 3 to 86 years, and the mean age was 32 years. The age groupsof 3 to 6 years old, 7 to 17 years old, 18 to 59 years old, and 60 years old and above accounted for 6.7% (199), 21.5% (637), 58.6% (1734), and 13.2% (390) of the total people, respectively[16,37,38].

In this study, vegetable oils collected in the survey included peanut oil, corn oil, tea seed oil, and soybean oil. According to the production conditions, vegetable oils were classified into commercial vegetable oil and bulk vegetable oil. Commercial vegetable oil was defined as the vegetable oil produced by licensed manufacturers and had underwent sampling inspection by the Chinese Food and Drug Administration. Bulk vegetable oil was produced by family workshops in the suburban areas, where this inspection usually did not in place. In this case, bulk vegetable oil referred to home-made peanut oil.

**Estimation of daily intake of $AFB_1$.** The total dietary intake of $AFB_1$ was calculated as an estimateddaily intake (EDI) by using Eq. (1)[39].

$$EDI = \sum_{i=1}^{n} = \frac{Di * Mi}{W} \tag{1}$$

EDI was the estimation of daily dietary $AFB_1$ intake (ng kg−1 body weight day−1). Di was the daily consumption of each food in each age group (gperson$^{-1}$ day$^{-1}$). Mi was the mean level of $AFB_1$ in each food category (ngkg$^{-1}$). When $AFB_1$ was not detected in certain types of food, Mi was then assumed to be LOD/2[40]. The WHO recommended an alternative method to calculate the undetected value[41–43]. When the undetected samplevalueswere less than 60%, the non-detected value was replaced by the value of LOD / 2.When more than 80% of the sample values were not detected, the undetected valueswere replaced by 0 or LOD, respectively, as the lower bound and upper bound. However, in our study, the LODappears to be highcompared with those of other regions, such as Japan and Taiwan, China, where LODs ranged from0.001 to0.1 μg kg$^{-1}$,but it was consistent withvalue in the Chinese National Food Contamination Monitoring Program.If the upper bound is used to estimate the mean value, the exposure risk might be overestimated. Our approach was to replace all the undetected values by LOD / 2, which ishighly conservative and doesn't overestimatethe risk. W was the body weight of each respondent (kg). The average weight of respondents aged 3 to 6 years was determined to be 20 kg[44], the average weight of respondents aged 7 to 17 years was determined to be 40 kg[45], and members of the other two age groups were determined to average 60 kg[46]. Mean daily exposure to $AFB_1$ was estimated by using the @RISK software.

**Risk characterization.** *Margin of exposure (MOE).* TheMOE method estimates the risk of genotoxic carcinogens[21]. It calculates the risk by the ratio of carcinogenic dose (or population carcinogenic dose) to population intake. The higher the MOE value is, the lower the risk of genetic carcinogen exposure.

MOE is calculated as the ratio between the points of departure (PODs) on the dose-response curve (animal or population carcinogenic dose) for a critical effect and the exposure level of the population. The formula is as follows: MOEs = PODs/dietary exposure (EDI). The European Food Safety Authority (EFSA) Scientific Panel on Contaminants in the Food Chain proposed the use of a benchmark dose lower confidence limit for 10% extra risk (BMDL10) and a benchmark dose lower confidence limit for 1% extra risk (BMDL1) for characterizing the MOE as PODs[25]. The value of BMDL10 (the lower limit for the 95% confidence interval of the 10% incidence of liver cancer in the control group) was 340 ng kg$^{-1}$ bw day$^{-1}$ for $AFB_1$as referenced by the EFSA[25]. In reference to the dose-response relationship based on the data of Peers[47,48] and Carlborg[49], the value of BMDL1 (the lower limit for the 95% statistical confidence interval of the 1% incidence of liver cancer in the control group) was estimated as 78 ng kg$^{-1}$ bw day$^{-1}$. The reference value for a chronic dose that causes 25% of test animals to develop liver cancer (T25) during their standard lifespan was varied. The most widely used values were390 ng kg$^{-1}$bw day$^{-1}$(according to Benford[50])and 500 ng kg$^{-1}$ bw day$^{-1}$(recommended by Wogen[51]). For safety considerations, we referred to the conservative T25 value of 390 ng kg$^{-1}$bw day$^{-1}$as the POD.

*Quantitative risk assessment of liver cancer.* Quantitative liver cancer riskassessment is one of the popular low-dose extrapolationapproaches used for $AFB_1$ dietary exposure risk assessment. The low-dose extrapolation approachassumes that there is a linear dose-response relationship between the carcinogenic dose and the incidence of cancer in a population within a low-dose response range[15,52–54]. This methodtakes advantage of the exposure andpotency of carcinogens, providing quantitative data on human carcinogenic risk.This method was consistent with the formula proposed by the JECFA[20]. Because hepatitis B could synergistically increase the risk of $AFB_1$-induced liver cancer, we separately estimated the carcinogenic potency in people who had hepatitis B and in peoplewho were hepatitis B negative. Studies have shown that the carcinogenic efficacy of AF in hepatitis B virus carriers is 30 times higher than that in nonviral carriers[27,53,55]. For hepatitis B surface antigen-positive individuals (PHBsAg+), the potency was 0.3 cancers per year ng$^{-1}$ $AFB_1$ kg$^{-1}$bw day$^{-1}$per 100,000 population. For hepatitis B surface antigen-negative individuals (PHBsAg-), the potency was 0.01 cancers per year ng$^{-1}$$AFB_1$ kg$^{-1}$bw day$^{-1}$per 100,000 population[53,56,57].

The cancer riskwas estimated by using Eq. (2).

$$\begin{aligned} P_{\text{cancer}} &= (\text{PHBsAg+ xpop. HBsAg+}) + (\text{PHBsAg-xpop. HBsAg}-) \\ \text{Cancer risk} &= P_{\text{cancer}} \times \text{Estimated Daily In take} \end{aligned} \tag{2}$$

The prevalence of HBsAg+ was estimated to be 12.5% in Guangzhou, with 7.1% in urban areas and 16.1% in suburban areas[58].

