

The aflatoxin situation in Africa

Systematic literature review

Executive summary of RIKILT report 2018.010



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1. Introduction

Aflatoxins are highly toxic fungal metabolites produced by certain strains of *Aspergillus* species. Aflatoxins thwart Africa's efforts at achieving food security, improving nutrition and health outcomes and attaining agricultural-led economic growth. They pose major risks to human and animal health, nutrition, as well as intra-regional and international trade. The difficulty African producers, traders and manufacturers face in sourcing high quality raw materials and producing high quality products hampers agribusiness development, job creation and economic growth. This makes the attainment of the UN Sustainable Development Goals (SDGs), especially as they pertain to food security, more challenging. They also undermine continental priorities such as the Malabo Declaration Commitments of 2014 of the African Union. Despite the fact that the above mentioned impacts of aflatoxin to the African situation are clear, quantitative evidence is lacking, and the information that is available is scattered.

The aim of this project was to provide insight into the aflatoxin situation in Africa. These insights can be used to enhance effective management of the major challenges to combat aflatoxin contamination. The following research questions have been defined for the systematic literature review:

1. What is the scale and geographical spread of aflatoxin contamination in food, feed, and associated commodities and key value chains, in African countries?
2. What is the scale of aflatoxin disease burden for African countries?
3. What are the economic effects of aflatoxins on African countries?
4. What are current and additional possible mitigation measures and what is the cost-effectiveness of mitigation of aflatoxin contamination in key commodities / value chains in African countries?

2. Scientific background

Scale and geographical spread of aflatoxin contamination in food, feed, and associated commodities/key value chains

Widespread aflatoxin contamination of certain African staple foods, particularly maize, other cereals, groundnuts, and peanuts, had been reported prior to the year 2010, which marked the start of the considered review period in this report. In general, these crops which are particularly vulnerable to *Aspergillus* infection and aflatoxin contamination pre- and post-harvest showed high proportions of samples being positive, both in raw commodities as well as derived and processed products.

Regulations on maximum limits of aflatoxins in food vary among countries worldwide. Of a total of 55 countries in Africa, only 15 countries have established regulations on aflatoxins level. Some countries refer to EU regulation to set the limit for food for human consumption. In the EU, maximum limits for AFB1 range from 2 µg/kg for groundnuts (peanuts) and processed products thereof, intended for direct human consumption or use as an ingredient in foodstuffs, to 20 µg/kg for feed. It should be taken into account that aflatoxins are carcinogenic substances and concentrations in food should therefore be as low as reasonably achievable.

For maize in Africa, a majority of samples was contaminated with aflatoxins. Aflatoxin concentrations also commonly exceeded internationally established legal limits (EU, Codex) in a substantial fraction of the samples analysed. There were only a few reports of absence or very low levels of aflatoxins. Consumption of maize contaminated with high levels of aflatoxins accounted for large outbreaks of acute aflatoxicosis, particularly in Kenya in 2004, leading to morbidity and, in some cases, mortality. In that year, of the maize sold in markets in the affected four districts, seven percent turned out to be contaminated with more than 1,000 parts-per-billion (µg/kg) of aflatoxin, with a maximum of

46,400 µg/kg. For maize, the prevalence of aflatoxin, as reported, appears to be highest in Nigeria and Kenya. However, the mapping exercises also highlight a lack of studies on prevalence in other sub-Saharan countries. Whereas the environmental conditions appear to be favourable for mycotoxin contamination, yet the number of studies conducted in those countries is low.

