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Total Diet Studies

Protecting the Public from Chemical Hazards in Food

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Summary

While food is one of life's greatest pleasures, toxic chemicals in food may pose risks to health. In addition, the lack or excess of certain nutrients, particularly micronutrients, can also pose risks to health. As these chemicals are usually not detectable by the senses, assessing the potential exposure to hazardous chemicals in the food supply must be considered an essential public health function of any responsible government. To protect public health, the World Health Organization has recognized that total diet studies are the most cost-effective method for assuring that chemicals in the diet are at safe levels. Unlike routine surveillance monitoring, total diet studies are designed to be health-oriented and population based.
This paper describes total diet studies and discusses their importance for health. The difference between total diet studies and routine surveillance monitoring, the trade and environment aspects and cost of total diet studies are presented. Finally, suggestions for promoting total diet studies in countries and conclusions are provided.

Keywords: total diet studies, food safety, toxicology, risk assessment, toxic chemicals in food, contaminants, health risks, public health

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Introduction

As early as 1863, Ludwig Feuerbach wrote *„Der Mensch ist, was er ißt"* [1], which conveys the notion that to be fit mentally and physically, one needs to eat good food. One of the first references to the parallel concept in English appeared in the 1940s when the nutritionist Victor Lindlahr authored his article entitled "You are what you eat" [2].

Of course today, these ideas are taken for granted because it is obvious that our health is directly linked to the quantity and quality of the food we eat. Over the past 100 years, nutrition has evolved into one of the most important health sciences, but controversies and debate continue. For example, the dietary recommendations that are offered to Americans concerning fat, cholesterol, and salt are likely to be revised based on critical analyses of supporting data [3, 4]. In a larger context, most observational studies involving the diet may not be replicable [5].

However, the basic questions always remain "What is beneficial in the human diet?", and its counterpart, "What is harmful in the diet?". Beginning in the 1960s, the discovery of contaminants and other toxins in the food supply has raised public health concerns and most societies have taken steps to address these risks.

Human exposure to toxic chemicals in food and nutritional imbalances are now known to be responsible for a range of human health problems and are implicated in many others. These problems include various cancers, kidney and liver dysfunction, hormonal imbalance, immune system suppression, musculoskeletal diseases, birth defects, premature births, impeded nervous and sensory system development, reproductive disorders, mental health problems, cardiovascular diseases, genitourinary diseases, old-age dementia, and learning disabilities. These maladies are prevalent in all countries, and, to some extent, they can be attributed to past and current exposures to chemicals in the foods we eat.

The World Health Organization (WHO) recognizes total diet studies as the most cost-effective method for assessing health risks posed by chemicals in food [6]. The Beijing Declaration on Food Safety, adopted by the 688 participants from 47 countries and regions, as well as 13 international organizations, urged all countries to establish total diet programs [7]. A survey carried out in 2015 by Health Canada in cooperation with WHO revealed that 53 countries have conducted total diet studies [8], and many more including Germany have since begun such studies.

What are total diet studies?

The primary purpose of total diet studies is to measure the average amount of a wide range of chemicals present in the diet that are ingested by various age/sex groups and other cohorts of interest living in a country.

> **A total diet study consists of purchasing foods that are representative of the diet at the retail level, processing them as for consumption, often combining the foods into food composites, homogenizing them, and analyzing them for toxic chemicals and certain nutrients.**

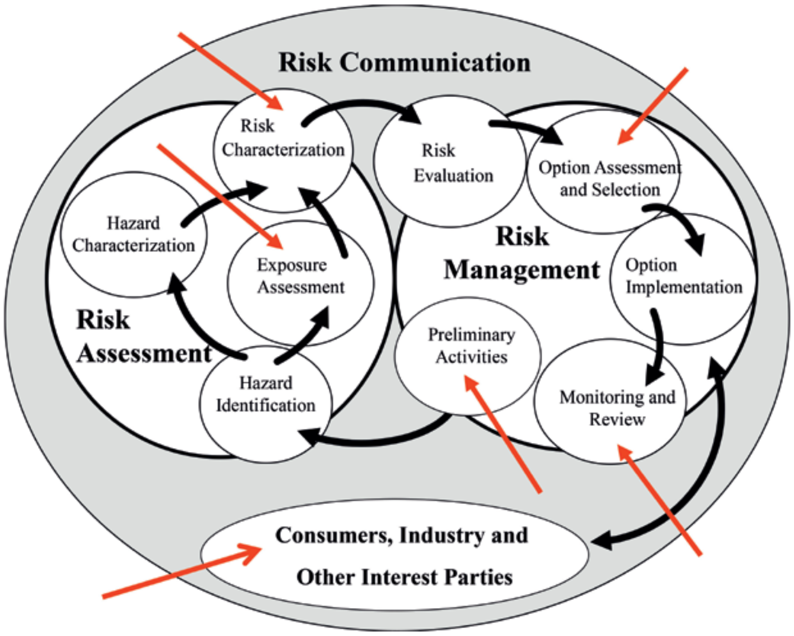

Figure 1: **Risk Analysis Paradigm** (adapted from [12])
Red arrows indicate activities where total diet studies can contribute