**Statistical analysis.** Descriptive analysis was performed to describe the concentration of $AFB_1$ in foodstuffs by using the mean ± standard deviation. Probabilistic risk assessment model calculations for $AFB_1$ dietary exposure, MOE values, and cancer risk were performed by @RISK software (Palisade Corporation, 7.6. Industrial, 2018) based on a Monte Carlo simulation with 10000 iterations. The results are displayed as the mean values (range from the 5$^{th}$ percentile to the 95$^{th}$ percentile).

Due to the difference in vegetable oil consumption habits between urban and suburban residents, we conducted a sub-analysis by stratifying suburban residents from urban residents to see the difference in dietary exposure to $AFB_1$. We found that the dietary intake of home-made peanut oil was reported among only suburban residents because such oil was predominantly sold in suburban areas.

| Food Category | Number of samples | <LOD | AFB$_1$ level($\mu$g kg$^{-1}$) Mean ±standard deviation | P50 | P95 | Range |
|---|---|---|---|---|---|---|
| Rice and rice Products | 490 | 483 | 0.13 ± 0.001 | ND | ND | 0.28~1.00 |
| Wheat and wheat products | 436 | 430 | 0.13 ± 0.001 | ND | ND | 0.28~1.46 |
| Maize and maize Products | 339 | 336 | 0.17 ± 0.001 | ND | ND | 1.50~6.30 |
| Nuts | 96 | 93 | 0.14 ± 0.001 | ND | ND | 0.62~1.37 |
| Tea | 128 | 105 | 0.36 ± 0.62 | ND | 1.68 | 0.25~4.0 |
| Vegetable oil [a] | 365[b] | 223[e] | 6.32±25.99 | ND | 30.45 | 0.26~283.0 |
| 1. Commercial vegetable oil | 269[c] | 201 [f] | 0.67 ±1.81 | ND | 3.01 | 0.35~7.30 |
| 2 Home-made peanut oil | **96[d]** | **22 [g]** | **38.74 ±47.45** | **3.21** | **141.40** | **0.26~283.0** |
| Total | 1854 | 1670 | 1.40±11.94 | ND | 2.20 | 0.25~283.0 |

**Table 1.** AFB$_1$ levels of foods in Guangzhou from2015 to 2017. a = vegetable oil equalsthe sum of commercial vegetable oil and home-made peanut oil. b = c+d. e = f+g. AFB$_1$: Aflatoxin B$_1$; LOD: Limit of detection; ND: Not detected.

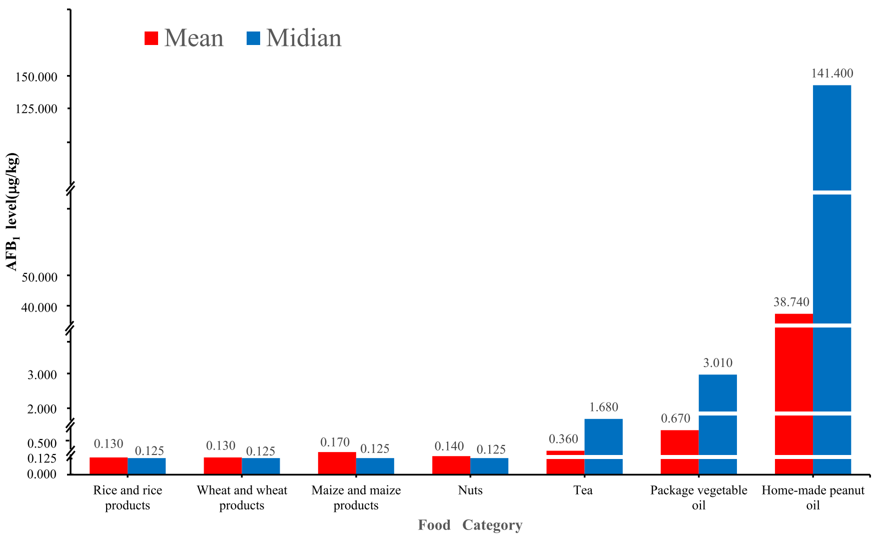


**Figure 1.** Aflatoxin B$_1$ levels in seven kinds of foods in Guangzhou City.

## Results and discussion

**AFB$_1$ levels in foods.** The levels of AFB$_1$ in 1854 food samples are summarized in Table 1. The levels of AFB$_1$ levels in food samples between 2015, 2016, and 2017 were comparable (see Supplementary Table 2).The mean level of AFB$_1$ in all samples was 1.4 µg kg$^{-1}$, and the 50$^{th}$ percentile (P50) and 95$^{th}$ percentile (P95) values were not detected (ND) and 2.2 µg kg$^{-1}$, respectively. In total, 9.9% (184/1854) of the test samples had AFB$_1$ levels above the LOD. Home-made peanut oil had the highest concentration of AFB$_1$, with detected values ranging from 0.26 to 283.0 µg kg$^{-1}$, a median value of 3.21 µg kg$^{-1}$ and a mean value of 38.74 ±47.45 µg kg$^{-1}$. In rice and rice products, wheat and wheat products, maize and maize products, and nuts, AFB$_1$ concentration levels were very low, and most results were under the detection limit (Fig. 1).

Comparisonsof data from someSoutheast Asian countries show that the level of AFB$_1$ contamination in some foods in Guangzhou, such as rice and maize, was relatively lower than that in some foods in Vietnam, where AFB$_1$ contamination levels in maize, rice products and other cereals were 2.1~31.1 µg kg$^{-1}$ [59], 2.7 µg kg$^{-1}$ and 3.2 µg kg$^{-1}$ [23], respectively. In addition, the contamination level of AFB$_1$ in nuts (including peanut) was low in Guangzhou compared with other provinces of China[16] and Malaysia (ranging from 0.40 µg kg$^{-1}$ to 222 µg kg$^{-1}$)[12]. However, the samples cited were raw peanut or maize samples, while in this study, all the samples were processed products. Generally, raw samples were relatively more contaminated with aflatoxins than were processed samples. For commercially processed samples, the levels of aflatoxin in peanut oil and maize were higher in Guangdong Province than in Fujian[60] and Chongqing[61,62]. This situation promptedGuangzhouto pay attention to the contamination of AFB$_1$ in peanut oil and find the source of the problem.

