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A Quantitative Approach for Estimating Exposure to Pesticides in the Agricultural Health Study

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We developed a quantitative method to estimate long-term chemical-specific pesticide exposures in a large prospective cohort study of more than 58000 pesticide applicators in North Carolina and Iowa. An enrollment questionnaire was administered to applicators to collect basic time- and intensity-related information on pesticide exposure such as mixing condition, duration and frequency of application, application methods and personal protective equipment used. In addition, a detailed take-home questionnaire was administered to collect further intensity-related exposure information such as maintenance or repair of mixing and application equipment, work practices and personal hygiene. More than 40% of the enrolled applicators responded to this detailed take-home questionnaire. Two algorithms were developed to identify applicators' exposure scenarios using information from the enrollment and take-home questionnaires separately in the calculation of subject-specific intensity of exposure score to individual pesticides. The 'general algorithm' used four basic variables (i.e. mixing status, application method, equipment repair status and personal protective equipment use) from the enrollment questionnaire and measurement data from the published pesticide exposure literature to calculate estimated intensity of exposure to individual pesticides for each applicator. The 'detailed' algorithm was based on variables in the general algorithm plus additional exposure information from the take-home questionnaire, including types of mixing system used (i.e. enclosed or open), having a tractor with enclosed cab and/or charcoal filter, frequency of washing equipment after application, frequency of replacing old gloves, personal hygiene and changing clothes after a spill. Weighting factors applied in both algorithms were estimated using measurement data from the published pesticide exposure literature and professional judgment. For each study subject, chemical-specific lifetime cumulative pesticide exposure levels were derived by combining intensity of pesticide exposure as calculated by the two algorithms independently and duration/frequency of pesticide use from the questionnaire. Distributions of duration, intensity and cumulative exposure levels of 2,4-D and chlorpyrifos are presented by state, gender, age group and applicator type (i.e. farmer or commercial applicator) for the entire enrollment cohort and for the sub-cohort of applicators who responded to the take-home questionnaire. The distribution patterns of all basic exposure indices (i.e. intensity, duration and cumulative exposure to 2,4-D and chlorpyrifos) by state, gender, age and applicator type were almost identical in two study populations, indicating that the take-home questionnaire sub-cohort of applicators is representative of the entire cohort in terms of exposure.

Keywords: exposure assessment; pesticide exposure; agricultural exposures; farmers; pesticide applicators; occupational exposures

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INTRODUCTION

Several environmental and biological monitoring techniques have been used to characterize human exposure to pesticides (Rutz and Krieger, 1992; Van Hemmen, 1992; Brouwer *et al.*, 1994). These data, however, have rarely been incorporated into epidemiological studies of cancer or other chronic diseases (Zahm *et al.*, 1997).

In chronic disease research, assessment of exposure to agricultural pesticides has been limited to the use of surrogates of exposure such as type of farm operation, chemicals used, job title and duration of employment (Zahm *et al.*, 1997). A limited number of studies have obtained information on years of use, days of application per year and use of protective equipment while handling specific pesticides (Blair and Zahm, 1995).

Since it is unlikely that monitored exposures will be available for studies of chronic disease in the near future, it is necessary to develop other techniques to quantify long-term exposure levels. Exposure to pesticides may occur while transporting, mixing, loading or applying chemicals, through cleaning or repairing equipment or from re-entering treated fields. Factors affecting the level of exposure include type of activity (e.g. application, mixing, loading or harvesting), method of application (e.g. air blast, backpack, aerial spray, hand spray or ground boom application), pesticide formulation (e.g. dilute spray, aerosol or dust), application rate (e.g. weight of active-ingredient/acre), use of personal protective equipment (PPE) (e.g. gloves, respirators, face-shields, boots or overalls), and personal work habits and hygiene (e.g. changing into clean clothes/washing hands or taking bath/shower after the use of pesticide, frequency of healthcare visits). The challenge is to incorporate these exposure modifiers into an estimation of intensity of pesticide exposure.

The National Cancer Institute (NCI), the National Institute of Environmental Health Sciences (NIEHS) and the US Environmental Protection Agency (EPA) are conducting a prospective cohort study (the Agricultural Health Study, AHS) of more than 90000 farmers, farmers' spouses and commercial applicators in Iowa and North Carolina to evaluate cancer and other disease risks associated with pesticides, other agricultural exposures and lifestyle factors (Alavanja *et al.*, 1996). In this report, we describe a quantitative approach developed for the AHS to estimate applicator exposure to more than 50 individual pesticides, using questionnaire responses and pesticide information published in the literature.

