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Modeling for Nuclear Disaster Planning and Preparedness

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Abstract

Mathematical modeling projects consequences of disasters based on algorithms and parameters, with explicit assumptions that can be varied to explore potential variation in outcomes. Modeling of mechanical trauma, thermal burn, and ionizing radiation injuries due to nuclear detonations has been used at the Department of Health and Human Services, Administration for Strategic Preparedness and Response (HHS/ASPR) to inform needs assessments for medical countermeasures. Physiological modeling for the Defense Threat Reduction Agency (DTRA) projects outcomes of injury from ionizing radiation combined with mechanical trauma and/or thermal burns including effects on physical capabilities, which are used to evaluate the population consequences of nuclear detonations. Public health response modeling explores the effects of variation in operational practices such as triage and allocation of resources for treatment, which informs decisions and practices toward improvement in planning for response to nuclear detonations. Research can inform assumptions and algorithms of modeling, and strategic use of modeling can further inform planning for such topics as shielding, survival, and survivor behavior like sheltering and evacuation.

Introduction

A common characterization of modeling has been that "all models are wrong, but some are useful."[1] Emphasizing the positive purpose, models are designed to be useful, but they require assumptions and other simplifications of reality, including aspects that cannot be known before the situations modeled arise. Therefore, they cannot predict future conditions or consequences.[a] The nuclear and radiological model uses described here result from endeavors to balance representing reality simply enough to keep analysis manageable while including adequate complexity accurately enough to be substantially useful in projecting outcomes.

Modeling is a way to represent reality, using mathematical relationships and algorithms to project outcomes under defined assumptions and conditions. Modeling results are used to inform planning and preparedness for potential disasters by assessing potential impacts, including immediate and evolving injuries, for possible incidents that have not specifically occurred. This paper provides a sampling of ways mathematical modeling has been used to inform policy and planning decisions and guidance for disaster preparedness and response related to nuclear and radiological incidents, particularly nuclear detonations; this paper includes advances made since the 2011 issue of *Disaster Medicine and Public Health Preparedness* (DMPHP) addressing scarce resources.[2] The examples here are not intended to be a comprehensive review, but rather to provide key instances of endeavors and advancements in the mission space, as well as to highlight some areas where gaps remain. For a general overview of modeling as used in emergency response, see Greening and Meltzer.[3]

Because the range of possible incidents of a given type requiring a particular set of capabilities to respond is wide, the approach to modeling to inform national preparedness capability requirements at the Administration for Strategic Preparedness and Response (ASPR) and across the nuclear and radiological community has been to use models in which a wide variety of assumptions can be adjusted by varying key parameters. For nuclear detonations, these parameters include location (city, with variations in population size, population density, building

[a]Hurricane and other weather modeling is a special case, in which the modeling has become accurate enough to forecast near-future occurrences with some fidelity.

distribution and structure, and more), detonation yield (magnitude), detonation height (above ground), and time of year (associated with weather). Collectively, the results provide an estimate of the greatest need for response capabilities from among all modeled scenarios—potentially not the same scenario for every capability.

Using this approach, modeling can inform decisions associated with costs and benefits relative to managing risks for public health caused by specific radiological-nuclear incidents—with information about the types and quantities of public health, medical, and associated resources that could be needed to serve as insurance in case an incident occurs, the projected costs for the resources, and the potential benefits in improved outcomes. Issues include these:

(1) How much need will result from the incident and what types? Approaches to assessing need for medical response and resources are addressed in the sections of this paper on *Medical Needs: Health Effects Modeling at HHS/ASPR* and on *Combined Injury: DTRA Physiological Modeling*.
(2) What are the relationships among (a) the overall needs, (b) capabilities required to meet the needs, (c) response activities required to provide those capabilities, and (d) the operational capacity to engage those response activities? How do these relationships inform decisions that affect the outcome? Aspects of this second topic are addressed in the section of this paper on *Public Health Response Modeling*.
(3) How can we interpret and improve the modeling to help design improvements in concepts of operations in response and guidance for survivors and responders? This third question is addressed in the *Discussion*.

Medical Needs: Health Effects Modeling at HHS/ASPR

The U.S. Department of Health and Human Services (HHS), through ASPR, uses modeling to project health effects and inform capability requirements, including for medical countermeasures (MCMs), for a wide range of threats and hazards, including chemical, biological, radiological, and nuclear. MCM requirements are developed in the context of the Public Health Emergency Medical Countermeasures Enterprise[4] and inform development and acquisition decisions of ASPR.

ASPR's nuclear modeling capability was initially developed to project consequences of the Department of Homeland Security (DHS) National Planning Scenario (NPS) #1, a nuclear detonation in a large metropolitan area,[5] and the Homeland Security Presidential Directive (HSPD)-18, *Medical Countermeasures Against Weapons of Mass Destruction*,[6] which extended the scope to additional cities and addressed the need for medical intervention in the aftermath of an attack by terrorist adversaries using a weapon of mass destruction. This became the ASPR nuclear incident health-effects model (ASPR Model). The ASPR Model has been continually iterated for internal use[b] to estimate the number of people with mechanical trauma, thermal burn, and/or ionizing radiation injuries[c] and the quantities of MCMs required to treat them in the aftermath of a nuclear detonation. Results of this modeling inform investment in the development of MCMs, including novel life-saving devices and therapies, and directly inform the requirements for types and quantities of products recommended for federal programs that support national preparedness.

Modeling Concepts

The ASPR Model uses a deterministic approach that generates population-level estimates, relying on gridded population data and mathematical formulas to project outcomes. The model does not track individuals and their symptoms; rather, it tracks groups of people over a geographic grid and assigns injuries to the population in each grid cell based on weapon effects[d] from the detonation and assumptions about locations of people within buildings. This approach allows the model to handle a nuclear incident affecting millions of people.

Development of a deterministic model capable of projecting the number of individuals with various types of injuries requires a comprehensive and robust dataset. The accuracy of such a model directly depends on the quality and relevance of the data used. Where real-world data was unavailable or incomplete, substitute data was incorporated from analogous scenarios or experiments. For instance, data describing mechanical trauma injuries resulting from buildings collapsed by a nuclear blast are scarce. Because the most serious trauma-injured people in Hiroshima and Nagasaki perished before they could be hospitalized, little data are available regarding the types and severity of injuries they sustained. In this case, data on trauma injuries from the 2001 World Trade Center attacks and from major earthquakes provided valuable insights into potential trauma injuries from a nuclear detonation.[7] Experimental data from animal tests were also used to establish methods for estimating the extents of specific injuries.[8]

Modeling also requires various assumptions and parameters. Similar models exist within the federal response establishment; the ASPR Model is tailored to serve ASPR-specific concerns in preparing for the medical consequences of a nuclear detonation (e.g., stocking required medical interventions). A host of assumptions, many of them data-informed, are necessary to project types and numbers of injuries. Examples include city characteristics (e.g., building types, associated radiation-protection factors, collapse thresholds), population location (inside versus outside, line of sight to the detonation flash), and population behavior (sheltering in place versus evacuation, evacuation routes). Criteria, such as fatality and injury thresholds, were determined with the purpose of informing health care needs of the injured population. For instance, using higher weapon effects thresholds for modeling immediate fatality rather than modeling deaths within 6 weeks[e] results in lower immediate fatality projections and higher projections of injured people that need care until they die, which is appropriate for projecting medical needs.