Our study is the first to include home-made peanut oil in the assessment of AFB$_1$ in Guangzhou. The results showed that the alarmingly high AFB$_1$ level in home-made peanut oil poses a potential public health threat among suburban residents in Guangzhou. Home-made peanut oil is widely consumed in many underdeveloped cities of China. People prefer home-made peanut oil because of traditional cooking styles and eating habits, particularly in rural areas[28]. Two factors might contribute to the contamination of home-made peanut oil by AFB$_1$. One factor

| Food category | 3~6years old | | 7~17years old | | 18~59years old | | More than 60 years old | | total | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Dietary Consumption Reference Person± Standard Deviation (g day$^{-1}$) | $AFB_1$EDI (ngkg$^{-1}$bwday$^{-1}$) (90% confidence interval) | Dietary Consumption Reference Person± Standard Deviation (g day$^{-1}$) | $AFB_1$EDI (ng kg$^{-1}$bwday$^{-1}$) (90% confidence interval) | Dietary Consumption Reference Person± Standard Deviation (g day$^{-1}$) | $AFB_1$EDI (ng kg$^{-1}$bwday$^{-1}$) (90% confidence interval) | Dietary Consumption Reference Person± Standard Deviation (g day$^{-1}$) | $AFB_1$EDI (ng kg$^{-1}$ bwday$^{-1}$) (90% confidence interval) | Dietary Consumption Reference Person± Standard Deviation (g day$^{-1}$) | $AFB_1$ EDI (ng kg$^{-1}$bwday$^{-1}$) (90% confidence interval) |
| Rice and rice products | 78.5±45.5 | 0.50 (0.02~0.98) | 121.3±73.8 | 0.38 (0.01~0.77) | 146.5±90.5 | 0.31 (0.01~0.63) | 126.5±90.7 | 0.27 (0.05~0.58) | 135.8±86.9 | 0.29 (0.01~0.59) |
| Wheat and wheat products | 32.6±22.3 | 0.21 (0.03~0.44) | 48.4±38.2 | 0.16 (0.04~0.35) | 52.3±38.7 | 0.11 (0.02~0.25) | 50.6±33.1 | 0.12 (0.03~0.44) | 49.3±36.3 | 0.11 (0.03~0.27) |
| Maize and maize products | 6.3±4.8 | 0.04 (0.01~0.09) | 7.0±4.5 | 0.02 (0.01~0.04) | 9.2±8.7 | 0.02 (0.01~0.12) | 14.7±3.1 | 0.03 (0.01~0.03) | 8.8±5.3 | 0.02 (0.01~0.05) |
| Nuts | 2.5±1.9 | 0.02 (0.01~0.03) | 2.2±1.8 | 0.01 (0.01~0.02) | 2.3±2.2 | 0.01 (0.01~0.02) | 1.14±1.1 | 0.01 (0.01~0.02) | 2.0±1.9 | 0.01 (0.01~0.02) |
| Tea | 0.1±0.9 | 0.00 (0.00~0.02) | 2.2±1.5 | 0.01 (0.01~0.02) | 4.5±4.0 | 0.01 (0.01~0.05) | 3.8±3.1 | 0.01 (0.01~0.03) | 3.6±3.3 | 0.01 (0.01~0.03) |
| Vegetable oil | 11.3±9.6 | 0.17 (0.01~3.37) | 22.3±18.5 | 0.17 (0.01~3.31) | 26.4±17.3 | 0.13 (0.01~2.43) | 9.6±5.3 | 0.05 (0.01~0.88) | 26.6±16.8 | 0.13 (0.01~2.50) |
| Total | | 0.94 (0.29~4.24) | | 0.75 (0.22~3.64) | | 0.59 (0.20~3.11) | | 0.48 (0.16~1.41) | | 0.57 (0.21~3.16) |

**Table 2.** Dietary consumption and $AFB_1$ EDI for each $AFB_1$-analysed food in different age groups in Guangzhou. $AFB_1$: Aflatoxin $B_1$;EDI: Estimateddaily intake.

is that poor-qualityoil extraction machines and simple traditional procedures are unabletodegrade $AFB_1$and that effective techniques to control $AFB_1$ are difficult to apply in family workshops[63]. The other factor is that the peanuts used for oil extraction might becontaminated by $AFB_1$ to different degrees.If the harvested peanuts that were not ready to be pressed soon for peanut oil were stored in a warm and humid environment,the $AFB_1$ level could easily increase. If mouldy peanuts were not removed, the $AFB_1$ level of peanut oil would hardly be reduced[28].

Due to a lack of awareness of $AFB_1$ contamination and the maximization of profits,oil mill ownerstend to use mouldy peanuts for oil extraction, which would not significantly affect the flavour of home-made peanut oil. This poor manufacturing practice is common because it is difficult for consumers to identify. Therefore, regulation-and supervision of home-made peanut oil should be enhanced in Guangzhou.Findings from this study are also meaningful to regions where home-made peanut oilis widely available but whose production is unsupervised by food safety regulators.

**Dietary $AFB_1$ exposure.** The EDI of $AFB_1$ in each $AFB_1$-detected food in all age groups is presented in Table 2. The EDI in each $AFB_1$-detected food for urban and suburban areas is presented in Table 3.In all age groups, the intake was the highest for rice and rice products among the contributed foods, and rice and rice product intake was the main contributor to $AFB_1$ exposure in Guangzhou.Despite the low dietary consumption of vegetable oil, it was the second contributor due to its high $AFB_1$ concentration. Wheat and wheat products were the third contributor to therelatively high consumption. However, the$AFB_1$ concentration in wheat and wheat products was low. In addition, maize and maize products, tea, and nuts had little effect on the EDI due to their low consumption and $AFB_1$ concentrations.