MATERIALS AND METHODS

To estimate levels of exposure to pesticides, we used self-reported exposure information on pesticide use from questionnaires as well as pesticide monitoring data from the literature, the Pesticide Handlers Exposure Database, and results of EPA pilot AHS pesticide monitoring surveys.

Questionnaire information

At enrollment into the study, approximately 58000 pesticide applicators completed a questionnaire with time- and intensity-related pesticide exposure questions. The time-related information consisted of the duration (i.e. number of exposed years) and frequency (i.e. average annual number of days used) of handling (i.e. mixing, loading and/or application) for 22 pesticides [i.e. ten herbicides (atrazine, dicamba, cyanazine, metolachlor, EPTC, alachlor, imazethapyr, glyphosate, trifluralin and 2,4-D), nine crop or livestock insecticides (pyrethroid, terbufos, fonofos, trichlorfon, cabofuran, chlorpyrifos, coumaphos, permethrin and dichlorvos), one fumigant (methyl bromide) and two fungicides (chlorothalonil and captan)]. These chemicals were selected because of their importance in Iowa and North Carolina agriculture, where the study is being conducted, or because of human or animal data suggesting their possible adverse health effects. Intensity-related information included frequency of mixing pesticides, method of application, repairing application equipment and use of PPE.

All applicators who completed the enrollment questionnaire were also given a self-administered take-home questionnaire to obtain additional information for two time periods (10 years ago and 1 year ago). Information includes pesticide handling, use of an enclosed mixing system, type of tractor (open cab or enclosed cab with or without a charcoal air filtration system), procedures used to clean pesticide application equipment, personal hygiene (e.g. timing of changing into clean clothes/washing hands, or taking bath/shower after application), the practice of changing clothes after a spill, and frequency of replacing old gloves, as well as information on lifestyle factors. In this questionnaire we obtained time- and intensity related information for additional 28 chemicals [i.e. eight herbicides (chlorimuronethyl, metribuzin, paraquat, petroleum distillate, pendimethalin, butylate, 2,4,5-TP and 2,4,5-T), 13 insecticides (lindane, malathion, parathion, carbaryl, diazinon, aldicarb, phorate, aldrin, chlordane, dieldrin, DDT, haptachlor and toxaphene), three fumigants (aluminum phosphide, carbon disulfide and ethylene dibromide) and four fungicides (benomyl, maneb, metalaxyl and ziram)]. More than 40% of the enrolled applicators returned this take-home questionnaire.

Development of algorithms

The questionnaire responses were used to develop chemical-specific exposure scenarios. Quantitative intensity levels for a given exposure scenario were calculated using two algorithms based on the reported information from the enrollment questionnaire and take-home questionnaire. The general algorithm based on the enrollment questionnaire has fewer exposure variables than the detailed algorithm, which is based on the information both from the more detailed self-administered take-home questionnaire and the enrollment questionnaire.

The general algorithm

The algorithm and weights for the variables from the enrollment questionnaire are presented below.

Enrollment algorithm

Intensity Level = (Mix + Appl + Repair) * PPE

where:

Mix (mixing status):

if [Mix] = Never	then score = 0
if [Mix] = <50% of time mixed	then score = 3
if [Mix] = 50%+ of time mixed	then score = 9

Appl (application method):

if [Appl] = Does not apply	then score = 0

The following application methods are identified for five different groups of pesticide:

For herbicides

if [Appl] = Aerial-aircraft	then score = 1
if [Appl] = Distribute tablets	then score = 1
if [Appl] = In furrow/banded	then score = 2
if [Appl] = Boom on tractor	then score = 3
if [Appl] = Backpack	then score = 8
if [Appl] = Hand spray	then score = 9

For crop insecticides

if [Appl] = Aerial-aircraft	then score = 1
if [Appl] = Seed treatment	then score = 1
if [Appl] = Distribute tablets	then score = 1
if [Appl] = In furrow/banded	then score = 2
if [Appl] = Boom on tractor	then score = 3
if [Appl] = Backpack	then score = 8
if [Appl] = Hand spray	then score = 9
if [Appl] = Airblast	then score = 9
if [Appl] = Mist blower/fogger	then score = 9

