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TOWARD AN INTEGRATED ASSESSMENT OF HEALTH RISKS FROM MULTIPLE CBRN EXPOSURES

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Abstract. *The individual components of the CBRN (Chemical, Biological, Radiological, and Nuclear) category of hazardous agents are characterised by distinct properties, particularly in terms of their health effects. This makes assessing the overall impact of exposure to two or more CBRN agents on human health highly complex. Each agent interacts with human tissues and organs through specific mechanisms, making it difficult to consolidate their effects into a single measure or express the total harm as a response to multiple exposures using one unit or parameter. Furthermore, health effects from low-level CBRN exposure may be limited to stochastic outcomes, while higher exposure levels can lead to deterministic effects. Comprehensive assessment of total CBRN health risk is essential in all contexts where such hazardous substances are managed or used—whether under controlled conditions or in cases of malicious or terrorist misuse. The paper provides an overview of current methodologies for quantifying the health risk associated with CBRN exposure, highlighting the need to account for the contributions from more than one individual CBRN component.*

Keywords: *CBRN, hazardous agents, health effects, multiple exposure, assessment of total risk*

1. INTRODUCTION

CBRN stands for chemical, biological, radiological, and nuclear substances or agents that pose risks to human health and the environment. These agents can be released intentionally, for example in acts of terrorism, or accidentally, causing harm through toxicity, infection, or radiation exposure. Proper management of CBRN materials throughout their entire lifecycle—production, use, transport, storage, and disposal—is essential to prevent incidents. Both accidental and intentional releases require specific prevention, response, and mitigation strategies. In some cases, the term CBRNE is used to include explosives as an additional category of threat. Comprehensive knowledge of these agents and their impacts is critical for effective emergency preparedness and response.

The health impacts of CBRN agents are influenced by various factors, such as how the agents are delivered, how they interact with human tissues, the type of physiological response they trigger, the level of physical protection available, and the application of additional measures like decontamination or isolation. Important aspects also include the agent's classification and its chemical, physical, and biological properties, along with the time delay before symptoms emerge. To protect both people and the environment—especially during emergencies—it is crucial to use reliable detection and monitoring systems. These systems help track CBRN agent concentrations and allow for a swift response if hazardous levels are detected whether in workplaces or public spaces. Such precautions are essential for the safety of workers and others who may be at risk of exposure.

In some cases, it is helpful to assess the overall risk of CBRN agents by using measurement units specific to each type—chemical, biological, radiological, and nuclear. Each category has distinct features that influence how it spreads, enters the body, or affects organs, and the severity of harm it can cause. For instance, when only radiological and nuclear agents are involved, such as with ionising radiation, the hazard may seem easier to evaluate since the damage results solely from radiation exposure [1,2].

Radiological threats generally arise from radionuclides, which may be naturally occurring or created through neutron irradiation of stable isotopes. Nuclear threats, on the other hand, stem from fission or fusion reactions that generate radioactive substances emitting ionising radiation. In both scenarios, the biological effects are determined primarily by the dose and type of radiation exposure rather than by the source of the radioactive material. Consequently, health risks are mainly linked to the way radiation interacts with human tissue rather than its specific origin.

Additionally, when dealing with radiological and nuclear components, it is possible—through radiation detection and spectrometry—to determine the nature of the radioactive source with high accuracy, often detecting levels even below natural background radiation. This level of precision is not achievable with chemical or biological agents, where distinguishing between stochastic (delayed) and deterministic

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(immediate) health effects is extremely challenging. This complexity makes it difficult to assess the biological impacts of chemical substances or biological agents.

Chemical agents exist in countless variations, making it nearly impossible to apply a single detection method to identify all forms or quantities. In contrast, radioactive materials can usually be identified quickly and reliably using a detector, often with just one sensor. Preliminary results are typically available almost instantly, with more detailed analysis following within minutes.