The EDI of $AFB_1$ in each age group was estimated to range from 0.48 ng kg$^{-1}$bw day$^{-1}$ to 0.94 ng kg$^{-1}$bw day$^{-1}$, and the average EDI was estimated to be 0.57 ng kg$^{-1}$bw day$^{-1}$(the 90% confidence interval extended from 0.21 to 3.16). Among all age groups, the 3–6 years of age group had the highest EDI, with a value of 0.94 ng kg$^{-1}$bw day$^{-1}$. The difference in EDI between urban and suburban residents was large, with 0.29 ng kg$^{-1}$bw day$^{-1}$ and 2.26 ng kg$^{-1}$bw day$^{-1}$ for urban and suburban residents, respectively. The main source of suburban resident exposure to $AFB_1$ was home-made peanut oil.

**Risk characterization using the MOE Approach.** Table 4 presents the MOE values for $AFB_1$ exposure. All MOE values were below the safe threshold of 10000. Probabilisticrisk analysis resultsshowed that most of the lower bound MOE values ranged from 10 to 100, indicating a concern for risk management.

Age-group analysis suggestedthat we should pay close attention to the 3~6 years of age group, whose MOE value was the lowest. This result reflected that preschool children might have the highest risk of being exposed to $AFB_1$.This agreed with the results from a studyfrom Taiwan in 2018 that found thatbabies and toddlers were at the highest risk of $AFB_1$ exposure[64].

Meanwhile, our results showed that the MOE value of suburban residents was lower than that of urban residents.$AFB_1$ dietary exposure among urban residents in Guangzhou was similar to that of the urban residents in Shenzhen, an adjacent city to Guangzhou that is the most economically developed city in South China[38]. However, Guangzhou as a whole had a higher level of $AFB_1$ risk than Shenzhen, probably because of the consumption of home-made peanut oil by suburban residents. In Guangxi Province, which neighbours Guangdong

| Food Category | Urban District | | Suburban District | |
|---|---|---|---|---|
| | Dietary Consumption Reference Person (g day$^{-1}$) | $AFB_1$ EDI (ngkg$^{-1}$bwday$^{-1}$) | Dietary Consumption Reference Person (g day$^{-1}$) | $AFB_1$EDI (ngkg$^{-1}$bwday$^{-1}$) |
| Rice and rice products | 118.5 ± 83.9 | 0.25 (0.04~0.54) | 159.3 ± 90.1 | 0.33 (0.02~0.65) |
| Wheat and wheat products | 51.6 ± 37.2 | 0.11 (0.02~0.24) | 47.4 ± 35.3 | 0.10 (0.02~0.23) |
| Maize and maize Products | 8.3 ± 5.8 | 0.02 (0.01~0.04) | 9.0 ± 4.9 | 0.02 (0.01~0.04) |
| Nuts | 2.5 ± 2.4 | 0.01 (0.01~0.03) | 1.8 ± 1.7 | 0.01 (0.01~0.02) |
| Tea | 3.5 ± 3.0 | 0.01 (0.01~0.03) | 3.7 ± 3.2 | 0.01 (0.01~0.03) |
| Vegetable oil [a] | 25.9 ± 14.8 | 0.14 (0.01~0.37) | 27.1 ± 18.1 | 1.78 (0.10~6.13) |
| 1. Commercial vegetable oil | 25.9 ± 14.8 | 0.14 (0.01~0.37) | 25.0 ± 17.8 | 0.13 (0.00~0.38) |
| 2. Home-made peanut oil | / | | 2.1 ± 1.95 | 1.65 (0.05~5.72) |
| Total | | **0.29(0.08~0.56)** | | **2.26(0.35~6.59)** |

**Table 3.** $AFB_1$ exposure in each $AFB_1$-analysed food between urban and suburban areas in Guangzhou. A: Total vegetable oil intake was equal to commercial vegetable oil plus home-made peanut oil (a = 1 + 2). $AFB_1$: Aflatoxin $B_1$;EDI: Estimateddaily intake.

| Characteristic | POD(ng kg$^{-1}$bwday$^{-1}$) | | | Exposure (ng kg$^{-1}$bwday$^{-1}$) | MOE | | |
|---|---|---|---|---|---|---|---|
| | $T_{25}$ | $BMDL_{10}$ | $BMDL_1$ | | $T_{25}$ | $BMDL_{10}$ | $BMDL_1$ |
| ***Age group*** | | | | | | | |
| 3~6 years old | | | | 0.94 (0.29~4.24) | 417(65~1086) | 363 (62~931) | 83 (14~215) |
| 7~17years old | | | | 0.75 (0.22~3.64) | 519 (65~1382 | 453 (51~1234) | 104 (14~276) |
| 18~59years old | 390 | 340 | 78 | 0.59 (0.20~3.11) | 654(96~1604) | 570 (98~1478) | 131 (20~347) |
| More than 60 years old | | | | 0.48 (0.16~1.41) | 812(231~2199) | 708 (204~1998) | 162 (48~455) |
| ***Region*** | | | | | | | |
| Urban | | | | 0.29 (0.08~0.56) | 1364 (657~4612) | 1189 (573~4020) | 273 (131~922) |
| Suburban | | | | 2.26(0.35~6.59) | 172 (57~1055) | 150 (50~920) | 34 (11~211) |
| Total | | | | 0.57 (0.21~3.16) | 681 (107~1719) | 594 (88~1509) | 136 (20~346) |

**Table 4.** Risk characterization of $AFB_1$ exposure in different age groups and different regions in Guangzhou based on the MOE approach. $AFB_1$: Aflatoxin $B_1$; MOE: Margin of exposure; POD: Point of departure. $BMDL_{10}$: Benchmark dose lower confidence limit for 10%; $BMDL_1$: Benchmark dose lower confidence limit for 1%; $T_{25}$: The reference value of a chronic dose that causes 25% of test animals to develop liver cancer.

