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The aflatoxin situation in Africa: Systematic literature review

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Abstract

Contamination of African staple foods is a major issue for human and animal health, nutrition, and trade. This review aimed to collect and synthesize the available evidence on geographical spread, scale of contamination, disease burden, economic impact, and mitigation measures for aflatoxins in Africa by way of a systematic literature review. This knowledge can enhance management strategies for the major challenges to combat aflatoxins. The search was conducted by applying a predefined search strategy, using bibliographic databases and websites, covering the period 2010 to 2018. Results showed that maize, peanuts, and animal feeds were the most studied commodities. For maize, all studies indicated mean AFB_1 to exceed the European Union legal limit. From studies on contamination levels and biomarkers, it is clear that overall exposure is high, leading to a substantial increase in long-term disease burden. In addition, concentrations in food occasionally can reach very high levels, causing acute aflatoxicoses. The trade-related impact of aflatoxin contamination was mainly evaluated from the standpoint of aflatoxin regulation affecting products imported from Africa. There was a limited number of studies on health-related economic impacts, pointing out a gap in peer-reviewed literature. A number of mitigation measures have been developed, but proof of cost-effectiveness or even costs alone of the practices is often lacking. We recommend more emphasis to be put in peer-reviewed studies on evidence-based cost-effective mitigation strategies for aflatoxins, on the scale and spread of the problem and its impacts on public health and economics for use in evidence-based policies.

KEYWORDS
economic effects, health effects, mitigation, mycotoxin, scale

1 | INTRODUCTION

In Africa, aflatoxins pose major risks to human and animal health, nutrition, as well as intraregional and international trade. Aflatoxins are some of the most common toxic fungal metabolites, collectively known as mycotoxins, produced by certain strains of the fungus *Aspergillus* (Klich, 2007). After infection and growth of *Aspergillus* spp. in crops in the field or on produce during storage, the fungus can produce aflatoxins. Commodities mostly affected by aflatoxins worldwide are peanuts, tree nuts, dried fruits, and maize (Pitt, Taniwaki, & Cole, 2013). Widespread contamination of these African staple foods is a major issue in affected countries.

Aflatoxins are rated as Group-1 carcinogens by IARC, meaning that there is sufficient evidence of carcinogenicity in humans (IARC Working Group, 2012). Because aflatoxin is a genotoxic carcinogen, there is no safe level of exposure, and levels should, therefore, be as low as reasonably achievable ("ALARA"). Children in many African countries are exposed to aflatoxins from the very early stages of life (Akbari et al., 2017; Wild, Kensler, & Groopman, 2016). Long-term exposure to subacute 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 (Probst, Njapau, & Cotty, 2007; Udomkun et al., 2017; Yard et al., 2013). HCC may take up to two decades to develop (Afum et al., 2016) and, therefore, a causal relation with aflatoxin exposure via food is not always recognized. Furthermore, HCC can be the result of multiple causes and other factors. For example, simultaneously being exposed to hepatitis B and aflatoxins may shorten the period for HCC to develop (Kensler, Roebuck, Wogan, & Groopman, 2011; Palliyaguru & Wu, 2013; Wogan, Kensler, & Groopman, 2012). A study from the Africa Liver Cancer Consortium shows that HCC tends to develop at a younger age in Africa than in other regions of the world (Yang et al., 2017).

Recently, several reviews on aspects related to aflatoxins in Africa were published (Darwish, Ikenaka, Nakayama, & Ishizuka, 2014; Flores-Flores, Lizarraga, López de Cerain, & González-Peñas, 2015; Gibb et al., 2015; Shephard, Kimanya, Kpodo, Gnonlonfin, & Gelderblom, 2013; Udomkun et al., 2017; Wild et al., 2016). Most of these reviews focus only on one aspect of the subject, such as geography, toxicity, or social/economic impact. Udomkun and coauthors have presented a study combining a number of these aspects of interest: contamination in specific crops; food security, society and economic impacts; awareness and knowledge; legislation and regulation; and measurement. However, for mycotoxins, this information was only presented for the sub-Saharan regions (Udomkun et al., 2017).

Sourcing high-quality raw materials and producing high-quality products are challenges in some African regions due to aflatoxin contamination. This may hamper agribusiness development, job creation, and economic growth (Adenle, Manning, & Azadi, 2017). Although the mentioned adverse impacts of aflatoxin to the African situation seem clear, as underpinned by studies published in the gray (not peer-reviewed) literature; quantitative evidence as well as evidence published in peer-reviewed literature appears to be lacking (Okoth, 2016). Insights on the geographical spread, scale of contamination, disease burden, economic impact, and mitigation measures for aflatoxins in Africa is a pressing issue to enhance management strategies for the major challenges to combat aflatoxin contamination. This review aimed to collect and synthesize the available evidence on these four topics related to the aflatoxin situation in Africa.

2 | MATERIALS AND METHODS

A systematic literature review was performed following 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). The EPPI guideline refers to Gough, Oliver, and Thomas (2017), which provided flexibility to combine different disiciplines other than natural or medical science. This made the EPPI guideline and software tool well suited for our systemic review. The essential processes of conducting systematic reviews, and their respective outcomes, consist of five phases: (1) defining research questions for the systematic review; (2) searching databases for literature; (3) screening of papers; (4) classification (key wording) based on full-text; and (5) data synthesis of studies for the specific theme being investigated (Petersen, Feldt, Mujtaba, & Mattsson, 2008). The web-based software tool for systematic reviews designed by the EPPI (EPPI Reviewer v4) was used.

2.1 | Research questions

The following research questions were defined to guide the systematic literature review:

1. What is the scale and geographical spread of aflatoxin contamination in food, feed, and associated commodities in African countries?
2. What is the scale of aflatoxin disease burden for the African population?
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 and their value chains in African countries?

2.2 | Conducting searches of studies

The literature search was conducted by applying predefined search strategy, using bibliographic databases and websites. For each research question, a search strategy was developed for identifying relevant studies. Search terms originated from personal knowledge, searches on websites, screening key (review) papers, and screening the results of preliminary searches in bibliographic databases. The search queries are presented in Tables S1 to S11. Bibliographic scientific databases (i.e., CAB Abstracts, Scopus, PubMed, AGRIS, and EconLit) were searched for potentially relevant publications, covering the period 2010 to 2018 and written in the English language.

To verify whether the use of the search queries indeed enabled retrieval of relevant references, the outcomes of preliminary searches with these queries were checked against "benchmark publications." These were scientific journal articles that had been predefined as being relevant for the respective research question, based on expertise of the authors. The benchmark publications are listed in Table S12. If retrieval was incomplete, that is, not all benchmark studies resulted from the database searches, then the search queries were further modified so as to achieve 100% coverage.

