Interaction of Occupational and Personal Risk Factors in Workforce Health and Safety

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Most diseases, injuries, and other health conditions experienced by working people are multifactorial, especially as the workforce ages. Evidence supporting the role of work and personal risk factors in the health of working people is frequently underused in developing interventions. Achieving a longer, healthy working life requires a comprehensive preventive approach. To help develop such an approach, we evaluated the influence of both occupational and personal risk factors on workforce health. We present 32 examples illustrating 4 combinatorial models of occupational hazards and personal risk factors (genetics, age, gender, chronic disease, obesity, smoking, alcohol use, prescription drug use). Models that address occupational and personal risk factors and their interactions can improve our understanding of health hazards and guide research and interventions. (*Am J Public Health.* 2012;102:434–448. doi:10.2105/AJPH.2011.300249)

Work and workplace hazards are known to compromise the health of workers and represent a significant national financial, social, medical, and emotional burden, but health is also affected by an array of individual risk factors such as genetics, age, gender, obesity, smoking, alcohol use, and the use of prescription drugs.[1,2] Despite their awareness of these hazards, decision-makers and stakeholders do not strongly emphasize taking a holistic view of the health of working people.

Historically, work has been compartmentalized from other human activities. This separation is in part because of legislative limitations with respect to worker safety and health and the practice of limiting liability and determining the cause of injury or illness among workers.[3] Although some work-related conditions are de facto triggers for compensation in various jurisdictions and the historical practice has been to take workers "as is" (with existing disabilities and propensities for injury), some compensation and tort systems apportion the cause of an injury or illness among various work-related and non-work-related causes and compensate only work-related causes.[4,5] However, determining the extent to which workers' illnesses or disabilities are influenced by work and nonwork factors is not a precise science.

THE PROBLEM

Most of the diseases, injuries, and other health conditions experienced by working people are multifactorial. The underlying evidence for the role of various risk factors in the overall health of working people is frequently underused in developing interventions, and most research focuses on a single risk factor through the lens of a single discipline or topic. For example, an investigator interested in smoking may treat all other factors as confounders or effect modifiers when assessing smoking–disease relationships. Thus, smoking is the primary focus, and the overall impact of all risk factors is not directly considered or studied.

Similarly, in assessing workplace risk factors, personal risk factors (PRFs) are treated as confounders or sources of bias, and the complete range of workplace risk factors and PRFs that affect the health of working people are rarely comprehensively studied. This is partly because society tends to appropriate resources to address certain specific problems such as smoking, drinking, and occupational disease. Rarely do societal programs focus on research and interventions addressing the composite effect of those risk factors.

Understanding the interactions between risk factors may help to target and determine the effectiveness of health protection and health promotion interventions. Specific problem-driven research focuses on a marginal effect that is averaged over the other risk factors in a given context. Such problem-driven research, although beneficial in understanding a specific risk factor, has led to a lack of comprehensive research on the combined role of PRFs and occupational risk factors (ORFs) in work-related illness and injury. ORFs and PRFs are not only potential confounders or effect modifiers of associations of each risk factor with disease, but they may also be on a causal pathway to each other. For example, shift work may be associated with higher rates of obesity or smoking, or the use of prescription drugs may interact with workplace chemical exposures in affecting various organ systems.

To isolate the effects of risk factors, epidemiologists usually study them in isolation while assuming that other factors are constant or ensuring that they are part of a uniformly distributed background (and hence they are disregarded in terms of interfering with the assessment of this single factor). One challenge in epidemiological research is to identify major modifying factors when they are not uniformly distributed.[6] Determination of effect modification requires analyses that include interaction terms in statistical models or stratification based on candidate variables. Identifying effect modification is important because failure to do so can lead to misinterpretation of exposure–disease relationships and to inefficiencies, including incorrect targeting, in developing interventions.[7,8]

The overarching rationale for considering the interaction of ORFs and PRFs is that the health of the contemporary workforce is critical to the well-being of the nation and its international competitiveness.[9–11] The growing burden of illness and injury and the subsequent increased use of health care services are driving up health care costs.[12] Ultimately, the impact of shortages in skilled labor and rising health care costs on productivity and profitability can affect business and national economic health.[2] Many developed nations with an aging population face the challenge of increasing workforce participation, especially among older workers.[13] As a means of meeting this challenge, governmental policies are being implemented to increase the age of full retirement to balance the ratio of dependent to employed individuals (the dependency ratio).[14]

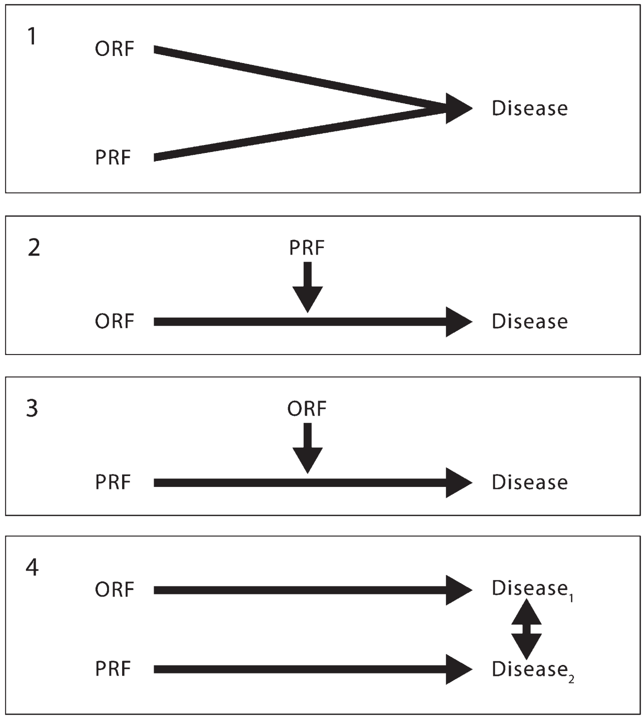
We address various ways in which ORFs and PRFs can combine or interact and develop a conceptual approach to describing the interaction of these 2 types of risk factors among workers. The goal is to begin to develop a theoretical framework for considering the health of working people in a comprehensive manner.