Province(where Guangzhouis located),grains and oil crops were also prone to mildew due to its subtropical climate with abundant year-round rainfall[63]. It should be noted that the residents of Guangxi Province have a similar habit of consuming home-made peanut oil. The mean $AFB_1$ level of home-made peanut oil in the Guangxi study was 41.50 μg kg$^{-1}$, slightly higher than the result in our study[35]. In a comparison of this study and studies from other low- and middle-income countries, dietary health risk exposure to $AFB_1$ in Guangzhouappeared to be lower than that in other countries, and the risk of cancer was also lower than that in Indonesia[13] and Vietnam[23]. The MOE values in our study were much greater than those in Japan[27] and South Korea[22],where socioeconomic statusisvery developed.

**Risk characterization using quantitative risk assessment of liver cancer.** The potential cancer risk of $AFB_1$ in Guangzhou residents was estimated by age group and by region (Table 5). In general, the risk of liver cancer in the entire population was estimated at 0.0264 cancers(year100 000 people)$^{-1}$on average, which was far less than the incidence of liver cancer in China of 24.6 cancers(year 100 000 people)$^{-1}$ [65]. These results indicated that foods currently contaminated by $AFB_1$ had low health risks for residents and that dietary exposure to $AFB_1$may not account for the occurrence of liver cancer in Guangzhou.However, the EDI of suburban residents was nearly ten times higher than that of urban residents. The cancer risk among suburban residents was much higher than that among urban residents. These results were comparable to the results of a study conductedin-Guangxi Province[66], where dietary exposure to $AFB_1$ was mainly caused by home-made peanut oil. Nonetheless, with the increasing vaccination rate for the hepatitis B vaccine in China, it is believed that the cancer risk will gradually decrease in the future.

**Uncertainty analysis and limitations.** The entire process of food safety risk assessment has been accompanied by uncertainty. There are two main sources[67,68]. One source is extrapolation, wheredose levels inanimal studies exceed human exposure possibilities. Models used for extrapolation could cause results to differ by orders of magnitude, but uncertainty analysis can still improve transparency and assessment accuracy. The other source is data limitations, mainly including the inability to obtain theno observed adverse effect level(NOAEL), differences in exposure pathways, and differences in exposure time.Use of anuncertainty factor is a common method for dealing with these uncertainties[68]. Dividing the NOAEL obtained from animal experiments or other reference

| Characteristic | Exposure (ng $kg^{-1}$bwday$^{-1}$) | Fraction of population with hepatitis B | Annual hepatocellular carcinoma (HCC) incidence(cancers (year 100 000people)$^{-1}$) |
|---|---|---|---|
| *Age group* | | | |
| 3~6 years old | 0.94(0.29~4.24) | 12.45 | 0.0432(0.0001~1.4733) |
| 7~17years old | 0.75(0.22~3.64) | | 0.0346(0.0001~1.3403) |
| 18~59years old | 0.59(0.20~3.11) | | 0.0275(0.0001~0.8368) |
| More than 60 years old | 0.48(0.16~1.41) | | 0.0221 (0.0001~0.4958) |
| *Region* | | | |
| Urban | 0.29(0.08~0.56) | 7.10 | 0.0088(0.0001~0.3507) |
| Suburban | 2.26(0.35~6.59) | 16.14 | 0.1284(0.0001~24.422) |
| **Total** | **0.57(0.21~3.16)** | **12.45** | **0.0264(0.0058~1.3802)** |

**Table 5.** Estimated cancer risk in different age groupsand different regions in Guangzhou residents.

doses by theuncertainty factor can obtain a reference dose that is considered safe or without appreciable risk. The uncertaintyfactor is a coefficient that increases the level of protection of the health guidance value. The BMDL (with the uncertainty factor considered) used in the calculation of the exposure assessment in this study is a scientific method for dealing with data uncertainty.

Two factors need to be taken into consideration when these results are interpreted. First, AFs are jointly produced in nature, occurring as a mixture of $AFB_1$, $AFB_2$, $AFG_1$, $AFG_2$, etc.In our study, we assessed the risk of only $AFB_1$, which wouldunderestimate the health risk of total AFs. However, $AFB_1$ is the most toxic and frequent mycotoxinin AFs. Thus, the risk assessment for$AFB_1$can reflect the overall risk of AFs. Second, although the consumption of home-made peanut oil among urban residents might be rare, the high concentration of $AFB_1$ in home-made peanut oil requires the attention of the entire population. It would thus be necessary to expand the scale of home-made peanut oil consumption surveys to all residents instead of focusing on only suburban residents.

## Conclusions

This study is one of the few studies on probabilisticrisk assessment of dietary exposure to $AFB_1$in China. Instead of studying the limited category of $AFB_1$-contaminatedfood that is found in most studies, our study covered a wide variety of foods that mightcontribute to contamination by$AFB_1$[16,64,69]. Thoughthe overall risk of dietary health risk exposure to $AFB_1$ for liver cancer was low, there is a risk to health especially with continuous consumption. Furthermore, the health risk of suburban people was higher than that of urban people because of the common habit of consuming home-made peanut oil in the former group.In addition, 3~6-year-olds need special attention. Supervision of the production and sales of home-made peanut oil should be in place to reduce the risk of $AFB_1$ exposure.