By comparison, evaluating exposure to chemical and biological agents is far more complex. The effects vary greatly not only between the C and B categories but also among individual substances within each group. Given the vast number of chemicals—each with distinct biological effects—and the variability of biological agents, it is practically impossible to apply a standardised method for assessing their impact [1,2].

2. BASIC CHARACTERISTICS OF INDIVIDUAL COMPONENTS OF THE CBRN GROUP

A common characteristic of most CBRN agents is that they are difficult to detect or recognise once they are released. For instance, they may be odourless and colourless chemicals or biological agents, or radioactive materials that emit invisible and imperceptible radiation. Consequently, recognising or confirming exposure can be challenging, often leading to delays or complications in identifying the specific agent involved and assessing the extent of adverse health effects in affected individuals [3].

Chemical agents are poisonous substances designed to injure or disable people by disrupting normal physiological functions. They fall into families such as nerve, blister, blood, and choking agents, each affecting the body in different ways. Some are persistent and remain on surfaces for long periods, while others are non-persistent and evaporate or disperse quickly — a distinction that matters for emergency response and clinical care. Although chemical agents are not biological, their effects can mimic those of viruses, toxins, or pathogenic microbes. They may appear as gases, liquids, or solids and have the potential to cause large-scale harm. Both armed forces and terrorist actors have employed chemical agents to produce mass casualties, spread fear, and destabilize societies. Examples include purpose-made warfare agents like sarin, VX, and mustard gas, as well as toxic industrial chemicals used in industry — for instance chlorine, phosgene, ammonia, and cyanide [4,5].

Biological agents are microorganisms or toxins that can cause diseases or infections in humans, animals, or plants. They may exist naturally or be modified genetically to increase their virulence or resistance. Examples include bacteria, viruses, fungi, and toxins derived from living organisms. These agents can be transmitted through various means, such as direct contact, airborne particles, or vectors like insects. They are generally divided into two main types: (a) Live agents, which include bacteria (e.g., Rickettsia and Chlamydia), viruses, and fungi, and (b) Toxins, which are poisonous substances produced by organisms such as bacteria, fungi, plants, or animals (for example, venoms) [6,7].

Radiological agents are radioactive materials that, when released, can cause harm to humans and the environment. They are characterised by their ability to emit ionising radiation, which can damage biological tissues and disrupt cellular processes. These agents can be naturally occurring or artificially produced, and their impact depends on factors like the type of radiation, the amount of exposure, and the duration of exposure. Radioactive agents emit one or a mixture of the following types of ionising radiation: a) Alpha radiation (heavy, positively charged particles; easily stopped by paper or skin), b) Beta radiation (electrons - light charge particles, more penetrating than alpha), c) Gamma photons (high-energy electromagnetic waves; can pass through the body, stopped by lead or concrete), d) Neutrons (uncharged particles; can cause secondary radiation such as alpha, beta, or gamma; characterised by high penetration) [8,9]. Formally, it would be more appropriate to refer to these agents as *radioactive* rather than radiological since the latter term also includes sources of radiation produced by X-ray machines or other charged particles.

Nuclear agents, in the context of CBRN, primarily involve materials that can release radiation and cause harm through nuclear reactions, typically fission or fusion. These agents include radioactive materials and the neutrons and other particles emitted during nuclear reactions. The effects of nuclear agents include blast, heat, and radiation, with radiation being particularly harmful over extended periods and large areas [10-12].

Although the substances classified under the CBRN category are often treated as a single, homogeneous group, there are significant differences among the individual components—particularly regarding their health effects and the feasibility of their detection and identification. These distinctions are most pronounced between chemical and biological agents on one hand, and radiological and nuclear agents on the other.

The R and N categories are relatively uniform in their characteristics, as their health risks stem exclusively from radiation exposure. Moreover, radiation levels can be detected with high precision using sensitive monitoring equipment, often capable of measuring values even below natural background levels. This allows for a clear distinction between deterministic effects (which occur above specific dose thresholds) and stochastic effects (which are probabilistic and can occur at any dose).

