CHAPTER 8.

Economics of mycotoxins: evaluating costs to society and cost-effectiveness of interventions

Summary

The economic impacts of mycotoxins to human society can be thought of in two ways: (i) the direct market costs associated with lost trade or reduced revenues due to contaminated food or feed, and (ii) the human health losses from adverse effects associated with mycotoxin consumption. Losses related to markets occur within systems in which mycotoxins are being monitored in the food and feed supply. Food that has mycotoxin levels above a particular maximum allowable level is either rejected outright for sale or sold at a lower price for a different use. Such transactions can take place at local levels or at the level of trade among countries. Sometimes this can result in heavy economic losses for food producers, but the benefit of such monitoring systems is a lower risk of mycotoxins in the food supply. Losses related to health occur when mycotoxins are present in food at levels that can cause illness. In developed countries, such losses are often measured in terms of cost of illness; around the world, such losses are more frequently measured in terms of disability-adjusted life years (DALYs). It is also useful to assess the economics of interventions to reduce mycotoxins and their attendant health effects; the relative effectiveness of public health interventions can be assessed by estimating quality-adjusted life years (QALYs) associated with each intervention. Cost-effectiveness assessment can be conducted to compare the cost of implementing the intervention with the resulting benefits, in terms of either improved markets or improved human health. Aside from cost-effectiveness, however, it is also important to assess the technical feasibility of interventions, particularly in low-income countries, where funds and infrastructures are limited.

1. Introduction

Two important topics are central to a discussion of the economics of mycotoxins: (i) the overall economic impact of mycotoxins on society, and (ii) the benefits and costs of strategies to control mycotoxins in food.

A common misunderstanding about the overall economic impact of mycotoxins on society is that only market impacts – losses from food lots rejected due to excessively high mycotoxin levels, as well as losses related to livestock and poultry – are included in this estimation. In estimating the economic impact of mycotoxins, human health impacts matter just as much, if not more so, particularly in low-income countries (LICs). Since the 1990s, the field of health economics has developed sufficiently that now improved methods exist to evaluate human health impacts of diseases and conditions, including those associated with mycotoxin exposure in food. To derive an estimate for the total cost to society of mycotoxins in food and feed, both market impacts and health impacts must be included in the calculation.

Strategies to control mycotoxin contamination should also be subject to economic analysis. Multiple strategies have been developed to reduce mycotoxin risks before harvest (in the field), after harvest (in storage, transportation, or processing), in diets, and in clinical settings (see Chapter 9). If these mycotoxin control strategies are to be adopted in the parts of the world where they are most needed, then their expected benefits, or effectiveness – in terms of both market and health outcomes – should exceed their costs. Moreover, their capital costs should not be so high that LICs would find it impossible to adopt the strategies. Low-tech strategies may prove the most economically feasible option to control mycotoxins in LICs. Finally, cultural acceptability of the interventions is crucial, to ensure long-term adoption and effectiveness in mycotoxin reduction.

In addition to the overall economic impact of mycotoxins and the cost-effectiveness of control strategies, another important economic consideration is the technical feasibility of these strategies, which includes risk assessment of potential health and environmental impacts. These issues are also discussed in this chapter.

It is important to remember that values for the different variables in economic models can change substantially with time. Hence, when the models are used at any point in time, the results should not be overinterpreted, to avoid the danger of making long-term decisions based on analyses of current (limited) information.

2. Market and trade impacts of mycotoxins

The primary way in which mycotoxins affect markets is to lower the value of the commodity being traded. The price paid for a particular lot of food or feed is reduced, or the lot is rejected entirely, or the lot must be treated at additional cost before being sold at a higher price. This can occur at multiple different levels of trade, from local all the way to international. Depending on the demands of the buyer, the stakeholder group that bears the burden of mycotoxin cost can be individual farmers, handlers, processors, distributors, consumers, or government.

2.1 Dynamics of market supply and demand due to mycotoxin contamination

Microeconomic theory explains how the overall market and trade costs of mycotoxins can be evaluated. Simply, mycotoxin contamination decreases the available supply of acceptable food to be sold or bought. Fig. 8.1 illustrates the dynamics of supply and demand for food for human consumption when supply is decreased. The demand curve represents the quantity of a particular food that consumers are willing to buy at a particular price. At very high prices, less demand will exist for the food, whereas at lower prices, demand will be higher. The supply curves (labelled S_0 and S_1) represent the quantity of food that producers will provide at different prices per unit of food. Hence, the original equilibrium of quantity of food supplied, Q_0, and price per unit of food, P_0, is the intersection of the demand curve with the original supply curve, S_0. However, when the supply curve is shifted left, to S_1 (as happens when food supply is decreased due to excessively high mycotoxin levels), a new equilibrium is reached, represented by the intersection of the demand curve with the new supply curve, S_1. The reduced quantity of units of food sold, Q_1, demands a higher price per unit of food, P_1.