Exposures through drinking water and water used in cooking are typically included in the total diet study assessment. Dietary exposure from a single food is calculated by combining the concentration of the chemical in the food sample with the average amount of the corresponding food ingested by each population age/sex group. This is repeated for all the foods or food groups in the diet and the sum of these exposures is the total diet exposure [10]. The dietary exposure of the chemical can be compared with its corresponding national or international health-based guidance value to assess whether or not the specific chemical poses an unacceptable risk to health. Thus, a single total diet study can provide a scientific assessment of the safety of the diet from numerous potential hazards in the food supply. For most substances, the total diet approach is relevant [9].

Composite samples are essential features of any total diet studies because they reduce uncertainty in the results and saves on the cost of analysis. The composite samples can consist of various individual food items of the same type. For example, one composite apple sample is made up of different varieties of apples. Another type of composite sample mixes together several different foods that are usually from the same food group. For example, one composite citrus fruit sample might be made up of oranges, lemons, limes and grapefruit.
In countries where dietary exposure to chemical hazards in unknown, a basic total diet study is recommended as a useful screening tool for identifying priority hazards in the main food groups. The simpler protocol of such a study is easier and less expensive to implement than more refined total diet studies, but the information provided is limited. On the other hand, a refined total diet study provides details on specific foods that contribute significantly to exposure and on exposures of specific population subgroups, including extreme percentiles. A refined total diet study requires not only individual food consumption survey information, but also the analysis of many more food samples to correspond to the foods reported in the food consumption survey.

Why are total diet studies important?

It was the Swiss-German alchemist and physician Paracelsus who first recognized that all chemicals were poisonous and it was only a matter of dose that differentiated a remedy from a poison. He is famous for his dictum *„Die Dosis macht das Gift"* (The dose makes the poison) [11]. While Paracelsus is often called the Father of Toxicology, he should rather be considered the Father of

Total Diet Studies because of his emphasis on the importance of exposure (dose) in determining whether or not an adverse health effect will occur.
In the modern risk analysis paradigm (◆ Figure 1), the output of risk assessment (risk characterization) is a combination of knowledge of the toxic effects and potency of a chemical (hazard characterization) and the dietary exposure to that chemical. One of the key advantages of total diet studies is that the resulting dietary exposure is one of the most accurate and reliable estimate of chronic dietary exposure. This is because many of the conservative assumptions contained in other types of dietary exposure assessments are absent. A total diet study more realistically represents the levels of the compounds in the edible portion of the food at the point of consumption because it takes into account changes during food processing, preparation and storage.
Total diet studies can also contribute to risk management by identifying priorities for mandatory and/or voluntary measures. In option selection, total diet studies can be used to identify the food or foods that contribute the most to exposure. If measures are taken to reduce exposure, total diets studies can be used to assess the effectiveness of such measures. Total diet studies are also important for risk communication because they are easy to understand by policy- and decision-makers as well as the food industry and consumers.

When the exposure to various cohorts has been calculated by total diet studies, the results are directly compared with appropriate health-based guidance values [13]. For exposure to food additives and residues of pesticides and veterinary drugs, the comparator is the Acceptable Daily Intake (ADI) which is the amount on a kilogram body weight basis that can be safely consumed every day over a lifetime. For contaminants and toxins, the comparator is the Provisional Tolerable Intake (PTI), which is the amount of a contaminant or toxins that may be consumed (usually weekly) with no appreciable risk to health. For chemicals that have no threshold of toxicity, such as certain carcinogens (acrylamide) and neurotoxins (lead), total diet studies are also essential for calculating the Margin of Exposure (MOE) in which the Benchmark Dose (BMD) at the Lower Confidence Limit serves as the hazard characterization component.
In addition to contaminants, most total diet studies include the assessment of the long-term intake of selected nutrients, especially micronutrients. Because of the nature of nutrients, defaults are adjusted to provide estimates of intake for low percentile consumers for nutrient deficiencies (Recommended Daily Intake [RDI]) as well as estimates of exposure for high percentile consumers for nutrient toxicity (Maximum Daily Intake or Tolerable Upper Intake Level [UL]).