For animal insecticides

if [Appl] = Ear tags	then score = 1
if [Appl] = Inject animal	then score = 2
if [Appl] = Dip animal	then score = 5
if [Appl] = Spray animal	then score = 6
if [Appl] = Pour on animal	then score = 7
if [Appl] = Powder duster	then score = 9

For fungicides

if [Appl] = Seed treatment	then score = 1
if [Appl] = Distribute tablets	then score = 1
if [Appl] = In furrow/banded	then score = 2
if [Appl] = Boom on tractor	then score = 3
if [Appl] = Backpack	then score = 8
if [Appl] = Hand spray	then score = 9
if [Appl] = Airblast	then score = 9
if [Appl] = Mist blower/fogger	then score = 9

For fumigants

if [Appl] = Gas canister	then score = 2
if [Appl] = Row fumigation	then score = 4
if [Appl] = Pour fumigant	then score = 9

Repair (repair status):

if [Repair] = Does not repair	then score = 0
if [Repair] = Repair	then score = 2

PPE (Personal Protective Equipment use):
Four groups of PPE categories are identified considering combinations of PPE used:

PPE-0 (0% PROTECTION):
[PPE] = never used PPE
PPE-1 (20% PROTECTION):
[PPE] = Face shields or goggles
[PPE] = Fabric/leather gloves
[PPE] = Other protective clothing, such as boot
PPE-2 (30% PROTECTION):
[PPE] = Cartridge respirator or gas mask
[PPE] = Disposable outer clothing
PPE-3 (40% PROTECTION):
[PPE] = Chemically resistant rubber gloves

Then the scores for each PPE type are:

PPE-0 = 1.0
PPE-1 = 0.8
PPE-2 = 0.7
PPE-3 = 0.6
PPE-1 & PPE-2 = 0.5
PPE-1 & PPE-3 = 0.4
PPE-2 & PPE-3 = 0.3
PPE-1 & PPE-2 & PPE-3 = 0.1

The enrollment questionnaire provided the time-related information, such as duration and frequency for each chemical-specific pesticide, however, the intensity-related information (i.e. Mix, Appl, Repair and PPE) was obtained for all pesticides combined, rather than individual chemicals or chemical class. If the subject marked more than one application method, then the mean of scores for marked methods were used in the calculation the 'Appl' variable. For example, in a following scenario for 2,4-D, the intensity level of exposure was calculated as follows:

2,4-D used: Yes
Mixing status: Personally mixes pesticides more than 50% of time *[score = 9]*
Application method: Backpack spray *[score = 8]*
Repair status: Personally repairs application equipment *[score = 2]*
PPE status Wears rubber gloves and boots *[PPE-1 & PPE-3; score = 0.4]*

Intensity level = (Mix + Appl + Repair) * PPE
= (9 + 8 + 2) * 0.4 = 7.6

The detailed algorithm

In the take-home questionnaire, we have more pesticide-specific exposure information than that from the enrollment questionnaire. For example, intensity variables, such as mixing conditions, application type and PPE used, were collected by group of chemicals (i.e. herbicides, crop insecticides, livestock insecticides, fungicides and fumigants). In addition, we asked detailed questions about work practices such as washing pesticide equipment after application, frequency of replacing old gloves, personal hygiene behavior on changing into clean clothes and washing hands or taking bath/shower after application, and changing clothes after a spill.

For the information obtained from the take-home questionnaire, we used the following algorithm to calculate the intensity level for each exposure scenario.

Detailed algorithm

Intensity Level = [(Mix * Enclosed) + (Appl * Cab) + Repair + Wash] * PPE * Repl * Hyg * Spill

where:

Mix (Status of pesticide mixing):
if [Mix] = Never mixed then score = 0
if [Mix] = Mixed then score = 9

Enclosed (Using enclosed mixing system):
if [Enclosed] = Yes then score = 0.5
if [Enclosed] = No then score = 1.0

Appl (Application methods for herbicides, crop insecticides, fungicides):
if [Appl] = Does not apply then score = 0
if [Appl] = Aerial-aircraft hen score = 1
if [Appl] = In furrow/banded then score = 2
if [Appl] = Boom on tractor then score = 3
if [Appl] = Backpack then score = 8
if [Appl] = Hand Spray then score = 9
if [Appl] = Mist blower/fogger then score = 9
if [Appl] = Airblast then score = 9