Collection of relevant references from the selected sources was done by the use of Endnote reference citation management software. Due to a general lack of studies identified on the topic of economic effects through the systematic searches for peer-reviewed literature, additional literature on economic effects was identified via "snowballing." This refers to using the references of relevant studies with the aim to identifying further studies.

2.3 | Screening

The screening of papers was done by applying predefined exclusion/inclusion criteria to the papers that were found via the searches. First, these publications' titles, keywords, and abstracts were screened for relevance; followed by screening of the full text of the article. Inclusion and exclusion criteria were applied in the screening, in order to ensure that relevant studies were identified for further synthesis. General exclusion criteria consisted of the following:

- Topic: Studies that do not consider aflatoxins specifically (e.g., focusing on general health effects of aflatoxins rather than on the disease burden in Africa, as well as studies that focused on mitigation measures outside of Africa, studies focusing on development of analytical methods, and studies on the population biology of fungi producing aflatoxins);
- Date: Publications concerning data predating 2010;
- Geography: Data either do not specifically pertain to or are otherwise irrelevant for the aflatoxin situation in Africa (as a continent, region, country, or locality);
- Language: studies that were not written in English.

2.4 | Classification and data synthesis

The studies retained after the previous screening step were classified using keywords that signified their relevance to each of the four research questions. Data from these studies were subsequently synthesized by "coding" the specific subjects and information covered by each publication. For the coding, a "questionnaire" was applied to the relevant studies. In this way, questions about the relevant information were systematically answered by using the research findings of the studies. The questionnaire included topics such as: type of publication (article in a scientific journal, book chapter, etc.) and technical details, such as the type of aflatoxin being described in the study. Using the key wording and coding, a high-level understanding of the nature and contribution of the research was achieved. For the coding, we used the tool designed by the Evidence for Policy and Practice Information and Co-ordinating Centre (EPPI, University of London), referred to hereafter as "EPPI tool." More specifically, the "questionnaire" was programmed in the EPPI tool and subsequently used for data synthesis by the reviewers.

For every study, general coding consisted of assigning the type of publication, the geographical area, and the aflatoxins studied. Subsequently, for each research question, several additional questions were considered. For the research question on the scale and geographical spread of aflatoxin contamination, specific additional questions concerned the part of the production chain considered, type of product sampled and analyzed, questions on methods used for analysis (if applicable), and nature of results (qualitative/quantitative). For the topic of disease burden, additional questions considered the populations studied, route of aflatoxin exposure, how exposure was estimated, disease symptoms investigated, which outcomes were used (e.g., epidemiological, clinical, etc.), and parameters provided (incidence, DALY, etc.). More specific questions were asked on studies related to biomarkers, pertaining to the type of biomarker considered, method used for analysis, and nature (qualitative/quantitative) of results. For the topic of economic impact, additional questions considered the type of economic impact studied (trade-related, firm-level, or health effect), and the method used to estimate the economic impact. Finally, for the topic of mitigation measures, additional questions considered the economic operators' characteristics, production stage, type of mitigation measure (cultural, biological, chemical, etc.), and types of outcomes described.

3 | RESULTS

Using the final search strategy, 6,374 references were retrieved in total; of which 2,308 references were included for the next steps; after eliminating studies published before 2010 or in a language other than English. After deduplication (−1.116); screening on title and abstract (−534); and finally screening on full-text (−204); a total of 330 studies were found to be relevant for synthesis. Full texts for 23 publications could not be retrieved. Of the remaining 307 papers, 88 papers dealt with multiple research questions. Most included studies (275) were on the topic of contamination of food or feed, followed by studies on mitigation methods (60), on disease burden (49), and finally the economic impact (11). The aflatoxin metabolite most frequently reported was AFB_1, which was reported in 179 publications (58%), followed by AFB_2 (36%), AFG_1 (34%), and AFG_2 (32%). Around 30% of the publications focused on aflatoxin in general, while around 19% studied AFM_1, and two publications (2%) investigated AFM_2 and AFP_1. Multiple publications reported more than one type of aflatoxin in their studies. The included publications are presented and discussed in the following sections.

3.1 | Geographic spread and scale of aflatoxin contamination

3.1.1 | Geographical spread of available information on aflatoxin contamination

Of the 275 retrieved papers focusing on aflatoxin contamination levels, the most studied country was Nigeria (56 studies), followed by Egypt (41), and Kenya (33). Around half of the included studies (145) were on a variety of other African countries, including Tanzania (26), Ghana (12), and South Africa (15). Multiple papers also reported results of studies that focused on aflatoxin contamination in more than one country. For Egypt and Kenya, the focus of included studies was largely on processed/retail/marketed products. The part of the production chain that is covered in the relevant papers is more evenly distributed among studies conducted in Nigeria.

3.1.2 | Scale of aflatoxin contamination

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, followed by food and feed ready for consumption at households or farms where animals are kept (56). Food or feed during transportation were least studied (8). The most commonly investigated commodities in the included papers were maize and peanuts, and animal feeds.

Table S13 shows the contamination levels as presented in the included papers, specifically for AFB_1. In general, in various products analyzed in the various countries, AFB_1 contamination was relatively high, with the highest mean AFB_1 concentration recorded in maize from Egypt; 440 μg/kg (El-Shanshoury, El-Sabbagh, Emara, & Saba, 2014). The highest concentration found in an individual sample was 6,738 μg/kg; this sample was from Nigeria in 2012 (Adetunji et al., 2014). Only few studies indicated relatively low mean AFB_1 concentration (< 1 μg/kg): sugarcane juice from Egypt (Abdallah, Krska, & Sulyok et al., 2016), maize from Gert Sibande District Municipality (GDSM, Mpumalanga Province), South Africa (Mngqawa et al., 2016), wheat from Egypt (El-Shanshoury et al., 2014), fufu (maize dish) from Cameroon (Abia et al., 2017), iru from Nigeria (Adedeji et al., 2017), maize and sesame from Senegal (Savannah Guinea zone-Kolda and Sedhiou); and sesame from Sudan Savannah zone Kaffrine and Nioro (Diedhiou, Bandyopadhyay, Atehnkeng, & Ojiambo, 2011) and sesame from Sudan (Idris, Mariod, Elnour, & Mohamed, 2010) and Nigeria (Ezekiel et al., 2012). Concentrations in samples of animal feed taken from manufacturers ranged between <1 and 4,682 μg/kg (Senerwa et al., 2016).

In 27 of the included papers, AFB_1 was quantified in various products, with maize as the most frequently studied product in nine publications. All studies indicated a mean AFB_1 level in maize of > 5 μg/kg, which is the legal limit for AFB_1 in maize prior to being sorted, according to EU legislation (Regulation (EC) No 1881/2006), except for one study by Mngqawa et al. (2016) in South Africa and one by Diedhiou et al. (2011) in Senegal. In both studies, AFB_1 levels were found to be below 1 μg/kg. Not all studies reported the prevalence of positive samples, but the highest reported prevalence was 67.1% (total samples 70) in Nigeria (Adetunji et al., 2014). The lowest prevalence rate was 0% in South Africa; specifically, samples from GDSM, Mpumalanga Province in the sampling time year 2011 (Mngqawa et al., 2016).

