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Integrating exposure measurements into epidemiologic studies in agriculture

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Agricultural epidemiology studies frequently rely on questionnaires to assess pesticide exposure. Farmers can provide accurate information regarding their pesticide use history. However, pesticide exposure is influenced not only by the pesticide, but also by factors related to pesticide application and behavior; estimates of exposure can be improved by incorporating data on these factors. Exposure measurement studies help to elucidate influential factors with regard to pesticide dose. These factors can be incorporated into exposure estimates to reduce measurement error and allow for better resolution of the exposure distribution. In the Agricultural Health Study, two exposure algorithms were developed to evaluate exposure intensity; this exposure intensity score was used to modify the lifetime days of pesticide application. This metric, along with additional refinement as a result of on-going field studies, will allow better assignment of exposure levels in the cohort. Future work to develop exposure metrics that incorporate both chemical and behavior characteristics for all farmworkers and farm residents will further improve epidemiologic studies in agriculture.

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Epidemiologic studies frequently rely on questionnaire information to assess exposures. Measured exposure data can provide critical information to improve pesticide exposure estimates in epidemiologic studies in agriculture. Measurement data can facilitate improved exposure estimation if they are used to identify the predictors and determinants of exposure. This, in turn, can result in better use of questionnaire information and better design of future questionnaires. As indicated by other papers (1, 2), exposure measurement studies are very rigorous, resource intensive operations that capture a snapshot of the pesticide exposure experience of the population at one point in time. The challenge is how to incorporate the results of these studies into epidemiologic studies in which exposure information is primarily questionnaire based.

The assignment of pesticide exposure in epidemiologic studies has evolved from crude surrogates, such as farming or living in a rural area, to personal application history of pesticides. Farmers have been shown to provide reliable information regarding their personal pesticide use (3–6). Proxies for farmers have been able to report the types of chemicals used (herbicides, insecticides, etc), but are not as accurate with regard to individual chemicals (4). Conversely, farmworkers, who are not farm owners or operators, often do not know what pesticides have been used on the crops on which they work, but can accurately report crops worked and geographic region (7). This information can be combined with other data regarding crop and pesticide usage to estimate potential pesticide exposures. Since working with a pesticide does not determine the extent of exposure, as indicated by Lunchick et al (2), questionnaires may also obtain information to determine the extent of exposure associated with pesticide usage.

The workhorse of epidemiologic studies in agriculture is the questionnaire. Questionnaires can be used to obtain information regarding chemicals used, application methods, use of personal protective gear, and work practices that may contribute to pesticide exposure. Questionnaires frequently address both current and historical pesticide use practices, while exposure measurement data can only be obtained for current application practices. Questionnaire data can be combined with other resources to create appropriate exposure metrics, through the use of job exposure matrices (8) or algorithms such

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as the one developed to assess the intensity of pesticide exposure among applicators in the Agricultural Health Study (9).

The primary goal of exposure estimation in epidemiology is to rank persons correctly with regard to exposure level in the population. While quantitative exposure measures may be optimal for some purposes (eg, risk assessment), much can be learned from data that provide relative exposure ranking. To reduce exposure misclassification, it is important to separate the unexposed from the low-exposed and to correctly identify highly exposed persons. Because pesticide exposures can be highly variable, exposure assessment tools in epidemiology need to correctly classify a person's average exposure. The exposure period of interest depends on the outcome; for example, for cancers, we are more interested in past exposures than current exposures, while, for birth defects, we may be more interested in in utero and preconception exposures.

Exposure measurement studies, particularly those including both environmental and biological measures of exposure, provide critical information regarding the predictors and modifiers of pesticide exposure to farmers and their families. They often collect information regarding chemical properties and formulation, application rate, mixing methods and behavior, such as the use of personal protective equipment. These studies have contributed a wealth of information regarding factors associated with pesticide application. The Pesticide Handlers Exposure Database (PHED) was developed to standardize pesticide exposure estimates, and it contains exposure information from over 100 studies of pesticide mixing, loading, and applying methods without individual chemical information (10). These data, along with those in the open literature that provide chemical-specific information, allow for the evaluation of the determinants of pesticide exposure and their relative contribution to personal pesticide exposure. Determining which exposure factors are chemical- or product-specific and which factors can be considered generically (as in the PHED) is best answered by field-monitoring studies.