THE INITIAL FRAMEWORK

We used 4 basic conceptual models to evaluate the relationships among ORFs, PRFs, and disease outcomes (including both illness and injury) in working populations. The roles of PRFs and ORFs in causing illness and injury can be very complex. We focus on an initial framework in which to consider issues associated with these 2 risk factor categories.

The models presented here are not meant to delineate specific molecular-, cellular-, or organ-level etiological steps; epidemiological mechanisms; or statistical relationships with respect to the diseases discussed. Rather, we developed these models to describe theoretical frameworks through which PRFs and ORFs affect health outcomes (Figure 1). They were adapted from previous work,[15,16] specifically the work of Ottman[17] on gene–environment interactions. Conceptual models have been used in epidemiology to represent causal relations among factors, to identify potential confounders or sources of bias, and to categorize effect modifiers.[18–22]

The 8 PRFs assessed were genetics, age, gender, chronic disease, obesity, smoking, alcohol use, and prescription drug use. We selected these PRFs because they represent common risk factors for various diseases. They are not meant to be exhaustive but to illustrate how most PRFs can be assessed with respect to their interaction with ORFs.



Note. ORF = occupational risk factor; PRF = personal risk factor. Model 1 depicts a model in which the PRF and ORF are independent of each other with respect to their impact on disease. Models 2, 3, and 4 present a framework in which PRFs and ORFs can have interaction effects on disease. In models 2 and 3, PRFs and ORFs affect the same disease or disease stage, whereas in model 4 risk factors can affect different diseases or disease stages that can affect each other or disease stages that can exacerbate or compound the disease. In some cases, placement of examples in one model versus another can change on the basis of scientific information or interpretation of that information. References to disease may also include injury.

FIGURE 1—Conceptual models delineating PRF and ORF effects.

LITERATURE SEARCH STRATEGY

We employed a 2-stage search strategy for identifying examples of PRFs and ORFs. Initially, we searched combinations of general ORFs, PRFs, and work-related terminology in all fields using the PubMed database; the search strategy terminology is listed in Table 1.

We then identified articles addressing specific diseases and disease processes through further investigation of primary sources in relevant journal articles and review articles, again using all fields in the PubMed database. This next stage of the literature search focused on specific hazards and health effects terms derived from articles identified in the first stage of the search.

We based the examples used to illustrate each type of model for each PRF examined on studies that were peer-reviewed, original research articles; meta-analyses; or systematic reviews of studies that tested hypotheses and noted statistically significant effect sizes based on relative risks or odds ratios.

THE MODELS

According to model 1 (Figure 1), a PRF and an ORF can both cause the same disease with possibly independent effects. Here we define an independent effect to mean that a given level of effect is seen if there is no relationship other than an additive one between the 2 sets of factors that cause a particular outcome.[23] Examples for model 1 may be transitory because further research might suggest that other models are more suitable.

Models 2 and 3 conceptualize ORFs and PRFs, alternately, as effect-modifying variables that affect a disease association. Thus, in an ORF–disease association a PRF would be an effect modifier. Conversely, a PRF–disease

TABLE 1—Initial Search Strategy for Evaluating the Literature on Occupational and Personal Risk Factors for Occupational Illness and Injury

PRF Category	Previous 2 Years	Previous 5 Years	All Years[a]
Genetics			Genetics and work
Age		Age and work	
Gender		Gender and work	
Chronic disease	Stress and work: terms in title only (preceding 3 y); work-related diseases, injuries (preceding y only)	Chronic diseases/conditions and work; stress, acute and work; stress, chronic and work	Preexisting conditions, occupational exposure, occupational diseases and work; preexisting conditions (terms in title/abstract) and workplace terms in title field only
Obesity			Exercise, occupational exposure, occupational diseases and work; physical fitness, occupational exposure, occupational diseases and work
Smoking	Smoking, occupational exposure, occupational diseases and work	Smoking and work: terms in title field only	
Alcohol		Alcohol and work (title field only)	
Prescription drug use			Prescription drugs, occupational exposure, occupational diseases and work; prescription drugs and work: terms in title field only

Note. PRF = personal risk factor. Literature searches for each personal risk factor combined with various occupational risk factors were conducted. Search strategies differed in number of years back in the literature the search was conducted, and this was dictated by individual characteristics of the PRF or occupational risk factor being searched. General searches refer to search terms that were not specific to any single PRF.

[a]General searches for all years included the following terms: work, work-related, workplace, worksite; workforce, workers; occupation, occupations, occupational; employment, employee; job; health behaviors and work (title field only); lifestyle and work (title field only); multifactorial etiologies, occupational exposures, occupational diseases and work.

association could be modified by an ORF. Model 4 illustrates the situation in which ORFs and PRFs affect different diseases or disease stages with subsequent interactions between multiple diseases or disease stages.