Received: 9 October 2019; Accepted: 14 April 2020;
Published online: 14 May 2020

## References

1. Saracci, R. & Wild, C. P. Fifty years of the International Agency for Research on Cancer (1965 to 2015). *Int. J. Cancer* **138**, 1309–1311, https://doi.org/10.1002/ijc.29929 (2016).
2. Wu, F., Groopman, J. D. & Pestka, J. J. Public health impacts of foodborne mycotoxins. *Annu. Rev. Food Sci. Technol.* **5**, 351–372, https://doi.org/10.1146/annurev-food-030713-092431 (2014).
3. Schroeder, H. W. & Boller, R. A. Aflatoxin production of species and strains of the Aspergillus flavus group isolated from field crops. *Appl. Microbiol.* **25**, 885–889 (1973).
4. Klich, M. A. & Pitt, J. I. Differentiation of Aspergillus flavus from A. parasiticus and Other Closely Related Species. *Trans. Br. Mycological Soc.* **91**, 99–108 (1988).
5. Frisvad, J. C. *et al.* Taxonomy of Aspergillus section Flavi and their production of aflatoxins, ochratoxins and other mycotoxins. *Stud. Mycol.* **93**, 1–63, https://doi.org/10.1016/j.simyco.2018.06.001 (2019).
6. Geiser, D. M., Dorner, J. W., Horn, B. W. & Taylor, J. W. The phylogenetics of mycotoxin and sclerotium production in Aspergillus flavus and Aspergillus oryzae. *Fungal Genet. Biol.* **31**, 169–179, https://doi.org/10.1006/fgbi.2000.1215 (2000).
7. Adamson, R. H., Correa, P., Sieber, S. M., McIntire, K. R. & Dalgard, D. W. Carcinogenicity of aflatoxin B1 in rhesus monkeys: two additional cases of primary liver cancer. *J. Natl Cancer Inst.* **57**, 67–78 (1976).
8. Sengstag, C.The molecular mechanism of aflatoxin B1-induced liver cancer: is mitotic recombination involved?*Mol Carcinog***19**, 147-152, doi:10.1002/(SICI)1098-2744(199707)19:3<147::AID-MC1>3.0.CO;2-B (1997).
9. Liu, Y., Chang, C. C., Marsh, G. M. & Wu, F. Population attributable risk of aflatoxin-related liver cancer: systematic review and meta-analysis. *Eur. J. Cancer* **48**, 2125–2136, https://doi.org/10.1016/j.ejca.2012.02.009 (2012).
10. Li, Q. W., Lu, C. R., Ye, M., Xiao, W. H. & Liang, J. Evaluation of DNA repair gene XRCC1 polymorphism in prediction and prognosis of hepatocellular carcinoma risk. *Asian Pac. J. Cancer Prev.* **13**, 191–194, https://doi.org/10.7314/APJCP.2012.13.1.191 (2012).
11. Abrar, M. *et al.* Aflatoxins: biosynthesis, occurrence, toxicity, and remedies. *Crit. Rev. Food Sci. Nutr.* **53**, 862–874, https://doi.org/10.1080/10408398.2011.563154 (2013).
12. Leong, Y. H., Rosma, A., Latiff, A. A. & Ahmad, N. I. Exposure assessment and risk characterization of aflatoxin B1 in Malaysia. *Mycotoxin Res.* **27**, 207–214, https://doi.org/10.1007/s12550-011-0097-4 (2011).
13. Nugraha, A., Khotimah, K. & Rietjens, I. Risk assessment of aflatoxin B1 exposure from maize and peanut consumption in Indonesia using the margin of exposure and liver cancer risk estimation approaches. *Food Chem. Toxicol.* **113**, 134–144, https://doi.org/10.1016/j.fct.2018.01.036 (2018).

