New Tools to Assess Community-Based Cumulative Risk and Exposures

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Timothy M. Barzyk, Ph.D.

Multiple agents and stressors can interact in a given community to adversely affect human health and ecosystem conditions. A cumulative risk assessment (CRA) analyzes, characterizes and potentially quantifies effects from multiple stressors, which include chemical agents (e.g., benzene), as well as biological (e.g., vector-borne illness), physical (e.g., housing characteristics) and psychological (e.g., socioeconomic) ones. The distinguishing feature of a CRA is an analysis of combined effects and interactions.

In risk assessment, the term 'community-based' indicates a focus on a given population. A community may be defined by geophysical boundaries, such as a watershed, by geopolitical limits such as county or state borders, or by socio-economic criteria within a defined geographic boundary. These assessments may also include community participation in project formulation and implementation, such as by providing test kits to residents to take measurements of environmental pollutants (Johnson *et al.*, 2009).

Cumulative assessment challenges.

Single-chemical risk assessments typically involve the process of hazard identification, dose-response, exposure assessment, and risk characterization. These source-based assessments are typically performed in the context of regulatory requirements or isolated actions, such as the issuance of an air permit for an industrial facility (EPA, 2008). In contrast, population-based assessments focus on identifying persons exposed, chemicals or stressors to which they were exposed, and characterizing risks (USEPA, 2003). This approach is more effective for implementing risk reduction strategies based on public or ecological health.

Single chemicals often have various sources or exposure pathways, which describe full source-to-receptor paths for a particular agent. Aggregate exposure is exposure to a single stressor across all sources, pathways, routes and time, such as a pesticide. Cumulative risk is the combined risk from aggregate exposures to multiple agents or stressors. Aggregate exposure can be calculated with deterministic approaches that combine single-point exposure values for various pathways, or with probabilistic approaches that produce a distribution of exposure values. The latter produces a better idea of sources of uncertainty and variability, which can lead to a clearer picture of where additional data are needed (USEPA, 2006).

A cumulative assessment can be quantitative, such as a cancer risk assessment of inner-city teenagers to urban air pollutants (Sax *et al.*, 2006), or more qualitative in nature, such as by drawing from various sources of information to visually display potential risk factors. Multiple stressors, sources, dose-response relationships, and health effects may be involved. Stressors may be chemical, biological, radiological, physical or psychological and be related to a range of health effects. Multi-stressor, multi-effect cumulative assessments are considerably more complex methodologically than aggregate or single-chemical assessments (USEPA, 2003). Indoor sources of pollution are an example of multiple stressors that can impact health (Table 1).

Publicly available tools.

A community-based cumulative risk assessment (CBCRA) typically begins with a characterization of initiating factors, which prompt decisions to undertake a CBCRA and may include multiple pollutant sources within a community, increases in illness in the population, or elevated chemical concentrations either in the environment or in humans (e.g., blood or urine samples) (Figure 1, Initiating Factors). Next steps involve defining the relevant population and study area, generating a list of environmental stressors related to initiating factors, and identifying links between exposures and vulnerabilities within the population. Several factors may be examined throughout this process, including population vulnerabilities, public health information, toxicological and epidemiological data, exposure pathways, differential exposures, and contact with environmental media and pollutant sources (Figure 1, Data Elements) (USEPA, 2007a).

One of the primary differences between communities is in their patterns of exposure. While emission source and dose-response characteristics are common across communities, susceptibility and vulnerability differ. Tools that isolate exposure routes and pathways for a given community and then incorporate toxicity information will lead to a better characterization of risk. A number of tools are publicly available that provide information on initiating factors and data elements (Barzyk *et al.*, 2009), including web-based mapping tools, databases, guidance documents and exposure models. Several types of measurement test kits are also available (Medina-Vera *et al.*, 2009) for a variety of chemical-related stressors.

Current assessment tools.