Models 2, 3, and 4 can all contain interaction effects of risk factors on outcomes. We define an interaction effect to mean that a given magnitude of effect would be observed if there is a relationship different from an additive one between the 2 sets of factors. Although many interaction effects may be important in a given model, not all interaction effects have meaningful consequences. This concept is important in situations in which ORFs and PRFs interact with each other but such interactions have only minimal effects on disease outcomes. Inclusion of such interactions may allow more accurate characterization and description of disease mechanisms. For each of the 8 PRFs, 4 models of interaction with ORFs are identified in Figures 2 through 9.[15,24–164] In the case of each PRF considered, these figures present examples with descriptions and references for each type of model.

Genetics

Inherited genetic factors can contribute to variable responses of workers to occupational hazards.[165–171] In most cases, inherited genetic factors alone may not lead to adverse outcomes; however, such factors combined with an occupational risk factor can alter risk.

For example, among chemical industry workers, polymorphism in the *NAT2* gene itself does not cause bladder cancer, but in workers with a particular *NAT2* genotype, exposure to aromatic amines increases the risk of bladder cancer.[33,34,36] Furthermore, other *NAT2* polymorphisms may be protective for bladder cancer in workers exposed to benzidine in the absence of other aryl amine exposures (such as 2-naphthylamine or 4-aminobiphenyl), indicating that genetic variations in the same gene can have different effects on a disease outcome according to exposure and mechanism of action.[172] Increasingly, patterns of genes within genomes may be associated with various PRF and ORF combinations.[173,174]

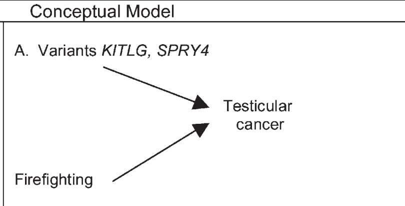
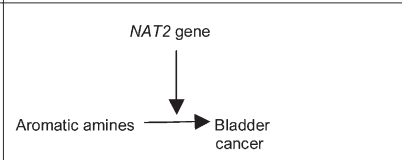
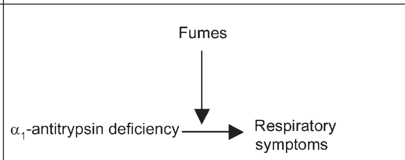
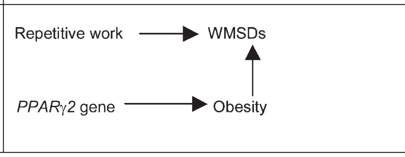
Age

Age is a widely studied effect modifier with a complex biology.[175] Age influences people's susceptibility to disease or dysfunction. Generally, the incidence of disease increases with age, but aging and disease are not synonymous.[176] Aging can influence workers' susceptibility or resistance to various hazards. Becker et al.[45] presented data supporting age, among other factors, as an independent risk factor for work-related musculoskeletal diseases. Factors such as high perceived job stress and non-work-related stress may be strongly associated with these diseases as well.[47] In the complex disease process involved in work-related musculoskeletal diseases, modeling the effects of age and psychosocial work factors on disease outcomes (Figure 3) illustrates a way to refine targets for intervention and prevention.

The variable development of occupational illness and injury according to age will have implications for disease prevention in an aging workforce. In particular, given the societal and economic pressures of maintaining working populations with larger and larger numbers of older workers, understanding the role of age in the development of disease and the subsequent impact on occupational illness and injury will be crucial in early disease intervention, health promotion, and workplace interventions for aging workers.

Gender

Similar to age, gender has often been used to stratify the workforce into subpopulations with different ORF–disease risk profiles. Despite its importance, epidemiological studies often ignore

Conceptual Model		Examples	Reference(s)
1. Genetics and an ORF are independent risks for occupational disease		A. KITLG and SPRY4 genes associated with testicular cancer, increased testicular cancer in firefighters B. APOE gene polymorphisms associated with CHD risk, low job control associated with CHD	24–31
2. Genetics modify an ORF–occupational disease association		Workers with certain *NAT2* genes, exposed to aryl amines, have an increased risk of bladder cancer	32–35
3. An ORF modifies a genetics–occupational disease association		Workers with α_1-antitrypsin gene deficiency, when exposed to certain fumes, gases, and dusts, have worsening lung function and respiratory symptoms	36,37
4. Genetics are a risk factor for one disease/disease state, an ORF is a risk factor for another, and the 2 interact		*PPARγ2* and *ADRβ2* genes associated with obesity; repetitive work associated with WMSDs; obesity linked to WMSDs	38–44

Note. CHD = coronary heart disease; ORF = occupational risk factor; WMSD = work-related musculoskeletal disease. Bidirectional and unidirectional arrows indicate flow of effect in the models exemplified.

FIGURE 2—Examples of 4 Conceptual Models of the Relationships Between Genetics and Occupational Risk Factors

the impact of gender, although within occupations the magnitude of an ORF can vary by gender.[74,177] Classic occupational epidemiology has paid less attention to women's health issues. Recent studies have begun including gender interactions, but more effort is needed in this regard.[178] Rarely have studies taken into account the potential interactions between gender, social class, employment status, and family roles.[179] In general, methods have not been systematized or used to quantify gender differences in clinical research.[180]

Chronic Disease

All individuals enter the workplace with a set of characteristics that may affect their vulnerability to occupational risk factors. These characteristics may include a broad range of chronic diseases, many of which vary according to the age of the employee (Table 2).[181a] Some chronic diseases, such as hypertension, also can be risk factors for other diseases such as ischemic heart disease.