Injuries—Baseline

The first nuclear incident health effects model developed for ASPR included about 200 different scenarios of plausible detonation yields, detonation heights, cities, and weather (which affects the direction and extent of the fallout footprint); selected results have been published in the 2011 scarce-resources issue of DMPHP.[9] Gridded nuclear weapon effects data for these scenarios were provided by Lawrence Livermore National Laboratory (LLNL)

[b]The ASPR Model has been for internal HHS use only and is unpublished.
[c]Sometimes referred to subsequently simply as trauma, burn, or radiation injuries, respectively.
[d]Airblast, thermal radiation, and nuclear (ionizing) radiation.
[e]Fatalities from nuclear detonations have historically been considered to be deaths within 6 weeks.[8]

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and the Defense Threat Reduction Agency (DTRA). Population distribution for each city was provided by the LandScan™ Global Population Database developed and maintained by the Oak Ridge National Laboratory (ORNL).[10]

The baseline model uses building collapse and window breakage data to estimate the number of people with various severities of mechanical trauma injuries. Radiation exposure criteria account for radiation dose from both prompt radiation and fallout as well as building-specific shielding. Published thermal burn injury criteria,[8] with free-field thermal effects adjusted for clothing and line of sight to the detonation flash, are used to estimate the number of people with thermal flash burns of various degrees and extents. Mechanical trauma injuries are subdivided based on severities associated with injury severity score ranges.[11] Radiation injuries are divided into over 30 radiation exposure bins. Thermal burn injuries are categorized by degree (depth) and extent (total body surface area) of burn. The initial ASPR Model provided results of the number of people with each type of injury for each scenario, including injury severity.

Response Resources and Procedures—Beyond Baseline of Injuries

Adapting ASPR's nuclear incident health effects model to assess the need for specific MCMs or other medical interventions requires defined treatment protocols, including dosages, start and duration of treatment, injury-specific treatments, and the percentage of injuries of various severities that would require treatments. Treatment protocols are gathered from extensive literature reviews and subject matter experts (SMEs), including interviews with burn and trauma doctors. Useful treatment information is detailed in this type of statement, for example: 10 percent of people with radiation exposure between 0.75 and 3 Gy will need antibiotic A for 2 weeks and 20 percent of those people will experience antimicrobial resistance and need to be switched to antibiotic B for another 2 weeks.

Specific Applications of the ASPR Model

ASPR's nuclear incident health effects model has been adapted for various purposes to guide requirements for MCMs, capture specific injury types, inform complementary models designed for emergency response planning, and provide data for use in planning exercises.

MCM acquisition and stockpiles

Blood and tissue products. The original ASPR Model was developed to support the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Blood and Tissue Working Group to estimate the blood component requirements in the aftermath of a nuclear detonation. Treatment protocols for blunt and penetrating injuries were based on a meta-analysis of large trauma datasets provided by the authors of various published trauma studies (e.g., references 11–13). Treatment protocols for radiation injuries were based on the percentage of the population with different radiation-absorbed dose levels expected to need the various blood products until recovery or death.[14–17] Treatment protocols for thermal burn injuries were based on standards of care from the American Burn Association,[18] which are in 3 time-dependent phases: fluid resuscitation, maintenance, and skin grafting. Based on the treatment protocols and the population injury estimates, the model provided the numbers of people who would need platelets, red blood cells, intravenous (IV) fluids, hematopoietic stem cells, and skin grafts for thermal burns, with the time-dependent quantities that would be consumed.

The available supply of blood and tissue products was based on stockpiles, reserves, and donor programs. The estimated results for need, compared to existing national inventories, informed the analysis of the time-dependent gap in blood and tissue products.

Thermal burn treatment products. The ASPR Model was also used to support the ASPR Center for the Biomedical Advanced Research and Development Authority (ASPR/BARDA) thermal burn team's investigation into which thermal burn products would be used to treat burn casualties sustained from a nuclear detonation and to quantify the needs for these thermal burn products. Although burns incurred because of a nuclear detonation would be different from those typically encountered by burn doctors, the team worked with burn practitioners to discuss available treatment products. A list of point-of-care (0-72 hours) and definitive-care (after 72 hours) burn products was selected and treatment protocols were described for each product, focusing on the timing and quantities to be administered. Point-of-care burn products included oral rehydration, nutrition, pain medicines, EpiPens in case of respiration issues, anti-emetics, and anti-infective silver-based coverings. Definitive care burn products included IV fluids, nutrition, pain medicines, anti-emetics, anti-infective silver-based coverings, Xeroform bandages, skin (autograft), and skin substitutes (allograft and xenograft).

Burn injuries were categorized by the percentage of total body surface area for which the patient had partial thickness (second-degree) or greater burns. The model provided estimates of the number of people expected to suffer shallow partial-thickness burns, deep partial-thickness burns, and full-thickness burns. The model then calculated hospital days, the number of burn beds and burn surgeries needed, and the quantities of thermal burn products for both the point-of-care and definitive-care phases of treatment. Results were estimates that informed development of acquisition requirements for treatments.

Cytokines for neutropenia. The Director of the PHEMCE Radiological/Nuclear Integrated Program Team (Rad-Nuc IPT) asked the modeling team to estimate the number of people that could benefit from anti-neutropenic MCMs and the associated number of doses of filgrastim required to treat them. Nuclear radiation exposure thresholds for anti-neutropenic treatment were set and agreed upon by the Rad/Nuc IPT. Modeling assumptions included the initiation of treatment within 24 hours after the nuclear detonation, daily dosing until recovery, perfect biodosimetry (i.e., every survivor had a projected threshold radiation dose), and treatment including supportive care with antibiotics in addition to the anti-neutropenic. Treatment duration was based on published data (e.g., McVittie et al. 2005[19]) and varied by radiation dose. The model also included an estimate of the number of appropriately concerned survivors who did not, in fact, have enough exposure to warrant treatment. Time to death was incorporated into the model to ensure the number of required filgrastim doses would not be incorrectly inflated by the inclusion of people at the highest radiation exposure doses. In providing projections of the scale of the impact of a nuclear detonation and therefore of the response required, including the number of potential recipients of cytokines, the model helped in assessing key challenges associated with cytokine eligibility screening and administration during response.[20]

Broad-applicability MCMs. The ASPR Model was expanded to include additional MCMs under scarce-resource conditions. As a proof-of-concept study, the need was determined for 3 classes of

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analgesics: morphine class, oxycodone class, and ibuprofen class. Triage rules for scarce-resource environments with crisis standards of care were implemented to categorize certain high-severity injuries as expectant, limiting their treatment to palliative care only rather than the previously established treatment protocols. Analgesic needs were calculated and reported by analgesics class and by day, and palliative care needs were calculated and reported for morphine, IV fluids, and anti-emetics.

