

UNCERTAINTY MODELING APPROACHES IN HEALTH RISK ASSESSMENT: A REVIEW

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Abstract

Risk assessment is an important aid in decision making process while uncertainty is an unavoidable component of risk assessment. Uncertainty may arise due to inherent variability, natural stochasticity, lack of knowledge, measure uncertainty, small sample size etc. In this article, we discuss different process of risk assessment, sources and nature of uncertainty, the important aspect of uncertainty encountered in risk assessment, different ways of uncertainty modeling and uncertainty propagation.

Keywords: Uncertainty, Risk assessment, Uncertainty Modeling, Uncertainty propagation.

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1. Introduction

Throughout our life each and every one of us has to make some kind of decisions often under uncertain environment. For example (Lindley D. V., 2006), ‘*it will rain tomorrow*’ this statement is uncertain because it will be confirmed after tomorrow has passed; ‘*the defendant is guilty*’ this is uncertainty in a court of law, and ‘‘guilt’’ here refers to what

truly happened, not to the subsequent judgment of the court. Here it will usually remain forever uncertain, though the primary function of the court is, by the provision of evidence, to remove much of that uncertainty with the court's decision; *'Shares in companies will rise over the next month'* the buying and selling of stocks and shares are uncertain activities because we do not know whether they will rise or fall in value; *'Inflation next year will be 3.7%'* statements of this type are often called either predictions or forecasts. In general, predictions or forecasts should be avoided, because they have an air of spurious precision, and replaced by claims of the form "inflation next year will most likely be between 3.1% and 4.3%," though even here "most likely" is imprecise; *'The proportion of HIV cases in the population currently exceeds 10%'* here the uncertainty arising partly because not every member of the population will have been tested; *'There will be a serious nuclear accident in India next year'* the uncertainty here is generally admitted and discussed. Two important features are the extreme seriousness of the statement if true, and the very small chance that it will be true. The balance between these two aspects is not easy to resolve and is of very real concern in a society where people are more comfortable with small risks of moderate chance like road accidents, than with accidents of a nuclear type; *'The planting of genetically modified (GM) crops will damage the environment'* most people consider this statement uncertain, while others are so sure it is true that they are prepared to take action to destroy any GM crops that are planted. Indeed, some will go so far as to destroy those grown to provide information about them and thereby remove, or at least reduce, the uncertainty. Others recognize the value of GM rice in improving the diets of some people in the third world. Issues concerning genetic modification are complex because they can affect both our health and the environment and also have economic consequences.

Uncertainty is everywhere, so it is interesting to see that it is only in the twentieth century that the concept has been systematically studied and, as a result, better understood. Special types of uncertainty, like those arising in gambling, had been investigated earlier but the understanding of the broad notion, applicable to everyday life, is essentially a modern phenomenon. Because uncertainty is everywhere and affects everyone, a proper appreciation of it is vital for all persons. Here, in section 2 we study on risk assessment

and different risk assessment process, section 3 deals with different sources and different nature of uncertainty. Section 4 explores the important aspect of uncertainty encountered in risk assessment. Section 5 summarizes different ways of uncertainty modeling and uncertainty propagation.

2. Risk Assessment Process

According to United States Environmental Protection Agency, (**USEPA**) risk is the chance of harmful effects to human health or to ecological systems resulting from exposure to an environmental stressor. A stressor is any physical, chemical, or biological entity that can induce an adverse response. Stressors may adversely affect specific natural resources or entire ecosystems, including plants and animals, as well as the environment with which they interact.

Environmental Protection Agency (EPA) uses risk assessment to characterize the nature and magnitude of health risks to humans (e.g., residents, workers, recreational visitors) and ecological receptors (e.g., birds, fish, wildlife) from chemical/radiological contaminants and other stressors, which may be present in the environment. In risk assessment, risk consists of both the probability and impact of disease. So risk reduction can be achieved either by reducing the probability of disease or by reducing its severity.

Health-risk assessment is a quantitative evaluation of information on potential health hazards from exposure to various agents and involves four inter-related steps, namely, Hazard identification; Dose response assessment; Exposure assessment, and Risk characterization.