It is likely that some chronic conditions, such as skin diseases (e.g., eczema, psoriasis) and autoimmune disorders (e.g., inflammatory bowel disease), are undercounted yet constitute a significant disease burden in the workforce. Coexisting conditions may interact with occupational risk factors.[182] Workers are often healthier than the rest of the population, in part because continued employment requires good health or the development of disease causes workers to leave employment.[183–185] This "healthy worker effect" may influence the study of risk factor interactions, with workers having lower rates of chronic disease than the population at large has. One US study suggested that, after adjustment for this effect, the exposure–outcome association (in this case, the association between arsenic and ischemic heart disease) became stronger with a statistically significant increasing trend.[186]

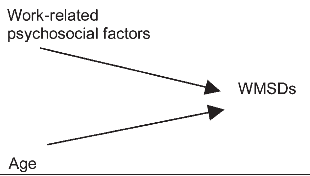
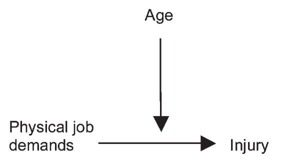
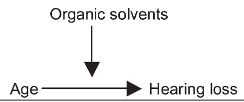
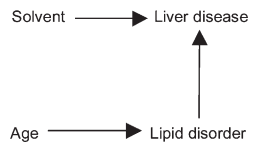
Obesity

Obesity is rapidly increasing in most developed countries. It is a contributing factor in cardiovascular disease, diabetes, asthma, some cancers, and many other diseases and is associated with workplace absenteeism and reduced productivity.[187–189] Obesity appears to have genetic and environmental determinants.[190] Lack of physical activity and high consumption of energy-dense foods are the primary causes of obesity.

Occupational hazards and obesity are part of a complex matrix of risk factors that are a function of technological development as well as social, economic, and demographic factors. Numerous studies have reported increases in body weight among shift workers.[15,191] In addition, a relatively large number of studies have demonstrated the association of job stress with body mass index.[15,192,193] Long work hours have also been associated with higher body mass indexes.[191,193] Obesity has been related to decreased participation in the workforce and other life activities.[194]

Smoking

Smoking is an extremely significant determinant of adverse health outcomes. It has been shown to be an independent variable, a confounder, and an effect modifier in occupational epidemiological relationships.[195–201] Smoking

Conceptual Model		Examples	Reference(s)
1. Age and an ORF are independent risks for occupational disease		A. Age and psychosocial factors are both a risk for WMSDs B. Age and outdoor work are both risks for macular degeneration	45,46
2. Age modifies an ORF–occupational disease association		Risk of injury associated with physical job demands (e.g., vibration, high force, awkward postures, high-pace work, high physical workload) increases with age ≥45 y (after control for other lifestyle factors)	47
3. An ORF modifies an age–occupational disease association		Hearing acuity decreases with age; organic solvents affect age-related hearing loss	48–51
4. Age is a risk for one disease/disease state, an ORF is a risk for another, and the 2 interact		Dyslipidemias increase with age; solvent exposure is linked to liver disease; lipid disorders may account for 5%–30% of US cryptogenic hepatocellular carcinoma cases; of relevance are the effects of lipid disease and solvent exposure on workers' livers	52–59

Note. ORF = occupational risk factor; WMSD = work-related musculoskeletal disease. Bidirectional and unidirectional arrows indicate flow of effect in the models exemplified.

FIGURE 3—Examples of 4 Conceptual Models of the Relationships Between Age and Occupational Risk Factors

as an exposure is a risk factor for many diseases, including heart disease and cancer.

In the workplace, shift work has been shown to affect workers' rates of smoking.[196] Other occupational risk factors demonstrated to affect smoking rates include work at sea,[197] construction and cleaning work,[198] and work-related stress.[199] Quantification of the role of smoking in occupational health has been difficult but is becoming increasingly exact.[200,201] Smoking may also exert a healthy worker effect, with workers who have a stronger smoking history and possibly shorter work lives affecting the interpretation of studies of interactions with ORFs.

Alcohol Use

Alcohol consumption is highly prevalent in many countries and is associated with extensive morbidity and mortality.[202,203] It has been estimated that alcohol misuse contributes extensively to lost workdays and lost productivity.[204] Workplace harassment has been reported to lead to alcohol misuse,[205] suggesting that occupational hazards can lead to increased alcohol consumption. In addition to alcohol consumption as a general risk factor, an estimated 8.9 million workers in the United States consume alcohol during the workday and 2.3 million do so before beginning the workday.[206] Because of the significant health effects of alcohol consumption, loss of workforce members as a result of alcohol use may be another healthy worker effect that influences the understanding of interactions among personal and occupational hazards.

Prescription Drug Use

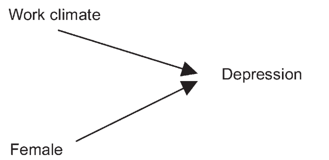
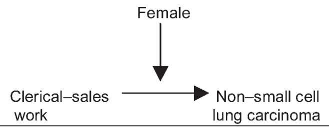
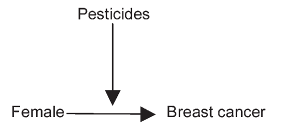
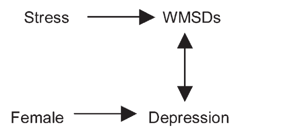
Prescription drug use has the potential to interact with ORFs, but detailed knowledge of its occupational safety and health impact remains limited. This interaction also may be related to the widespread presence of prescription drug use in developed and developing societies.[207] An aging workforce can be expected to have an increased need for acute and chronic pharmacological regimens.[207] Prescription drug use (the exposure, or PRF) can thus possibly lead to a range of occupational outcomes.