In contrast, the health effects of C and B agents are more complex and less predictable. Detection and identification are more challenging due to their variable properties, modes of action, and the often-delayed onset of symptoms. Furthermore, there is a lack of comprehensive statistical data on population-level health outcomes following major chemical or biological incidents—unlike the R and N domain, where events such as the Hiroshima and Nagasaki bombings or the Chernobyl disaster have provided substantial datasets for analysis. This data gap makes it virtually impossible to distinguish stochastic from deterministic effects in the context of C and B agents with the same degree of confidence as for R and N exposures.

Victims with combined injuries (e.g., trauma alongside chemical exposure or radiation) often face a significantly worse prognosis. This is due to factors such as bone marrow suppression, increased susceptibility to infection, and potential adverse interactions with anaesthetic agents. Fig. 1 illustrates the typical timeline of symptom onset in a CBRN incident. Here, one must apply right units for different biological effects: for stochastic effects and for deterministic effects.

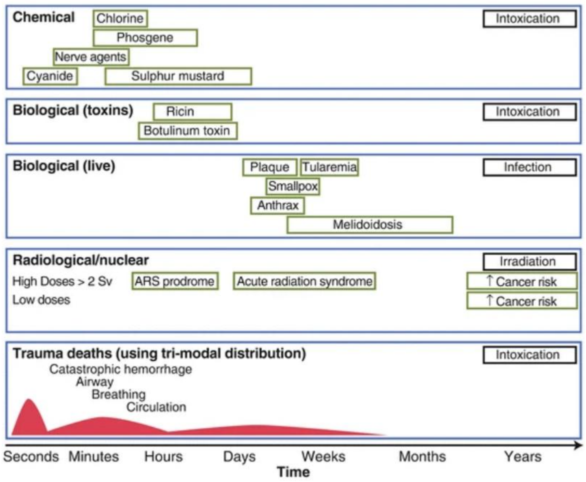

Figure 1. Illustrations of the specific properties of individual CBRN agents related to the onset of symptoms reflecting their biological effects (based on [12])

3. Detection, monitoring, and identification of individual CBRN agents

Detection, monitoring, and identification (DMI) of CBRN agents are essential components of an effective response to potential threats. This process focuses on quickly determining the type of agent involved, as well as its location and concentration, to guide appropriate protection and response actions. Reliable measurement systems depend on a combination of technologies and techniques, with the chosen approach differing according to the nature of the agents (C, B, R/N) and the specific circumstances.

The roles of individual DMI processes can be characterise as follows: *Detection* - involves using sensors and other technologies to identify the presence of CBRN agents; *Monitoring* - refers to the ongoing tracking of agent concentration and distribution, often using real-time data acquisition and analysis; and *Identification* - reflects determination of the specific type of CBRN agent present, which is essential for selecting appropriate response measures.

Technologies and methodologies of DMI differ substantially among the three most important groups of CBRN. In the case of chemical agents, an important role is played especially by mass spectrometry, gas chromatography-mass spectrometry, and ion mobility spectrometry for detecting and identifying chemical warfare agents and toxic industrial chemicals. For the DMI of biological agents, some of the following methods are applied: DNA microarrays, polymerase chain reaction, and other advanced molecular techniques for identifying pathogens. The relatively simplest methods are available for the detection, monitoring and identification of radiological and nuclear agents since here universal gauges and methods based on the use of radiation detectors, including GM counters, scintillation detectors, and other specialised instruments for identifying and measuring radiation levels and exposures in terms of personal doses [13-15].

Results of detection and identification are extremely important for implementing protection and decontamination procedures, which can serve as a reliable source of information for medical countermeasures as well as for information system planning (Fig. 2).