Scale of aflatoxin disease burden

Disease burden is generally defined as the impact of a health problem, and can be measured by indicators such as cost-of-illness, mortality or morbidity. The latter two are often combined and represented by Disability Adjusted Life Years (DALYs). Since aflatoxin is a genotoxic carcinogen there is no safe level of exposure, thus a tolerable daily intake (TDI)



In various African countries, other cereals derived products have been reported to contain elevated levels of aflatoxins, in particular sorghum, barley, millet, rice, teff, and wheat. In peanut, another important staple crop, inoculation with aflatoxigenic moulds occurs primarily in the soil, during the plant development stage in which the pod enters the soil and directly comes into contact with soil-borne *Aspergillus* species. Cassava and derived products, such as flour and chips, generally show low aflatoxins contamination even in case of *Aspergillus* infection, with relatively rare cases of contaminations exceeding regulatory limits.

cannot be determined. Instead, a margin of exposure (MOE) approach can be used in the risk assessment, defining the difference between estimated intake levels (EDI) and the lower confidence limit of the benchmark dose (BMD) related to cancer induction (BMD/EDI).

Ingestion of aflatoxins via food can lead to both acute and chronic toxic effects in humans, depending on the concentration of aflatoxin in the diet. Long-term exposure to sub-acute concentrations of aflatoxins are related to various adverse health effects in humans. Particularly, the development of hepatocellular carcinoma (HCC) is related to chronic aflatoxin

intake. It is well documented that people who are chronically infected with the hepatitis virus B (HBV) or C (HCV) are at high risk to develop hepatocellular carcinoma even when exposed to low concentrations of aflatoxins. There is an “extremely strong association between high AF-alb levels of aflatoxin-albumin adducts (AF-alb) in blood serum and stunted growth in children” (Gong et al., 2003).

Biomarkers can give an indication of exposure of a person to a certain mycotoxin at a certain time. The level of exposure can be estimated from the biomarker concentration only when the transfer rate (intake versus excretion) is validated in studies. Biomarkers of exposure can be measured in blood plasma and urine. There are no validated biomarkers of effect. In plasma, “AFB1-lysine is the most reliable biomarker of chronic aflatoxin exposure” (Vidal et al., 2018). Urinary biomarkers are more suitable for measuring short-term exposure.

Economic effects of aflatoxins

In published studies that focus on the economic effect of aflatoxin, the situation of aflatoxin is usually described, but not quantified. Some early studies investigated the effect of aflatoxin contamination in Africa and the measures imposed by developed countries, namely the legal maximum levels for aflatoxin in the European Union. Wilson and Otsuki (2001) estimated an annual loss amounting to USD 670 million for African food exporters from attempting to meet EU aflatoxin standards.

The cost of disease burden can be measured in the value of statistical life (VSL). However, the lack of data available on Africa restricts the analysis. At best, the health economic effect and the trade effect are estimated, but the production effect, the costs and overall loss for the economy were not determined due to the lack of data.

Mitigation measures

Prior to the period covered by the systematic bibliographic searches, various accounts of mitigation measures being implemented or developed specifically for African countries were already given. For peanut, breeding efforts towards resistance to *Aspergillus* infection and aflatoxin formation were well under way, yet total resistance still needs to be achieved. Another agronomic measure to prevent aflatoxin contamination in the field is ‘biocontrol’ through the use of non-aflatoxigenic mould strains that compete with *Aspergillus* for the same niche but that do not form aflatoxins.

Other agronomic measures already being tested and further elaborated in more recent years include for instance: crop rotation and chemical and biological control with pesticides or natural enemies to prevent pest insect damage that may facilitate mould infection as well as control of moulds. Further post-harvest measures include: drying of harvested seeds or grains and sorting and fractionation (e.g. flotation) of harvested seeds or grains. In addition, awareness raising, good practices for agricultural and hygienic food production, as well as regulation and enforcement have been forming part of contamination-mitigating strategies. Mitigation may also focus on preventing the health effects caused by aflatoxins in consumers.

3. Methodology

A systematic literature review is a ‘structured process of review synthesis’. Systematic literature reviews rely on the following core principles: (i) systematic approach; (ii) reproducible; (iii) rigorous reviewing of literature; (iv) including the quality of studies when drawing conclusions. Compared to the narrative type of literature review commonly performed within research projects, systematic literature reviews have several benefits, including that a well-defined methodology reduces bias. The current literature review covered the period 2010-2018.