(Application methods for livestock insecticides):
if [Appl] = Does not apply then score = 0
if [Appl] = Ear tags then score = 1
if [Appl] = Hang pest strips then score = 2
if [Appl] = Rope wick then score = 2
if [Appl] = Dip animal then score = 5
if [Appl] = Spray animal then score= 6
if [Appl] = Spray buildings then score= 6
if [Appl] = Dust animals then score= 7
if [Appl] = Pour on animal then score= 7
if [Appl] = Fog/mist animal then score= 9

(Application methods for fumigants):
if [Appl] = Does not apply then score= 0
if [Appl] = Gas canister then score= 2
if [Appl] = Row fumigation then score= 4

Cab (Tractor with enclosed cab and/or charcoal filter):
if [Appl] = Boom, in furrow, hand spray, mist blower, or airblast on tractor
and
if [Cab] = Yes; and [Filter] = Yes
then score = 0.1
if [Cab] = Yes; and [Filter] = No
then score = 0.5
if [Cab] = No; or don't use tractor
then score = 1.0

Repair (Status of repairing equipment):
if [Repair] = No then score= 0
if [Repair] = Yes then score= 2

Wash: (Status of washing pesticide equipment after application)
if [Wash] = Don't wash then score = 0
if [Wash] = Hose down sprayer
then score = 0.5
if [Wash] = Hose down tractor then score = 0.5
if [Wash] = Clean nozzle then score = 3
if [Wash] = Rinse tank then score = 1

PPE (Personal Protective Equipment use):
Four groups of PPE categories are identified, considering combinations of PPE used:

PPE-0 (0% PROTECTION):
[PPE] = never used PPE
[PPE] = Hat only
PPE-1 (20% PROTECTION) one or more indicated PPE:
[PPE] = Dust mask
[PPE] = Full face shields
[PPE] = Goggles
[PPE] = Fabric/leather gloves
[PPE] = Apron
[PPE] = Cloth overall

PPE-2 (30% PROTECTION) one or more indicated PPE:
[PPE] = Cartridge respirator, gas mask
[PPE] = Chemically resistant boots
[PPE] = Disposable outer clothing (Tyvek)
PPE-3 (40% PROTECTION):
[PPE] = Chemically resistant rubber gloves

Scores for combinations of PPE use:

PPE-0 = 1.0
PPE-1 = 0.8
PPE-2 = 0.7
PPE-3 = 0.6
PPE-1 & PPE-2 = 0.5
PPE-1 & PPE-3 = 0.4
PPE-2 & PPE-3 = 0.3
PPE-1 & PPE-2 & PPE-3 = 0.1

Repl (Replacing old gloves):
if [PPE] = Fabric/leather gloves
and
[Repl] = Change after each use then score = 1.0
or
[Repl] = Change once a month or 1–4 times per season then score = 1.1
or
[Repl] = Change when they are worn out then score = 1.2

Hyg (Personal hygiene: changing into clean clothes and washing hands or taking bath/shower):

Five categories of personal hygiene habits are identified:

Hyg-1: (80% protection; score = 0.2)
if [Change clothing] = Right away; or always use disposable clothing
and
[Wash or shower] = Hands/arms washed right away; Bath/shower right away; or Bath/shower at lunch
Hyg-2: (60% protection; score = 0.4)
if [Change clothing] = Right away; or use disposable clothing
and
[Hand wash/shower] = Bath/shower at the end of the day
or
if [Change clothing] = At lunch; or at the end of the day
and
[Hand wash/shower] = Hands/arms washed right away; Bath/shower right away; or Bath/shower at lunch
Hyg-3 (40% protection; score = 0.6):
if [Change clothing] = Right away; or use disposable clothing
and
[Hand wash/shower] = Hand/arms only at the end of the day
or
if [Change clothing] = At lunch; or at the end of the day
and
[Hand wash/shower] = Bath/shower at the end of the day
or
if [Change clothing] = At the end of the next day; or later in the week
and
[Hand wash/shower] = Hands/arms washed right away; Bath/shower right away; or Bath/shower at lunch
Hyg-4 (20% protection; score = 0.8):
if [Change clothing] = At lunch; or at the end of the day
and
[Hand wash/shower] = Hands/arms washed at the end of the day
or
if [Change clothing] = At the end of the next day; or later in the week
and
[Hand wash/shower] = Bath/shower at the end of the day
Hyg-5 (No protection; score =1.0):
if [Change clothing] = At the end of the next day, or later in the week
and
[Hand wash/shower] = Hands/arms only at the end of the day