Thus, both producers and consumers bear costs associated with mycotoxins. Producers sell less food and thus have reduced revenue, and consumers must buy the food at a higher price. Specifically, the decrease in food producers' welfare due to mycotoxin contamination is represented by the shaded area in Fig. 8.1. This area represents the difference between the producers' initial welfare (area of triangle bounded by P_0, Q_0, and the demand curve) and their resulting welfare (area of triangle bounded by P_1, Q_1, and the demand curve). The decrease in consumers' welfare because of mycotoxins is represented by the difference between their initial welfare (area of triangle bounded by P_0, Q_0, and supply curve S_0) and their resulting welfare (area of triangle bounded by P_1, Q_1, and supply curve S_1).

In practical terms, producers of commodities vulnerable to mycotoxin contamination may suffer market losses directly, if the buyers monitor and enforce limits for mycotoxins. Consumers suffer market losses indirectly, by facing a reduced supply of the commodity and therefore a higher price. (In contrast, consumers may suffer health-related losses directly, as discussed in Section 3.) Often, this cost to consumers is marginal, particularly in developed countries, where the bulk of the cost of food is made up of food processing rather than the commodity itself. But in LICs, reducing the supply of food by removing heavily contaminated commodities can result in food shortage crises. Moreover, for

Fig. 8.1. The impact of a strict food quality standard on supply and subsequent price. Source: Wu (2008); reproduced with the permission of the publisher.

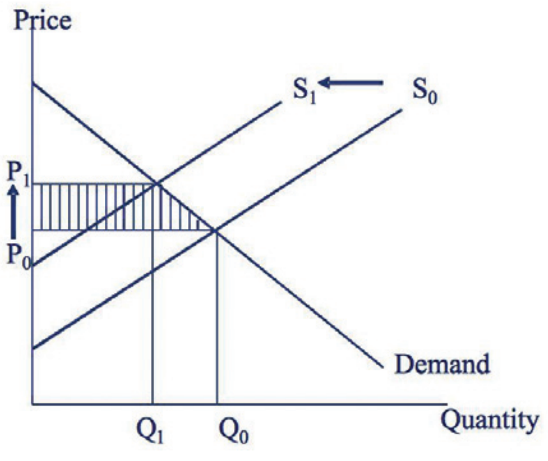
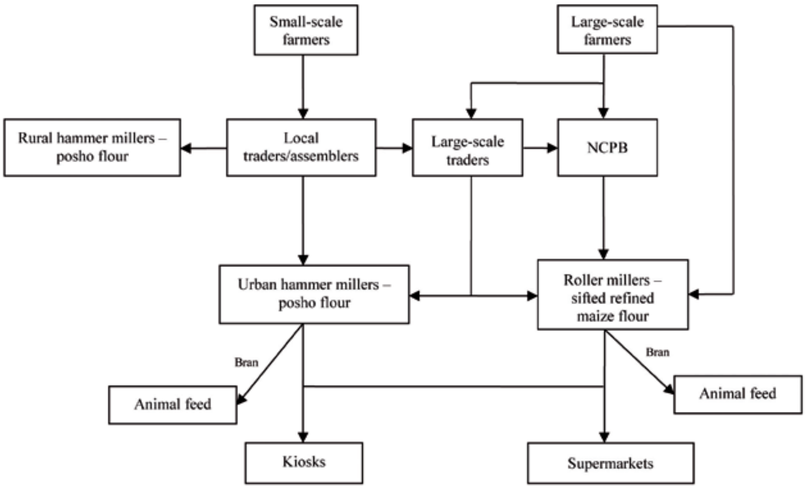


Fig. 8.2. Complexity of the value chain of maize in Kenya, and points at which aflatoxin control strategies could be implemented. NCPB, National Cereals and Produce Board of Kenya. Source: Dr Jonathan Hellin, International Maize and Wheat Improvement Center (CIMMYT), personal communication.



staple food items such as maize, the price elasticity of demand is usually very low, which means that demand will not change significantly in response to a change in price; consumers will purchase staples even if the price becomes much higher, because staple foods are a necessity.

2.2 Mycotoxin costs in local and regional markets

The complexity of local and regional commodity markets varies considerably among countries, and thus the extent to which mycotoxins may impose market costs varies. In the USA, for example, crop value chains are relatively simple. Farmers may sell their crops to grain elevators (e.g. maize, wheat) or to shellers or other handlers (e.g. groundnuts, tree nuts), who may then further process the crop and sell it to animal operations or to food processors for human consumption. After processing, the food is sold to distributors, who then sell it to retail markets to be purchased by consumers.

For the USA, mycotoxin action levels (for aflatoxin, specifically) or industry guidelines (for fumonisin and deoxynivalenol) set by the United States Food and Drug Administration are enforced at different levels, such as at grain elevators or by food handlers. Crops with the lowest mycotoxin levels can be sold for human food or for feed to the most sensitive animal species at a higher price, whereas crops with higher mycotoxin levels can be sold for animal feed at a lower price or are rejected outright. Within each commodity, different stakeholder groups are affected differentially by mycotoxins. In the USA, producers of grain commodities generally bear the burden of costs related to mycotoxins, whereas shellers and handlers, not growers, bear the largest burden of mycotoxin-related costs associated with groundnuts and tree nuts (Wu *et al.*, 2008).