The guidelines for the qualified application of systematic review by the Evidence for Policy and Practice Information and Co-ordinating Centre (EPPI centre, University of London) and the Cochrane Handbook for Systematic Reviews of Interventions were followed. In particular, the software tool for systematic reviews designed by the EPPI, University of London was used.

For each research question, a search strategy was developed for identifying relevant studies. Bibliographic scientific databases (i.e. CAB Abstracts, Scopus, PubMed, AGRIS, EconLit) were searched for potentially relevant publications. Search terms originated from personal knowledge, searches on websites, screening key (review) papers, and screening the results of preliminary searches in bibliographic databases. In order to verify whether the use of the search queries indeed enabled retrieval of relevant references, the outcomes of preliminary searches with these queries were compared to benchmark collections. Collection of relevant references from the selected sources was done by use of Endnote reference citation management software. In addition to these searches for peer-reviewed literature, additional literature on economic effects was identified via 'snowballing', which refers to using the references of relevant studies with the aim to identifying further studies.

Inclusion and exclusion criteria were pre-defined and applied to the screening in order to ensure that relevant studies were identified. Outside of the scope of this study were studies: not written in English; not on aflatoxins (e.g. on other mycotoxins); not conducted in Africa; and studies focusing on general health effects of aflatoxins.

The screening resulted in a list of studies that are relevant for answering one or more the four research questions of the systematic review, and only those studies were assessed in detail. These studies were classified in order to create systematic maps of categories of studies that are part of the database. For instance, by assigning all studies on biomarkers to a specific sub-category within the category disease burden. For the coding, a "questionnaire" was

applied to the studies. In essence, using the key wording and coding, a high level understanding about the nature and contribution of the research was achieved.

4. Results: Map of available literature

In total, 6.374 references were collected. Of these, 2.467 studies (39%) were published in the considered period of 2010 to 2018. After de-duplication; pre-screening; subsequent screening on title and abstract; and finally screening on full-text. A total of 361 studies was

found to be relevant for synthesis. An overview of the subsequent steps followed in this project, and the respective number of identified studies per step, is shown in Figure 1.

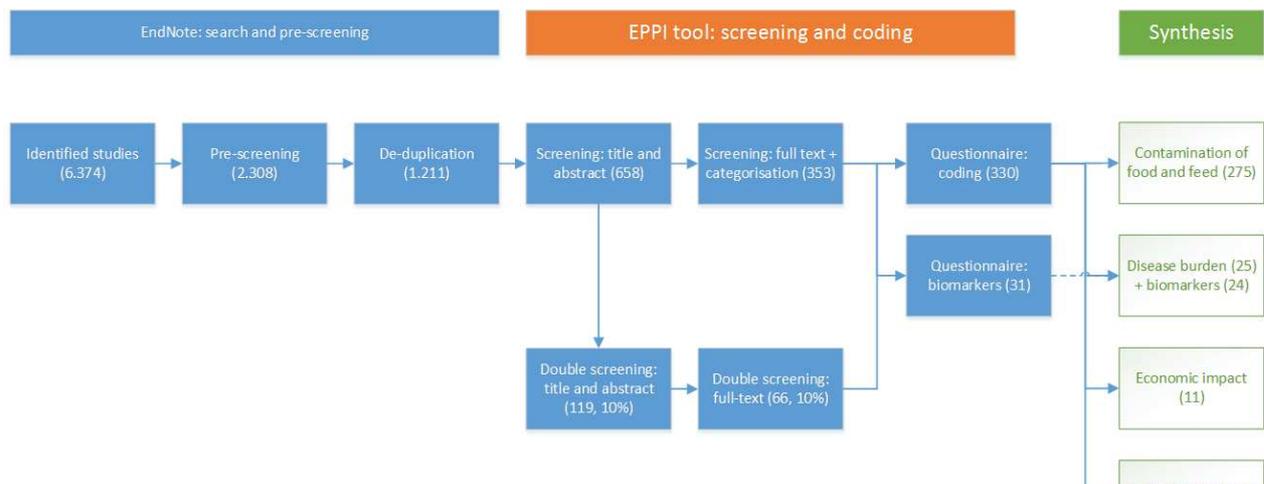


Figure 1: Overview of steps conducted in systematic review.