The included studies that investigated peanuts all reported AFB_1 concentrations in peanuts to be relatively high (> 15 μg/kg set by Codex Alimentarius [hereinafter: "CODEX"]), with only samples from Algeria having a lower mean concentration of 6.3 μg/kg (Magembe, Mwatawala, & Mamiro, 2016a; Magembe, Mwatawala,

& Mamiro, 2016b; Magembe, Mwatawala, Mamiro, & Chingonikaya, 2016c; Oyedele et al., 2017; Riba, Matmoura, Mokrane, Mathieu, & Sabaou, 2013). Mean AFB_1 concentrations in African dishes, such as ogiri, kuru-kuru, and dagwa, were found to be > 5 μg/kg, while AFB_1 concentrations in peanut cake ranged from 13 to 2,824 μg/kg. Kuru-kuru and dagwa are both groundnut-based snacks, ogiri is a flavoring made from fermented sesame seeds. Only fufu (a maize-based dough) and iru (fermented and processed locust beans) contained low AFB_1 concentrations of 0.9 and < 0.3 μg/kg, respectively (Abia et al., 2017; Abia et al., 2013; Adedeji et al., 2017; Ezekiel, Sulyok, Warth, & Krska, 2013; Nishimwe, Wanjuki, Karangwa, Darnell, & Harvey, 2017).

AFM_1 was estimated in seven studies covering milk, maize, and animal feeds. The highest mean concentration in milk was found in samples from the rural area of South Africa, being 2.38 μg/kg, while the maximum concentration was detected in Kenya, which was as high as 6.99 μg/kg, which is 140 times higher than the maximum level set by CODEX for AFM_1 in milk of 0.5 μg/kg (Mwanza, Abdel-Hadi, Ali, & Egbuta, 2015; Senerwa et al., 2016).

Infants and young children are exposed to aflatoxins via the complementary foods. In a study of aflatoxin contamination in Kenyan complementary foods, Obade, Andang'o, Obonyo, and Lusweti (2015) showed that infants and young children in the country might be at risk for aflatoxin exposure. All foods, except cassava, that are used as complementary food, were contaminated with aflatoxins (Obade et al., 2015). The researchers found AFB_1 levels between 0 and 34.5 μg/kg in foods, and AFM_1 levels from 0.012 to 0.127 μg/kg in processed milk and from 0.0002 to 0.013 μg/kg in raw milk (Obade et al., 2015).

3.2 | Disease burden

Aflatoxin exposure in young children is correlated to impaired growth leading to stunting in children (Wild et al., 2016). Studies from Dewey and Adu-Afarwuah (2008) and Bhutta et al. (2013) illustrate that successful feeding interventions in populations showed average rates of a 20% to 40% reduction in stunting in children in the best-performing countries (Bhutta et al., 2013; Dewey & Adu-Afarwuah, 2008), meaning other factors, besides exposure to aflatoxins, also play a role in stunting. The IARC working group on mycotoxin control in low- and middle-income countries concluded that aflatoxin might be one of several significant factors contributing to stunting (Wild et al., 2016). No additional evidence for a causal relationship between stunting and exposure to AFB_1 was identified among the included studies.

3.2.1 | Disease burden expressed as disability-adjusted life years

Disability adjusted life years (DALY) expresses the healthy life years lost as a result from the exposure to a certain hazard. The measure DALY combines the number of years of life lost (YLL) due to premature death with the number of years lived with disability due to the disease caused by the hazard (Havelaar et al., 2015). We retrieved one study discussing disease burden expressed as DALYs in relation to aflatoxins in Africa, performed by Havelaar et al. (2015). This study was based on data obtained in 2010. Median rates of aflatoxin-related DALY per 100,000 population were calculated for the global subregions used by WHO for the assessment of global disease burden that include the countries on the African continent. Aflatoxin was ranked as the fourth cause of nondiarrheal foodborne deaths, based on the number of DALY estimated (leading causes were: Salmonella Typhi, *Taenia solium*, and hepatitis A virus). Aflatoxins were ranked as by far the most important hazard in the group of the chemical hazards under investigation, followed by cassava cyanide and dioxins. Almost all countries reported the burden of aflatoxins as premature mortality (YLL), mainly in the population group older than 5 years of age. The median rates for aflatoxin-related DALY ranged from 0.04 to 28 DALY per 100,000 population for all global subregions. Aflatoxin was considered an important hazard in the African countries in the WHO Eastern Mediterranean subregion (EMR-D), of which six countries are situated in Africa (Egypt, Sudan, South Sudan, Djibouti, Somalia, and Morocco). Nevertheless, the authors indicated that incidence data on effects of aflatoxin are difficult to obtain and they extrapolated from neighbouring countries for the estimations (Havelaar et al., 2015).

3.2.2 | Disease burden expressed as the risk on adverse health effects resulting from exposure to aflatoxins

Ediage, Hell, and de Saeger (2014) estimated aflatoxin intake of the population in Cameroun at a concentration of 0.15 ng/kg body weight per day; which is the mean of the provisional range 0.11 to 0.19 ng/kg bw per day estimated in 1995, for African and Asian populations possible predisposed to HBV infection. This, what they call a "Tolerable Daily Intake" (TDI), was defined as a cancer risk level of 10^{-5}, which was considered to pose a negligible risk to health. It should be noted that TDI as a measure does not apply to carcinogens. They concluded that exposure of the Cameroun population to aflatoxin from maize, peanut, and cassava could exceed the "TDI" by 10^4- to 10^5-fold (Ediage et al., 2014).

There is evidence that maternal exposure to high AFB_1 concentrations via food during pregnancy leads to lower birth weight, although causality has not been established yet (Partanen et al., 2010; Andrews-Trevino et al., 2019; Smith et al., 2017).

Adetunji, Atanda, and Ezekiel (2017) based their risk assessment for Nigeria on the benchmark dose level (BMDL) of 170 ng/kg bw per day as established by the European Food Safety Authority in 2007 (EFSA, 2007). The margins of exposure (MOEs) for aflatoxins for the Nigerian population were below two in all four agro-ecological zones for infants, children, and adults when using the probably daily intake (PDI) approach for assessing the exposure. Since infants and young children were the categories at high risk, mitigation strategies would be to encourage breast-feeding in the first 6 months of life, and to diversify by using complementary foods less prone to mycotoxin contamination (Adetunji et al., 2017). An MOE well below 10,000 was calculated, also based a risk assessment on the BMDL10 of 170 ng/kg bw per day, for infants <6 months of age in Northern Tanzania consuming maize flour (N = 98) (Magoha et al., 2016 citing Kimanya et al., 2014). Azaiez, Font, Manes, and Fernandez-Franzon (2015) used the PDI as calculated by EFSA (EFSA, 2007) for aflatoxins from date consumption to get insight in the contribution of contaminated dates to the exposure of Tunisian people to aflatoxins. They compared their estimated PDI of 0.29 ng/kg bw per day for aflatoxin in dates in Tunisia with the PDI of 0.69 to 1.934 ng aflatoxins/kg bw per day from all food for the European Union (EU) population. It was emphasized that their study was limited to PDI of dates only and did not include other food sources of aflatoxin; also comparing PDIs is not generally accepted as a proper exposure assessment study for the risk assessment (Azaiez et al., 2015).