Afterward, an expanded analysis of MCM needs was completed for the nuclear detonation scenario-based analysis subgroup. New IV and oral MCM need estimations included antimicrobials, tetanus vaccine, vasopressors, anti-emetics, and rehydration therapies. With input from SMEs on the various injuries and the use of the standards of care from the American Burn Association,[18] the team developed MCM-specific treatment protocols for the various severities of injury. These protocols identified the percent cohort of patients to be treated, the quantity of patients per day, the initiation day for treatment, and the duration of treatment that would be used to treat each type of injury and determine overall needs. The model calculated estimates of the daily and total needs for MCMs and this information was used to inform national preparedness MCM acquisition requirements.

Cutaneous radiation injuries. Beta radiation from nuclear fallout poses a risk of cutaneous radiation injury (CRI) to evacuating populations. Therefore, the Rad/Nuc IPT asked for an estimate of the number of people at risk for CRI so they could determine if CRI should be included in the list of injuries considered by ASPR/BARDA in planning. The CRI model included a hazard module, a population movement module, and an injury aggregation module. The hazard module examined dose protraction for dry and moist desquamation by adapting the biological effective dose calculation to a hazard function calculation like those recommended by the National Council on Radiation Protection and Measurements for other acute radiation injuries.[21] The population movement module used battle injury data that estimated degraded soldier performance under various injury severity combinations of burn and radiation with trauma.[22] Performance degradation was used to approximate the impact of burn, trauma, and radiation injuries on the rates of civilian evacuation. The scenario data from the ASPR Model provided gamma radiation data to the hazard module and geospatial and population data to the population movement module.

The outputs from these 2 modules informed the injury aggregation module that projected the numbers of people with various degrees of CRI based on their location at the time of detonation and the radiation they were exposed to as they traversed the hot zone during evacuation. These results then informed the types and quantities of MCMs needed to treat CRI, assuming operational capacity to administer the MCMs.

Antimicrobial resistance. The ASPR Model's injury results have also been used to help analyze the potential for mass casualties to develop antimicrobial-resistant (AMR) infections and subsequent antibiotic needs. The initial broad MCM study included estimates of antibiotics that may be needed to treat various injuries. This study went a step further, providing more specificity on the types of injuries and infections that were likely to develop and the number of infections that would not respond to a given antibiotic regimen. The AMR model required infection prevalence in subjects with trauma, radiation, and/or burn injuries and overall rates of resistance to various antibiotics for those types of infections.

The AMR model used injury data from the ASPR Model to estimate the expected incidence of bacterial infection among survivors of a detonation. The model projected the number of resistant infections resulting from specific antibiotic treatments. Results of the study were used to reinforce the need for investment in novel therapeutics that focus on AMR bacteria and why they belonged in ASPR/BARDA's portfolio.

For additional information on modeling used to inform issues related to antimicrobial resistance see Phipps et al.[23]

Blast trauma injury. ASPR has expanded the ASPR Model to estimate the numbers and types of specific blast trauma injuries to a level of detail beyond the existing injury severity levels (minor, moderate, severe, and very severe). This was for the ASPR/BARDA Burn and Blast MCMs Program, which supports developing and integrating transformative MCMs into routine care to build national preparedness for mass-casualty incidents.

This blast trauma injury study involved an extensive literature review in conjunction with guidance from ASPR/BARDA burn and blast SMEs to formulate a portfolio-relevant list of specific trauma injuries, such as lacerations, fractures, crush, hemorrhage, and various others. Due to a lack of trauma injury data from nuclear incidents, the literature search focused on published analyses of trauma injury patterns reported in-hospital data from terror-related bombings and attacks, earthquakes, explosions, and battlefield casualties. These incidence values were adapted and applied to the number of people with blast trauma injuries by injury severity and damage zone. These blast trauma injury incidences and estimates of injuries from the ASPR Model were used to estimate the number of specific injuries resulting from a nuclear detonation incident.

A new modeling component was developed to complement this study and more realistically limit potential MCM estimates based on injury severity and assumed time to rescue.[24] The model merged the Department of Defense (DoD) triage protocols[25] with the consideration of damage zones and the presence in them of people who will not survive long enough to be rescued.

Combined Injury: DTRA Physiological Modeling

Physiological modeling provides estimates based on the relationship between physical models and biological/medical consequences for affected subjects when the relationship between the consequences of the detonation and the effects on survivors is not directly ascertainable or deducible. Such information has been applied in modeling described here to estimate effects of combined injuries—for which some, but incomplete, direct evidence exists from animal experiments.

DTRA serves as a Department of Defense combat support agency that safeguards the United States and its allies from weapons of mass destruction by providing capabilities to reduce, eliminate, and counter the threat, and mitigate its effects. More specifically, DTRA's Research and Development Directorate's Nuclear Survivability Division is tasked with developing, validating, implementing, and employing nuclear detonation human survivability modeling tools designed for the following aims:

- Address nuclear weapons environments, especially in the nuclear battlefield and urban settings.
- Support mechanistic and physiological casualty models for combined injury to project military and civilian patient outcomes.

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- Support combatant commander targeting consequence assessment, medical planning, and combat effectiveness applications, which can be applied to civilian situations to address survivors' functionality, including mobility and ability to evacuate.

A single individual may sustain more than one of the types of injury due to nuclear detonations, caused by ionizing radiation exposure, thermal fluence, and blast effects. Historically, over half of the resulting casualties exhibit radiation exposure combined with at least one other type of trauma.[26–29] Experiments to explore the consequences of combined injuries in humans cannot be performed and data from Hiroshima and Nagasaki lack detail on acute effects and clinical signs and symptoms. Animal experiments are particularly challenging and difficult to interpret, although some have been done.[8,27,30,31] For example, historical animal tests focusing on primary blast and penetrating injuries are only appropriate for estimating level of severity and not the specifics of the injury necessary to project combined effects. Combined injuries have synergistic effects, including a systemic wound-healing response; outcomes may be more severe than would be expected from adding the effects of the individual injuries.[26,32,33] Therefore, modeling these combined injuries using available animal data is a useful means to project the numbers of casualties and the negative effects of those casualties on performance for military purposes.