Scale and geographic spread of aflatoxin contamination

In total, 275 identified studies investigated the occurrence of aflatoxin in food and feed in Africa. Included studies were frequently for Nigeria (56 studies), followed by Egypt (41), and Kenya (33). Studies on food or feed of interest reported on sampling throughout the supply chain. Around half of the studies investigated products that were already processed and/or on the market (152 studies), while 69 studies reported the contamination on harvested or stored commodities. Samples from plants, and food and drinks for human consumption were most frequently reported in the included studies; accounting for 48% (plants, 132 studies) and 43% (food and drink for human consumption, 118) of the studies. Various analytical methods were used for aflatoxin detection. In general, the use of immunochemistry methods such as ELISA, dip stick test, sensor (82 studies, 30%) and liquid chromatography (HPLC) (85, 31%) with fluorescence detection or post-column

derivatization were most commonly reported, followed by detection using LC-MS (48, 17%) and TLC (33, 12%).

Disease burden

A total of 25 studies addressing disease burden were identified. An additional 24 studies focused on biomarkers. Most studies on disease burden were from Egypt, followed by Nigeria and Kenya. Most of the included studies focused on infants and children. Around 50% (12) of the studies investigated consumption of plant-based foods (cereals, groundnuts, etc.), dairy products and breast milk (26%), and other type of foods such as weaning food, meat, and food in general. Several included studies investigated disease symptoms in humans, most of them on hepatocellular carcinoma (33%) and growth impairment in children (38%).

Of the 24 included studies specifically for biomarkers, nine focused on urinary biomarkers and 17 on biomarkers in serum (e.g. AF-albumin adduct). The route of exposure for the

biomarker studies was mostly via plant foods (e.g. peanuts, cereals, etc.).

Most mitigation measures from the included studies focused on agricultural (16) or biological



Economic impact

In total, only 11 peer reviewed articles could be found related to the economic impact. Four of these included studies concerned results from Kenya. An econometric estimation was made in one study. Two studies measured the impact at firm level by assessing productivity losses due to contamination; four measured this via costs of managing aflatoxin at the farm level with regard to compliance costs.

Mitigation measures

A total of 60 peer reviewed papers were related to mitigation measures, many of which were reported for Kenya (13), followed by Nigeria (9) and Egypt (7). The operators studied were largely small scale: smallholder farms, village processing, local middlemen and vendors, etc.

(12) measures. The impact of mitigation measures in the included studies was described in varying manners. For six studies, the impact was described in monetary value, while many others did not quantitatively address the effectiveness of the mitigation measure. The cost-effectiveness expressed as investment per benefit gained (e.g. USD/DALY) was described in only a single study, which assessed the impacts of aflatoxin contamination of maize and groundnut in Tanzania and Nigeria on agriculture & food security, trade, and public health (Narayan et al., 2014).

5. Results: Synthesis of data

Scale and geographic spread of aflatoxin contamination

AFB1 was the most studied aflatoxin for all countries, followed by B2, G1, and G2, which are usually analysed together with AFB1 by using a multi-toxin analysis. In 27 studies, AFB1 was quantified in various products, with maize as the most frequently studied product in nine publications. Almost all studies indicated mean AFB1 levels in maize exceeding 5 µg/kg, which is the legal limit for AFB1 in the EU. Six included studies that investigated peanuts, found the AFB1 contamination concentrations in peanut to be relatively high (>15 µg/kg), with samples from Algeria only having a mean concentration of 6.3 µg/kg. The highest mean AFB1 was recorded in maize from Egypt; as high as 440 µg/kg.