A study among 249 infants 6 to 12 months of age in three agro-ecological zones in Tanzania revealed that the estimated intake of aflatoxin via food resulted in an estimated average MOE of 1.3. This really low MOE makes aflatoxin a priority for risk management and mitigation studies must be explored. This also implies that the remaining part of the population is also very likely at risk which highlights the need for urgent action (Kamala et al., 2017).

3.2.3 | Disease burden: biomarkers of exposure

AFM_1 was detected in 100% of the breast milk samples in Kenya and the PDI was estimated in the range of 1.13 to 66.79 ng/kg bw per day for the infants (Wambui, Karuri, Ojiambo, & Njage, 2017). In Egypt, AFM_1 was detected in 65% of the breast milk samples above 0.05 μg/L of 150 mothers of infants fed exclusively on breast milk. Blood of both mothers and children in the positive group contained significantly more liver enzymes alanine aminotransferase and aspartate aminotransferase than blood of both mothers and infants in the negative group. Elevated liver enzymes may indicate liver damage and be a trigger for future development of HCC biomarkers of effect (Tomerak, Shaban, Khalafallah, & El Shazly, 2011).

Ayelign et al. (2017) studied aflatoxins in urine of 200 children age 1 to 4 in Ethiopia in 2016. Aflatoxins B_2 (4.5%), G_1 (2.5%), G_2 (3%), and M_1 (7%) were detected in 17% of the urines. AFB_1 was not detected in any of the samples (Ayelign et al., 2017). Aflatoxins were more often detected and at a higher concentration in blood and urine from children in Nigeria suffering from protein energy malnutrition as compared to healthy children (Onyemelukwe et al., 2012). A study in Egypt showed a correlation between increased aflatoxin M_1 levels in blood and high hepatitis C virus titer in patients with chronic liver disease (El-Shahat, Swelim, Mohamed, & Abdel-Wahhab, 2012). Asiki et al. (2014) found that in Uganda in 2011, all of the studied 100 adults and 92 of the 96 children under 3 years of age had detectable levels of AF-albumin adduct in their blood. Among the children were five babies who were exclusively breast-fed (Asiki et al., 2014). In Kenya, AF-albumin adducts, insulin-like growth factor 1 (IGF1), and IGFBP3 were analyzed in blood of 99 schoolchildren. Children with the highest AF-albumin adducts had reduced length as compared to children with lower AF-albumin adduct concentration in their blood. In addition, AF-albumin adducts were inversely related to IGF1 and IGFBP3. It was calculated that IGF1 levels explained about 16% of the impact of aflatoxin exposure on child height ($P = 0.052$). The authors concluded that aflatoxin-induced changes in IGF protein levels could contribute to growth impairment when aflatoxin exposure is high (Castelino et al., 2015).

According to Afum et al. (2016), it may take up to two decades to develop HCC; it is, therefore, difficult to relate HCC to current exposure to aflatoxins as almost all volunteers had positive aflatoxin M_1 concentrations. They raise the fact that females are partly protected from developing HCC because of the suppression of interleukin 6 (IL-6) production by oestrogen. IL-6 promotes inflammation in response to liver injury, such as hepatitis B virus (Afum et al., 2016).

Table S14 gives an overview of 23 peer-reviewed included studies on biomarkers in African populations. Surveys were used in which AF-albumin adduct in serum was measured and/or aflatoxin M_1 in the urine. In general, AF-albumin adduct or aflatoxin M_1 was detected in almost all individuals in each group under investigation, meaning all the persons were exposed to aflatoxins at the time of the survey. The biomarkers are present in a large range of concentrations. Extremely high concentrations (up to 3,583.3 pg/mg for 21-day-old children) of aflatoxin M_1 in urine were detected for a group of children in the Ejura area in Ghana, and 100% of samples were tested positive in one other area (Hiawoawu); both for children aged 0 and 21 days (Kumi, Dotse, Asare, & Ankrah, 2015). It must be taken into consideration that some groups represent persons with a specific condition, which may influence the rate of transfer of mycotoxins from food to urine. It is uncertain if the elevated levels are a result of higher exposure or impaired excretion (Onyemelukwe et al., 2012).

3.3 | Economic impact

The economic impact of aflatoxin for Africa can be considered threefold: (1) trade-related impact that determines if a product can be sold internationally, for example, exports of African products to trade partner countries, measured in terms of trade loss, and (2) firm-level impact in terms of costs of production to avoid aflatoxin contamination by prevention, control, or mitigation measures, so as to comply with high standards; and (3) health impact leading to economic costs (cost of illness). Different types of economic impact of issues are measured in different ways and therefore cannot be directly compared. The economic impact is usually expressed in monetary terms (e.g., USD) as the value of products lost due to aflatoxin contamination.

3.3.1 | Trade-related economic impact

Edelman and Aberman (2015) estimated the limiting factors of groundnut exports to countries with legal limits of aflatoxins, such as the EU and South Africa, by means of qualitative methods (semistructured interviews and forum group discussions) and trade data for the years 2004 to 2014. However, they did not quantify the loss in monetary value. Their findings showed that Malawi was becoming more dependent on trade with countries enforcing less strict or no aflatoxin legal limits. Export to countries with more strict aflatoxin legal limits, such as the EU and South Africa, accounted for only 4% in 2014. However, Malawi's trading partners in Africa were working toward stricter common legal limits for aflatoxin. Thus, without promoting low-aflatoxin exports, there could at least be two consequences: a decrease of exports leading to a fall in the domestic price and an increase of informal exports leading to a loss of tax revenue and foreign exchange. Exporters are considered as the key actors in the chain of the Malawi groundnut sector, thus increasing price incentives for them to export low-aflatoxin groundnuts could generate incentives to other upstream actors, including the farmers.

Senerwa et al. (2016) discussed direct market loss due to aflatoxin contamination in the Kenyan dairy chain, in feed (feed manufacturers and dairy farmers) and milk (dairy farmers). This study lacks an elaboration on method and results, but indeed mentioned the estimated loss. By estimating the proportion of samples exceeding aflatoxin legal limits, the losses were estimated as a function of annual production. The estimated losses were USD 22.2, USD 37.4, and USD 113.2 million for feed manufacturers, feed used by dairy farmers, and milk produced by dairy farmers (Senerwa et al., 2016).