In other parts of the world, local commodity markets are far more complex. The value chain of maize in Kenya is illustrated in Fig. 8.2, to provide an example of trade of one commodity in one country. Maize growers (labelled in Fig. 8.2 as "Small-scale farmers") may sell their maize to a wide variety of different local maize traders, who may travel from household to household to purchase maize. These traders, in turn, may sell the maize to large-scale traders or to a variety of millers. Each step further in the value chain of maize provides different opportunities for both buyers and sellers.

This complexity of the value chain of crops in Africa means that it can be very difficult to implement mycotoxin control strategies that would have widespread effects. The control strategies would have to be implemented at multiple points, and these points would have to be coordinated. In the event of an outbreak of mycotoxicosis, interventions would need to be distributed, and communication among different stakeholders is absolutely crucial. Depending on available communications infrastructures, implementing interventions may be a difficult task.

2.3 Mycotoxin costs in international markets

The issue of mycotoxin control is becoming increasingly important for LICs as international trade becomes more prominent in a world of increasing demand for crops (to be used for food, animal feed, or even fuel). Hence, mycotoxin costs must also be considered in the context of international trade.

More than 100 countries have established maximum tolerable levels for aflatoxins in human food (FAO, 2004), whereas relatively few countries have established these levels for other mycotoxins such as fumonisin, ochratoxin A, and deoxynivalenol. Table 8.1, which lists maximum tolerated levels for foodborne aflatoxins in selected countries and regions as of August 2010, shows that aflatoxin standards vary greatly among countries, even for a small sample of countries; this difference may cause food trade barriers. Indeed, the Council for Agricultural Science and Technology states that one key goal for the 21st century is to "develop uniform standards and regulations for mycotoxin contamination" (CAST, 2003). These standards have implications not just for the country that imposes the standard but also for countries that attempt to export foods there.

From an international trade standpoint, mycotoxin contamination inflicts heavy economic burdens. It reduces the price paid for crops and can cause disposal of large amounts of food. In the USA, losses from mycotoxins – in the hundreds of millions of US dollars annually – are usually associated with these market costs rather than with health effects because enforcement of mycotoxin standards and pre-harvest and post-harvest control methods have largely eliminated harmful exposures in food in the USA (Wu, 2004).

In LICs, impacts of mycotoxins are far more severe. Many individuals are not only malnourished but also chronically exposed to high aflatoxin levels in their diet, resulting in deaths from aflatoxicosis, cancer, and other conditions (Wild and Gong, 2010). LICs often lack the resources, technology, and infrastructure necessary for routine tests of mycotoxin levels in food. Further complicating the problem in the case of aflatoxin is that for a given level of aflatoxin exposure, cancer risk may be more severe in LICs than in developed countries because of higher prevalence of chronic hepatitis B virus (HBV) infection, which synergizes with aflatoxins to significantly increase the risk of liver cancer (hepatocellular carcinoma [HCC]) (Groopman *et al.*, 2008).

Globalization of trade has exacerbated food losses due to mycotoxins in three ways. First, strict mycotoxin standards mean that LICs will export their best quality foods and keep more heavily contaminated foods for domestic consumption, resulting in higher mycotoxin exposure in LICs (Cardwell *et al.*, 2001). Second, even the best quality foods produced in LICs may be rejected for export, resulting in millions of US dollars in losses (Wu, 2004; Wu *et al.*, 2008). Third, the cost of a rejected food shipment is enormous (about $10 000 per lot in transportation, storage, and dockage fees; Wu *et al.*, 2008), even if the lot can be returned to the country attempting to export the food.

These dilemmas led former United Nations Secretary-General Kofi Annan to recognize the magnitude of the problem of setting appropriate aflatoxin standards worldwide. At the Third United Nations Conference on the Least Developed Countries, held in Brussels in 2001, he commented, "The European regulation on aflatoxins costs Africa $670 million each year in exports. And what does it achieve? It may possibly save the life of one citizen of the European Union every two years. Surely a more reasonable balance can be found."

Annan had based his statement on a report of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) (WHO, 1998), which assessed the effect of aflatoxin regulations on HCC incidence, depending on HBV prevalence. JECFA developed two scenarios to determine the effect of moving from an enforced aflatoxin standard of 20 µg/kg to a stricter standard of 10 µg/kg in two hypothetical countries: one with an HBV prevalence of 1% and another with an HBV prevalence of 25%. In the first country, tightening the aflatoxin standard would yield a drop in the estimated population HCC incidence by 2 cases per billion people per year. In the second country, tightening the aflatoxin standard would yield a drop in the estimated population HCC incidence of 300 cases per billion people per year. Hence, in high-income importing countries with low HBV prevalence, tightening the aflatoxin standard would reduce HCC incidence by an amount so small as to be undetectable (Henry *et al.*, 1999; Wu, 2004).