Nine out of eleven countries conducting studies on AFB1 had contaminations being high to very high. Sudan and Tunisia were the only studied countries with a very low levels of contamination. Maize and peanut tend to be heavily contaminated. Animal feeds also tend to have high levels of contamination as shown by studies in Ethiopia, Kenya, and Nigeria. With



regard to AFM1, only four studies reported concentrations in milk. One study on milk samples in South Africa showed concentrations above 0.5 µg/kg (the maximum limit set by CODEX). Mean concentrations reported from other countries, i.e. Morocco, Ethiopia and Kenya were below 0.5 µg/kg. Notable is that for

Egypt and Kenya, the included studies focused largely on processed / retail / marketed products. The part of the production chain (e.g. at the farm or in retail) studied is more evenly distributed among studies conducted in Nigeria.

Disease burden

Havelaar et al. (2015) was the only study that estimated disease burden expressed as DALYs. For all global sub-regions used by WHO for the global assessment of disease burden, the median rates for aflatoxin related DALY varied between 0.04 to 28 DALY per 100,000 population. Almost all countries report the burden of aflatoxin as premature mortality (YLL), and that the burden of aflatoxin lays in the group older than 5 years of age. Aflatoxin was considered an important hazard with a high disease burden in the sub-region AFR-D, which mostly encompasses West Africa. In that area, the median rates of aflatoxin related DALY per 100,000 population were 28 (7-78), while for East Africa (AFR-E), this was 3 (1-8).

Four included studies focused on disease burden expressed as the risk of adverse health effects resulting from exposure to aflatoxins via food. All of these studies described a partial risk assessment on aflatoxins in food in the respective regions. They all concluded that the risk of aflatoxin warrants policy interventions.

Economic impact

Only a few relevant peer reviewed studies that estimate the economic impact of aflatoxins in Africa were found. Data needed is not readily available, and collecting the data necessary for gauging the economic impact is costly and not straightforward. This complexity of economic analyses may add to the explanation of the gap in the literature.

The trade-related impact of aflatoxin contamination is mainly evaluated from the standpoint of how stringent aflatoxin regulation (mainly EU legal limits) affects products imported from developing countries, including Africa. One finding showed that even when

adopting the limits advised by CODEX (that are more lenient than EU standards), 83% of African exporters were still non-compliant. Thus, even a less strict legal limit might not cause a better impact for groundnut trade from Africa to the EU.

Considering the firm-level impact for the peanut marketing chain, the purchase price, selling price, and storage cost were considered as the most important factors contributing to business revenue. Thus, an economic incentive was deemed very important for the chain actors to adopt measures to reduce aflatoxin level in the peanut products. The willingness to pay for the products produced with AflaSafe® (a biocontrol strategy to mitigate aflatoxin contamination) was equal or larger than the original price of the product. Lack of awareness and usage experience were considered as the main reasons why farmers did not want to pay. Two studies investigated the awareness of consumers to aflatoxin contamination and estimated the willingness to pay for aflatoxin-free products in Kenyan market. Both studies showed that consumers were interested in aflatoxin-free certified products, specifically milk (average WTP of 9.7 KSh/ litre) and maize (clean-untasted maize for 31 KSh/2 kg). Based on an assessment of end market, regulation, and awareness levels; aflatoxin-related health problems contributed the largest impact of aflatoxin contamination.

Mitigation measures

For mitigation of mycotoxin contamination, a wide range of options at the various stages of food production, consumption and the general population are available. Measures specifically applied to the African situation in the included studies were divided into the following categories, according to the chain-step in which the intervention was tested: plant breeding, agricultural practices, post-harvest storage, processing, and reducing availability of aflatoxin from food and feed by the use of binders.

