EXPOSURE TO AFM_1 THROUGH MILK IN LEBANON

Risky or Not?

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Food and Chemical Toxicology 193 (2024) 115042

Contents lists available at ScienceDirect

Food and Chemical Toxicology

journal homepage: www.elsevier.com/locate/foodchemtox

Stochastic health risk assessment of aflatoxin M_1 in cow's milk among Lebanese population

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Aflatoxin M_1

- AFB_1 contaminates feed, metabolized by mammals into AFM_1, secreted in milk
- Milk = one of the main sources of exposure to AFM_1
- Chronic exposure to AFM_1 = hepatocellular carcinoma (HCC)
- Enhanced potency if Hepatitis B virus infection
- Maximum levels in place
- But hazard ≠ risk
  - Can the levels of AFM_1 in Lebanese milk lead to HCC?
  - If yes – Does the entire population face the same level of risk?

Risk Assessment

- To what dose of the hazard are we exposed to through food?

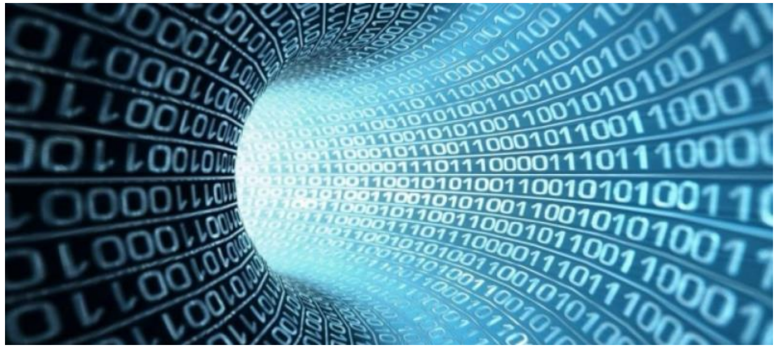
$$Exposure = \frac{AFM1\ concentration * Milk\ intake}{Body\ weight}$$

- Can this exposure lead to adverse health effects? (risk)
  - Number of additional HCC cases per year per 100 000 population
  - Margin of exposure < 10 000 = concern

- Deterministic (mean value) vs probabilistic (range of values)

Non-Aggregated Data

- ❑ Examples of risk assessment questions:
  - Which AFM_1 concentration levels result in adverse health effects?
  - Do different age/gender subgroups face different levels of risk?
  - If yes, which milk consumption levels result in adverse health effects for each population?
  - ...
- ❑ Need non-aggregated data to answer them



- ❑ Input variables as distributions → RA outputs as distributions

New Data/Models, Updated RA

- ❑ AFM_1 from milk in Lebanon not a new topic (Daou et al., 2020; Hoteit et al., 2024)
- ❑ New/better data + probabilistic approach = more informative results
  - AFM_1 concentration (Daou et al., 2020)
  - Adults’ milk consumption (Hoteit et al., 2024)
  - Adolescents’ milk consumption (this study)
  - Adults’ and adolescents’ body weights (Hoteit et al., 2024; this study)
  - Prevalence of Hepatitis B virus (Abou Rached et al., 2016) → cancer potency

Identification of Significant Differences

- Important preliminary step
- Are there significant differences within variables' subgroups / subpopulations?
  - AFM_1 concentration in milk per region?
  - Milk intake per age/gender subgroup?
  - Body weight per age/gender subgroup?
  - Prevalence of HBV per age/gender subgroup?
  - …

- If yes, need to differentiate them in the risk assessment

Exposure Variables

$$\frac{AFM1\ concentration\ *\ Milk\ intake}{Body\ weight}$$

AFM_1 in Lebanese milk: national distribution, did not investigate differences per region of production

Milk intake	Body weight
• Adults: M = F • Adolescents: M ≠ F	• Adults: M ≠ F • Adolescents: M = F

Fig. 1. Daily milk intake (kg) of Lebanese adolescents per gender (F = 169; M = 147). Means are shown with an asterisk (*).