Some countries conduct total diet studies on a regular basis, and consequently are in position to identify trends in levels of chemicals and nutrients, which allows them to anticipate potential problems before they occur.

For example, a decrease in iodine intakes was noted in total diet studies performed in New Zealand. This resulted in a risk management decision to fortify food with iodine to correct potential nutritional deficiencies [14]. The decline was later determined to be due to a change by the dairy industry away from iodophors[1] towards using other sanitizing agents.
Total diet study information often provides direct evidence of the contribution of different food items or food groups to the dietary exposure of chemicals. This information can be used to establish priorities of surveillance monitoring and assures that limited government resources are used for the greatest health benefit. For example, numerous total diet studies had shown that the overwhelming contributor to the dietary intake of methylmercury is fish. As a result, health and trade surveillance resources for methylmercury have been largely directed toward identifying those fish with the highest concentrations and to educate the public to limit their consumption of those types of fish.

Total diet studies, by their design, provide background concentrations of the chemicals in the foods analyzed. This baseline information is critical for quickly identifying contaminated foods when food safety emergencies arise. For example, during the Belgium dioxin incident in 1999, the availability of background concentrations of polychlorinated dioxins, dibenzofurans and biphenyls in Canadian foods ensured that foods imported into Canada from Belgium did not contain high levels of these chemicals.
Finally, total diet samples can be used to facilitate the investigation of new hazards or nutrients in the food supply. For example, total diet study samples that were stored frozen were used to assess past exposure to acrylamide, a new hazard that was discovered in cooked starchy food in 2002. Another example is: understanding the possible role of trace amounts of lithium in neurodevelopment. Data from total diet studies would help define low and high percentile exposures.

[1] Iodophors are preparations that contain iodine complexed with a solubilizing agent.

How do total diet studies differ from other surveillance programs?

In most countries, food safety legislation has placed the primary responsibility for ensuring the safety of food on commercial food enterprises that produce, process, distribute or prepare food for the consumer. Usually, governments will establish regulatory limits based on Good Agricultural Practices (GAP) and/or Good Manufacturing Practices (GMP). However, these limits are only indirectly linked to the actual risk posed by a chemical. Some countries, such as Germany, have used randomized surveillance data in conjunction with processing factors to estimate consumer exposure to certain chemicals, such as pesticide residues and heavy metals. However, in 2012 Germany embarked on its first total diet study [15] after concluding that the two approaches were complementary with both having advantages and disadvantages [16]. As surveillance programs are intended to ensure compliance with Good Agricultural/Good Manufacturing Practice (GAP/GMP), total diet studies differ in several aspects, namely:

- In most surveillance programs, a large number of targeted samples are analyzed to provide a basis for possible regulatory action. In total diet studies, the focus is on exposure to chemicals from across the whole diet, so that a wide range of different foods are randomly sampled and analyzed. It should be noted, however, that the variability of certain chemicals makes them more suitable for other exposure assessment methods than total diet studies.
- In a total diet study, foods are analyzed after being prepared as usual for consumption, such as washing, peeling and cooking. While some chemicals may be reduced, e.g. pesticide residues, and certain nutrients, others chemicals may be formed, e.g. acrylamide, and polycyclic aromatic hydrocarbons. Thus, the chemicals in the foods analyzed in a total diet study are more closely representative of what is actually ingested by the consumer rather than what is present in raw agricultural commodities.
- Surveillance for trade purposes is conducted to assess whether a commodity meets regulatory requirements. For pesticides, the whole raw commodity (including the husk and other inedible portions) is analyzed for compliance with national Maximum Residue Limits (MRLs), which usually are in the parts per million ranges. Analytical methods used to monitor MRLs commonly yield results that are below the limit of quantification. In contrast, methods with very low sensitivities are used in total diet studies so that actual levels can be measured and exposures calculated. For this reason, more expensive analytical equipment, such as high-resolution mass spectrometers, are often required.
- In most surveillance programs, individual foods are analyzed separately. In the total diet study, individual food items from different sources (brands, regions, and seasons) may be combined into composite food samples, or if resources are limited, individual food items are combined into food group composites.
- Unlike most surveillance samples, total diet samples are usually analyzed for many different chemicals to save sampling and analytical costs. For example, fish samples are typically analyzed for methylmercury, a range of fat-soluble chemicals, such as DDT (dichlorodiphenyltrichloroethane), dioxins and polychlorinated biphenyls, and omega-3-fatty acids.
- Total diet studies are used to assess long-term, i.e. chronic, exposure to chemicals in the diet. In contrast, surveillance monitoring is the best tool for identifying chemicals in food that may pose an acute risk to health. Exposure from a single highly contaminated commodity unit, e.g. one apple,

The costs of total diet studies depend on the number of chemicals and food samples in the study.

may exceed the Acute Reference Dose (ARfD). In cases where high levels are encountered, immediate action by risk managers may be necessary to protect public health.