The PRFs associated with prescription drug use may reflect adverse side effects from single medications, interactions between drugs, or polypharmacy. For example, workplace musculoskeletal trauma can lead to greater consumption of prescription nonsteroidal anti-inflammatory agents and narcotics,

TABLE 2—Common Chronic Diseases or Conditions Present in the Workforce, by Age

Age < 45 Years	Age 45–54 Years	Age 55–64 Years	Age Not Specified
Asthma	Stress	Coronary heart disease	Allergies
	Depression	Hypertension	Respiratory infections
	Anxiety	Arthritis	Migraines/other headaches
		Musculoskeletal pain	Bipolar disorder (with depression)
		Diabetes	Hypercholesterolemia (with coronary heart disease)
			Cancer

Source. Adapted from Munir et al. and Hymel et al.[181a,181b]

Conceptual Model		Examples	Reference(s)
1. Gender and an ORF are independent risks for occupational disease		A. Women have more risk of depression; poor work climate, skill level associated with depression; gender differences in depression in the workplace may be significant B. Scleroderma is 14 times more common in women; solvents, vibration, etc. are associated with scleroderma; gender differences in occupational scleroderma may be important	60–69
2. Gender modifies an ORF–occupational disease association		A. Non–small cell lung carcinoma increased in clerical, transportation, and service workers, with gender differences B. Workplace injuries/WMSDs sometimes greater for women	38,70–73
3. An ORF modifies a gender–occupational disease association		Exposure to some pesticides, metals, acid mists, sterilizing agents (ethylene oxide), light at night (shift work), and tobacco smoke increases women's risk of breast cancer	74–78
4. Gender is a risk for one disease/disease state, an ORF is a risk for another, and the 2 interact		Psychosocial stress is associated with musculoskeletal disorders; depression may affect the development of chronic musculoskeletal disease; women have a greater risk of depression; the interaction of depression and WMSDs may vary by gender	69,79–81

Note. ORF = occupational risk factor; WMSD = work-related musculoskeletal disease. Bidirectional and unidirectional arrows indicate flow of effect in the models exemplified.

FIGURE 4—Examples of 4 Conceptual Models of the Relationships Between Gender and Occupational Risk Factors

increasing the risk of adverse side effects from these drugs.[208]

Exposures during the manufacturing and processing of drugs can lead to adverse outcomes such as allergy and urticaria.[209] An additional factor for pharmaceutical industry workers is the impact of concomitant exposures to chemicals that can interact with prescribed drugs. Rates of prescription drug use vary by occupation, with high-stress occupations associated with increased use of psychotropic prescription drugs.[210] Use of prescription medicine can also ameliorate the effects of occupational risk factors.[211] A high-stress job can exacerbate hypertension, but workers' use of antihypertensive medications can result in work performance improvements and reductions in absenteeism.[212]

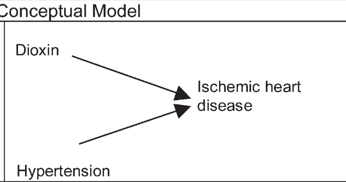
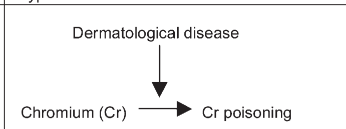
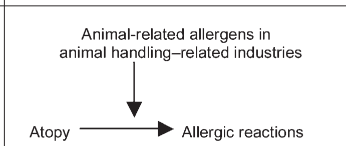
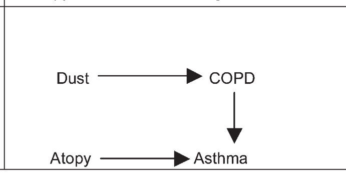
A precondition may lead to both the use of a prescription drug and an adverse outcome, the so-called effect modification by proxy.[21] The drug is not the cause of the adverse outcome but is a modifier, by proxy, of the effect of interest.[213] Differentiation of true effect modifiers from effect modifiers by proxy will be a critical issue in evaluating prescription drugs as PRFs, and future research should take this into consideration.

OVERVIEW

We have described and illustrated 4 conceptual models for the evaluation of the role of ORFs and PRFs in the development of disease. At an initial stage, a model theorizing an isolated ORF–disease relationship is potentially useful in developing interventions in the workplace. The seemingly reasonable nature of such a model, however, is perhaps a result mainly of the state of knowledge at a given point in time. In the case of many diseases, such a rudimentary model is inappropriate because the relationship between risk factors and disease is shown by epidemiological and other data to be complex.

Model 1 represents independent effects of ORFs and PRFs on outcomes. Some examples of such effects, such as the roles of genetic variants in testicular cancer and the link between firefighting and testicular neoplasms, highlight the potential independent action of PRFs and ORFs on certain diseases. However, other examples used to illustrate model 1 (Figures 2–9), such as the effects of fatigue and sedatives on workplace injuries, could easily require more complex modeling frameworks as research provides new insights. This potentiality underscores the fluidity required in such modeling efforts.