2.1 Hazard Identification

Anything (e.g. condition, situation, practice, behaviour) that has the potential to cause harm, including injury, disease, death, environmental or property and equipment damage is known as hazard. The hazard identification step involves the determination of the adverse effects which may be associated with a biological, chemical, or physical agent has an inherent capacity to cause (Kushwaha, 2009). It involves gathering and evaluating data on the types of health effects or disease that may be produced by a toxic pollutant and exposure conditions under which environmental damage, injury or disease will be produced.

It is the likelihood of harm due to exposure which distinguishes risk from hazard. The observed effects in humans may include a range of effects; reversible to irreversible such as increase body weight, gain to congenital birth defects, neurological disorder or cancer. Ecological hazards include structural and functional effects.

In hazard identification, an association between dose/risk and the presents of pollutants in environmental or food chain is documented. Hazard identification involves data collection regarding the type of industries in the area and the process involved in it. It may also involve characterization of the behaviour of a contaminant within the body and its interaction with organs, cells or genetic material.

2.2 Dose Response Assessment

Dose-response assessment describes the relationship between the dose of the contaminant and the incidence of adverse health effects in the exposure population. Typically, as the dose increases, the measured response also increases (USEPA). At low doses there may be no response. At some level of dose the responses begin to occur in a small fraction of the study population or at a low probability rate. Both the dose at which response begin to appear and the rate at which it increases given increasing dose can be variable between different pollutants, individuals, exposure routes, etc.

Dose-response assessment is a two-step process. The first step is an assessment of all data that are available or can be gathered through experiments, in order to document the dose-response relationship(s) over the range of observed doses (i.e, the doses that are reported in the data collected). However, frequently this range of observation may not include sufficient data to identify a dose where the adverse effect is not observed (i.e., the dose that is low enough to prevent the effect) in the human population. The second step consists of extrapolation to estimate the risk (probably of adverse effect) beyond the lower range of available observed data in order to make inferences about the critical region where the dose level begins to cause the adverse effect in the human population.

2.3 Exposure Assessment

USEPA defines exposure as 'contact between an agent and the visible exterior of a person (e.g. skin and openings into the body)'. Exposure assessment is the process of measuring or estimating the magnitude, frequency, and duration of human exposure to an agent in the environment, or estimating future exposures for an agent that has not yet been released. It involves determining the emissions, pathways and rate of movement

of a substance and its transformations or degradation in order to obtain concentrations or doses to which human population or environmental components are or may be exposed. Exposure assessment involves describing the nature and size of the population or compartments exposed to a substance, and the magnitude and the duration of their exposure. The evaluation may concern past, or current exposure, or anticipated future exposure.

It is important that the exposure assessment takes into account different levels of exposure that may be experienced by different groups. Exposed populations will include the general population, those most exposed and those most susceptible. The most exposed will be those who for some reason are likely to be exposed to higher levels of the hazard than the general population. This may include workers on the project, those living near known sources of the hazard and those who may be exposed to other sources of the hazard. The possibility of multiple exposure routes may arise from exposure to a combination of air, water, soil and food sources, from occupational sources and even from lifestyle factors such as diet and tobacco smoking. The level of exposure is also influenced by the environmental persistence of a substance. The longer a substance persists in the environment, the longer it persists as a potential source of exposure.

Any model used to represent exposure should include several pieces of information (FAO/WHO Report, 1995):

- the level of an agent measured in a commodity or the levels measured in soil, plants, or animals that supply this commodity;
- the depletion/concentration ratio which defines changes in the level of an agent as a result of processing, preparation, and dilution;
- the frequency and magnitude of human intake of a commodity;
- the duration of contact or the fraction of a lifetime during which an individual is exposed to a commodity; and,
- the averaging time for the type of health effects under consideration to be clinically detectable.

2.4 Risk Characterization

Risk characterization involves integrating the information gathered in the previous steps to estimate the risk to a population, or in some case, to a particular type of consumer (Kushwaha, 2009). It summarizes and combines outputs of the exposure and toxicity assessments to characterize risk, both in quantitative expressions and qualitative statements. A risk characterization conveys the risk assessor's judgment as to the nature and presence or absence of risks, along with information about how the risk was assessed, where assumptions and uncertainties still exist, and where policy choices will need to be made (USEPA). Risk characterization takes place in both human health risk assessments and ecological risk assessments.

This final step brings together all the information from the previous steps to describe the risks to different groups. It will make conclusions by weighing up all the information, taking into consideration the quality of the data, the amount of evidence and levels of uncertainty, to prepare an overall picture of risk.