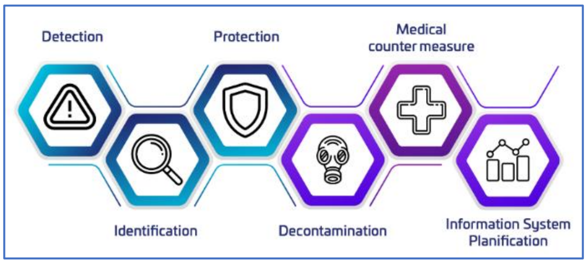

Figure 2. CBRNe capability chain for defence and security

4. Health effects and detection of the impact of multiple exposures to more CBRN agents

CBRN agents may produce health effects that vary from minor illness to serious injury or death, depending on the type of agent, the dose, and the route of exposure—whether through inhalation, ingestion, or skin contact. Detecting these agents involves multiple approaches, such as the use of specialized sensors, laboratory testing of collected samples, and observation of atypical symptoms.

Multiple agents can cause distinct health effects, and sometimes their combined impact is more complex than the sum of each agent alone. While in the case of R/N agents, the situation is relatively straightforward, in the case of other agents, the health impact assessment and prediction are more complicated.

Chemical substances can produce a wide range of effects on the human body, such as breathing difficulties, skin blistering, nerve damage, and organ failure. For instance, nerve agents like sarin can cause respiratory collapse and paralysis, blister agents like mustard gas led to skin lesions and lung injury, and choking agents like chlorine trigger respiratory irritation and pulmonary oedema. Evaluating the health impact of exposure to multiple chemicals simultaneously is extremely complex.

A comparable situation exists, to some extent, with biological agents—such as bacteria, viruses, and toxins—which can cause various infectious diseases. These agents are often hard to detect and may have long incubation periods, making their management challenging. As a result, their presence is frequently identified only after some delay.

On the other hand, the occurrence of radiation exposure can be identified almost immediately using even simpler monitors. They are susceptible and are also able to identify radionuclides present in the contaminated area. The intensive radiation exposure can result in immediate effects like burns and nausea, as well as long-term effects like cancer and genetic damage. The severity of these effects depends on the type and amount of radiation and the duration of exposure. The advantage of assessment of R/N consequences is that the effect depends entirely on the radiation exposure, and it is enough to get information about this exposure and there is usually no need to identify the radioactive source of this exposure. The advantage is also that there are now available single monitors which can measure both radiation doses and other parameters of radiation based on which one can easily assess the biological impact of radiation exposure.

The situation with other than radiation related agents is much more complicated since there is no universal method to evaluate the danger potentially caused by two or more chemical or biological agents. The current in-field sensors are typically limited to detecting only one class of threat at a time. Current detection techniques for chemical and biological agents are generally complex and require highly specific and ultra-sensitive methods. For example, biological threats, such as anthrax or ricin, are routinely analyzed offsite through a laboratory response network, where samples of interest are first sent to a sentinel lab, followed by a reference laboratory, and then, if the biological threats are not ruled out at the first two laboratories; the samples are sent to a national laboratory. This network uses fixed laboratory equipment, such as mass spectroscopy techniques, which are highly sensitive. Unfortunately, they require complex data analysis, especially for biological samples, which have numerous fragments and potential matrix effects that can interfere with the determination of the analyte. Accordingly, improved sensor technology for simultaneously detecting multiple CBRN threats, including different types of threats, would be welcomed in the field. So far, however, this problem has not been solved satisfactorily.

Even more complicated cases involve multiple combinations of various types of CBRN agents, with circumstances also arising where at least two agents from the CBRN group are present. Moreover, cases exist where two or more types of the same C and B agents are present. A universal new quantity should be introduced to express the total risk from the exposure to multiple CBRN agents, where different elements of the same agent will also be considered [16].