Various studies indicated that selection of maize and other crop varieties for resistance to fungal infection, by using 'kernel infection rate' as a

selective criterion, has started to take off in Africa. In addition, several studies indicated the enhanced effectiveness against mould infection and mycotoxin formation of a combination of fertilizer regime with the planting of resistant varieties. At the farm stage before harvest, studied effective measures described for Africa in literature include the use of non-aflatoxigenic fungal strains, also including strains that have been locally sourced, which will compete with the ones forming aflatoxin and therefore resulting in an infected crop with relatively low levels of Aflatoxin. Findings also suggested a correlation between a reduced aflatoxin contamination of maize and various agronomic practices, such as time of planting seeds, non-mechanical weed removal, and use of insecticides.

Post-harvest measures that were successfully applied to reduce aflatoxin contamination of maize, sorghum and peanut include drying of the harvested product above ground or on particular surfaces, or sorting out of visibly contaminated kernels or other products, and ventilated storage. In addition, storage of cereals and groundnuts in certain types of plastic bags (PICS, polypropylene) has been shown to help reduce post-harvest aflatoxin formation. A wide variety of processing techniques, depending on the product in question, can be applied to effectively mitigate aflatoxin formation, as shown in several of the included studies. Several studies also indicated that combinations of processing techniques can further reduce mycotoxin contamination, such as cooking or fermentation combined with chemical treatment (ammonisation, oxidation). Examples of techniques, of which effectiveness was demonstrated in multiple studies, include roasting and decortication of groundnuts/peanuts, and various forms of microbial fermentation, such as of various local, maize gruel/porridge or yoghurt fermented with lactic acid bacteria. The experimental use of binders, particularly clay, has shown to help in reducing availability of aflatoxins from food and feed. Use in food appears to reduce the level of aflatoxin biomarkers, but potential side-effects are unknown. Most studies on the effects of binders in feed focused on aqua-feed for cultured fish. Interventions substantially

reduced aflatoxin contamination as compared to the positive control fed AFB1-tainted diets. In addition, fast detection methods such as immunochemical tests (e.g. dipstick) and thin-layer chromatography may be used in local settings for screening for potentially contaminated samples, prior to the technically more demanding confirmatory laboratory analyses if needed.

6. Discussion

Scale and geographical spread of aflatoxin contamination in food, feed, and associated commodities/key value chains

The included studies reported most commonly on the commodities maize and peanuts, and animal feed – which are generally the products most commonly associated with aflatoxigenic mould contamination in Africa. All studies indicated mean AFB1 in maize > 5 µg/kg which is over the EU legal limit for AFB1. The results imply that reduction of overall aflatoxin levels in food and feed in Africa is still a major challenge. The included studies give insight in the geographic areas and foods that were studied, but extrapolation or generalization of specific results to other areas is difficult.

A large number of the included studies was assessed to be relevant for the question on scale and geographical spread of aflatoxin contamination in Africa, but a much smaller number of studies gave quantitative results (36). Included studies were frequently for Nigeria, followed by Egypt, and Kenya. Although the included studies do give insight in the studied areas and foods; there is a lack of prevalence studies in certain countries.

Scale of aflatoxin disease burden

Populations in Africa can be exposed to high concentrations of aflatoxin via food, causing acute aflatoxicoses, even to this day. For various reasons it is likely that this problem might be larger than described since diseases in

the developing world may often go unreported, thus the described cases in the included studies on acute toxicity may represent only a portion of the problem. Incidents in Kenya and Tanzania with human fatalities in 2004 and 2016 were analysed by specialised investigation teams and lessons learned were published. This approach should be encouraged and will contribute significantly to early warning systems, and prevent fatalities.

Diseases related to chronic aflatoxin exposure may result from more causes and/or diseases can be enhanced when people are chronically exposed to aflatoxins, which complicates the estimation of the disease burden. This systematic review did reveal relatively many studies on biomarkers for aflatoxins. Although biomarkers may give a good indication of current and recent exposure to aflatoxins, they do not relate to the source or exposure earlier in life. Biomarker studies may be useful to study the impact of mitigation strategies, however.