What are the trade and environment aspects of total diet studies?

While unsafe levels of chemicals in food may cause serious health problems, they also pose threats to trade and environment. Food production, processing, and distribution are important economic activities for all countries and any disruption caused by toxic chemicals in food can have enormous impact on a country and on consumer confidence in the food supply. It is estimated that the global economic and trade burden from such contamination in food totals many billions of dollars annually [17]. This has become a critical issue not only because global trade in food now exceeds US$ 1 trillion a year, but also because such trade is highly complex, which makes the tracing of contaminated food from the importing country back to the producer in the exporting country a daunting task [18]. For developing countries, the foreign exchange earned from food exports is often essential for their stability and economic development.

Food exports may be threatened by unjustified health and safety requirements, which can serve as non-tariff trade barriers. Beginning in 1995, the World Trade Organization (WTO) under its Agreement on the Application of Sanitary and Phytosanitary Measures has since required its member states to base their health and safety requirements for food on sound scientific risk assessments [19]. Since that time, governments have used total diet study data to support their positions in trade disputes before the WTO.

For example, the Czech Republic used the results of its total diet study to support safety measures taken to halt the importation of chicken with high levels of arsenic. The exporting country complained to the WTO and sought damages of US$ 15 million, but the Czech Republic risk assessment argument prevailed.

Total diet studies are now routinely included in the safety evaluation of chemicals performed by international risk assessment bodies, such as the Joint FAO/WHO Expert Committee on Food Additives [20].

Such evaluations are used by the Codex Alimentarius Commission in establishing limits for contaminants and toxins in food which are recognized by the WTO as representing the international consensus on harmonized health and safety requirements [21].

In addition, total diet study results can be indicators of environmental contamination by chemicals. For example, persistent organic pollutants, the so-called POPs, have been the subject of an international treaty to eliminate or reduce their emission into the environment [22]. Being highly fat soluble, POPs concentrate in the food chain and as a result, human exposure is almost exclusively through food. Human milk has been selected as a media to monitor the effectiveness of the treaty in achieving its goals. Therefore, it is increasingly important to assess the dietary exposure to POPs as well as the other environmental pollutants that may migrate to food. The WHO/United Nations Environment Programme Global Environment Monitoring System/Food Contamination Monitoring and Assessment Programme (GEMS/Food) has encouraged all countries, and in particular developing countries, to undertake total diet studies as a matter of public health importance, while recognizing the significance of total diet studies to environmental risk management. Global climate change also has implications for the assessment and management of risks from chemicals in food. Higher levels of contaminants, such as mycotoxins, as well as altered pathways from the natural environment are predicted to increase exposures in certain parts of the world. In addition, dietary changes, psychosocial stress and stressors such as high temperatures, are likely to increase the vulnerability of humans to chemicals [23].

What is the cost of total diet studies?

The assessment of the safety of the food supply is an essential responsibility of governments. Given this responsibility, the first question is often, "Can a government afford to conduct a total diet study?". Perhaps the more appropriate question to ask is, "Can a government afford not to?".

In Canada, a study of the economic impact on Parkinson's disease, hypothyroidism, diabetes mellitus, and nervous system and IQ effects suggested that the current negative impact of previous and current human exposure to toxic chemicals, including nutritional imbalances, likely exceeds US$ 800 for every man, woman, and child each year [24]. While methods that estimate the health burden of environmental contaminants are still being refined, lead exposure alone is estimated to comprise almost 1 % of the total global burden of disease, due to mental retardation and cardiovascular diseases [25]. As noted above, total diet studies are now important for trade in food and are accepted as scientific evidence by WTO dispute panels. Repeated incidents of food contamination can adversely affect consumer confidence not only in the food supply, but also in the competence of government. In short, total diet studies have health, economic, environmental, social and political benefits.