Ideally, CBRN sensors should be capable of instantaneous detection of multiple threats. Specifically, the present subject matter relates to a multifunctional sensor that can simultaneously detect two or more different CBRN threats of the same or different classifications on a single nano-sized platform using energy transfer-based technology. The disclosed sensors can be used to simultaneously detect CBRN threats with high selectivity, high confidence, and reduced false positives. Disclosed sensors are based upon the energy transfer from an excited donor molecule to an acceptor through nonradiative dipole-dipole interactions.

Humans are constantly exposed to a wide variety of CBRN chemicals from food, air, and water. A major challenge in risk assessment is to determine the degree of exposure to multiple agents of more than one agent of category C, B, R and N, or different substances of the same agents. This is especially relevant for a group of chemical dangerous agents where chemical hazard is associated with combined exposure to different chemicals, which generally interact in a specific way. Predicting risk from exposure to chemical mixtures is complex, as chemicals in mixtures can interact in terms of both toxicokinetics and toxicodynamics. Such interactions may result in effects that are either antagonistic or synergistic. The temporal nature of the exposures may play a leading role in determining these interactions.

In some cases, it can be relevant to assess aggregate exposure of humans to the same industrial chemical or other contaminant 1) Via the environment, 2) Through use of consumer products and 3) At the workplace. Attention should be paid to the spatial and temporal scales at which these exposures occur. In general, aggregate exposure can be of relevance when long-term exposure to a chemical with widespread use and emissions occurs. Exposures from different scenarios and routes are added, considering differences in bioavailability of the chemical via different exposure routes. In the risk characterization, the total daily intake estimated is then compared with a no-effect level for humans at the right spatial and temporal scales.

Finally, many chemicals are intentionally applied for purposes, such as pesticides, biocides, veterinary medicines, or food additives, which can lead to human exposure. This exposure may occur through inhalation, skin contact, or other external pathways.

5. QUANTIFICATION OF THE TOTAL HAZARDS OF THE CBRN GROUP

In some cases, it can be relevant to assess aggregate exposure of humans to the same industrial chemical or other contaminant 1) Via the environment, 2) Using consumer products, and 3) At the workplace. Attention should be paid to the spatial and temporal scales at which these exposures occur. Aggregate exposure is especially relevant for chemicals widely used and emitted over long periods. Exposures from different scenarios and routes are added, considering differences in bioavailability of the chemical via different exposure routes. In the risk characterisation, the total daily intake estimated is then compared with a no-effect level for humans at the right spatial and temporal scales. Below, the approach for exposure of humans to contaminants via the environment is explained.

The use of CBRN weapons is not a recent phenomenon. Although such incidents are uncommon, they remain a global concern due to their capacity to cause mass casualties and threaten international stability [17]. Studying the deployment of CBRN weapons by non-state actors, through analysis of specific databases, can help healthcare systems better understand the potential risks and consequences of these events. In this study, 565 events were documented. Of these, five hundred events (89.4%) involved a single agent, while sixty events (10.6%) involved multiple agents. Fatalities totalled 965 for chemical agents, nineteen for biological agents, and none for radiological or nuclear incidents. The number of injuries was 7,540 for chemical agents, fifty-nine for biological agents, fifty for radiological events, and zero for nuclear attacks. On average, each chemical event resulted in 2.22 deaths and 17.37 injuries, while each biological event caused 0.15 deaths and 0.48 injuries.

Between 1990 and 2020, violent non-state actors were responsible for 565 distinct incidents worldwide involving CBRN weapons. The countries with the highest number of occurrences were the United States (118), Russia (49), and Iraq (43). Although such events are relatively uncommon, advancements in technology could make the deployment of these weapons easier, potentially integrating them into hybrid warfare strategies with serious consequences for public health and healthcare infrastructure.

The results of this unique study conducted from 1990 through 2020 [17] are summarised in Table 1 displaying how number of events involving one up to all four agents are distributed among 565 cases recorded. The data given in Table 1 seem to be a good illustration and reflection of the most frequently occurred typical frequencies of the occurrence of various combinations where different components of the CBRN family are involved. It looks like most frequently occurring events are related to the single agents C, B, and R, as well as the two agents C and B. Much less is the probability that other combinations of C, B, R, N components occur.