In practice, each component of the risk assessment (e.g. hazard assessment, dose-response assessment, exposure assessment) has an individual risk characterization written to carry forward the key findings, assumptions, limitations, and uncertainties. The set of these individual risk characterizations provide the information basis to write an integrative risk characterization analysis.

The overall risk characterization thus consists of the individual risk characterizations plus an integrative analysis.

3. Sources of Uncertainty and Nature of Uncertainty

3.1 Sources of uncertainty

There are a number of distinct sources of uncertainty and these come under the heading of model or structural uncertainty and parameter uncertainty. Sources of uncertainty are discussed in USEPA Documents. A few concepts are summarized in Christopher et al. (2002).

The structure of mathematical models employed to represent scenarios and phenomena of interest is often a key source of uncertainty, due to the fact that models are only a simplified representation of real world problem and problem boundary encompassed by a model may be incomplete or incorrect. Significant approximations are often an inherent

part of the assumptions upon which a model is built. Competing models may be available based on different scientific or technical assumptions. Furthermore, the limited spatial or temporal resolution of many models is also a type of approximation that introduces uncertainty into models results. Uncertainties arising out of the above situations are usually referred as model uncertainty.

On the other hand, the inputs of a model are hardly accurately known. Either due to lack of data or randomness, uncertainty exists in the inputs. This is called parameter uncertainty. This is often dealt with by assigning probability distribution or possibility distribution to the parameters, representing the analyst's knowledge about them.

Granger et al.(1992) have identified a number of different types of quantities used in models. These include empirical data, defined constants, decision variables, value parameters, model domain parameters etc. Of the different types of quantities used in models, only empirical quantities are unambiguously subject to uncertainty. The other types of parameters represent quantities which are almost always more properly treated as point estimates reflecting convention, the explicit preference of a decision maker, or a discrete quantity by its nature (e.g., grid size). Uncertainty in empirical quantities may be for the following reasons:

- Random Error and Statistical Variation: This type of uncertainty is associated with imperfection in measurement techniques.
- Systematic Error: The mean value of a measured quantity may not converge to the 'true' mean value because of biases in measurements and procedures.
- Variability: Some quantities are variable over time, space or some population of individuals rather than for any individual event or component.
- Inherent Randomness or Unpredictability: Some quantities may be irreducibly random even in principle, the most general example being Heisenberg's Uncertainty principle. However, this concept is often applied to quantities that are in principle measurable precisely but as practical matter (e.g., due to cost) are not.
- Lack of Empirical Basis: lack of experience about or knowledge of a process or system is a source of uncertainty. This type of uncertainty cannot be treated

statistically because it requires predictions about something that has yet to be built, tested or measured.

Uncertainty may also occur due to missing or incomplete information to fully define exposure. It originates from the fact that not all contributions to risk are addressed in risk analysis models. For example, it will not be feasible to overcome all possible initiating events in a risk analysis.

Knowing the source of uncertainty in the analysis plays an important role in the overall handling of uncertainty. First of all, different kinds of uncertainty call for different methods of treatment. Another aspect is the possibility of reducing uncertainty. If one knows why there are uncertainties and what kinds of uncertainty are involved, one has a better chance of finding the right methods for reducing them.

3.2 Nature of Uncertainty

Comprehensive taxonomy of uncertainty has been offered by several authors. At an even more fundamental level, two major group of uncertainty are recognized in most of the literature (Vose, 2002). They are defined as follows:

3.2.1 Aleatory Uncertainty

It arises from inherent variability, natural stochasticity, environmental or structural variation across space or through time, manufacturing or genetic heterogeneity among components or individuals and variety of other sources of randomness. It is also called randomness, variability, stochastic uncertainty, objective uncertainty, dissonance, irreducible uncertainty. It may be tied to variations in physical and biological process and cannot be reduced with additional research or information although it may be known with greater certainty. The data like demographic data on food intake, water intake which depends on the height, body weight, socio-economic status life style and inherent variation in dietary habits faces this type of uncertainty. Variability usually has different levels. For example, daily consumption rate of meat/fish vary from person to person, vary between consecutive days, vary between seasons, vary between countries etc. Similarly height, hair colour, food consumption, breathing rate etc vary. This type of uncertainty cannot be reduced by any means. However the uncertainty can be reported

with high level of confidence and can be modelled using various statistical test and tools.