But the question of cost is open ended because it depends on the number of chemicals and number of food samples in the study as well as other factors. While some total diet studies have modest budgets, the usefulness of the results is limited, particularly for risk management purposes. However, these studies are valuable in developing countries where little or nothing is known about chemicals in the food supply. On the other hand, more comprehensive total diet studies can provide greater assurance that the food supply does not pose unacceptable risk to health from particular chemicals and foods. Such data offer the possibility to assess special subgroups of the population as well as newly discovered threats, such as acrylamide. While the cost of such comprehensive studies may exceed US$ millions, the cost-effectiveness and value of such studies should be seen in the context of the many developed countries who have found them to be indispensable. For example, Australia has carried out its 24th total diet study [26] and the United States of America has continuously conducted total diet studies for over 50 years [27].
A major expense associated with conducting a total diet study is often related to food consumption data. If these data are not available in a country, countries can use one of the GEMS/Food Consumption Cluster Diets [28] to estimate the per capita consumption of foods in their country. National per capita food production statistics (Food Balance Sheets) can also be used. However, more detailed individual food consumption data are preferred which allows specific exposure estimates for the different age/sex groups as well as population groups of special interest, such as vegetarians. In this regard, total diet studies have found that children are most often the most exposed group on a kilogram body weight basis. It has also been found that food coding differences, and total diet food lists not directly derived from food consumption data, may result in insufficient coverage of some subgroups [29].
Many countries use the 24-hour recall method on two non-consecutive days, which is supplemented by a food frequency questionnaire. The cost of such a food consumption survey will vary depending on the local cost of labor. However, the cost should be averaged over a number of years, as dietary patterns usually change slowly. The cost of the survey may also be shared with other stakeholders with an interest in such data, including the agriculture sector and the food industry.
Another major cost of a total diet study is the expense of analyzing samples at low limits of quantification. For some chemicals, new and more sophisticated instruments may need to be purchased and staff trained in their use. Another option is to have the analysis of certain chemicals, such as dioxins, performed by a contract laboratory. In Australia, all of their total diet samples are analyzed on a contract basis. The cost of total diet studies can also be reduced by limiting the size of the food list, reducing the number of samples, and restricting the range of chemicals to be analyzed. If a total diet study indicates that exposure to a chemical is well within its safe limits, then the next total diet study may omit this chemical. Finally, total diet studies can be run over a number of years to spread out the costs.

How can total diet studies be promoted in countries?

Government policy- and decision-makers need to be aware of the importance of total diet studies for assuring the safety of the food supply. In this regard, realistic risk assessments simply cannot be performed without an assessment of exposure.

WHO has recognized total diet studies as the most cost-effective means for governments to protect public health from chemicals in the food supply.

As a first step, the food safety and applied nutrition communities in countries need to mobilize support for total diet studies. This includes stakeholders in government, academia, and industry as well as consumer groups. For the food industry, total diet studies provide a sound scientific basis for the establishment of standards and for the orderly development of the food trade. Consumers and their advocacy groups should recognize that total diet studies are essential public health measures that serve to safeguard the food supply from potentially hazardous chemicals and to ensure adequate levels of nutrients in the diet.
Governments, particularly in developing countries, need to support the development of human and infrastructure capacities to undertake total diet studies in their countries. In order to promote the availability of competent people with the technical and logistical skills to conduct total diet studies, workshops and training courses at regional and international levels should be held periodically. Practical experience can also be gained by placement of personnel in institutions already conducting total diet studies. A network of total diet practitioners, including WHO Collaborating Centers for Food Contamination Monitoring, is maintained by WHO to promote collaboration and cooperation.
Once a country has completed its first total diet study, experience has shown that support for further total diet studies are almost always assured. For example, China has completed its 4th total diet study. The ability of policy- and decision-makers and consumers to understand total diet studies and their significance for human health, de-

velopment and food industry, has contributed to this continuity. Because they are based on a transparent internationally-accepted scientific method, total diet studies are increasingly recognized as the key to providing essential assurance that people's diets are safe and nutritionally adequate.
General information on food contamination monitoring, including total diet studies, is available in a number of publications [30, 31]. In addition, EFSA in cooperation with WHO and FAO has developed a harmonized protocol for European Union countries that may be useful to consult [32].

Conclusion

Total diet studies have demonstrated their cost-effectiveness and value over the past several decades and more countries, including those of the European Union, are adopting them to assess consumer exposure to contaminants, nutrients and other chemicals through the foods in their diets. Governments and international organizations should support total diet studies to ensure that the food supply is safe and wholesome. Total diet studies can provide essential information that is needed to assess, manage and communicate risks posed by chemicals in the food supply.

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Conflict of Interest
The author declares no conflict of interest according to the guidelines of the International Committee of Medical Journal Editors.

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