Table 1. Number of events involving CBRN and their combinations in mixed agents [17]

Event agent	Number of events
Chemical only	380 (67%)
Biological only	74 (13.1%)
Radiological only	40 (7.1%)
Nuclear only	11 (2.0%)
C + B + R + N	1 (0.2%)
C + B + R	4 (0.7%)
C + B + N	1 (0.2%)
C + R + N	1 (0.2%)
C + B	42 (7.4%)
C + R	5 (0.9%)
B + R	1 (0.2%)
R + N	5 (0.2%)

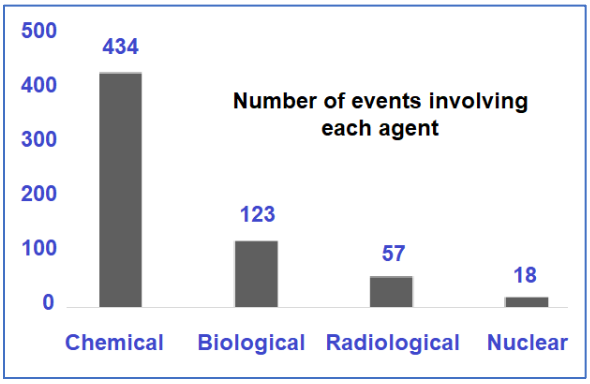

Figure 3. Results related to the number of chemical, biological, radiological, and nuclear events

Another illustration of the results is in Fig. 3 showing the distribution of 434 events involved chemical agents, 123 involved biological agents, 57 involved radiological agents, and eighteen involved nuclear agents.

Evaluating the overall health impact of CBRN agents requires consideration of both synergistic and antagonistic interactions. Synergistic interactions happen when one hazard amplifies the effect of another, whereas antagonistic interactions occur when one hazard diminishes the effect of another. In some cases, the total risk may simply equal the sum of the individual risks of each CBRN component. Alternatively, different components may contribute to distinct aspects of the overall risk. This concept is illustrated in Fig. 4, which considers two components (based on [18]).

In the example described in Fig. 4, when two or more hazards interact, they can produce a combined outcome characterized by two principal types of effects. Typically, the total impact may correspond to a simple additive effect or manifest as synergism—ranging from partial to strong—where the combined outcome exceeds the sum of individual effects. In the context of radiation-induced effects, immunosuppression may heighten an individual's vulnerability to biological agents, as a weakened immune system is less capable of combating infections. Such interactions are often complex, dose-dependent, and may differ across various organisms and biological systems.

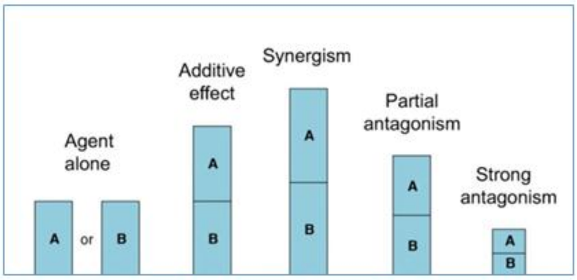

Figure 4. Schematic view of how the specific circumstances can be used to describe additive, synergistic, and antagonistic interactions between different two agents. For simplicity, the effects A and B are of equal height, but similar images can be constructed for any number of agents.

A somewhat different outcome occurs when antagonistic effects are present. In such cases, one hazard diminishes the impact of another, producing a combined effect smaller than the sum of their individual effects. This typically happens when certain agents counteract one another or when specific interventions reduce the influence of a particular hazard. Understanding these dynamics is essential for accurately evaluating the overall risk of CBRN exposures and designing appropriate response measures. Recognizing whether interactions are synergistic or antagonistic helps identify the most effective actions—such as decontamination, medical treatment, or evacuation. However, the range of potential interactions among different CBRN agents is extensive and often difficult to anticipate.