3.2.2 Epistemic Uncertainty

It arises from incompleteness of knowledge about the world. Sources of epistemic uncertainty include measure uncertainty, small sample size, detection limit and data censoring, ignorance about the details of the physical mechanisms and processes involved and other imperfections in scientific understanding. For example the length of a crack in a pipe line in a plant is not measured precisely due to its inaccessibility. It is clear that crack length has a fixed value but not measured due to practical constraints. When dealing with these kinds of uncertainty one often has to rely on experts and their subjective judgements. So it is also known as subjective uncertainty. Incertitude, ignorance, non-specificity, reducible uncertainty are other terms used for this uncertainty. Unlike variability, epistemic uncertainty can be reduced by further study such as additional experimentation, collection of additional bit of data etc. For example, model uncertainty is an example of epistemic uncertainty which can be reduced with more understanding of the physical phenomena. Parameter uncertainty in a random variable also falls in epistemic uncertainty which is not measured precisely due to scarcity or lack of data. (Ferson et al., 2004; Stephen, 1996).

Keeping epistemic uncertainty and aleatory uncertainty separate is very important from a mathematical viewpoint. Mixing both the uncertainties will make it difficult to ascertain how much of the total uncertainty comes from epistemic and aleatory uncertainties. If one knows that a large part of the total uncertainty is due to epistemic uncertainty then by collecting further information, and thereby reducing total uncertainty, one would be able to improve the estimate of the future, on the other hand, total uncertainty is due to variability, then the only way to reduce the total uncertainty would be to change the physical system.

4. Uncertainty in Risk Assessment Process

At the fundamental level risk can be explained as a structured process for identifying and analysing the most important contributions to the overall risk that an establishment or activity poses to people, the environment or some other vulnerable part of society (Kushwaha, 2009). Every step of the risk assessment process is tainted with uncertainty. Uncertainty in risk estimation may arise from many different sources such as measure or estimates of parameters, environmental monitoring of data, natural variability in individual response, variability in environmental concentration in toxicants or radionuclides over time and space and unverifiable assumptions in dose response models or extrapolations of results of these models. In risk assessment available information are collected and utilize to make decisions regarding the associated with a particular stressors such as a chemical, biological or physical (radionuclides) agent. Uncertainty analysis is a part of risk assessment that focuses on uncertainties in the assessment. Important components of uncertainty analysis include qualitative analysis and identifying the uncertainties, quantitative analysis of the effects of the uncertainties on the decision process and communication of the uncertainty.

4.1 Uncertainty in Hazard Identification

Three issues are considered potentially significant that contribute to uncertainty and variability in hazard identification (FAO/WHO Report, 1995). First, is the misclassification of an agent - either identification of an agent as a hazard when it is not or the reverse. Second, is the issue of the reliability of the screening method both for appropriately identifying a hazard and the reliability of the assays to give the same result each time the assay is performed. Third, is the issue of extrapolation because all screening methods are used to extrapolate the information provided by the test to predict human hazards. Epidemiological studies are used to predict the impact of exposures on human populations in the future. As an example, in epidemiological studies, the extent of the extrapolation needed to predict health hazards for future human populations is generally minimal; whereas, other assays have substantially greater need for extrapolation to produce predictions of potential adverse health effects for human populations.

4.2 Uncertainty in Dose response Assessment

Although uncertainty is common in every step of the risk assessment process, dose-response assessment by far contributes the most uncertainty (Toxprobe Inc., Toronto). This is in part because of the frequent need to extrapolate from animal data to humans. It is also always necessary to estimate risk at low environmental levels from known risk at high occupational exposure levels or from animal data obtained at high exposure levels. These extrapolations are difficult to undertake and are potential sources for large errors. This is why the estimates of potency prepared by different agencies for a given toxicant often vary substantially even if they have used the same sets of data to derive their estimates. It is therefore reasonable to assume that the uncertainty of the RfD (Reference Dose) or RSD (Risk Specific Dose) of a typical chemical ranges from ten- to a hundred-fold.