3.3.2 | Firm-level economic impact

Six studies evaluating firm-level economic impact (producer side) were identified as being relevant, five of which assessed the impact on the costs of managing aflatoxins (compliance cost) and one study assessed the productivity loss due to aflatoxin contamination. None of the five studies estimated the same or comparable effect and/or considered the same or similar products using the same analytical method, and thus no comparison of the studies under review could be performed.

Moser and Hoffmann (2015) and Hoffmann and Moser (2017) showed that products with a higher price tend to be less contaminated than products sold for a lower price. Thus, when managing aflatoxin levels in foods and building its brand reputation as a safe food producer, a firm can apparently charge a higher price than other firms without this value. Note that the costs of compliance to aflatoxin regulation were not estimated in these studies.

Ayedun et al. (2017) estimated the Nigerian farmers' willingness to pay (WTP) for AflaSafe® goods, as a biocontrol strategy to mitigate aflatoxin contamination in maize and groundnuts. The WTP estimates for AflaSafe® are found to be equal or larger than USD 10 (which is the price of the AflaSafe® product). The lack of awareness and the farmer's experience were considered as the main reasons why farmers did not want to pay for AflaSafe® (Ayedun et al., 2017).

N'Dede, Jolly, Vodoube, and Jolly (2012) investigated the financial risk associated with several steps contributing to aflatoxin reduction along the peanut marketing chain in Benin, such as sorting and storing. 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 levels in the peanut products (N'Dede et al., 2012).

Ayyat, Abd Rahman, El-Marakby, El-Hakem, and Hessan (2014) examined the effect of several treatments to alleviate the effects of aflatoxin contamination in feed of Nile tilapia in Egypt. The results showed that feed treated with absorbent materials could reduce the effect of aflatoxins in Nile tilapia and increased body weight resulting in higher price. The economic analysis shows a profitable result of using feed with absorbent materials (Ayyat et al., 2014).

3.3.3 | Consumers' WTP for aflatoxin-free products

Two studies showed that awareness level of consumers and occurrence of aflatoxins in food in Kenya increased the WTP for aflatoxin-free products. Specifically, the WTP for uncontaminated milk was estimated to be 64% higher and for maize, this was 50% higher (de Groote et al., 2016; Mtimet et al., 2015).

3.4 | Mitigation measures

In this study, we specifically focused on mitigation measures that had been tried and tested under African conditions. Proceeding "from farm to fork," we considered measures at the following stages: plant breeding, agronomic practices, postharvest measures, food processing, reduction of mycotoxin availability using binders, and education and awareness. In total, 60 studies were included related to mitigation measures. Included studies were mainly reported for Kenya (13); followed by Egypt (7) and Nigeria (9). The impact of mitigation measures described in the included studies was done in varying manners. For six studies, the impact was described in a monetary value. It appears that most studies did not quantify the impact of the mitigation measure.

3.4.1 | Plant breeding

Resistance to *Aspergillus* ear rot infection (indicated, for instance, by "kernel infection rate") and aflatoxin contamination are relatively new targets for African maize variety selection (Kwemoi, Okori, & Asea, 2010; Okoth et al., 2017). Okoth et al. (2017) describe the results field testing of 23 inbred three maize lines (which can be used in breeding of hybrid maize varieties). These lines had been bred with a particular focus on *Aspergillus* ear rot resistance and reduction of aflatoxin formation in both South Africa and Kenya. Three lines were thus identified that scored favorably on these two traits, two of them adapted to tropical lowlands and the third to mid-altitude (Okoth et al., 2017). Various reports highlight the relationships between resistance of the maize variety, type of maize (flint or dent; early or late maturing), and particularly the nitrogen fertilizer regime (Manoza et al., 2017; Mutiga et al., 2017). These relationships are important in choosing appropriate combinations of agricultural practices and crop variety.

3.4.2 | Agronomic practices

Marechera and Ndwiga (2014) surveyed farmers in lower Eastern Kenya for mitigation practices. Particular practices applied by many farmers (approx. 50%) were crop rotation, and pest control on the farm. Irrigation, bio-control, and smearing of cobs with soil were less commonly employed (Marechera & Ndwiga, 2014). In a survey of Tanzanian maize farmers from three different climatic zones, it was observed that early and mid-planting resulted in lower aflatoxin levels than late planting. This also held true for hand-hoeing and ox-tillage versus tractor tillage, as well as for the use of insecticides (Kamala et al., 2016; Nyangi et al., 2016).

Boaz, Wachira, Kagot, and Okoth (2017) surveyed West-Kenyan groundnut farmers for their agronomic practices and awareness of aflatoxin issues. They also checked for possible correlations with aflatoxin residues in harvested and stored groundnut samples, as well as for aflatoxigenic fungi in these samples and the farm soil. A statistically significant correlation was found between drought during cultivation and the state of storage, that is, in-shell versus unshelled, with the latter showing lower aflatoxin levels than shelled groundnuts. In addition, if groundnuts were grown in rotation with maize, the population of molds capable of forming aflatoxin was high (Boaz et al., 2017).

Wambui et al. (2017) estimated that reductions in the occurrence of HCC among rural dwellers in Kenya could be achieved through combinations of various agronomic measures, such as the use of farmyard manure, lime in groundnut, and the use of nonaflatoxigenic strains.

In crop fields, encouraging experimental results have been obtained with the addition to soil of preparations of molds that compete for the same ecological niche as aflatoxin-forming *Aspergillus* molds but that do not produce aflatoxins themselves. Following the successful application of such preparations in cotton, maize, pistachio, and peanut farming fields in the United States, nonaflatoxigenic strains were tested with support from the International Institute of Tropical Agriculture (IITA) and commercialized among African maize and peanut farmers under the brand name AflaSafe® (Bandyopadhyay et al., 2016). A recent study explored the use of preparations of local nonaflatoxigenic strains of *A. flavus* applied to maize field soils experimentally in Nigeria. The results thus showed the persistence of the applied molds in the field, and a reduction of aflatoxin levels in maize kernels by 95% at most, which persisted even after harvest as a continued effect (Atehnkeng et al., 2016). Whereas sorghum kernels are commonly used to produce AflaSafe® preparations, Okike et al. (2015) showed how these could be replaced by farmers with cassava peels, a by-product of cassava production. While a certain eagerness to buy AflaSafe® has been observed among African farmers, such as 82% among Kenyans, awareness of the public health implications of aflatoxin contamination appears not to play a decisive role in this decision (Johnson et al., 2017; Marechera & Ndwiga, 2015). The cost-effectiveness of control measures, such as AflaSafe® and other solutions which need to be used on a regular basis, largely depends on their lifespan. If this span only extends to 1 year, for example, then the product would not be cost-effective (Narrod, 2013; Njoroge et al., 2016).