Incorporating measurement data into epidemiologic studies is challenging. One key aspect is that measurement studies evaluate one point in time and obtain detailed information regarding all aspects of pesticide application, while epidemiologic studies are often interested in the long-term and chronic effects of pesticide exposure and are limited with respect to the amount of information that can be collected regarding the lifetime history of pesticide application. What predicts pesticide levels on a given day may not be relevant for long-term exposure. Conversely, one short event with a spill or other events involving high pesticide exposure may contribute greatly to someone's annual pesticide dose. Farming and pesticide applications are highly variable and are subject to change as a result of a variety of factors, including temperature, wind, rain fall, insect burden, and application methods; thus extrapolation from short-term exposure measurements to long-term estimates of exposure should occur with caution. While many predictors of exposure have been identified, combining information regarding exposure factors across studies and assigning the relative weights of these factors are not trivial tasks.

In the Agricultural Health Study, Dosemeci and his colleagues (9) have developed two algorithms that use measured exposure data to assign weights to estimate exposure intensity in association with pesticide application. These exposure intensities are used to modify the reported lifetime cumulative pesticide application history (lifetime days of application) for each chemical. The general algorithm (equation 1) uses questionnaire information from over 58 000 licensed pesticide applicators enrolled in the Agricultural Health Study to calculate an exposure-intensity factor. The intensity factor assigns weights for mixing and applying pesticides and repairing pesticide equipment, based on their relative contributions observed in monitoring studies. These weights are further modified by the use of personal protective equipment (PPE), such as chemically resistant gloves. The general intensity score is not chemical-specific and relies on information from the PHED and other studies to create the weights used. These weights were used to modify chemical-specific cumulative durations to create intensity-adjusted lifetime duration values. The use of PPE as a reduction measure is consistent with the data that Lunchick et al (2) presented for MoCap workers, for whom the use of gloves and closed mixing systems dramatically reduced potential exposure.

$$\text{Intensity}_{\text{general}} = (\text{mix} + \text{apply} + \text{repair}) \times \text{PPE}, \qquad \text{(equation 1)}$$

where mix = the frequency of mixing pesticides (0, 3, 9), apply = application method (0–9), repair = repair of application equipment (0, 2), PPE = personal protective equipment (0.1–1.0), and the range of weights is in parentheses.

For the approximately 23 000 pesticide applicators who completed the more-detailed take-home questionnaire, a more-detailed algorithm (equation 2) was developed that created different intensity scores for different functional classes of pesticides (herbicides, crop insecticides, livestock insecticides, fungicides, and fumigants) and incorporated more information regarding pesticide handling behavior and other practices that may influence exposure intensity, such as enclosed mixing systems, cabs on tractors, glove replacement, clean up after spills, and general occupational hygiene practices. While the detailed algorithm incorporated additional information, the intensity scores for the general and detailed algorithm were highly correlated (9).

$$\text{Intensity}_{\text{detailed}} = [(\text{mix} \times \text{enclosed}) + (\text{apply} \times \text{cab}) + \text{repair} + \text{wash}] \times \text{PPE} \times \text{replace} \times \text{hygiene} \times \text{spill}, \quad \text{(equation 2)}$$

where, enclosed = enclosed mixing system (0.5, 1), cab = cab on tractor (0.2, 0.5, 1), wash = washing equipment after application (0, 2), replace = frequency of replacing gloves (1–1.5), hygiene = personal hygiene (0.2–1), spill = changing clothes after spill (0.2–1), and the range of weights is in parentheses.

These algorithms allow for the differentiation between people with similar exposure durations to help identify the truly highly exposed people, and they have been applied in epidemiologic analyses involving this cohort (11). These algorithms will evolve over time. Current efforts are underway by the Environmental Protection Agency and the National Institute for Occupational Safety and Health in the United States to evaluate these metrics using field measurements and biological measures of exposure. These and other current studies are attempting to expand our understanding of the important predictors of exposure and build on a growing literature. These studies will also allow us to refine our questionnaires to include key exposure predictors while removing redundant and uninformative questions. In addition, efforts are underway to develop the best predictive models of exposure to identify strategies to improve exposure estimation via questionnaires. Some of the standardization parameters that are the most useful in model building, such as the amount of active ingredient applied, may be outside the range of recall in a large questionnaire survey, but appropriate surrogates for this metric may also be identified. Behavior characteristics based both on fieldworker observations and applicator self-report will be considered for inclusion in revised algorithms. Future work should focus on developing exposure algorithms for all farm workers and residents, since very limited data are available for farm spouses and children.

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