Now that a global push exists to harmonize mycotoxin standards

Table 8.1. Maximum tolerated levels for aflatoxins in human food in selected countries and regions[a]

Country or region	Total allowable level of total aflatoxins in human food (μg/kg)
Australia[b]	5 or 15
China	20
European Union[c]	4, 10, or 15
Guatemala	20
India	30
Kenya	20
Taiwan, China	50
USA	20

[a] A more complete list can be found in FAO (2004).
[b] The Australian standard for maximum allowable aflatoxins in groundnuts is 15 μg/kg, more permissive than those for other foods.
[c] The European Union standard for maximum allowable aflatoxins is 4 μg/kg for cereals and all products derived from cereals, except maize to be subjected to sorting, which has a standard of 10 μg/kg. The standard for groundnuts, almonds, hazelnuts, and pistachios "ready to eat" is 10 μg/kg, whereas the standard for groundnuts, almonds, hazelnuts, and pistachios intended for further processing is 15 μg/kg.

(CAST, 2003), it is important to consider on a global scale what the economic impacts would be of harmonizing different standards, which range from relatively strict to relatively permissive. Wu (2004) provided a framework for assessing losses related to markets, as outlined below.

Given a particular internationally imposed mycotoxin standard, the total national export loss of a particular food crop can be calculated as the product of the price of the food crop per unit weight on the world market, the total amount of that crop exported, and the fraction of the export crop that is rejected as a result of that mycotoxin standard (Wu, 2004):

$$\text{Export loss}_{i,j,k} = P_i * W_{i,j} * r_{i,j,k},$$

where i is the crop (e.g. maize, groundnuts); j is the country; k is the international mycotoxin standard (e.g. for fumonisin or aflatoxin); P_i is the world price for food crop i per unit weight; $W_{i,j}$ is the total export amount (in metric tons) of crop i from country j; and $r_{i,j,k}$ is the fraction of export volume of crop i from country j rejected at international mycotoxin standard k.

A sensitivity analysis on k reveals how export losses for food crops in a particular country change as a function of the harmonized standard chosen. Values for $r_{i,j,k}$ are calculated by fitting probability density functions $PDF_{i,j,k}$, based on the relevant literature, of concentrations of fumonisin and/or aflatoxin in crop i in country j. The particular country j to study is chosen by looking at the most important exporting countries of crop i. Cumulative distribution functions are estimated from the probability density functions of the percentage of the crop having mycotoxin levels at or lower than a given concentration. Then, the fraction of export volume rejected at that concentration is:

$$r_{i,j,k} = 1 - \int PDF_{i,j,k}\, dk,$$

where $PDF_{i,j,k}$ is the probability density function of the percentage of crop i from country j having mycotoxin levels at or lower than standard k, and its integral over k is the cumulative distribution function. Then, export losses calculated for each country are summed across major food exporting countries to derive a total global burden of export loss at different mycotoxin standards.

3. Health economic impacts of mycotoxins

Looking at the market and trade impacts of mycotoxins is only one side of the story. The other important facet to consider is the public health impact of setting different mycotoxin standards worldwide, assuming they could be enforced. The human diseases and conditions caused by mycotoxin exposure must first be evaluated.

Evaluating the human health economic impacts of mycotoxins is crucial to understanding their total economic impact because mycotoxins primarily affect LICs, where trade-related losses are not nearly as prominent as adverse health effects from consuming food contaminated with mycotoxins. Subsistence farmers and local food traders occasionally have the luxury of discarding obviously mouldy food, but in conditions of drought or food insecurity, poor people often have no choice but to eat the contaminated food or starve.

Until recently, it was difficult to put an economic value on health effects. Fortunately, the field of health economics has made great strides in the past two decades. Health economics strives to quantify health benefits and costs in such a way as to be comparable with monetary benefits and costs. Otherwise, it can be difficult to understand how much a particular risk affects human society, especially if death is not a significant outcome, or, conversely, how much a public health intervention benefits human society, if no direct market outcomes exist. Putting monetary values on these health outcomes helps decision-makers to understand how important a risky agent or a disease is, how useful an intervention might be, and how to compare the relative importance of risks and the relative effectiveness of interventions (Wu and Khlangwiset, 2010a).

Much of the literature in health economics focuses on medical treatments, with relatively few applications in food and agriculture. Some examples of health economic assessments of food additives include studies of the potential cost-effectiveness of transgenic golden rice in reducing vitamin A deficiency (Stein *et al.*, 2008) and the cost-effectiveness of biofortifying foods in reducing micronutrient deficiency (Meenakshi *et al.*, 2007). Havelaar (2007) provided a notable example of estimating the health costs of foodborne zoonoses, such as those caused by *Campylobacter*, *Salmonella*, or *Cryptosporidium* in Europe.