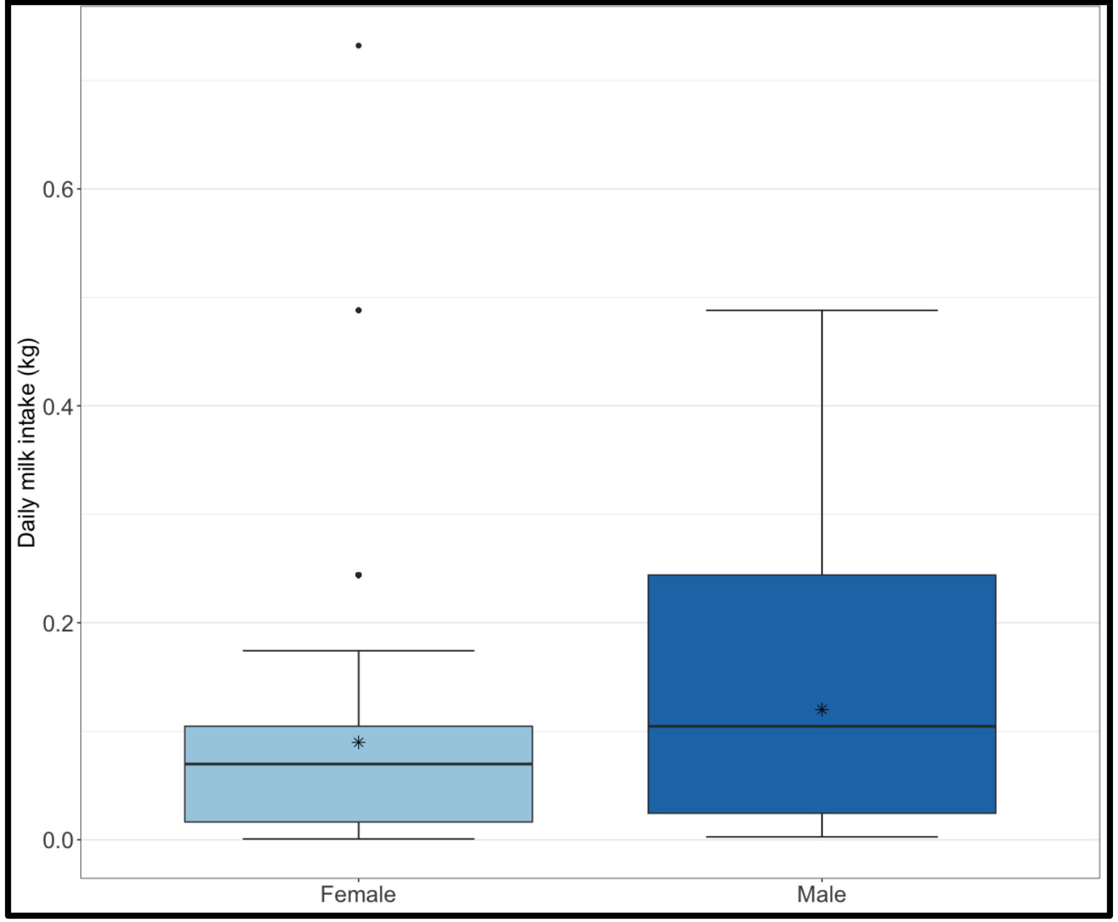
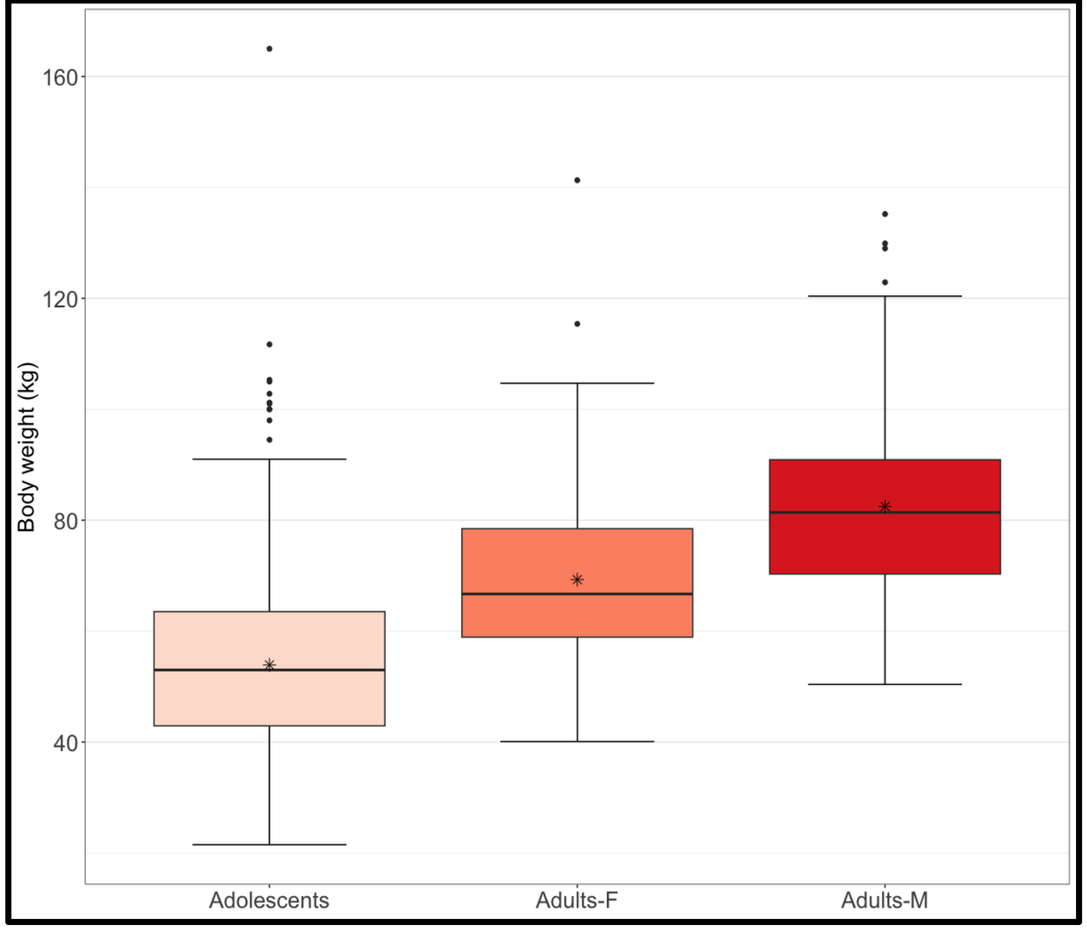