The comprehensive evaluation of health effects resulting from CBRN agents remains a complex and ongoing challenge. Several factors contribute to these difficulties:

- *Complexity and diversity of agents:* Each type of CBRN agent causes harm through distinct mechanisms, making it difficult to apply a single framework for assessing overall health impacts.
- *Detection and identification challenges:* Many agents lack visible signs, noticeable odours, or cause delayed symptoms, which hamper timely detection. Without accurate identification, medical diagnosis and epidemiological assessments remain highly uncertain.
- *Latent and long-term consequences:* In the case of biological and radiological agents, health effects may appear only after prolonged periods—ranging from days to years—making immediate evaluation difficult and often leading to underestimation or misinterpretation of their impact.
- *Combined and synergistic interactions:* Simultaneous exposure to multiple CBRN agents, or to CBRN agents along with

conventional injuries (such as blast trauma), can produce complex and compounded effects that are not yet fully understood or easily predicted. This complicates both medical treatment and broader health impact assessments.

- *Absence of standardized metrics and baselines:* There is no globally accepted system for quantifying the overall health burden caused by CBRN exposures. Differences in healthcare infrastructure, preparedness, and diagnostic capacity among countries further increase the variability of assessments.

6. Conclusion

Determining the combined health effects of multiple CBRN agents is a highly complex process. This complexity stems from the potential for synergistic, additive, or antagonistic interactions between different agents, leading to health outcomes that cannot be accurately predicted by studying individual agents in isolation. As a result, comprehensive assessment requires a multidisciplinary approach, incorporating risk analysis, exposure monitoring, and advanced modelling or simulation techniques.

A meaningful total CBRN exposure assessment must go beyond evaluating agents separately. It must account for individual and combined effects, interactions, mechanisms of action, exposure routes, and the intensity and duration of exposure. This holistic evaluation aims to estimate the overall risk posed by multiple CBRN agents present in a specific situation and guide effective protective and response measures.

In current practice, quantitative assessments tend to concentrate mainly on radiation risk—especially at low exposure levels and usually as an isolated factor. However, the simultaneous presence of other toxic substances, whether of natural or human origin, is seldom considered. It is precisely these combined exposures that can lead to health effects that differ from those expected by simply adding individual risks, as interactions between agents or their joint effects on tissues may either intensify or reduce overall health impacts.

Consequently, any valid CBRN risk assessment must consider whether interacting agents could alter expected health outcomes to the extent that standard risk predictions—based on isolated exposures—need to be revised. This is especially relevant in real-world incidents, where populations may be exposed to multiple agents simultaneously or sequentially. The challenge is particularly acute with chemical and biological agents, which pose significant difficulties in terms of detection, monitoring, and quantification. Their effects are often delayed, non-specific, and influenced by individual susceptibility, making risk modelling inherently more uncertain. In contrast, radiological and nuclear exposures are better characterized. These agents are typically limited to natural or anthropogenic radionuclides, including fission products from nuclear reactors or weapons, and can be measured and modelled with relatively greater precision.

Importantly, the total risk from CBRN agents must be expressed using appropriate quantities and units specific to each agent type, reflecting their environmental behaviour and capacity to cause harm. While the radiological risk is primarily a function of radiation dose, chemical and biological risks are more challenging to quantify due to their variable toxicity, infectivity, and mechanisms of action.

This paper aims to highlight the conceptual and practical inconsistencies between the assessment of C and B agents and that of R and N agents. Notably, there is a lack of rigorous evaluation of deterministic and stochastic health effects associated with chemical and biological exposures. These inconsistencies underline the urgent need for more integrated, harmonized, and scientifically robust methods to assess the total risk posed by all CBRN agents in both acute and long-term scenarios.

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