Economic effects of aflatoxins

In general, little evidence was found in this systematic literature review on the economic effects of aflatoxin contamination and a conclusive result on the trade-related impacts of aflatoxins regulations for African exporters could not be determined. In general, the limited number of studies estimating economic impacts of aflatoxins contamination points out a gap in literature. The bottom line in this literature gap is the lack of available data for the estimations, particularly for health-related impacts.

At the country level, most economic impacts studies were conducted in Kenya. According to the results of multiple studies in this review, economic incentives are needed to reduce aflatoxin contamination and, subsequently, aflatoxin exposure to humans. Two studies in Kenya showed that awareness level of consumers and occurrence of aflatoxicosis in their region increased their willingness to pay for aflatoxin-free products. At the same time, awareness on reducing aflatoxins should also be built in producers' side to stimulate them implementing mitigation measures. Moreover,

the additional costs of reducing aflatoxins should be equally distributed along the chain rather to put the burden on one side, for example, producers or consumers only.

Mitigation measures

Considering mitigation strategies, the systematic review further highlights the multitude of methods and stages from farm to fork, at which the contamination, exposure and adverse effects can be prevented, mitigated or reversed. Proof of cost-effectiveness, or even only the costs of the practices, appear to be lacking. Many included studies were on the use of 'biocontrol' agents, particularly the AflaSafe® product currently being applied to maize cultivation – but it has certain drawbacks, such as the need for yearly application. Other promising developments aiming at mitigation of aflatoxin contamination at various stages of the supply chain were identified. Dietary diversity to mitigate mycotoxin exposure should be encouraged.

7. Conclusion, knowledge gaps and recommendations

In this study, evidence from systematic literature review shows that different research areas have been covered by the four subtopics of contamination, economics, disease burden, and mitigation; illustrating the diversity of aspects of aflatoxin contamination of human food and animal feed. Given the results of this study, it is apparent that aflatoxins are a multi-faceted problem with a large contribution to a variety of negative health effects with high impact on society. This report underpins the need for effective management of the aflatoxin situation in Africa, in line with numerous previous reports [e.g. (Okoth, 2016; Udomkun et al., 2017; Wild et al., 2016)]. A number of mitigation measures have been developed, both on the production side to reduce contamination, and on the consumer side to reduce or mitigate the effects of exposure. It is clear however that aflatoxin levels in food and feed are too high,

and the priority should therefore be to reduce these levels substantially.

Some general inferences can be drawn across the four subtopics. Much of the data for aflatoxins in Africa reported in the included studies in the last 10 years, were executed in studies in three countries, namely Egypt, Kenya, and Nigeria. With regard to the disease burden caused by aflatoxins; this cannot be easily estimated. A holistic approach focusing on a combination of co-occurring mycotoxins and other contaminants, rather than an isolated strategy, is required to increase the total quality of life. Many of the retrieved studies focusing on economic impacts focused on exportability of produce to the European Union in the light of the legal limits set there, or more generally on Codex Alimentarius limits. Given that much of the trade is intra-African, and also other markets besides the EU are being catered to, such as Asia and the Americas, it would be useful to have a more global broader view on the trade impacts.

For mitigation measures, the success may be measurable both in the short and long-term, given that, for example, the health impacts can be acute (aflatoxicosis) as well as chronic (e.g. liver cancer). The contribution to the latter may be difficult to establish, although it is conceivable that any measure reducing the exposure to aflatoxins will ultimately result in a decrease in disease burden. There is a broad range of mitigation measures that are possible, and have been tested. However, a limited number of these measures is practically feasible for small farmers and downstream chain actors up to rural households. These measures include, for example, using resistant plant varieties, bio-control agents, hand-sorting, and fermentation of food products. Moreover, only few publications have comprehensively considered the cost-effectiveness of measures, which makes it difficult to compare them. We therefore recommend research on the cost-effectiveness of intervention measures so that available resources can be directed as efficiently as possible.

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