Fig. 2. Body weight (kg) of Lebanese adolescents (F = 246; M = 196) and adults (F = 234; M = 171). Means are shown with an asterisk (*).



Risk Variables

Additional HCC cases per year per 100 000 population, considering AFM1 cancer potency for 1 ng/kg bw/day

$$Exposure * Cancer\ potency$$

Previous RAs used 0.0083 (JECFA, 1999).

For non-European countries, assumes 25% HBV prevalence and 60 kg bw.

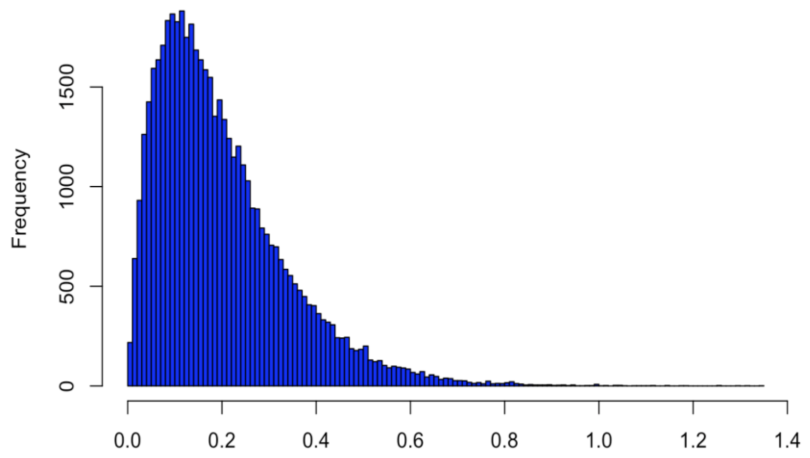
Estimated AFM_1 cancer potency for 1 ng/kg bw/day (in 100 000 person years) used in this risk assessment.

	HBsAg+	HBsAg-
AFM_1 cancer potency[a]	0.0562	0.0049
HBV prevalence in Lebanon	0.0174[b]	0.9826
AFM_1 cancer potency considering HBV prevalence	0.00098	0.00481
AFM_1 cancer potency used in this risk assessment	0.00579	

[a] One tenth of the 95% upper bound estimate of AFB_1's cancer potency reported by FAO/WHO (2017) for 1 ng/kg bw/day (in 100 000 person years).
[b] Abou Rached et al. (2016).