DTRA's Health Effects of Nuclear and Radiological Environments (HENRE) Model

DTRA's Nuclear Detonation Human Survivability Modeling (NDHSM) project focuses on developing health-effects models to better understand the impact on affected populations after nuclear detonation scenarios. The program supports development of a spectrum of models (environment, human response, injury criteria, physiological, and medical planning models) and their integration into operational tools. The research has focused on 3 key areas over the last decade:

- Survivability: Population-based analysis of who would survive a nuclear denotation.
- Medical planning: For initially survivable injuries, analysis of who will need medical care, illness progression over time, and the schedule of the needed care.
- Combat power: Performance degradation analysis of those who survive and do not need immediate medical attention.

The modeling uses physiological and mechanistic approaches to understand how animal data relate to humans, to estimate the impact from combined injuries and to project the time course of injury.[34] The granularity of models employed in this work is tailored to meet the specific requirements. For example, high-level empirical models may be sufficient to project the number of casualties from radiation or burn, whereas mechanistic models enhance understanding of the synergistic effects of combined injury or enable cross-species extrapolations. Once fully developed, the individual models are bundled into a single application programming interface (API), Health Effects of Nuclear and Radiological Environments (HENRE).[34,35]

What Is HENRE and How Does It Work?

HENRE is a modeling tool for projecting human effects after a nuclear detonation, developed for DTRA's nuclear survivability and forensics program, as well as DTRA's customers, including interagency partners in nuclear human survivability mission areas. HENRE is a collection of physiologically based and empirical mathematical models sharing a common workflow to enable analyses for medical planning and combat power assessment using minimal computational resources.[36]

In HENRE, users or modeling tools define nuclear detonation environment insult inputs (blast, thermal, radiation) and then run a simulation to assess effects on an individual. HENRE's medical outcome outputs can be aggregated to determine the impact across an urban area or battlefield at any echelon and to estimate collective capabilities.[35]

HENRE at its core is a consequence assessment tool to project health effects from multiple types of injuries due to a nuclear detonation. HENRE is currently structured as an API within a Jupyter-based run environment, available upon request or accessed through the DTRA Experimental Laboratory. This framework provides users with flexibility to design and efficiently execute common analyses, running parameter studies in parallel and generating fast-running surrogate models. HENRE provides a robust consequence assessment capability that provides both civilian and military medical planning outputs and combat effectiveness for essential military tasks. Through integration with the Hazard Prediction and Assessment Capability (HPAC) and the Nuclear Capabilities Services (NuCS) programs of DTRA, HENRE's models currently provide probability-of-casualty estimates for prompt and fallout exposures across the entire hazard area, shown in Figure 1 for 48-hour mortality and for thrombocytopenia with clinical implications. HENRE also projects an initial casualty stream to pair with the Joint Medical Planning Tool to estimate medical resources required for treatment and recovery.[36,37]

Performance Decrement and Combat Power

In recent years, the focus of NDHSM has transitioned from medical planning to modeling battlefield effectiveness and performance decrement to support combatant commanders' understanding of available combat power. Besides its importance for military purposes, such modeling is relevant to civilian response with consideration for survivor functionality, including mobility and ability to evacuate. Current focus areas on the human effects models are (a) improving estimates of blast-induced, region-specific injuries for individuals at a distance where blast injuries are expected to dominate and (b) projecting sign/symptom severity resulting from combined injury as a function of time to inform task-specific combat effectiveness and combat power calculations. The projection of combined injury dynamics following a nuclear detonation is achieved through a systemic combined injury model. The systemic model is a general framework extension of the physiological models accounting for the body's systemic responses to combined injury following a nuclear detonation.[38]

The Widespread Irradiation Thermal Burn Model and the Synergistic Algorithm for Performance provide a framework to estimate a single task-specific metric for the combined impact of ionizing radiation, thermal stressors, and blast-related injuries on performance. The model incorporates the additional systemic dynamics of immune cell proliferation in the bone marrow, cellular differentiation and maturation in the bone marrow and lymphatic tissues, and supply and circulation of immune cells in the blood vessels to the injury site in response to biomolecular signals. The inclusion of these dynamics improves calculations of wound-healing progression for combined injury and widespread radiation

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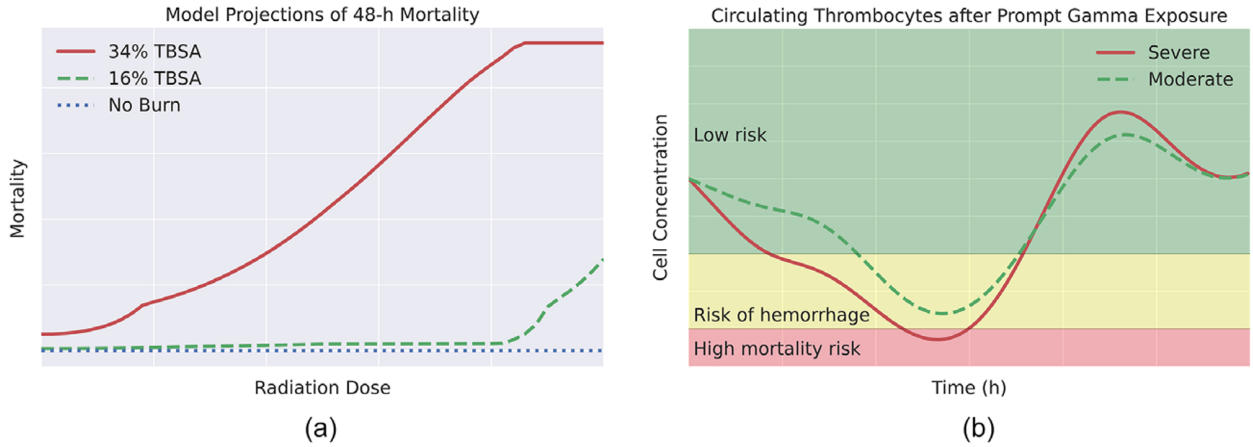


Figure 1. (a) Mortality at 48 hours with radiation dose, showing increase of about 70 percent in lethality due to shock with severe burn and high radiation dose. (b) Thrombocytopenia progression with clinical implications, showing projected time course of clinical symptoms and critical circulating thrombocyte levels.

exposure through analysis of the inflammatory conditions and signaling biomolecule expression responsible for physiological responses, which can be used to project the onset and severity of adverse systemic effects impacting performance. The model consists of a set of 21 ordinary differential equations capturing hematopoietic and immunologic dynamics, modeling the progression of healing in the injury site, the synergistic effects resulting from combined injury, and the effects of widespread radiation exposure on the wound-healing response. The model has been fit to purpose for the first 72 hours post-insult when the inflammatory response to injury is governed principally by the body's innate immune response. Notional results for the first 48 hours are shown in Figure 2.