4.3 Uncertainty in Exposure Assessment

Exposure assessment is associated with less uncertainty (Toxprobe Inc., Toronto). The sources of uncertainty include environmental levels at the points of exposure and the lifestyle/activity characteristics of potentially exposed populations. In general, however, the range of uncertainty is much less than ten-fold. The uncertainty associated with exposure assessment is to a large extent captured in the range of exposures estimated for different exposure scenarios for different subpopulations.

Defining exposure pathways is an important component of the exposure assessment (FAO/WHO Report, 1995). An exposure pathway is the course that a biological, chemical, or physical (radionuclides) agent takes from a known source to an exposed individual. In the case of agents in food, concentrations of chemicals and/or organisms (microbes, parasites, etc.) can change between what is measured in soil, plants, animals and raw food and what is ingested by an individual. In the case of chemicals, there can be some increases of contaminant concentration due to process (i.e. distillation), but more likely the storage, processing and preparation of the food product will result in a reduction of contaminant concentration. For organisms, there might be significant

increases of microbe or contaminant concentration due to replication under favourable environmental conditions. Thus, significant uncertainties might be expected in the ratio of the concentration of a bacterial agent in food at the time of consumption to the concentration measured in raw foods or measured in animals, plants, or soil.

4.4 Uncertainty in Risk Characterization

Once hazard characterization and exposure information have been collected, risk characterization is carried out by constructing a model for the distribution of individual or population risk (FAO/WHO Report, 1995). This is done by summing the effect of overall exposure routes. Because of the uncertainties and variability involved in its constituent steps, the overall process of risk characterization might involve potentially large uncertainties.

An important final step in the risk characterization process is the characterization of uncertainties. In order to directly characterize uncertainties in risk assessments, it is necessary to take a tiered approach to uncertainty analysis. Three tiers can be used. First, the variance of all input values should be clearly stated and the impact of these variances on the final estimates of risk assessed. Second, a sensitivity analysis should be used to assess how model predictions are impacted by model reliability and data precision. The goal of a sensitivity analysis is to rank the input parameters on the basis of their contribution to variance in the output. Finally, variance propagation methods should be used to carefully map how the overall precision of risk estimates is tied to the variability and uncertainty associated with the models, inputs, and scenarios.

5 Various Approaches of Modelling Uncertainty

Based on the nature and availability of data uncertainty can be modelled using any of the following methods:

- Interval Representation
- Probability Representation
- Fuzzy Set Theory
- Probability Bounds Analysis

- Two –D Monte Carlo Analysis
- Evidence Theory

5.1 Interval representation

When only information available regarding a variable is the maximum and minimum value it can attain then the obvious choice for representing such a variable is an interval where the left end point is the minimum value and the right end point is the maximum value. Representing possible value in interval is empirical way of representing uncertainty in measured values (Moore, 1979). Interval mathematics is used to address data uncertainty that arises (a) due to imprecise measurements, and (b) due to the existence of several alternative methods, techniques, or theories to estimate model parameters. Interval analysis can be used to propagate these uncertain values through calculations. The rules of interval arithmetic permit us to compute rigorous bounds on all the elementary mathematical operations (Moore, 1979). For example interval analysis may be used to represent interval estimates of likelihood and impact resulting in an overall interval estimate of risk using the product rule for interval numbers (Kumar, 2008). The basics of interval mathematics are fairly obvious, although still it is an active area of research in computer science because of its profound implications for handling round-off error (Alefeld, 1983). Although it's vastly simpler than probabilistic analysis, it can be a little trickier to use in complex modelling scenarios (Moore, 1979).

5.2 Probability Representation

The most common approach used to represent uncertainty regarding a quantity which is random in nature is to use probabilistic distribution. Probabilistic analysis is the most widely used method for characterizing uncertainty in physical systems, especially when estimates of the probability distributions of uncertain parameters are available. This approach can describe uncertainty arising from stochastic disturbances, variability conditions, and risk considerations. Uncertainty is characterised by the probability associated with events. The probability of an event can be interpreted in terms of frequency of occurrence which can be defined as the ratio of the number of favourable events to the total number of events. In this approach, the uncertainties associated with

model inputs are described by probability distributions, and the objective is to estimate the output probability distributions (Kumar, 2008).