It is also important to consider the health economic impacts of mycotoxins, which can impose an enormous socioeconomic cost. As stated above, in developed countries it is relatively straightforward to estimate the costs of mycotoxins because these costs are primarily related to markets. Commodities that contain mycotoxins at levels exceeding regulatory guidelines for human food or animal feed are discarded or sold at a lower price for a different use (Wu *et al.*, 2008). One can estimate the cost of mycotoxins to a particular commodity group by estimating how much of the commodity must be discarded or discounted due to mycotoxin contamination. In LICs, in contrast, health-related costs are usually much higher than market-related costs, and health economic impacts are more difficult to evaluate.

The burden of human diseases, such as those caused by mycotoxin consumption, can be calculated in two primary ways. The first is cost of illness (COI), which is more appropriate in developed countries because a large portion of the estimate is health-care cost. The second is disability-adjusted life years (DALYs), which is appropriate for both developed and developing countries. A third metric, quality-adjusted life years (QALYs), is more often used to estimate the relative effectiveness of different public health interventions in improving overall quality of life.

3.1 Cost of illness

For an individual or for a particular population, COI caused by a disease or condition is calculated as the sum of three factors: direct health-care costs (DHC), direct non-health-care costs (DNHC), and indirect non-health-care costs (INHC):

$$COI = DHC + DNHC + INHC.$$

DHC are costs associated with medical services. These include general practice consultations, consultations with specialists, hospitalization, any surgery or treatments required, drugs, supplements (e.g. intravenous fluids), and rehabilitation. DNHC are costs associated with the disease that do not relate to the medical system. These include travel costs to medical centres, costs of childcare, and co-payments by patients for medicines.

INHC are defined as the value of production lost to society due to the disease or condition, as a result of temporary absence from work, permanent or long-term disability, or premature mortality (Havelaar, 2007; Wu and Khlangwiset, 2010a). To the extent that they can be evaluated, the costs of pain and of suffering associated with the condition would also be included in this category.

3.2 Disability-adjusted life years

The DALY, like COI, is a measure of the overall burden of disease. It extends the concept of potential years of life lost due to premature mortality to include equivalent years of healthy life lost in states of less than full health, broadly termed disability (Havelaar, 2007; Wu and Khlangwiset, 2010a). One DALY can be thought of as one lost year of healthy life. The total DALYs associated with a particular disease are calculated as follows:

$$DALYs = YLL + YLD,$$

where YLL is the years of life lost due to premature mortality from the disease and YLD is the years lost due to disability. YLD is estimated as the number of years lived with the disability multiplied by a weighting factor, between 0 and 1, that reflects the severity of the disability.

The World Health Organization (WHO), among other organizations, has estimated DALYs for many diseases and conditions in different parts of the world. DALYs for any given disease are estimated separately for high-income, middle-income, and low-income countries. This stratification is based on assumptions about how many years individuals will live with a disability in different parts of the world and what resources are available to alleviate disability (Wu and Khlangwiset, 2010a).

3.3 Quality-adjusted life years

The QALY is used to assess the value for money of a medical or public health intervention. It is based on the estimate of the number of years of life that would be added by the intervention, and hence is used to rank the relative effectiveness of different interventions for a particular condition. Every year of "perfect health" is assigned a value of 1, whereas a year not lived in perfect health is assigned a value between 0 and 1 that reflects the quality of life (similar to the weighting factor for YLD in DALYs).

QALYs are calculated as follows. Individuals with a serious, life-threatening condition (as is often the case with excessive exposure to aflatoxin) can receive a standard treatment (which, in LICs, may be no treatment at all) that will allow them to live for *X* more years with a quality of life of *A*. However, if they receive a new treatment instead, they will live for *Y* more years with a quality of life of *B*. The difference between the new and the standard treatment in terms of QALYs gained is

$$\text{QALYs gained} = Y * B - X * A.$$

To assess the relative effectiveness of an intervention, the cost of the new treatment must also be taken into account. The difference in treatment costs divided by the QALYs gained is used to estimate the cost per QALY, i.e. how much would need to be spent to provide one additional QALY.

3.4 Challenges to evaluating health economic impacts of mycotoxins

To use either the cost of illness or the DALYs method to calculate socioeconomic costs, one must first identify human health end-points, i.e. diseases or conditions, to assess. Otherwise, it is impossible to gather data on the necessary factors to assess the economic impact: mortality and morbidity, incidence, duration, and severity associated with the disease.

The challenge in calculating the socioeconomic costs of mycotoxins is that, with the exception of aflatoxins, specific human health end-points are difficult to attribute quantitatively or even qualitatively to a particular mycotoxin. For example, fumonisins have been associated with oesophageal cancer and neural tube defects in humans, but these associations are not clearly established and there are no human dose–response data, i.e. doses of fumonisins causing particular levels of disease incidence, by which to perform a reliable quantitative risk assessment. Further complicating the issue is that each mycotoxin may have multiple health end-points, including cancer, acute toxicity, and immunomodulation. Even if quantitative relationships could be established for each end-point, an analyst would need to ensure that every possible human health outcome of a mycotoxin was included in the calculation, to derive an accurate health economic estimate.