Many tools developed for general risk assessments can be applied to CRAs. They fall into one of four categories based on which aspect of risk assessment they inform: 1) planning, scoping and problem formulation, including stakeholder involvement; 2) contaminant fate and transport and subsequent exposure; 3) toxicity evaluation; and 4) characterization of risk and uncertainty, and presentation of results (USEPA, 2007a). Various types of tools are included in these categories. Guidance documents and facility or air quality web-based mapping tools fall under the first category. Computer models often inform the second category, in addition to monitoring methods and databases of information. The third includes toxicity databases, interaction profiles and regression models for meta-analysis of toxicology data. Probabilistic approaches (e.g., Monte Carlo methods) and geospatial analysis tools (e.g., geographic information systems) address the fourth category.

To assess differences between community-specific exposures, the second category of tools should address certain exposure-related questions: 1) How are people exposed to multiple chemicals? 2) In which media, at what levels, where and when? 3) What are the intensity and duration of these exposures? 4) Are there uniquely susceptible or vulnerable subpopulations? Exposure models that incorporate human activity patterns and pollutant concentration fields begin to address many of these questions; however, they are not widely available, and generally require specific inputs and technical expertise to operate. Exposure metrics, such as proximity to a pollutant source, provide screening level assessments and could prove to be more transferable across communities, but generally lack the precise concentration estimates necessary for dose-response relationships.

Emerging tools.

Additionally, emerging scientific tools are also being applied to better understand environmental risks, especially with respect to multi-chemical toxicity. These tools coincide closely with recent advances in high performance computing, and in genomics research and chemical structure-biological activity relationships. They address processes that occur within a physiological system after exposure to an agent or stressor. Biomarkers are a product of physiological processes that occur after exposure to an agent or stressor. Some biomarkers reflect actual exposure concentrations, such as total blood lead levels for lead exposure, whereas other contaminants may be better reflected by measuring chemical byproducts that result from the metabolism and detoxification process.

Computational toxicology and research in genomics, proteomics, metabolomics and metabonomics (the "omics") have potential to address multi-chemical toxicity at the molecular and cellular level. This precludes the necessity for whole animal toxicity testing, and addresses risk based on specific molecular changes. They provide high-throughput assessments and facilitate research on effects of multiple chemicals on various physiological systems (NRC, 2007).Three examples within these fields include quantitative structure-activity relationships (QSAR), physiologically-based toxicokinetic (PBTK) models, and *in vitro* toxicity pathways.

QSAR assumes a sufficiently strong relationship between chemical structure and biological activity, so toxicities of minimally tested compounds could be estimated from those of better known compounds with similar structures (USEPA, 2007b). QSAR can relate physiochemical properties of a given chemical to its Lowest Observed Adverse Effect Level (LOAEL), Effective Concentration (EC50) and carcinogenicity. An extension of QSAR is Virulence Factor-Activity Relationship (VFAR), which extends the application to biological agents.

PBTK models describe the transport and metabolism of a chemical entering the body, and estimate and predict internal doses for organs, tissues or groups of both (Figure 2). PBTK models incorporate parameters such as partition coefficients, organ and body volumes, blood flows, ventilation rates, absorption rates, clearance, and metabolic transformation rates. PBTK models effectively act as *in silico* mimics of body tissues, organs or systems.

The omics relate to advances in mapping and evaluating changes in the human genome. Those described above specifically refer to research on full DNA sequences, structures and functions of proteins, metabolites (chemical fingerprints) left behind from specific chemical processes, and the quantitative measurement of metabolic responses to pathophysiological stimuli or genetic modification. For risk assessments, the omics can relate perturbations in *in vitro* biocellular pathways to chemical stressors, such as activation of specific genes to arsenic exposure (NRC, 2007; Fry *et al.*, 2007; USEPA, 2009).

Moving forward.

Community-based cumulative risk assessments include two key components, one is involvement of community stakeholders, and another is the cumulative risk assessment. This article focuses on developing tools for communities and researchers to perform a CRA. One of the defining features that differentiate communities from one another is their differences in exposure to chemical agents. While toxicity and dose-response remain fixed across communities, exposure will determine a community's susceptibility to an agent or stressor. Each community may also have different demographics of especially vulnerable populations, such as children or the elderly.