Public Health Response Modeling

Projecting the number of people injured and the consequent need for medical countermeasures is an initial step in the overall planning process. While useful for ranking scenarios by impact and ascertaining needs, injury numbers need more context to help guide overall planning. Outcomes of a nuclear detonation depend not only on the direct and indirect effects of the detonation but also on many other factors, including those that can be influenced by guidance, operational decisions, and policy. Examples include how survivors behave after the detonation and how the response is engaged and executed—the concept of operations, including triage and treatment. These are typically assumptions included in

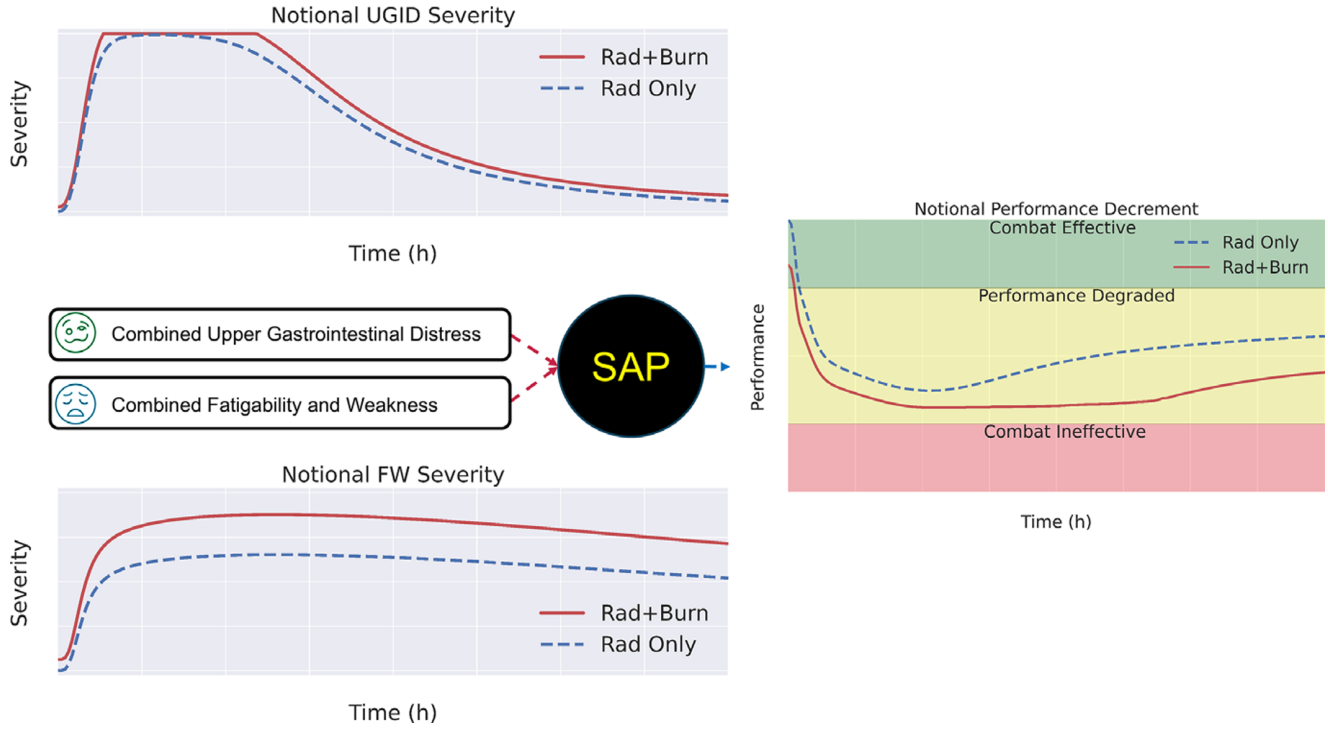


Figure 2. Notional performance decrement due to radiation exposure only and combined radiation and thermal burn. The combination of radiation and burn increases the severity of upper gastrointestinal distress (UGID) and fatigability and weakness (FW) symptoms and therefore further degrades task-specific performance over the first 48 hours after the nuclear detonation. SAP: Synergistic Algorithm for Performance.

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consequence modeling but can be a subject of study in themselves to determine projected effects of variation for assessing effectiveness of alternative approaches to them.

Public health response (PHR) modeling is the use of mathematical methods to model the patient stream, triage, treatment, and outcomes of people injured following a nuclear detonation or other incident. To examine triage and treatment, PHR modeling requires the modeler to understand both where people who require treatment are and where resources for treatment are, including staff, durable resources, and one-use resources. At each step during the 2 major phases modeled in PHR modeling, triage and treatment, the model must project the number of people who die from injuries (both treated and untreated), assess and allocate available triage resources, assess and allocate available treatment resources, and determine if any treated individuals need to re-enter the patient stream (e.g., because of post-treatment infection or development of acute radiation syndrome symptoms). The patient stream also can be analyzed in terms of how people enter the stream, including issues of evacuation from the incident site and transport to a triage site. PHR modeling data needs are extensive and include both scenario-specific and injury-specific information (Figure 3).

PHR modeling has several overarching goals, including estimation of current capabilities to mitigate the injuries from a nuclear detonation and the requirements for complete treatment. The difference between the current capabilities and the resources needed to treat all individuals in need represents the gap that may be bridged by improved medical response to a nuclear incident and can inform additional investments, policy, or operational changes to improve national medical response posture.

PHR modeling can also inform how uncertainty in the scenario or response could affect outcomes. Differences in the detonation location and weather can affect what parts of health care infrastructure are affected and how they are affected, including availability of transportation, water, power, and fuel, among other interdependencies. Understanding how these affect the availability of medical supplies, staff, and resources, as well as how they affect the patient streams in terms of injuries and where they present, can facilitate effective planning by affording exploration of the projected outcomes of a range of possibilities for what an actual incident might look like and what courses of action could be taken.

This examination allows for improving effectiveness of response. PHR modeling can represent how changes in triage methodology, resource placement, and response operations may allow existing resources to go further and save lives. Additionally, including new technologies such as rapid and simple biodosimetry screening or improved medical treatments for trauma, burns, or radiation injury in PHR modeling can allow exploration of how novel technologies may impact outcomes. Such analyses can inform requirements and priorities for future development.

By its nature, PHR modeling is undertaken using results of blast and radiation transport modeling, injury modeling, and evacuation modeling. Uncertainty in those modeling steps will accumulate in PHR modeling results. Interpretation therefore needs to account for these accumulated uncertainties and focus on substantial, approaching order-of-magnitude, differences in modeling results, not precise estimations.