With aflatoxins, more progress has been made in quantifying the link between exposure and disease incidence. Aflatoxins cause a multitude of conditions, including acute aflatoxicosis and HCC, and are believed to contribute to immunosuppression and stunted growth in children. In an aflatoxicosis outbreak in Kenya in 2004 (Strosnider *et al.*, 2006), it was possible to estimate the total number of cases, the number of deaths, and the concentrations of aflatoxins in the contaminated maize that caused the toxicoses. Decades of work have likewise established dose–response relationships between aflatoxins and HCC in HBV-positive and HBV-negative individuals, from which aflatoxin cancer potency factors can be derived for quantitative cancer risk assessment (WHO, 1998). The immunosuppressive effects of aflatoxins cannot yet be quantified in humans, but limited quantitative data are available to assess the link between aflatoxin exposure and stunted growth in children (Gong *et al.*, 2002).

4. Evaluating total economic impacts of mycotoxins

If both the market and the health economic impacts of mycotoxins can be estimated, the cost-effectiveness of different interventions to reduce mycotoxin risk can then be assessed.

Various studies have attempted to quantify the potential market losses associated with mycotoxins in crops. In the USA, Vardon *et al.* (2003) estimated the total annual losses due to three mycotoxins – aflatoxin, fumonisin, and deoxynivalenol – to reach as high as US$ 1 billion. Almost all of this loss was borne by maize, groundnut, and wheat growers. However, a small portion of this loss was estimated to be suffered by livestock producers due to adverse animal health effects.

In three Asian countries – Thailand, Indonesia, and the Philippines – the total estimated annual loss due to aflatoxin was about 1 billion Australian dollars (Lubulwa and Davis, 1994). This loss was a combination of market impacts, through rejected lots with excessively high mycotoxin levels, and adverse health effects – specifically the impacts of HCC in these populations.

Wu (2004) estimated the market impacts to the world's top maize-exporting and groundnut-exporting countries and regions of conforming to hypothetical harmonized standards for fumonisin in maize and aflatoxin in groundnuts. If the current United States Food and Drug Administration (FDA) total fumonisin guideline of 2 mg/kg were adopted worldwide, the total annual maize export losses for the USA, Argentina, and China would be US$ 100 million, whereas if a fumonisin standard of 0.5 mg/kg were adopted worldwide, those total annual losses would increase to US$ 300 million. If the current FDA total aflatoxin action level of 20 μg/kg were adopted worldwide, total annual groundnut export losses for the USA, Argentina, China, and Africa would be US$ 92 million, whereas if an aflatoxin standard of 4 µg/kg were adopted worldwide, those total annual losses would increase to US$ 450 million.

Liu and Wu (2010) and Liu *et al.* (2012) estimated the global burden of aflatoxin-related HCC using two different approaches: quantitative cancer risk assessment and population attributable risk (PAR), respectively. The quantitative cancer risk assessment methodology (Liu and Wu, 2010), relying on dietary surveys and cancer potency factors, yielded an estimate of 5–28% of total global HCC cases attributable to aflatoxin. Similarly, the PAR approach (Liu *et al.*, 2012), making use of a systematic review and meta-analysis of human biomarker studies on aflatoxin-related cancer, yielded an estimate of 21–24% of global HCC cases attributable to aflatoxin. Because the total number of new HCC cases worldwide is hundreds of thousands each year and each HCC case is associated with 13 DALYs (Wu and Khlangwiset, 2010a), aflatoxin-related HCC alone may cause > 2 million DALYs each year.

5. Assessing cost-effectiveness of interventions to control mycotoxins

Multiple public health interventions exist by which to control mycotoxins or their burden in the human body. Interventions to reduce illness induced by mycotoxins can be roughly grouped into three categories: agricultural, dietary, and clinical. Agricultural interventions are methods or technologies that can be applied either in the field (pre-harvest) or in drying, storage, and transportation (post-harvest) to reduce mycotoxin levels in food. Agricultural interventions can thus be considered primary interventions because they directly reduce mycotoxin levels in food. Dietary and clinical interventions can be considered secondary interventions. They cannot reduce actual mycotoxin levels in food, but they can reduce mycotoxin-related illness either by reducing the bioavailability of mycotoxins (e.g. through enterosorption) or by ameliorating damage induced by mycotoxins (e.g. through inducing phase 2 enzymes that detoxify metabolites of mycotoxins). These control strategies are described in greater detail in Chapters 7 and 9.