Models 2 and 3 represent interaction effects (effect modification) of ORFs and PRFs in the etiology of occupational disease. Both of these models illustrate effect modification. Assessing effect modification may be useful in at least 3 ways.[7,8,21,22] First, understanding effect modification may define subgroups most in need of intervention. Second, effect modification may help elucidate how the joint biological effects of 2 exposures inhibit or enhance each other. Third, effect modification may reveal different mechanisms. For example, as discussed in the section on genetics, recent investigations have suggested that certain aromatic amines, such as benzidine, use genetic pathways for the development of cancer that are different from

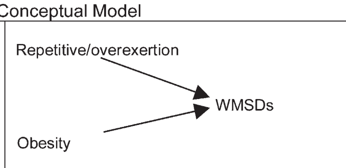
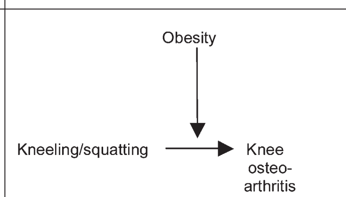
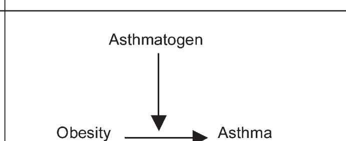
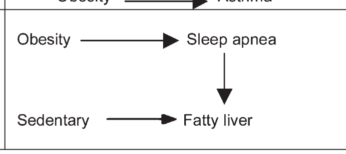
Conceptual Model		Examples	Reference(s)
1. A chronic disease and an ORF are independent risks for occupational disease		Dioxin may be a risk for ischemic heart disease; hypertension is a risk for ischemia; combined impact will be significant	82–84
2. Chronic disease modifies an ORF–occupational disease association		Eczema and dermatitis increase risk of poisoning from occupational chromium exposure	85,86
3. An ORF modifies a chronic disease–occupational disease association		Exposure to animal dander/furs/dusts in workers with atopy-based allergic reactions	87–92
4. A chronic disease is a risk for one disease/disease state, an ORF is a risk for another, and the 2 interact		Atopy can lead to asthma; psyllium workers, bakers, and laboratory animal handlers with atopy have greater risk of IgE-dependent asthma than those without; occupational dust is a risk factor for COPD; COPD can compound asthma	93–96

Note. COPD = chronic obstructive pulmonary disease; ORF = occupational risk factor. Bidirectional and unidirectional arrows indicate flow of effect in the models exemplified.

FIGURE 5—Examples of 4 Conceptual Models of the Relationships Between Chronic Disease and Occupational Risk Factors

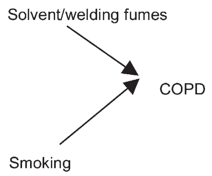
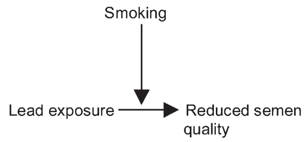
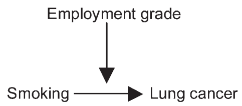
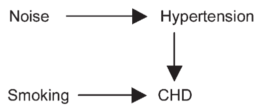
those of other compounds such as 2-naphthylamine and 4-aminobiphenyl.

Model 4 represents more complicated effects of ORFs and PRFs on occupational illness and injury. Although our examples focus on model 4 in its basic form, this model can also be described in an expanded format, which enables consideration of more complex relationships between ORFs and PRFs. For example, in some contexts, obesity can be considered a PRF that is a result of an ORF, such as shift work, that in turn can subsequently interact with that same ORF to affect another adverse outcome, such as cardiovascular endpoints. However, presenting examples

Conceptual Model		Examples	Reference(s)
1. Obesity and an ORF are independent risks for occupational disease		Obesity is an independent risk factor for WMSDs; skill, psychosocial factors associated with WMSDs	28,42,44,46, 81,97–99
2. Obesity modifies an ORF–occupational disease association		A 14-fold increase in risk of osteoarthritis among those with high body mass index and significant prolonged kneeling at work vs those with low body mass index who were not exposed to kneeling in the workplace	100,101
3. An ORF modifies an obesity–occupational disease process		Obesity increases asthma risk; exposure to work asthmatogens may exacerbate obesity-related asthma	15,96,102–105
4. Obesity is a risk for one disease/disease state, an ORF is a risk for another, and the 2 interact		Obesity can lead to sleep apnea; occupational risk factors may lead to fatty liver; sleep apnea increases risk for fatty liver disease	106–108

Note. ORF = occupational risk factor; WMSD = work-related musculoskeletal disease. Bidirectional and unidirectional arrows indicate flow of effect in the models exemplified.

FIGURE 6—Examples of 4 Conceptual Models of the Relationships Between Obesity and Occupational Risk Factors

Conceptual Model		Examples	Reference(s)
1. Smoking and an ORF are independent risks for occupational disease		A. Smoking, organic solvents associated with COPD; welding fumes, polycyclic aromatic hydrocarbons modify the relationship between smoking and adenocarcinoma B. Smoking, occupation are independent risks for amyotrophic lateral sclerosis	109–127
2. Smoking modifies an ORF–occupational disease association		A. Smoking affects the relationship between lead exposure and lead-induced reduction in semen quality B. In a review of occupational asthma, smoking appeared to increase the risk of IgE-mediated occupational asthma C. Occupational exposure to noise leads to hearing loss at 4000–6000 Hz; smoking leads to hearing loss at 8000 Hz	128–139
3. An ORF modifies a smoking–occupational disease association		Association of smoking and lung cancer in the Whitehall study; link between employment grade and malignant neoplasms of the lung in earlier Whitehall cohort	140,141
4. Smoking is a risk for one disease/disease state, an ORF is a risk for another, and the 2 interact		Meta-analysis estimates that for each 5 decibels of occupational noise exposure, systolic blood pressure increases by 0.51 mmHg; smoking is the most important modifiable risk factor for CHD; hypertension is a major risk factor for CHD	142–144

Note. CHD = coronary heart disease; COPD = chronic obstructive pulmonary disease; ORF = occupational risk factor. Bidirectional and unidirectional arrows indicate flow of effect in the models exemplified.