14. Sun, G. *et al*. Co-contamination of aflatoxin B1 and fumonisin B1 in food and human dietary exposure in three areas of China. *Food Addit. Contam. Part. A Chem. Anal. Control. Expo. Risk Assess.* **28**, 461–470, https://doi.org/10.1080/19440049.2010.544678 (2011).
15. Asim, M., Sarma, M. P., Thayumanavan, L. & Kar, P. Role of aflatoxin B1 as a risk for primary liver cancer in north Indian population. *Clin. Biochem.* **44**, 1235–1240, https://doi.org/10.1016/j.clinbiochem.2011.07.017 (2011).
16. Ding, X. *et al*. Risk Assessment on Dietary Exposure to Aflatoxin B(1) in Post-Harvest Peanuts in the Yangtze River Ecological Region. *Toxins* **7**, 4157–4174, https://doi.org/10.3390/toxins7104157 (2015).
17. CODEX. in *General Standard for Contaminants and Toxins in Food and Feed(Codex Alimentarius Comission* (2015).
18. European Commission (EC). in *Setting maximum levels for certain contaminants in foodstuffs* Vol. No. 1881/2006 (2006).
19. National Health and Family Planning Commission of thePeople's Republic of China. (2017).
20. Evaluation of certain food additives and contaminants. Forty-ninth report of the Joint FAO/WHO Expert Committee on Food Additives. *World Health Organ. Tech. Rep. Ser.* **884**(i-viii), 1–96 (1999).
21. European Food Safety Authority. Opinion of the Scientific Committee on a request from EFSA related to Exposure Assessments. *EFSA J.* **3**, 249, https://doi.org/10.2903/j.efsa.2005.249 (2005).
22. Ok, H. E. *et al*. Natural occurrence of aflatoxin B1 in marketed foods and risk estimates of dietary exposure in Koreans. *J. Food Prot.* **70**, 2824–2828, https://doi.org/10.4315/0362-028x-70.12.2824 (2007).
23. Huong, B. T. M., Tuyen, L. D., Tuan, D. H., Brimer, L. & Dalsgaard, A. Dietary exposure to aflatoxin B1, ochratoxin A and fuminisins of adults in Lao Cai province, Viet Nam: A total dietary study approach. *Food Chem. Toxicol.* **98**, 127–133, https://doi.org/10.1016/j.fct.2016.10.012 (2016).
24. IARC. Monographs on the Evaluation of Carcinogenic Risks to Humans. (INTERNATIONAL AGENCY FOR RESEARCH ON CANCER (2002).
25. EFSAPanelon Contaminants in the Food Chain. Opinion of the Scientific Panel on contaminants in the food chain [CONTAM] related heptachlor as an undesirable substance in animal feed. *EFSA J.* **5**, 478, https://doi.org/10.2903/j.efsa.2007.478 (2007).
26. Summary of Evaluations Performed by the Joint FAOWHO Expert Committee on Food Additives (JECFA). Nutrition Reviews58, 90, https://doi.org/10.1111/j.1753-4887.2000.tb01846.x (2000).
27. Sugita-Konishi, Y. *et al*. Exposure to aflatoxins in Japan: risk assessment for aflatoxinB1. *Food Addit. Contam. Part. A Chem. Anal. Control. Expo. Risk Assess.* **27**, 365–372, https://doi.org/10.1080/19440040903317497 (2010).
28. Qi, N. *et al*. Aflatoxin B1 in peanut oil from Western Guangdong, China, during 2016-2017. *Food Addit. Contam. Part. B Surveill.* **12**, 45–51, https://doi.org/10.1080/19393210.2018.1544173 (2019).
29. Zhang, W. *et al*. [Analysis on contamination of aflatoxinB1 in food and oil in Guangzhou from 2009 to 2013]. *Chin. J. Food Hyg.* **27**, 4, https://doi.org/10.13590/j.cjfh.2015.03.015 (2015).
30. Gao, X. *et al*. Aflatoxin contamination of corn samples collected from six regions of China. *J. Hyg. Res.* **40**, 46–49, https://doi.org/10.1631/jzus.B1000265 (2011).
31. Wang, J. & Liu, X. M. Contamination of aflatoxins in different kinds of foods in China. *Biomed. Env. Sci.* **20**, 483–487 (2007).
32. Bircan, C. The determination of aflatoxins in spices by immunoaffinity column extraction using HPLC. *Int. J. Food Sci. Technol.* **40**, 929–934, https://doi.org/10.1111/j.1365-2621.2005.01025.x (2010).
33. Roch, O. G., Blunden, G., Haig, D. J., Coker, R. D. & Gay, C. Determination of aflatoxins in groundnut meal by high-performance liquid chromatography: a comparison of two methods of derivatisation of aflatoxinB1. *Br. J. Biomed. Sci.* **52**, 312–316 (1995).
34. Chen, L., Molla, A. E., Getu, K. M., Ma, A.&Wan, C.Determination of Aflatoxins in Edible Oils from China and Ethiopia Using Immunoaffinity Column and HPLC-MS/MS.*Journal of Aoac International*, https://doi.org/10.5740/jaoacint.18-0106 (2019).
35. Zhang, Y. *et al*. [Food consumption and nutrients intake among residents in Guangzhou city]. *Chin. J. Public. Health* **33**, 4, https://doi.org/10.11847/zgggws2017-33-06-26 (2017).
36. Yuexin, Y.*China Food Composition*. (Peking University Medical Press (2009).
37. Wang, J., Liu, X. M. & Zhang, Z. Q. [Exposure assessment of liver cancer attributed to dietary aflatoxins exposure in Chinese residents]. *Zhonghua Yu Fang. Yi Xue Za Zhi* **43**, 478–481, https://doi.org/10.1016/j.chb.2008.10.005 (2009).
38. Li, K., Qiu, F., Jiang, L. & Yang, M. [Dietary exposure assessment of aflatoxin of foodstuff and edible oil from Shenzhen residents]. *J. Hyg. Res.* **43**, 6 (2014).
39. Evaluation of certain food additives. Seventy-first report of the Joint FAO/WHO Expert Committee on Food Additives. ReportNo. 0512-3054, 1-80 (2010).
40. 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. *EFSA J.* **9**, 2450, https://doi.org/10.2903/j.efsa.2011.2450 (2011).
41. Vlachonikolis, I. G. & Marriott, F. H. Evaluation of censored contamination data. *Food Addit. Contam.* **12**, 637–644, https://doi.org/10.1080/02652039509374352 (1995).
42. Hecht, H. & Honikel, K. O. Assessment of data sets containing a considerable number of values below the detection limits. *Z. Lebensm. Unters. Forsch.* **201**, 592–597, https://doi.org/10.1007/bf01201592 (1995).
43. Kulmbach Germany: WHORegional Office for Europe. Second workshop on reliable evaluation of low-level contamination of food. (1995).
44. Lin, Z. & Chen, D. [A sampling survey of growth and nutritional status in preschool children in Yuexiu District of Guangzhou]. *Chin. Prim. Health Care* **24**, 44–45, https://doi.org/10.3969/j.issn.1001-568X.2010.08.019 (2010).
45. Gao, D., Dong, Y., Yang, Y., Zou, Z. & Ma, J. [Secular trends of height and weight in Chinese children from 2005 to 2014]. *Chin. J. Sch. Health* **39**, 252–255, https://doi.org/10.16835/j.cnki.1000-9817.2018.02.027 (2018).
46. China Institute of Nutrition and Health. China Nutrition Data Yearbook. (2012).
47. Peers, F. G., Gilman, G. A. & Linsell, C. A. Dietary aflatoxins and human liver cancer. A study in Swaziland. *Int. J. Cancer* **17**, 167–176 (1976).
48. Peers, F., Bosch, X., Kaldor, J., Linsell, A. & Pluijmen, M. Aflatoxin exposure, hepatitis B virus infection and liver cancer in Swaziland. *Int. J. Cancer* **39**, 545–553 (1987).
49. Carlborg, F. W. Cancer, mathematical models and aflatoxin. *Food Cosmet. Toxicol.* **17**, 159–166 (1979).
50. Benford, D., Leblanc, J. C. & Setzer, R. W. Application of the margin of exposure (MoE) approach to substances in food that are genotoxic and carcinogenic: example: aflatoxin B1 (AFB1). *Food Chem. Toxicol.* **48**(Suppl 1), S34–41, https://doi.org/10.1016/j.fct.2009.10.037 (2010).
51. Newberne, P. M. Carcinogenic effects of low dietary levels of aflatoxin B1 in rats. *Food Cosmetics Toxicol.* **12**, 681–685 (1974).
52. Barraud, L. *et al*. The role of duck hepatitis B virus and aflatoxin B1 in the induction of oxidative stress in the liver. *Cancer Detect. Prev.* **25**, 192–201, https://doi.org/10.1007/s002800000224 (2001).
53. Kew, M. C. Synergistic interaction between aflatoxin B1 and hepatitis B virus in hepatocarcinogenesis. *Liver Int.* **23**, 405–409, https://doi.org/10.1111/j.1478-3231.2003.00869.x (2003).
54. Campbell, T. C. Correspondence re: G-S. Qian, et al., A follow-up study of urinary markers of aflatoxin exposure and liver cancer risk in Shanghai, People's Republic of China. Cancer Epidemiol., Biomarkers & Prev., 3:3-10, 1994, and C.C. Harris, Solving the viral-chemical puzzle of human liver carcinogenesis. Cancer Epidemiol., Biomarkers & Prev., 3:1-2, 1994. *Cancer Epidemiol. Biomarkers Prev.* **3**, 519–521 (1994).
55. Li, Y. *et al*. Synergistic effect of hepatitis B virus and aflatoxin B1 in hepatocarcinogenesis in tree shrews. *Ann. Acad. Med. Singap.* **28**, 67–71 (1999).