In developed countries, it is relatively straightforward to estimate the cost-effectiveness of controlling mycotoxins because the costs and benefits are primarily market-related (Wu *et al.*, 2008). The cost of a particular mycotoxin to a particular commodity group is calculated by assessing how much of the commodity must be discarded or discounted due to contamination. Then, measuring the benefit accrued from a particular intervention requires estimating how much levels of the mycotoxin are reduced as a result of the intervention and how much more of the commodity can thus be sold. The difference between the total market value of the commodity with and without the intervention is a rough estimate of the cost-effectiveness of that intervention.

To calculate the cost of mycotoxin contamination in developed countries, three market economic factors need to be considered: the expected cost of mycotoxin contamination to growers or handlers in the absence of any interventions, the cost of purchasing and applying an intervention, and the expected net benefit of applying the intervention in terms of mycotoxin reduction. The cost per hectare, C, of mycotoxin contamination to growers in the absence of agricultural interventions can be expressed as

$$C = Y * P * R,$$

where Y is the crop yield per hectare, P is the price differential for high-quality use (low mycotoxin levels required) versus other uses, and R is the percentage of the crop with mycotoxin levels above the limit for high-quality use.

This cost C is compared with the benefits and costs of applying a mycotoxin control method. The <u>net</u> benefit per hectare, B, of applying the intervention can be expressed as

$$B = (E * C) - A,$$

where E is the percentage efficacy in reducing mycotoxins to levels that allow growers a premium, C is the cost per hectare associated with mycotoxin contamination (as shown in the previous equation), and A is the total cost of purchasing and applying the mycotoxin control strategy.

In LICs, however, interventions to reduce mycotoxins have both market and human health importance. How can the cost-effectiveness of a health intervention be determined if no direct market benefits exist? The WHO Commission on Macroeconomics and Health has provided the following guideline for thresholds of cost-effectiveness (WHO, 2001). An intervention is considered very cost effective if the monetary amount spent on the intervention per DALY saved is less than the per capita gross domestic product (GDP) of the country in which the intervention is applied. An intervention is considered moderately cost effective if the monetary amount spent on the intervention per DALY saved is less than 3 times the per capita GDP. An intervention is considered not cost effective if the monetary amount spent on the intervention per DALY saved is greater than 3 times the per capita GDP.

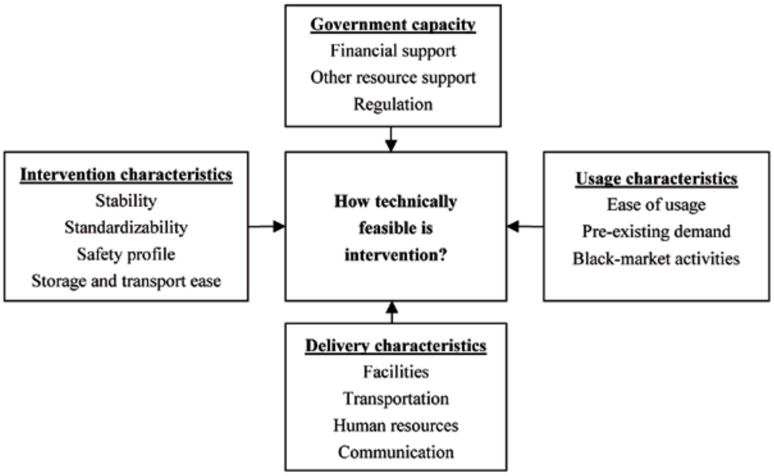
As described in Section 3.4, the health effects of the mycotoxin in question must be identified to estimate DALYs for this cost-effectiveness calculation. DALYs for any given disease are estimated separately for high-income, middle-income, and low-income countries. The DALYs estimate for each kind of country is based on assumptions about how many years individuals will live with a disability in different parts of the world and what resources are available to alleviate disability.

This WHO guideline is not without controversy. First, the cut-off of 3 times the per capita GDP for the cost-effectiveness of an intervention is a debatable metric. Second, using the average GDP in the estimation can be controversial in itself, especially for countries in which income is distributed bimodally rather than normally (i.e. average GDP can be meaningless in a country with very rich versus very poor populations and no middle class). Third, DALYs can be a controversial measure, particularly in selecting a weighting factor associated with each illness or condition. Finally, cost-effectiveness is but one component of the feasibility of aflatoxin reduction strategies in LICs. Many other factors are important, including the technical feasibility of the intervention, which is described next.

6. Technical feasibility of interventions to control mycotoxins

The cost-effectiveness of a mycotoxin control strategy is not enough to ensure its successful adoption in the parts of the world where it is needed. More questions must be addressed. Does the strategy entail countervailing health or environmental risks? What would the delivery mechanism be, and would local infrastructures support that mechanism? Do governmental regulations inhibit or promote the intervention? Is the intervention culturally appropriate and easily adopted by the target population? If an intervention to reduce mycotoxins fails in any or all of these points, then it is not likely to be adopted on the large scale, no matter how cost effective it may be.

Fig. 8.3. Framework for assessing the technical feasibility of public health interventions. Source: Wu and Khlangwiset (2010b); reproduced with the permission of the publisher.