FIGURE 7—Examples of 4 Conceptual Models of the Relationships Between Smoking and Occupational Risk Factors

of the expanded version of this model and discussing in detail various other statistical analysis issues were beyond the scope of the present work.

Future work should explore statistical and epidemiological considerations of basic and complex modeling approaches and issues associated with interactive effects. Other areas of investigation should include the role of particular statistical approaches in analyzing models with PRFs and ORFs, including, but not limited to, the utility of various regressions and other techniques. Assessment of the etiological fraction or relative strength of PRFs and ORFs was also beyond the scope of this study.

A Comprehensive Approach

From the vantage point of public health in the workplace, different exposures to workplace hazards leading to multiple adverse outcomes compound the medical burden on individual workers as well as the burden on the workforce as a whole.[1] The modeling of independent versus interactive effects of ORFs and PRFs on occupational illness and injury is the initial step in the process of defining the causes of illness and injury. In examining mechanisms, risk factors, or outcomes, modeling of this nature represents a theoretical framework for a comprehensive approach to the overall health of working people.

The bulk of our investigation involved assessing the scientific literature to obtain examples of the relationship of 8 PRFs (genetics, age, gender, chronic disease, obesity, smoking, alcohol use, and prescription drug use) to disease, individually and in relation to work, with a general focus on epidemiological studies. It should be noted that, in several cases, applying selection criteria to articles that might conventionally be considered disparate but were found to be relevant to a particular disease process illustrated the potential to link different domains of information to model ORFs, PRFs, and occupational disease and develop new hypotheses for subsequent analyses.

Although the examples we identified were not necessarily the only possible interactions with a particular PRF, or even the most important from a clinical or public health perspective, they do illustrate a range of important health conditions, many with significant societal burdens. Furthermore, these examples provide a roadmap for melding scientific and clinical knowledge that may have been divided by disciplinary boundaries so that we can develop broader models of occupational illness and injury.

The placement of an ORF, PRF, and disease process grouping in a particular model is also subject to the current level of scientific knowledge. This issue is reflected in various models for several of the PRFs presented here, including gender and prescription drugs. More research evaluating the impact of PRFs on the relationship of ORFs to occupational disease is needed. For example, given the extensive acute and chronic use of pharmacological agents in modern society, there is a need for studying the impact of this PRF and its role as an independent or modifying variable, which has significant implications for modern occupational health.

Conceptual Model		Examples	Reference(s)
1. Alcohol use and an ORF are independent risks for occupational disease	VCM → Liver cirrhosis; Alcohol → Liver cirrhosis	Occupational exposure to both VCM and alcohol have been associated with cirrhosis of the liver	145
2. Alcohol use modifies an ORF–occupational disease association	Alcohol ↓ (Job strain → Hypertension)	Job strain increases the risk of hypertension; alcohol use interacts with occupational risk factors in high-strain but not low-strain jobs	28,146
3. An ORF modifies an alcohol use–occupational disease association	Blue-collar work ↓ (Alcohol → Laryngeal cancer)	Blue-collar work status affects the association between alcohol use and laryngeal cancer	147
4. Alcohol use is a risk for one disease/disease state, an ORF is a risk for another, and the 2 interact	Health care work → HBV; HBV ↓ Cirrhosis; Alcohol → Cirrhosis	Alcohol use is a risk for liver cirrhosis; needle stick injuries in health care workers increase the risk of HBV; interactions may be important	148–153

Note. HBV = hepatitis B virus; ORF = occupational risk factor; VCM = vinyl chloride monomer. Bidirectional and unidirectional arrows indicate flow of effect in the models exemplified.

FIGURE 8—Examples of 4 Conceptual Models of the Relationships Between Alcohol Use and Occupational Risk Factors

In the example of the role of smoking and noise in coronary heart disease shown in Figure 7 (model 4), differences in disease mechanism may exist, with interventions and health promotions varyingly affected. However, more complex models incorporating multiple PRFs and ORFs may be more informative in identifying high-risk combination scenarios.

There is value in considering both ORFs and PRFs in epidemiological studies. At the design stage of such investigations, methodological issues regarding direct effects, confounding, effect modification, exposure misclassification, and conceptualization of the term "interaction," from a statistical as well as a biological

Conceptual Model		Examples	Reference(s)
1. Prescription drug use and an ORF are independent risks for occupational disease	Fatigue → Injury; Sedatives → Injury	Both sedating medications and workplace factors, such as fatigue, can independently lead to occupational injuries	154,155
2. Prescription drug use modifies an ORF–occupational disease association	Vaccine ↓ (Anthrax/lab work → Death)	Vaccination of laboratory workers to prevent diseases such as anthrax; vaccines may have role in postexposure prophylaxis	156–161
3. An ORF modifies a prescription drug use–occupational disease association	Hours worked/work schedule variability (after control for noise level) ↓ (Gastrointestinal medication → Medication use side effects)	Hours worked/work schedule variability, after control for noise level, was found to be associated with increased gastrointestinal medication use; increased gastrointestinal medication use may lead to increased side effects	162
4. Prescription drug use is a risk for one disease/disease state, an ORF is a risk for another, and the 2 interact	Health care work → HBV; HBV ↕ Liver injury; Nonsteroidal anti-inflammatory medication use → Liver injury	Needle sticks in health care workers increase the risk of HBV; drug-related liver failure is a growing issue; HBV secondary to needle exposure and drug-related liver failure may represent an important model	149–153,163, 164

Note. HBV = hepatitis B virus; ORF = occupational risk factor; PRF = personal risk factor. Bidirectional and unidirectional arrows indicate flow of effect in the models exemplified.