56. Wu, H. C. *et al*. Urinary 15-F2t-isoprostane, aflatoxin B1 exposure and hepatitis B virus infection and hepatocellular carcinoma in Taiwan. *Carcinogenesis* **29**, 971–976, https://doi.org/10.1093/carcin/bgn057 (2008).
57. Wang, J. S. *et al*. Temporal patterns of aflatoxin-albumin adducts in hepatitis B surface antigen-positive and antigen-negative residents of Daxin, Qidong County, People's Republic of China. *Cancer Epidemiol. Biomarkers Prev.* **5**, 253–261 (1996).
58. Liu, J., Cai, Y. & Wang, M. [Epidemiological survey of hepatitis B virus surface antigen positive in Guangzhou in 2008]. *Zhonghua Yu Fang. Yi Xue Za Zhi* **44**, 3, https://doi.org/10.3760/cma.j.issn.0253-9624.2010.03.029 (2010).
59. Trung, T. *et al*. Fungal mycoflora and contamination of maize from Vietnam with aflatoxin B1 and fumonisinB1. *World Mycotoxin J.* **1**, 8, https://doi.org/10.3920/WMJ2008.x010 (2008).
60. Qiu, W. & Fu, W. [Contamination of aflatoxins in peanuts and peanut products from Fujian]. *Chin. J. Health Laboratory Technol.* **22**, 2446–2448 (2012).
61. Zhang, X., Ding, J., Li, S. & Cheng, Y. Survey of aflatoxin contamination in foods sold in Wanzhou District, Chongqing, 2013-2014. *J. Practical Preventive Med.* **23**, 48–50, https://doi.org/10.3969/j.issn.1006-3110.2016.04.013 (2016).
62. Xu, W., Liu, D., Han, X., Lu, D. & Li, F. [Survey of aflatoxin contamination in edible vegetable oils sold in parts of China in 2015]. *Chin. J. Food Hyg.* **14**, 776–779, https://doi.org/10.13590/j.cjfh.2018.01.014 (2018).
63. Cheng, H. *et al*. Exposure risk assessment of aflatoxin B1 in edible vegetable oil by using the margin of exposure in Guangxi. *Chin. J. Food Hyg.* **29**, 4, https://doi.org/10.13590/j.cjfh.2017.04.022 (2017).
64. Wang, X., Lien, K. W.&Ling, M. P.Probabilistic Health Risk Assessment for Dietary Exposure to Aflatoxin in Peanut and Peanut Products in Taiwan. *Food Control*, S0956713518301828, https://doi.org/10.1016/j.foodcont.2018.04.021 (2018).
65. Zuo, T., Zheng, R., Zeng, H., Zhang, S.&Chen, W.[Analysis of liver cancer incidence and trend in China]. *Zhonghua zhong liu za zhi***37**, https://doi.org/10.3760/cma.j.issn.0253-3766.2015.09.013 (2015).
66. Ding, X., Li, P., Bai, Y. & Zhou, H. Aflatoxin B 1 in post-harvest peanuts and dietary risk in China. *Food Control.* **23**, 143–148, https://doi.org/10.1016/j.foodcont.2011.06.026 (2012).
67. Edler, L. *et al*. Selection of appropriate tumour data sets for Benchmark Dose Modelling (BMD) and derivation of a Margin of Exposure (MoE) for substances that are genotoxic and carcinogenic: considerations of biological relevance of tumour type, data quality and uncertainty assessment. *Food Chem. Toxicol.* **70**, 264–289, https://doi.org/10.1016/j.fct.2013.10.030 (2014).
68. International Programme on Chemical Safety (IPCS). Uncertainty and dataquality in exposure assessment. (2008).
69. Guo, Y. D., Chen, L., Yuan, Y. H. & Yue, T. L. Dietary Exposure and Risk Assessment of Aflatoxin B_1 in Corn-based Foods in China Using Probabilistic Approach. *Food Sci.* **34**, 24–27, https://doi.org/10.7506/spkx1002-6630-201311006 (2013).



## Acknowledgements
This work was supported by the Project for KeyMedicine Discipline Construction of Guangzhou Municipality (grant number2017–2019-07) and a medicalscientificgrantfrom Guangdong Province, China (B2018154). Minling Ye from McGill University (CA) helped with English language editing.


## Author contributions
Kuncai Chen is the corresponding author and was responsible for designing and organizing this study; Weiwei Zhang is the lead author and implemented the project, analysed the data and wrote the manuscript. Yufei Liu was responsible for project administration; Boheng Liang helped analyse the data; Yuhua Zhang and XianwuZhong contributed tothe foodsamples collected; XiaoyanLuo performed the experiments; Jie Huang and Yanyan Wang contributed to the food consumptionsurvey; Weibin Cheng provided important suggestions and revised the manuscript.

## Competing interests
The authors declare no competing interests.

## Additional information
**Supplementary information** is available for this paper at https://doi.org/10.1038/s41598-020-64295-8.

**Correspondence** and requests for materials should be addressed to K.C.

**Reprints and permissions information** is available at www.nature.com/reprints.


**Publisher's note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

**Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this license, visit http://creativecommons.org/licenses/by/4.0/.

© The Author(s) 2020