Triage

In any medical emergency, triage is the critical step to assess injuries both for allocation of resources and for prioritizing patients by need. In scarce-resource environments, where the number of patients and their medical needs far exceed the capacity of the health care system, triage has an extra role in increasing the life-saving value of available resources.[9] In either case, triaged patients are sorted into color-coded groups in order of treatment priority, including immediate (red), delayed (yellow), minor (green), and expectant (black). Triage is included in PHR modeling for 2 primary

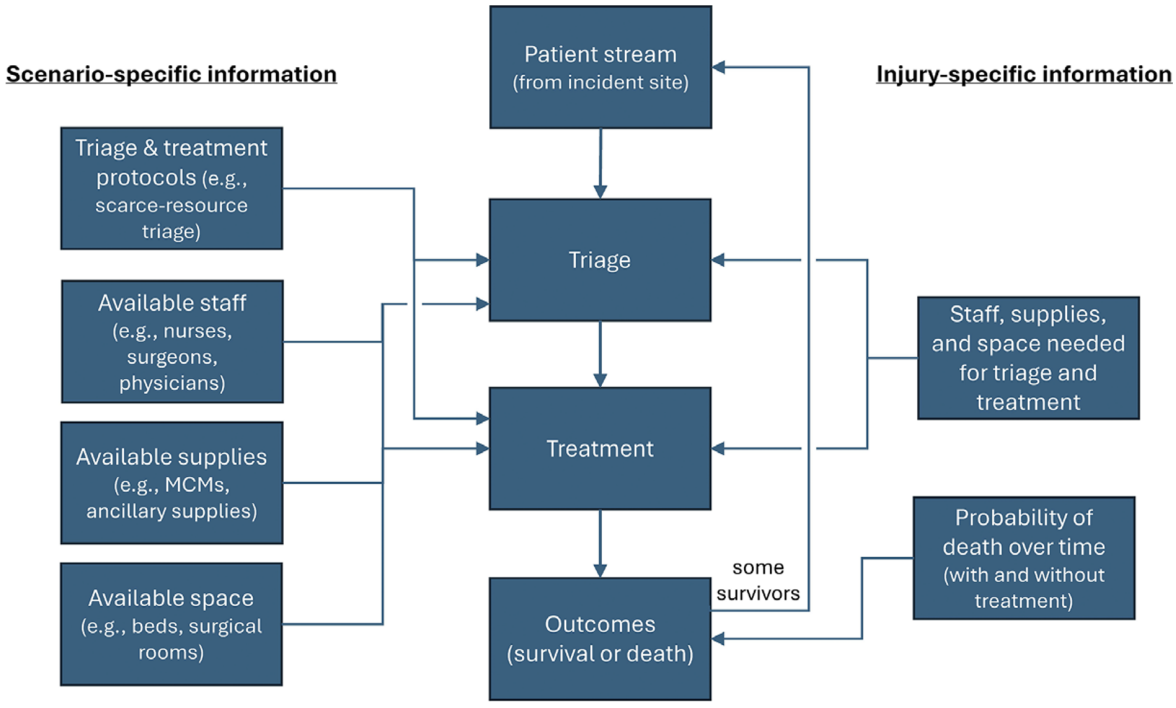


Figure 3. Information needed for public health response (PHR) modeling.

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reasons: triage takes time and resources, and the triage method used defines how limited resources are allocated.

A nuclear detonation will result in a scarce-resource environment with a need to enhance the overall lifesaving value of medical staff, resources, and space. Meeting this need requires a focus on treating patients whose survivability can be substantially increased with interventions that require a relatively limited use of resources, including all categories of limiting resources: staff engagement, supplies including medical countermeasures, patient space such as hospital beds, and systems supporting the use of the other categories of resources. When resources are scarcer, the threshold of severity of injury for exclusion from immediate and delayed treatment, i.e., for categorization as expectant under the circumstances, goes down—less serious injuries are considered expectant. An inappropriate triage protocol for the resource-availability circumstances will lead to inappropriate allocation of resources during treatment and the unnecessary loss of otherwise savable patients. Over-triage results in categorizing less severe injuries unnecessarily as expectant, leaving survivable injuries untreated. Under-triage results in more severe injuries categorized as immediate or delayed, using lifesaving value of available resources on patients for whom they are less effective. The threshold for expectant patients goes up as resources become more available and more people can be treated, until resources approach adequate availability for conventional triage and standards of care for all levels of injury.[9,39] Increasing overall survival for the available resources is the most critical aspect of triage methods. Appropriately triaging the patient stream, with as little as possible over- and under-triage for the resource availability situation, facilitates effective use of staff, supplies, and space. PHR modeling provides the opportunity to modify triage protocols used during a modeled incident and project how those changes could impact the ability of the health care system to save lives during the response.

One way that PHR modeling can address how changes in triage can save lives is by assessing how different allocations of staff and supplies to triage versus treatment may ultimately affect lives saved. Triage under conventional resource availability is typically performed by nurses at intake, who collect each patient's vital statistics and evaluate injuries based on severity. In a radiological or nuclear incident when resources are expected to be unusually constrained, including shortage of personnel who ordinarily perform triage, and crisis standards of care are invoked, triage may be able to be done by others with just-in-time training and well-designed instructions. Triage and subsequent treatment decisions may consider the assessment of the radiation component of injury using geographic assessment, rapid dosimetry, time-to-emesis or other clinical symptoms, single complete blood counts (CBCs), or more advanced biodosimetric tools (see reference 20 for challenges associated with screening and initial administration of cytokines in response to nuclear detonation). Ultimately active triage can conserve resources most needed to save lives; however, triage also requires resources and can potentially become a bottleneck, affecting the rate at which patients access treatment. Staff and supplies used for triage are not available to support treatment; PHR modeling can inform advantageous allocation of resources between triage and treatment.

Treatment

Assessment in PHR modeling of lifesaving effectiveness of treatment is data intensive. Data are required for each injury on the pre- and post-treatment probability of death with respect to time, as well as the required staff, supplies, and space for treatment. Modeled allocation of these resources to patients is based on triage group and availability of resources, specific to the chosen triage method (e.g., reference 39). Within each triage group (immediate, delayed, minor, expectant), PHR modeling typically uses a first-come-first-served method assuming resources are available at the level applicable to the triage rubric applied (conventional, contingency, crisis, catastrophic).