FIGURE 9—Examples of 4 Conceptual Models of the Relationships Between Prescription Drug Use and Occupational Risk Factors

perspective, should be explored, with rationales and models supported empirically or theoretically. For example, studies of gene–environment interactions, such as recent explorations representing environmental exposures with the concept of the "exposome" (a measure of all exposures of an individual in a lifetime and how those exposures relate to disease) and the interaction of such representations with genetic factors evaluated in genomic-wide association studies, may suggest future contexts in which to further evaluate the nature of interactions between ORFs and PRFs.[169,214]

These methodological considerations are germane not only to occupational epidemiological and other biological study designs but also to risk evaluation and assessment, interventional paradigms, and health promotion in the workplace. Such design, analysis, intervention, and promotion development requires careful consideration of the occurrence, direction, and magnitude of effects to optimally judge study designs or data relevant to risk or outcome analyses.[215] In addition, collection of PRF data will likely increase the cost of research on risk factor interactions. However, a more thorough appraisal of the health of the workforce may lead to more effective interventions.

Other Logistical Considerations

Evaluations of ORFs and PRFs in occupational safety and health research should be reinforced by other logistical considerations. Occupational factors need to be regularly included in medical records, particularly as new electronic record formats are being developed.[216] Clinicians may be able to provide a more thorough appraisal of a patient's condition with an occupational history.[217] Knowledge of the interaction of risk factors may foster enhanced management of occupational illness and injury. Occupational medicine clinicians may use information about risk factor interactions to better address workplace safety and health problems, particularly with respect to understanding and addressing health issues arising from exposures in the workplace versus those arising from PRFs. From the perspective of general medical practitioners, broader information about PRF and ORF interactions may assist in addressing general health issues in populations in which health prevention and promotion are a major focus.[217]

Workers' compensation efforts may necessitate a new category of cause, effect, and risk determination with implications for the use of worker's compensation and health care resources. Ethical, legal, and social issues relevant to long-held beliefs and approaches regarding disease causation, compensation, blame, and liability will also need to be considered. In addition, the recent passage of the Patient Protection and Affordable Care Act, which allows employers to offer a health plan premium differential based on employees meeting standards such as not smoking, reaching recommended weight levels, and having normal blood pressure, underscores a variety of ethical, legal, and social issues even as it promotes the broader use of comprehensive health promotion programs in workplaces.[218] Nonetheless, with an aging workforce and potential workforce shortages, there is a need to consider a comprehensive approach to the health of the workforce and to invest in studying its ramifications.

Globally, explaining the distribution of health and disease exclusively in terms of risk factors in individuals only partly addresses the health of the workforce. There is a need for contextual or multilevel analyses that address group- or macro-level variables given that various economic, social, cultural, and environmental group-level characteristics have been shown to be strongly related to the health of the workforce.[219–223]

Modeling that considers both PRFs and ORFs would provide a foundation for an integrated worklife approach that combines protection from workplace hazards and health promotion.[181b,224–228] This approach could include, for example, the development of wellness programs at worksites or funded by employers. These types of programs have been demonstrated to result in a positive return on investment for both workers and employers.[2,12,229,230] Nonetheless, attention to PRFs and wellness should not be a reason for employers to fail to provide a safe and healthy workplace or to blame workers for occupational health and safety problems.[11,15]

Conclusions

We have presented 32 examples of disease processes for 8 PRFs and 4 models, demonstrating an extensive catalog of combinations and interactions of ORFs and PRFs among workers. These examples clearly demonstrate the utility of new representations of PRF–ORF combinations and their impact on our understanding of disease with respect to hypothesis generation, study design, risk evaluation and assessment, workplace intervention, clinical evaluation, and health promotion in working populations. The models and examples offered here highlight the value of conceptual representations of relationships between ORFs, PRFs, and disease to drive more fully developed approaches to control occupational illness and injury and develop a comprehensive view of workforce health.

Models that combine ORFs and PRFs contain an inherent flexibility to model greater disease complexity; can guide various stages of epidemiological investigation, data analysis, and intervention development; and possess the capacity to incorporate intricate variables and analyses. Employing models and approaches that maximize consideration of factors impinging on the health of the workforce will allow researchers and practitioners to move beyond the historically fractionated approach to occupational illness and injury.

Thus, a comprehensive approach to the health of working people can form the basis for research and investigation into occupational illness and injury, address issues important for maintaining a healthy workforce despite pressures from factors such as aging and unsustainable dependency ratios, and contribute to the fostering of an integrated work life to better protect worker safety and health and fortify national and societal well-being. ■

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Contributors

P. A. Schulte conceptualized the article and developed the first draft with V. Wulsin. P. A. Schulte and

S. Pandalai made various revisions leading to the final article. S. Pandalai helped to reconceptualize the models and contributed extensively to the figure and tables. H. Chun contributed to writing early drafts and provided input to Figures 2–9. All of the authors participated in the literature review.

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Because no human participants were involved in this research, no protocol approval was needed.

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