5.3 Fuzzy Set Theory

Fuzzy set theory replaces the two-valued set-membership function with a real valued function; that is to say, membership is treated as a possibility or as a degree of truthfulness. Likewise, one assigns a real value to assertions as an indication of their degree of truthfulness. Membership functions define the degree of participation of an observable element in the set. Fuzzy numbers are the fuzzy set defined on the set of real numbers and have special significance. They represent the intuitive concept of *approximate numbers*, such as “*around, close to, approximately etc*”. The fuzzy set that contains all fuzzy numbers with a membership of $\alpha \in [0,1]$ and above is called the α -cut of the membership function (Abebe et al., 2000). So the α -cut represents the degree of sensitivity of the system to the behaviour under observation. Fuzzy α -cut technique is based on the extension principle (Zadeh, 1965), which implies that functional relationships can be extended to involve fuzzy arguments. It can be used to map the dependent variable as a fuzzy set. In simple arithmetic operations, this principle can be analytically used. However, in most practical modeling applications involving complex structural relationships (e.g. partial differential equations), analytical applications of the extension principle is difficult. Therefore, interval arithmetic can be used to carry out the analysis (Abebe et al., 2000). Arithmetic on fuzzy numbers can be defined in terms of arithmetic operations on their α -cuts (on closed intervals)(Kumar, 2008).

5.4 Probability Bounds Analysis

There are situations where parameter(s) (mean, variance) of a random variable may not be accurately known. Then the parameters are represented by intervals. Probability bounds approach combines probability theory and interval arithmetic to produce probability boxes (p-boxes), structure that allow the comprehensive propagation of both aleatory and epistemic uncertainty through calculation in rigorous way (Tucker et al., 2003; Morgan et al., 2006; Christopher et al., 2002). Williamson et al. (1990) provided

explicit numerical methods for computing bounds on the results of addition, subtraction, multiplication and division of random variables when only bounds on the distribution are given. All the necessary mathematical operations can be performed using p-boxes; the input distributions used in a probabilistic risk assessment need not be particular, well defined statistical distributions (Kushwaha, 2009).

5.5 Two-D Monte Carlo Analysis

Classically all sort of uncertainty have been modelled through simple probabilistic approaches (e.g. Monte Carlo analysis). However recently second order Monte Carlo or 2D Monte Carlo has been used to separate variability and epistemic uncertainty (Simon, 1999). The technique is utilized when the parameters of a probability distribution are modelled as distributions. (Kentelet al., 2005), (Kumar, 2008). Treatment of epistemic and aleatory uncertainties in the simulation approach is carried out by sampling epistemic variables in the outer loop and aleatory variables in the inner loop. For a problem of second order random variable, the epistemic uncertainty in the parameters of the distributions is sampled first and later the randomness in the distribution is propagated. Unlike probability bounds approach where it can solve only problem of second order random variables, simulation approach can provide solution where epistemic and aleatory variables are completely separate also. For instance model uncertainty has to be kept separate from input parameters of the model. Thus two-D Monte Carlo provides solution for two different problems of separating uncertainties. (Kushwaha, 2009).

5.6 Evidence Theory

Evidence Theory or the Dempster-Shafer theory of evidence (DST) was first introduced by Dempster (Dempster A., 1967) and latter extended by Shafer (Shafer G., 1976). In a finite discrete space, Dempster-Shafer theory can be interpreted as a generalization of probability theory where probabilities are assigned to *sets* as opposed to mutually exclusive singletons (Sentzet al., 2002). In traditional probability theory, evidence is associated with only one possible event. In DST, evidence can be associated with multiple possible events, e.g., sets of events. As a result, evidence in DST can be

meaningful at a higher level of abstraction without having to resort to assumptions about the events within the evidential set. Where the evidence is sufficient enough to permit the assignment of probabilities to single events, the Dempster-Shafer model collapses to the traditional probabilistic formulation. One of the most important features of Dempster-Shafer theory is that the model is designed to cope with varying levels of precision regarding the information and no further assumptions are needed to represent the information. It also allows for the direct representation of uncertainty of system responses where an imprecise input can be characterized by a set or an interval and the resulting output is a set or an interval (Sentzet al., 2002).

6. Conclusion

Risk assessment is an important tool in decision making process and every step of risk assessment process is tainted with uncertainty. So in this article, we discussed about risk assessment and risk assessment process, different sources and different nature of uncertainty. Also we discussed the important aspect of uncertainty encountered in risk assessment and finally summarized different ways of uncertainty modeling and uncertainty propagation.

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