Improving Effectiveness

Since PHR models can be run multiple times at low cost using different assumptions and triage methods, they represent a useful tool for planning associated with improving effectiveness of triage, treatment, and medical response operations. By varying each of these in turn, researchers can evaluate how changes could influence overall lifesaving during a response. Examination of triage rubrics can provide insight into what resource triggers indicate that a change in triage methodology is appropriate to increase lifesaving. This approach demonstrated increased survival under the assumptions of the model for crisis standards of care under scarce resource conditions in the original 2011 issue of DMPHP.[39] Some other such explorations have been done, and additional explorations could provide insights. For example, the potential utility of various applications of diagnostic protocols, new diagnostic tools (e.g., biodosimetry), or other new technologies can be explored.[20] Similarly, overall effectiveness of treatment may be improved by exploring ways to better allocate resources or develop new technologies that allow existing resources to go further.

Finally, PHR modeling can be used to improve effectiveness of response operations. Examination of the impact of various approaches on resource usage over time can help researchers examine how and where additional resources would be most effective and include plans for implementation of those projected to be advantageous. Examining deployment of Strategic National Stockpile (SNS) resources at different locations at 12, 24, and 48 hours after a nuclear detonation can clarify how and where staging those resources in a time-phased manner could save the most lives. Additionally, PHR modeling can be used to examine how medical evacuations; radiation triage, treatment, and transport (RTR) sites; and the interactions among local, regional, and national health care systems should work together to facilitate lifesaving during response to a nuclear detonation. Some of these topics are addressed in the discussion section of this paper on *Modeling gaps*.

The ASPR Model[f] has incorporated PHR modeling, including triage and treatment. Following are 2 examples of how the ASPR Model has been used toward improvement of response operations.

Hospital surge model

The ASPR modeling team was tasked internally in 2014[g] to replace the Agency for Healthcare Research and Quality (AHRQ)-funded hospital surge model built in 2006 with a modeling tool that incorporated updated data and improved methodologies for hospital emergency planners, local emergency managers, and federal medical preparedness stakeholders in assessment of needs for space, supplies, and staff in the aftermath of a range of scenarios. The ASPR Model was used to provide scenario input for a range of detonations of varying intensity, resulting in differing patient

[f]For internal government use.

[g]This was a project initiated by the then BARDA Division of Quantitative Analysis.

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classes and arrival streams. The model used the scenario input data to calculate the need for necessary medical interventions. Specific outputs included patient endpoints (discharged or dead), patient numbers by location and day, resource needs by day, and highlighted peak values. The surge model has been used internally in ASPR to estimate personnel needed for various types of incidents.

Exercises

To inform exercises, the ASPR Model has been used to provide credible injury numbers so responders can understand the scope and health impacts of a nuclear detonation in various damage zones, including severity of injuries. For the Gotham Shield exercise in 2017, the team provided the Centers for Disease Control and Prevention's response planners with estimates of numbers of people with radiation exposure, trauma, and burn injuries, and numbers of concerned survivors that would arrive at medical centers. Projections were provided for the number of injured people presenting daily at a medical center. These numbers helped medical professionals at the exercises consider and coordinate incoming patients and understand potential loads and bottlenecks, illustrating the depth of the scarce resource situation.

The ASPR Model also has been used to estimate the population displaced within the damage zones, as well as outside the light damage zone, from areas where radiation deposition exceeded relocation protective action guides (PAGs).[40] These numbers represented people who, at the time of detonation, were in a location that would exceed the relocation PAG for the next year. They helped responders consider and plan for the long-term needs of the affected population.

Discussion

Choice of what aspects of potential reality to represent in a model is important to make the modeling useful in developing guidance, concepts of operations, and policy for response. In this discussion we address some pertinent considerations, including types and sources of uncertainty and associated gaps that may be useful to address.

Improving Models: Handling Uncertainty and Gaps

Although modeling for nuclear detonations, including consequences and response options, has advanced substantially since 2011,[h] it is subject to several types of uncertainty. Aleatory uncertainty comprises aspects of a scenario that cannot be known before the incident, and is therefore unavoidable, such as location of a detonation, detonation yield, detonation height, and weather affecting fallout distribution. Epistemic uncertainty, uncertainty in what is known versus unknown, can be addressed by research. Uncertainty can also be due to modeling or representational gaps, in which something about the incident is not represented, or is not represented well, in the modeling.

Aleatory uncertainty

Although unavoidable, aleatory uncertainty can be addressed by considering results for various nuclear scenarios, as was done to explore the medical needs under multiple scenarios as described here in the *Medical Needs: Health Effects Modeling at HHS/ASPR* section and in Knebel et al 2011.[9] The consequent variability in results provides awareness for what might be expected in similar incidents. Other dimensions of aleatory uncertainty could be worth exploring. Health care infrastructure is interdependent with other critical infrastructure. Although hospitals typically have generators with fuel on site, prolonged loss of power and access to fuel will eventually impact operations. Additionally, hospitals are dependent on the availability of water from community water systems. Dependencies on transportation infrastructure influence how staff and patients arrive and the ability of facilities to transport patients to specialized facilities or to other facilities with additional capacity. Resource availability at the time of the incident is also aleatory. Although hospital systems are designed to have some limited surge capacity, this capacity varies for a variety of reasons, including other ongoing incidents or time of year (e.g., flu season). Aleatory uncertainty can be accounted for to an extent in PHR modeling by exploring multiple scenarios and providing results as a range of potential outcomes; however, strategic choices must be made regarding what is worth exploring since not all circumstances can be reasonably explored from among the infinite possibilities. A strategic choice can be made to explore those for which some preparation or action could reasonably reduce aleatory uncertainty, such as making provision for mitigating shortages of beds or ventilators.

Epistemic uncertainty

Epistemic uncertainty can be reduced or resolved with additional research. Epistemic uncertainty in projected health outcomes in the context of MCM administration is primarily related to the uncertainty about effectiveness of treatment for radiation and combined injuries. Literature reports efficacy for existing treatments for radiation injury as assessed under systematically controlled, favorable conditions (e.g., references 41–43) and does not provide sufficient information to understand how effective these MCMs are when treatment times are late or erratic or when treatment is incomplete, unless these conditions are systematically explored (e.g., references 44–47). Both variations are likely under the conditions during response to a nuclear detonation. Additionally, most existing data on radiation injury treatment are in non-human animal models, except for limited case studies of accidental radiation exposures and in clinical application of radiation for therapeutic purposes. Although the clinical applications do not match the dose rates and time courses likely during radiological-nuclear incidents, they can provide valuable information. This lack of pertinent human data presents challenges to estimate the efficacy of treatments in humans, and more so the effectiveness under real-world conditions. Typically, efficacy is estimated from animal models, under FDA's animal rule when seeking approval,[48] with treatment protocols designed to approximate the treatment protocols expected following a nuclear detonation. These data then need to be interpreted by comparing outcome rather than dose directly, due to the significant differences in radiation sensitivity among animals. Physiological modeling based on animal models is another approach to addressing this, as described in the section of this paper on *Combined Injury: DTRA Physiological Modeling*.