3.4.3 | Postharvest measures

Preventing infection with fungal spores from the soil, above-ground drying of the harvested product turned out as one of the successful measures toward reduction of the aflatoxin levels. Examples of above-ground drying include threshing sorghum on canvas (Taye, Ayalew, Dejene, & Chala, 2018) or drying of groundnuts in ventilated structures in the field or on plastic sheets (Seetha et al., 2017). For groundnuts, the handling and storage of unshelled rather than shelled peanuts were found to be associated with a reduced level of aflatoxins (Boaz et al., 2017).

Another effective mitigation practice is hand or automated sorting out of products that are contaminated to the eye, namely damaged, discolored, or moldy kernels, such as for maize, groundnut, and sorghum (Matumba, van Poucke, Ediage, Jacobs, & de Saeger, 2015; Njoroge et al., 2016; Seetha et al., 2017). Also, flotation of kernels is mentioned as a possible means of separating infected or contaminated kernels from the noninfected /noncontaminated ones. It showed to reduce aflatoxin contamination by as much as 95% (Matumba et al., 2015; Matumba et al., 2017).

Using plastic bags, such as PICS or polypropylene ones, to store dried kernels and protect them from mold infection and insect and rodent infestation also proved successful in a number of cases for reduction of mold growth and aflatoxin contamination during maize and groundnut storage (Baoua, Amadou, Ousmane, Baributsa, & Murdock, 2014; Magembe et al., 2016a; Maina, Wagacha, Mwaura, Muthomi, & Woloshuk, 2016; Ng'ang'a, Mutungi, Imathiu, & Affognon, 2016; Mutegi, Wagacha, Christie, Kimani, & Karanja, 2013). However, in groundnuts, higher levels of aflatoxins were seen in plastic bags (compared to jute bags), which were attributed to heat development in the bags. Also, the addition of grain protectants during storage has proven to afford adequate protection, such as with antifungal dried neem leaf powder (Magembe et al., 2016a).

The work of Christie, Kyamureku, Kaaya, and Devenport (2015) showed the contribution of Ugandan smallholder household education in postharvest practices toward changed practices for reduction of aflatoxin contamination. These practices included, for example, aboveground drying and sorting out of contaminated groundnuts. Particularly, also the role of women in awareness raising was acknowledged.

3.4.4 | Food processing

Removal of hulls from maize and groundnuts by household members before processing and consumption has shown to lead to reduced aflatoxin contamination of the resulting food products, such as maize meal. Also, handsorting and roasting of peanuts can further reduce aflatoxin levels (Afolabi, Ezekiel, Kehinde, Olaolu, & Ogunsanya, 2015; Kilonzo, Imungi, Muiru, & Njage, 2014; Xu et al., 2017). At the rural community level, a hyperspectral sorter such as developed by Stasiewicz et al. (2017) might be used to sort out infected maize kernels before the hammer mill: using this sorter, a reduction of aflatoxin contamination by 83% could be achieved experimentally.

Regarding processing methods that can be applied to foods in order to reduce levels of aflatoxin, a wide variety of techniques is available and has been tested, but not specifically for Africa. These include heating (e.g., cooking and boiling), fermentation, and chemical treatment (ammoniation and oxidation). Examples of nonintrusive techniques recently tested for application in African produce or within local environments include gamma-irradiation of foods, and their treatment with gaseous ozone. Seeds of sesame that had been sourced from local Nigerian markets were exposed to varying doses (0 to 15 kGy) of gamma-irradiation after being placed on a conveyor belt passing a ^{60}Co source. A statistically significant reduction of aflatoxin levels was consistently observed in all samples exposed to a 15-kGy dose (Akueche et al., 2012). Experimentally *A. flavus*-infected samples of Egyptian peanuts were placed within a fumigation chamber and exposed to gaseous ozone at 0 to 50 ppm for 5 to 10 min. AFB_1 and AFB_2 were largely reduced after this treatment, by more than 70% and 40%, respectively (Sahab, Hassanien, El-Nemr, Abdel-Alim, & Abdel-Wahhab, 2013).

Different forms of microbial fermentation have been applied successfully, such as the complete loss of aflatoxins in *amahewu*, a traditional fermented porridge, when prepared from aflatoxin-tainted maize meal (Chelule, Mbongwa, Carries, & Ggaleni, 2010). The production of fermented maize gruels (e.g., ogi and togwa) from maize has also been found to be associated with a substantial decrease in aflatoxins, by up to 68% for AFB_1 in togwa, for example (Okeke et al., 2015; Nyamete, Bennink, & Mugula, 2016). Also, fermentation of contaminated milk into yogurt-type dairy products, such as *leben* in Northern Africa, has shown to reduce contamination with AFM_1 originating from the milk (Ghislaine et al., 2016; Nduti et al., 2016).

In an industrial setting, the use of fast detection methods can help to verify the presence and level of aflatoxins in sourced raw materials and produced food products. Following a comparison of different fast detection methods, Mwanza et al. (2015) advised the application of a strategy by initially testing with thin-layer chromatography or with using dipsticks; and that positive tests should be followed up with a confirmatory high-performance liquid chromatography analysis.

3.4.5 | Reduction of mycotoxin availability using binders

During various clinical trials in rural African human volunteer populations exposed to typically aflatoxin-contaminated foods (e.g., maize), study participants consumed clay supplements (e.g., montmorillonite) on a daily basis. Results showed that in the supplement-administered groups, markers of aflatoxin exposure in serum or urine were substantially reduced, indicating reduced uptake of aflatoxins (Awuor et al., 2017; Mitchell et al., 2014).

In experimental feeding studies with Nile tilapia, an aquaculture species, the use of yeast or bentonite (clay) and their impact on aflatoxin residue levels in the fish product as well as on physiological markers was measured. It was observed that health and performance of the fish improved, and contamination levels decreased, when using these binders added to feed (Abdel Rahman, Abdellatief, & Mahboub, 2017; Ayyat, Abd Rahman, El-Marakby, Mahmoud, & Hessan, 2013).

3.4.6 | Education and awareness

When breastfeeding mothers from Malawi were instructed on food hygiene, preparation, and safety, their children showed less wasting and underweight than without this education. Wasting showed to be correlated with aflatoxin contamination of the consumed food (Seetha et al., 2018). Egyptian participants in a pilot awareness raising effort were more intent on preventing mold growth in their foods and to seek for medical assistance for HCC and hepatitis (Saleh et al, 2015).

4 | DISCUSSION

4.1 | Geographic spread and scale of aflatoxin contamination

The most commonly investigated commodities in the included papers were maize and peanuts, and animal feeds—which are generally the products most commonly associated with aflatoxigenic mold contamination in Africa. All studies indicated a mean AFB_1 concentration in maize of > 5 μg/kg, which is above the legal limit in the EU for AFB_1. The results imply that reduction of overall aflatoxin levels in food in Africa is still a major challenge.