CBCRAs represent real-world exposure scenarios, in which community members are exposed to a wide range of chemical, biological, physical and psychological stressors. The confluence of exposure assessment tools with ones that address multi-chemical toxicities, and their application by and within communities, represents the current multi-disciplinary drive towards tool development. Availability to community-based researchers and transferability across different communities are two logistical aspects that also need to be overcome. CBCRAs are becoming more common (http://www.epa.gov/care) and widely available tools would support this momentum and increase their effectiveness in decreasing exposure and subsequent risk.

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Pollutant	Source
Combustion Gases – CO and NO	Combustion – furnace, cooking stove, etc.
Volatile Organic Compounds	Outgassing of building materials
Formaldehyde and other aldehydes and carbonyls	Outgassing of pressed wood and insulation foam
Pesticides	Household products
Particulate matter	Combustion
Biological agents – molds, spores, dander	Contaminated ventilation systems, ceiling tile and wallboard, pets
Environmental tobacco smoke	Smoking in building
Radon	Infiltration from soil beneath structure
Asbestos	Construction coatings, tile, insulation

Table 1. Indoor air pollutants and typical sources.

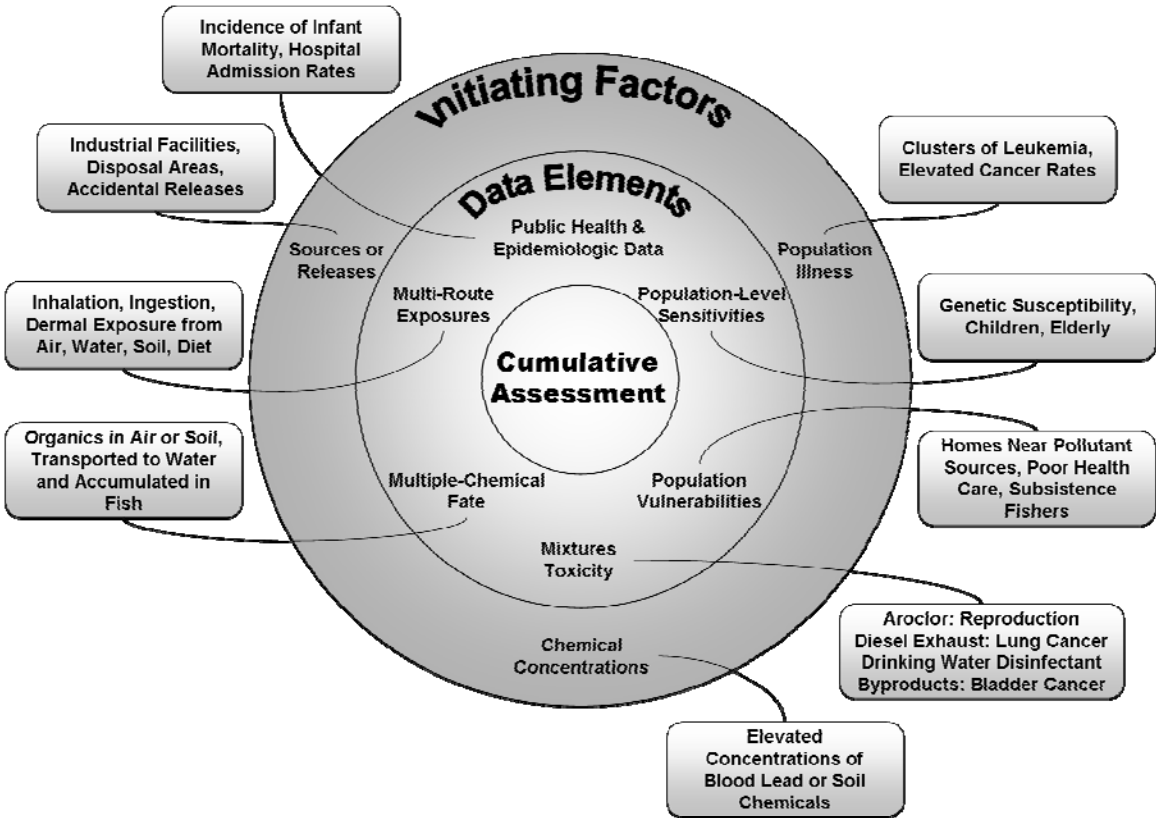

Figure 1. Examples of CRA initiating factors and data elements. Adapted from USEPA (2007a).