Epistemic uncertainty also exists around the effectiveness of partial treatments. In scarce-resource environments, the resources required to conventionally treat patients will not be available. Since the health care system is designed to have all resources available for injury treatment during normal operating conditions, a dearth of data exists on the impact of a lack of medical resources on the efficacy of treatment and resulting probability of death. In PHR

[h]Examples include numerous advances in HPAC and investments by DTRA and LLNL in the underlying transport and prompt effects modules.

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modeling, this uncertainty is typically managed by representing some patients as not treated at all within the model when resources are not available, but perhaps partial treatment of more patients would have better overall outcomes than complete treatment of fewer patients. To address this gap, additional research is needed.

Modeling gaps

Whereas aleatory and epistemic uncertainty are inherent in reality or in the state of knowledge, respectively, modeling gaps with substantial importance can often be addressed when their importance is recognized. Following are several modeling gaps we judge to be important to address in the near to medium future, because doing so would potentially improve consequence assessment or response effectiveness.

Shielding: Impact of built-up environment on prompt radiation. The protection offered by buildings, both for prompt and fallout exposures, is a topic that has been well studied.[49–53] One aspect that is important for accurately calculating prompt radiation dose but appears to be lesser studied is the impact of a built-up urban environment. Most studies evaluate the protection offered by a single building on an open plane; however, this is obviously not the environment of a city. If a detonation happened at ground level in the downtown of a major metropolitan area, multiple heavy buildings near the burst would contribute to the shielding of people located within farther buildings.

Urban shielding remains a computationally difficult problem. Attempts to evaluate it have been via ray tracing and other algorithms; due to complexity, these algorithms are not included in the most commonly used modeling applications. Failing to account for the additional shielding is likely to result in overestimates of the prompt radiation dose received by those most likely to survive the blast effects.

Survival and survivor behavior: Severe damage zone, sheltering, and evacuation. Modeling of the survival and behavior of injured people could be enhanced by considering damage zones. Many casualties in the severe damage zone are caused by building collapse. Given the expected prioritization of the moderate damage zone for responders during the early stage of the response, search and response operations would be unlikely to begin in collapsed buildings in the severe damage zone until at least 72 hours post detonation, if at all. At this point, any survivors, if reachable at all, would require treatment and at least basic medical care, since people with significant injuries and hemorrhaging would not have survived. A substantial number of people would not be expected to survive until the end of a recommended 24-hour sheltering-in-place timeframe, especially if they are without sufficiently uninjured companions able to provide care or to help them evacuate in time to reach the requisite lifesaving medical attention (at considerable risk to themselves since they would not be sheltering).

The unfortunate outcome is that many, perhaps most, of the severe blast trauma survivors would likely die before being rescued. First-level treatment facilities (RTR-1),[54] even if these people could reach them, are not intended to treat severely injured patients and would become quickly overwhelmed and unable to provide adequate treatment. The tragic result is that hospitals may not see as many severely injured patients as some modeling results imply. A solution to this disconnect is not to present raw casualty numbers but instead to incorporate assumptions on response and patient survival in the damage zones into casualty modeling. This additional step would allow planners to evaluate the implications of different response and triage options. An early example of this modeling was the Model of Resource and Time-Based Triage (MORTT).[39] Recently, the ASPR modeling team developed an approach to modeling that incorporates the impact of the extent of damage in the damage zones on the survival of casualties and their chances of reaching medical intervention.[23]

Current casualty modeling does not account for evacuation, whether via vehicles or on foot. This limitation is understandable given the difficulty of the problem and the hoped-for limited exposure during evacuation. The lack of modeling limits the ability of decision makers to evaluate potential trade-offs when making sheltering and evacuation decisions. Establishing evacuation corridors and relaying shelter-in-place messaging will need to be accomplished very quickly. The trade-off between sheltering in place versus evacuating is especially acute for those in the dangerous radiation zone (DRZ),[i] where sheltering longer would reduce exposure during evacuation but may push the survivors outside the window of maximum efficacy for cytokines.

The current lack of evacuation modeling may result in incorrect estimates of the projected number of people sustaining radiation injuries, with or without other types of injuries. People with trauma injuries are likely to attempt to self-evacuate to seek medical treatment rather than shelter in place, and given their untreated prognosis, this is a logical decision. For people in the DRZ, evacuating too soon can substantially increase radiation exposure. While current models treat these people as trauma-only casualties if they sheltered in a basement, they should be treated as combined-injury casualties due to radiation exposure during evacuation. In addition, people helping those requiring evacuation assistance would be exposed to fallout in the process.

Operational capacity and capabilities-based planning. An important realization since the DMPHP issue in 2011[1] has been the recognition of operational capacity as a limiting factor in framing how response could be carried out. Resource limitations on space, staff, supplies, and systems affect the capacity to respond. Stockpiling MCMs sufficient to treat the full need would result in some of the stockpile being unusable if the operational capacity to administer those treatments were not available in the required amounts at the required rates, as could easily occur in the aftermath of a nuclear detonation. For example, an intravenously administered MCM requires skilled staff to administer and appropriate ancillary supplies (e.g., syringe, saline, IV bag). Limited availability of one resource could limit the capacity and ability to provide a treatment that requires multiple resources. Another example is described in a study of the dependence of ventilator utility on the availability of trained personnel, regardless of how many ventilators are stockpiled.[56] The study and its recent practical applications[57,58] showed that more ventilators could be used during a response if more respiratory therapists and intensivists were available, or if new innovations in ventilators were developed to enable them to be administered to patients by others than respiratory therapists—respiratory therapist extenders. This issue of operational capacity is especially challenging due to uncertainty in the availability of resources and the inability to forecast and mitigate resource limits with planning and execution. Operational capacity modeling can help recognize bottlenecks and inform planning.

The concept of framing requirements in terms of capabilities is a broader approach than just focusing on the number of

[i]Where the exposure rate would be greater than 10 R/h.[55]

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medical countermeasures needed. This approach, adapted from the military, considers capabilities in several areas that could contribute to addressing a need: doctrine, organization, training, materiel, leadership and education, personnel, facilities—and policy (DOTmLPF-P).[59] Modeling of operational capacity can be useful for informing capability requirements for a broad range of public health emergency response planning.

Conclusion

Although a nuclear detonation would be devastating and cause many deaths and injuries, many lives could be saved and injuries could be mitigated through rational planning. Modeling provides useful estimates of the consequences of a detonation and of the effects of potential response resources and activities on mitigating the consequences, which is a basis of rational planning. Some modeling activities since the 2011 issue of DMPHP have informed and continue to inform planning. Additional modeling opportunities exist for future attention that will continue enhancing lifesaving response capabilities.

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