The included studies give an insight into the investigated geographic areas and foods, yet extrapolation or generalization of specific results to other areas and foods remains difficult. This observation is consistent with Atherstone, Grace, Waliyar, Lindahl, and Osiru (2014) and Wild et al. (2016) who mention that there is a lack of prevalence studies in certain countries. Research on aflatoxin contamination requires a substantial budget for sampling, storage, transport, and analysis of the samples, as well as interpretation of the outcome and publishing the results in peer-reviewed journals. The socioeconomic situation in a country or area may hinder mapping of the actual aflatoxin situation and special circumstances may lead to prioritizing aflatoxin after other health issues. Nevertheless, a lack of published data does not imply that aflatoxins are not a problem in those countries. In the opinion of the authors, a major step forward for countries where contamination is likely, but research funds or output of reports or scientific articles are not achievable, is to join one or more regional or pan-African partnerships that work on research, education, and capacity building on aflatoxin-related matters.

4.2 | Disease burden

Populations in Africa can be exposed to high concentrations of aflatoxin via food causing acute aflatoxicoses, even to this day (Kamala et al., 2018). Diseases in the developing world often go unreported and it is likely that this problem may even be larger than described (Strosnider et al., 2006). Incidents with human fatalities Kenya and Tanzania in the years 2004 and 2016 were investigated by specialized teams; and the lessons learned were published (Kamala et al., 2018; Probst et al., 2007). This approach should be encouraged by all governments because it will contribute significantly to early warning systems and it will prevent fatalities. Their recommendations included "continued mycotoxin awareness as a public health issue, strengthening laboratory and surveillance capacities as well as establishing early warning systems" (Kamala et al., 2018).

This systematic review revealed relatively many studies on biomarkers for aflatoxins. Such data could provide a useful tool to gauge the impact of mitigation measures by establishing a baseline and subsequently measure their trends so as to verify if these measures have the desired effect on exposure and related health impacts. Biomarkers can give an indication of exposure of a person to a certain mycotoxin at a certain time, but the level of exposure can be estimated from the biomarker concentration only when the transfer rate (intake vs. excretion) has been validated in studies. Vidal, Mengelers, Yang, de Saeger, and de Boevre (2018) reviewed mycotoxin biomarkers of exposure for aflatoxin. They indicated that AFB_1-lysine is the most reliable biomarker of chronic aflatoxin exposure in plasma. Other biomarkers of exposure are AFB-N7-guanine in urine, and some others in urine, which are more suitable as a measure of short-term exposure. It cannot be excluded that persons with impaired health have a different transfer rate. There are no validated biomarkers of effect. Here, it should be noted that the pathology of AFB_1 exposure in humans was not in the scope of this review.

Risk assessment for aflatoxins must be based on the MOE approach. A margin between the benchmark dose lower limit (BMDL10, the 95% lower confidence limit of the benchmark dose for a 10% increase in cancer incidence) and the exposure below 10,000 indicates a reason for concern and mitigation strategies must be explored. Governments should, therefore, protect the health of the population by enforcing legislation based on the "as low as reasonably achievable" or ALARA-principle. Legal limits should be based on risk assessments, scientific evidence, performed by competent authorities, such as the Joint FAO/WHO Expert Committee on Food Additives (JECFA) or European Food Safety Authority (EFSA), and published for the public.

A major gap in the peer-reviewed literature is the lack of studies expressing the disease burden of aflatoxin in Africa in DALY. Only one study was identified, which described data from 2010 (Havelaar et al., 2015). An update to this work with more recent figures is highly recommended. This would furthermore allow the assessment of the economic impact of disease burden on society.

4.3 | Economic impact

The trade-related impact of aflatoxin contamination is mainly evaluated from the standpoint of aflatoxin regulation affecting products imported from developing countries, including Africa. The aflatoxin legislation investigated mainly focuses on the EU legal limits that seems to have caught much attention in research of the quantitative effects of aflatoxin. In addition to the study by Xiong and Beghin (2012), several studies evaluated the impact of EU regulation to African exporters since the year 2001: Otsuki, Wilson, and Sewadeh (2001a), Otsuki, Wilson, and Sewadeh (2001b), and Wu (2004). These studies were cited as the main source of qualitative results reported in many studies that were identified as relevant by means of our snowballing strategy.

According to the World Bank studies by Otsuki et al. (2001a) and Otsuki et al. (2001b), meeting the EU harmonized aflatoxin legal limit announced in 1998 (which were more stringent than Codex Alimentarius standards) would decrease African exports by 64% or USD 670 million and, more specifically, for African groundnut exporters by 63%. The EU harmonized legislation at the time set a maximum limit of 4 μg/kg in cereals, edible nuts, dried and preserved fruits, and groundnuts intended for direct human consumption, and 10 μg/kg in groundnuts subject to further processing, while the Codex limit was 15 μg/kg for total aflatoxins, and no specific limit for AFB_1 (Otsuki et al., 2001a). However, a later study by Wu (2004) found that the losses of African groundnut exporters due to EU regulation on aflatoxins were lower, with trade between Africa and the EU being less affected than estimated by Otsuki et al. (2001b). This finding was later corroborated by Xiong and Beghin (2012) as the issues of groundnut exports were argued to be most relevant for domestic supplies and thus relate mostly to production rather than EU market access issues. Similarly, for the years 2010and 2011, Narayan, Beloya, and Haskell (2014) found that aflatoxin contamination was not the key constraint in increasing Tanzania's and Nigeria's exports of groundnuts and maize. Only a negligible percentage of these products was destined for exporting, given the domestic demand of these products for food, feed, and replanting (Narayan et al., 2014).

Diaz Rios and Jaffee (2008) looked at the EU rejections of groundnuts imports from Africa. Their findings showed that even when adopting the limits advised by Codex Alimentarius, which are more lenient than the EU standards, 83% of African exporters were still noncompliant. While the study by Diaz Rios and Jaffee (2008) dealt with the EU regulations, the same effect is likely to occur in other export destinations that apply Codex Alimentarius standards. It is interesting to note that the study by Diaz Rios and Jaffee (2008) applied a different counterfactual for measuring the trade impact than the one used in the studies by Otsuki et al. (2001a,b), such that results cannot be compared. In addition to groundnuts, economic losses for aflatoxins in maize were also estimated. For maize, countries worldwide seem to trade more with other countries enforcing similar aflatoxin regulations. Therefore, due to the relatively low quantity of maize export from Africa to the EU, it is not likely that African maize export would be adversely affected by the EU aflatoxin limits (Wu & Guclu, 2012). Scarcity of food not contaminated with aflatoxins is also likely to result in high costs for raw materials, which may hinder the sourcing of materials for food aid at the local or regional level.

Studies on health-related economic impacts for African countries were not found in the included scientific publications. Some gray literature was found, which resulted in a project report and presentation files for meetings (Narayan et al., 2014; Ndenn, Diedhou, & Atanda, 2015), both of which quantified the economic losses due to aflatoxins-related public health problems, specifically for liver cancer, and measured in terms of DALY and value of statistical life.