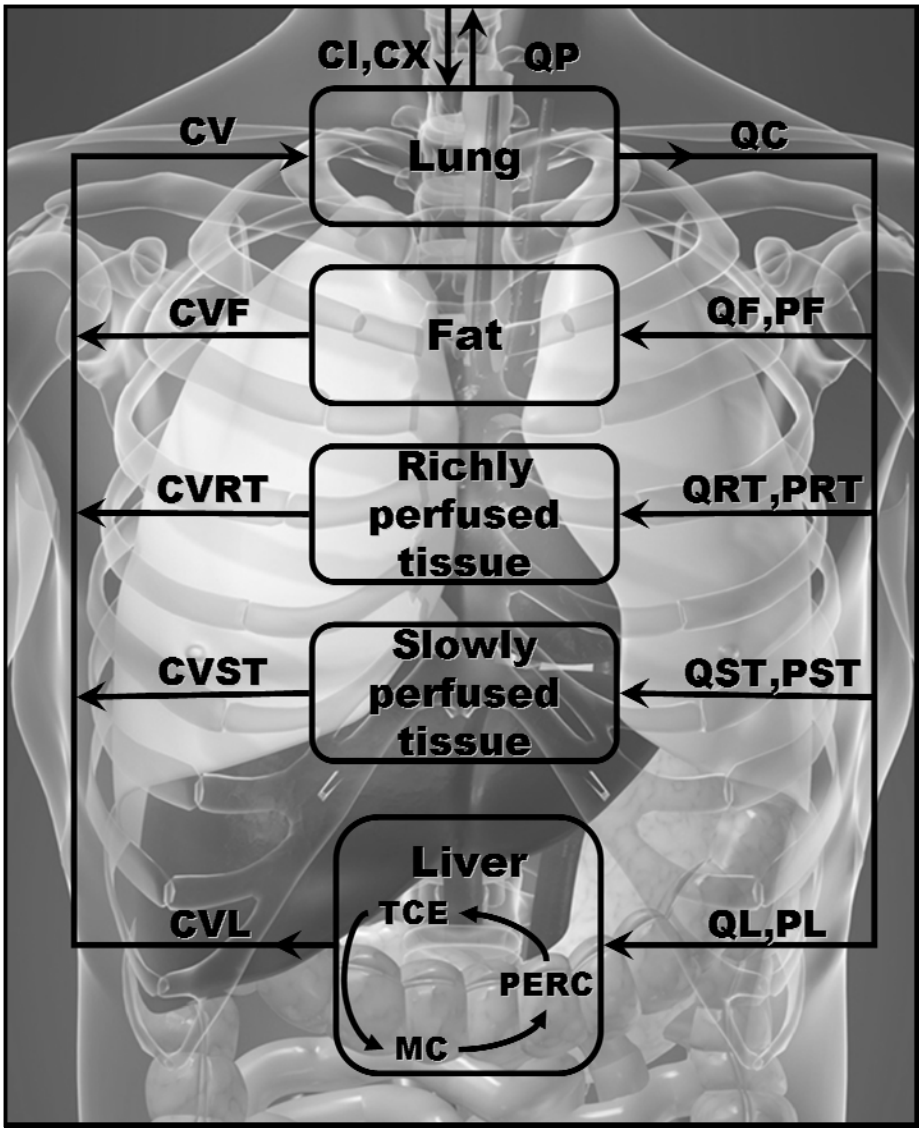

Figure 2. Ternary-mixture PBPK model representation for humans. Fat (F), richly perfused (RT), slowly perfused (ST), and liver (L) tissue groups are characterized with their volumes, perfusion rates (QF, QRT, QST, and QL), partition coefficients (Pf, PRT, PST, and PL), and concentrations of venous blood effluents (CVF, CVRT, CVST, and CVL). CV is the mixed venous blood concentration, QC and QP are cardiac output and pulmonary ventilation, and CI and CX are inhaled and exhaled air concentrations. Reproduced with permission: Ivan D. Dobrev, Melvin E. Andersen, and Raymond S.H. Yang, 2003, *Environmental Health Perspectives* Volume 110, Number 10.