Monte Carlo simulations

- Variables described as distributions, not point values
- 1 000 simulations, each considering 10 000 individuals consuming milk
- For each simulated individual, 1 value of each input variable's distribution is randomly selected and used to calculate outputs (exposure, risk)
- Result: 10 000 values per simulation for each output



Risk Assessment Model

VARIABLE	ADULTS		ADOLESCENTS	
	F	M	F	M
AFM1 PREVALENCE IN MILK	BERNOULLI			
AFM1 CONCENTRATION IN MILK	LOGNORMAL			
DAILY MILK INTAKE	WEIBULL		WEIBULL	GAMMA
BODY WEIGHT	LOGNORMAL	LOGNORMAL	LOGNORMAL	
EXPOSURE	✓	✓	✓	✓
AFM1 CANCER POTENCY	0.00579			
HCC RISK	✓	✓	✓	✓

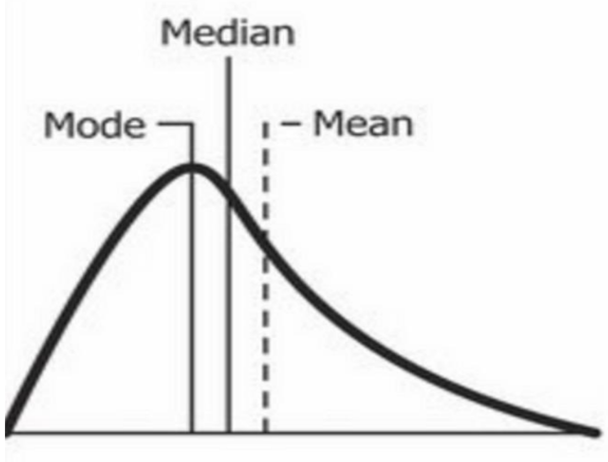
Exposure estimates

- ❑All subgroups significantly different

Distribution of the estimated exposure (ng/kg bw/person/day) to AFM_1 from milk.

Group	Subgroup	Min	25%	Median	Mean	75%	Max
Adults	Females	$<10^{-5}$	$<10^{-5}$	0.0056	0.0454	0.0445	2.63
	Males			0.0054	0.0371	0.0379	1.38
Adolescents	Females			0.0105	0.0592	0.0615	2.48
	Males			0.0112	0.0703	0.0678	5.14

- ❑WIDE range of exposure doses, skewed distribution
- ❑50% of estimated exposures were very low ($<10^{-4}$)
- ❑Mean values: adult males, lowest; adolescent males highest
- ❑Can these exposure result in adverse health effects?



HCC Risk

- All subgroups significantly different

Distribution of the number of estimated additional HCC cases per year per 100 000 population due to exposure to AFM_1 from milk.

Group	Subgroup	Min	25%	Median	Mean	75%	Max
Adults	Females	$<10^{-5}$	$<10^{-5}$	3.2×10^{-5}	2.6×10^{-4}	2.6×10^{-4}	1.5×10^{-2}
	Males			3.1×10^{-5}	2.2×10^{-4}	2.2×10^{-4}	8.0×10^{-3}
Adolescents	Females			6.1×10^{-5}	3.4×10^{-4}	3.6×10^{-4}	1.4×10^{-2}
	Males			6.5×10^{-5}	4.1×10^{-4}	3.9×10^{-4}	2.9×10^{-2}

- Mean values: adult males, lowest; adolescent males, highest
  - But notice adult males reach highest max values
- With these results we can rank risk, but are these values of concern?

Margin of Exposure

<10 000?

Adults: <25% of values

Adolescents: mean; <50% of values

Likelihood of MOE<10 000

Subgroup	Probability
Adult M	0.17
Adult F	0.20
Adolescent F	0.29
Adolescent M	0.31

Distribution of the Margin of Exposure (MOE) to AFM_1 from milk.[a].

Group	Subgroup	Min	25%	Median	Mean	75%	Max
Adults	Females	217	12 809	101 786	12 555	$>10^7$	$>10^7$
	Males	413	15 040	105 556	15 364		
Adolescents	Females	230	9268	54 286	9628		
	Males	111	8407	50 893	8108		

[a] MOE was calculated using an estimated BMDL10 for $AFM_1 = 570$ ng/kg bw/day (Udovicki et al., 2019). MOE ≥10 000 indicates low risk. More details in section 2.5.

Conclusions

General

- ❑Important to update RA as data becomes available
- ❑Value of aggregated data
- ❑Probabilistic assessment more informative and better adapted to input data (skewed)

This example

- ❑Lebanese adults low risk
- ❑Adolescents higher risk, more vulnerable population
- ❑Younger populations? Does ML provide adequate protection?


thank you
danke
謝謝
ngiyabonga
teşekkür ederim
gracias
рахмат
Баярлалаа
спасибо
mersi
kia ora
barka
welalin
spas
tack
dank je
misaotra
matondo
paldies
grazzi
mahalo
tapadh leat
faafetai lava
vinaka
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blagodaram
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hvala
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bayarlalaa
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