In general, the limited number of studies estimating economic impacts of aflatoxins contamination points out a gap in peer-reviewed literature. The bottom line in this literature gap is the availability of the data for the estimations, particularly for health-related impacts. This finding is in agreement with previous studies indicating that economic impacts of mycotoxins (including aflatoxins) are difficult to assess due to lack of data on health costs and mycotoxin-induced human illness (Coulibaly, Hell, Bandyopadhyay, Hounkponou, & Leslie, 2008; Dohlmann, 2003). For example, in order to estimate the cost of illness for aflatoxin-related HCC, various data sources are needed, including the epidemiology, medication costs, and so on. These data might not be readily available in many African countries. Scarcity of information on economic impact of aflatoxin contamination in animal feed is also a major limiting factor that prevents a full economic assessment to be performed. The authors concur with Coulibaly et al. (2008) in their assessment that establishing regional mycotoxin testing laboratories, facilitated by "development of both infrastructure and regulatory frameworks," would be a major step forward to getting such data. In addition, the use of fast testing methods that are affordable and low-key, and hence amenable to widespread use in the field and in industrial settings, should be promoted for the sake of greater situational awareness of the aflatoxin contamination across the food and feed production chains. Finally, performing baseline studies—using uniform protocols, methodologies, and standards—in countries where that baseline does not currently exist would enable comparative economic assessment (Coulibaly et al., 2008).

4.4 | Mitigation measures

While our literature search focused on mitigation measures reported specifically for Africa, a wide range of mycotoxin-reducing methods that have been described more globally or for other regions might also be of interest (Wild et al., 2016). Regarding mitigation measures tested specifically in Africa, this review of recent studies further highlights the multitude of methods and stages from farm to fork, and beyond, at which the contamination, exposure, and adverse effects can be prevented, mitigated, or reversed. However, proof of cost-effectiveness or even costs alone of the practices is often lacking. The following measures appear to be effective: use of resistant plant varieties adapted to the local agro-ecological situation; awareness raising and education of farmers; promotion of the use of competing, nonaflatoxigenic molds; proper use of storage options; introduction of good practices and enforceable food safety standards to protect public health; and advocating dietary diversity to mitigate mycotoxin exposure. Notably, a recent review highlights the high technology readiness level of various noninvasive postharvest measures, including fluorescence-based automatic sorting and ozone treatment, and less so for microbial decontamination and cold plasma treatment (Marshall et al., 2020). In order to gain insight into their practical implementability under local African conditions, it would be relevant to perform a cost–benefit analysis of these technologies. Much of the supplementary gray literature found, including book chapters, conference proceedings, flyers, and so on, appeared to corroborate the findings of this systematic literature search. In the opinion of the authors, certainly the mentioned mitigation measures should go hand-in-hand with strengthening national food safety control systems (including legislation), and increased capacity for surveillance and enforcement.

4.5 | Limitations

The methodological choices introduced some limitations of the study. First, we focused on publications written in the English language. Journals in, for instance, the French language were thus automatically excluded. Second, this literature review's focus was specifically on high-quality, peer-reviewed literature. Literature on certain aspects related to aflatoxin contamination, and the effects thereof, is lacking. For instance, literature on the economic effects of aflatoxin contamination in animal feed, in relation to consequences for the food-producing animals, was especially scarce. The disadvantage of this approach is, therefore, that certain findings, which could be of added value, were not included in this study because they had not been published in a peer-reviewed journal. In addition, the inherent disadvantages of a systematic literature review (as discussed in EFSA, 2010) apply, which are that they are time, resource, and expertise-intensive and primarily suitable for questions for which primary research is available. An inherent issue with literature reviews is that there is a bias toward publishing positive findings in literature (Haidich, 2010). Finally, because only studies from 2010 to 2018 were included in this review, the findings are inherently limited to that time period.

5 | CONCLUSION AND RECOMMENDATIONS

The systematic literature review covered various aspects related to the topic of aflatoxins in Africa: contamination, economics, disease burden, and mitigation. The retrieved relevant studies covered one or two of these aspects in combination, illustrating the diversity of research and types of methods applied in the analysis of these aspects of aflatoxins in human food and animal feed. Results show that aflatoxin levels in food and feed occasionally can reach very high levels, and that aflatoxins lead to a variety of negative effects, first and foremost health effects that have a high negative impact on society. Hence, results of the current review underpin the need for an effective management of the aflatoxin situation in Africa. A number of mitigation measures have been developed: to prevent and control the contamination during primary production, to control or reduce contamination, during processing, and to reduce or mitigate the effects of exposure on the consumer's side. The level of aflatoxin awareness at the farm and collector level is varied across the African continent and raising awareness and education is expected to have direct beneficial effects.

Based on the outcomes, it becomes apparent that aflatoxins are a multifaceted problem, for which a holistic approach addressing the wide variety of aspects will be needed to prevent, mitigate, or reverse aflatoxin-related negative impacts. Several research gaps have been identified. This study shows that more emphasis should be put in studies on evidence based cost-effective mitigation strategies for aflatoxins, on the scale and spread of the problem, and its impacts on public health and economics for use in evidence-based policies. The availability of data and published studies varies per country: performing baseline studies in countries where aflatoxin contamination and resulting exposure is likely but data are missing would, therefore, be a valuable first step. Using established research methodologies and expressing the results of such studies in internationally recognized measurement units, such as, *inter alia*, DALY and VSL, would allow for comparative assessment to take place and is, therefore, highly recommended. In order to establish such initiatives, joining existing regional and pan-African networks and partnerships that are working on aflatoxin education and capacity building should be a first step. Finally, it must be strongly encouraged to publish results in transparent peer-reviewed platforms.

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AUTHOR CONTRIBUTIONS

Nathan Meijer designed the study, drafted the manuscript, was responsible for project management, and interpreted the results on geographic spread and scale. Gijs Kleter contributed to the design of the study, drafted the search strategy, contributed to screening and synthesis of results, interpreted the results on mitigation measures, and reviewed and commented on the manuscript. Monique de Nijs contributed to the design of the study, contributed to screening and synthesis of results, interpreted the results on disease burden, and reviewed and commented on the manuscript. Marie-Luise Rau coordinated the implementation of the different steps and software of the EEPI centre, contributed to the design of the study, drafted the search strategy, contributed to screening and synthesis of results, interpreted the results on economic impact, and reviewed and commented on the manuscript. Ria Derkx contributed to the design of the study, contributed to the search strategy, executed the search strategy, and reviewed and commented on the manuscript. H.J. van der Fels-Klerx wrote the project proposal, started the study, contributed to the design of the study, and reviewed and commented on the manuscript.

CONFLICT OF INTEREST

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SUPPORTING INFORMATION

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