A conceptual framework has been developed for evaluating the technical complexity – and hence the feasibility – of public health interventions for LICs with limited resources (Gericke *et al.*, 2005). The framework has four relevant dimensions (see Fig. 8.3): intervention characteristics, delivery characteristics, government capacity, and usage characteristics. Each of these is discussed below.

6.1 Intervention characteristics

What aspects of the intervention itself make it more or less feasible for large-scale adoption? Gericke *et al.* (2005) pointed out that one of the most important aspects of the feasibility of an intervention, once it has been proven to have some level of efficacy in a field or clinical trial, is that it has the potential to be implemented on a much larger scale. This is crucial both spatially and temporally, to allow maximum effectiveness of the intervention in a target population. To achieve large-scale implementation, the following characteristics of the basic intervention would influence feasibility: (i) the stability of the product, including its usable lifetime and its risk of degradation or destruction; (ii) the degree to which the intervention can be standardized for production and sale; (iii) the safety profile of the intervention, in terms of both adverse health and environmental effects and risk associated with inappropriate use; and (iv) the ease of storage and transportation of the intervention.

In considering safety, it is important to recognize that implementing certain mycotoxin control interventions in LICs may result in health or environmental risks that would be less likely to occur in developed countries. Items to be considered include occupational hazards associated with producing or implementing the intervention, health risks to workers, quality control of production and application, immune status of the target population, local ecologies, and potential side-effects of dietary interventions (Wu and Khlangwiset, 2010b).

6.2 Delivery characteristics

How will a particular intervention be delivered to a target population? First, the target population must be identified, which can be a challenge in countries where food is grown in smallholdings. Communication of a need to those able to respond may pose difficulties. In addition, there are requirements for facilities, transportation, human resources, and communication (Gericke *et al*., 2005). Proper facilities are necessary to store and to administer the intervention and must be distributed widely enough within the target population so that most people have reasonably easy access to the intervention. Transportation may necessitate specific infrastructure (e.g. cold storage in vehicles for vaccines, and power to maintain cold temperatures). Transportation issues may also make a significant difference in cost if the intervention needs to be imported rather than produced locally. Human resources and communication are crucial when the public, or any subgroup thereof (such as farmers or food storage handlers), must be educated on proper use of the intervention and why it is important for health and economic reasons.

6.3 Government capacity

How would national or local governments either support or inhibit adoption of the intervention? Governmental financial support and other resource support, such as staff support and outreach activities, would be crucial for at least the start-up phase of an intervention. Moreover, governmental regulations can determine whether an intervention can be adopted broadly in a region. If, for example, regulations have been enacted against genetically modified organisms, certain food additives, or certain chemical or microbial agents, then particular interventions related to agriculture and food safety cannot be implemented on a scale that achieves widespread public health benefits (Wu and Khlangwiset, 2010b).

6.4 Usage characteristics

Generally, the more readily a target population can use or adopt an intervention, the more likely it is to be adopted with a frequency that actually makes a difference to public health (i.e. long-term use) and the more likely people are to adopt it (i.e. breadth of use). Gericke *et al*. (2005) identified three crucial dimensions of usage: (i) the ease of usage; (ii) the pre-existing demand for the intervention; and (iii) the risk of diminished effectiveness and efficiency because of illicit trade activities, such as counterfeit products.

Ease of usage includes the need for consumer information and education or training on how to use the mycotoxin control strategy effectively and safely. If no pre-existing demand exists for the intervention, adoption might be more difficult and would require more time. Finally, illicit trade activities can pose dangers, especially in the case of dietary interventions.

Understanding constraints on the feasibility of mycotoxin control interventions helps scientists and policymakers to think beyond efficacy, and even beyond material costs. For interventions to succeed in LICs, governments, scientists, international organizations, farmers, and consumers must work collaboratively to overcome challenges in implementing the intervention – challenges in terms of human resource needs; equipment, technology, and transportation requirements; financial aid; and user adoption constraints. Feasibility analyses can indicate research and development priorities to increase the likelihood of adopting interventions that can improve public health and market outcomes (Wu and Khlangwiset, 2010b).

7. Conclusions

For developed countries, it is relatively easy to estimate the cost to human society of mycotoxins as well as to assess the cost-effectiveness and technical feasibility of interventions to control them. This is because the costs of mycotoxins and the benefits of interventions are largely restricted to the marketplace; human health effects can largely be considered negligible. Moreover, in developed countries, the feasibility of mycotoxin control becomes an issue only if the intervention is extremely expensive, in which case another, less expensive intervention is usually available.

For LICs, including the impact of mycotoxins on human health results in much more complicated economic analyses. Health economic tools from the past two decades have improved the ability to place monetized values on human health effects. This, in turn, aids cost-effectiveness analysis because the monetary cost of interventions can be compared with the human health benefits of implementing the interventions. Evaluating the technical feasibility of interventions is still complex because the many impeding factors and external risks and benefits need to be considered.

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CHAPTER 8