Spill (Changing clothes after a spill):
if [Spill] = Right away then score = 1.0
if [Spill] = Always use disposable clothing then score = 1.0
if [Spill] = At lunch then score = 1.1
if [Spill] = At the end of the day then score = 1.2
if [Spill] = At the end of the next day then score = 1.4
if [Spill] = Later in the week then score = 1.8

In both algorithms, we used an additive model for mixing, application, repair and washing activities, because they are independent contributing factors for the overall body exposure, while we used a multiplicative model for the PPE and other potential protective factors, such as variables for ‘Enclosed’, ‘Cab’, ‘Repl’, ‘Hyg’ and ‘Spill’, because they are dependent on the basic exposure determinants. For applicators who used chlorpyrifos and completed the take-home questionnaire, the intensity level for an exposure scenario was calculated as follows:

Chlorpyrifos use:	Yes
Mixing status:	Always mixed insecticides personally *[score = 9]*
Mixing method:	Enclosed system *[score = 0.5]*
Application method:	Ground boom on tractor *[score = 3]*
Closed tractor cab:	Has closed cab without charcoal filter *[score = 0.5]*
Repair status:	Personally repaired application equipment *[score = 2]*
Washing equipment:	Rinsed pesticide tank *[score = 1]*
PPE status:	Wears fabric gloves, and respirator with cartridge *[score = 0.5]*
Replace of gloves:	Changes gloves after each use *[score = 1]*
Personal hygiene:	Washes and changes clothing at the end of the day *[score = 0.6]*
Spill treatment:	Changes clothing at the end of the day after a spill *[score = 1.2]*

Intensity level = [(Mix * Enclosed) + (Appl * Cab) + Repair + Wash] * PPE * Repl* Hyg * Spill

Intensity Level = [(9 * 0.5) + (3 * 0.5) + 2 + 1] * 0.5 * 1 * 0.6 * 1.2 = 3.2

Assignment of exposure weights

We used various sources of information to assign exposure weights for the variables in the algorithms. The main sources were the monitoring data in the published scientific literature. We extracted exposure data from more than 100 available published articles that had numerous measurements of pesticide exposures in relation to mixing, application or work practices in agricultural settings. More than 50% of these articles provided extensive monitoring data on applicators' dermal, inhalation and internal exposures.

Methods for determining dermal exposure include washing or wiping of the skin (Van Hemmen, 1992), the use of pseudo-skin (e.g. pads or patches, special clothing, coveralls, caps and gloves) (Durham and Wolfe, 1962; Nigg and Stamper, 1985) and fluorescent tracer techniques (Fenske, 1988, 1990; Archibald *et al.*, 1995). In the assignment of exposure weights, we relied on the results obtained by pseudo-skin and fluorescent tracer techniques, since the data from comparison studies suggested that washing or wiping may yield lower levels of exposure than sampling by means of pads and gloves (Davies *et al.*, 1983a,b; Fenske *et al.*, 1989). Respirators were used to trap inhaled particles and vapor to measure inhalation exposure in the early monitoring (Durham and Wolfe, 1962; Nigg and Stamper, 1985). Personal air sampling has been used to monitor the level of breathing zone pesticide exposure of applicators (Brouwer *et al.*, 1992). Internal doses of pesticides are usually monitored by measuring the parent compound or its metabolites in urine, blood, feces, exhaled air or sweat. The details of biological monitoring of internal doses of pesticides have been reported in two review articles (Coye *et al.*, 1986; Rosival *et al.*, 1986).

To generate weights for the variables in the algorithms, we compared the results of various monitoring data between individual exposure variables (e.g. mixing versus applying) as well as within a selected variable (e.g. for 'Appl' variable: ground boom versus backpack; for 'Cab' variable: open cab versus closed cab) using the results presented in these articles. The ratio between exposure levels of mixing and application depends on the method of application. For example, mixer/loaders have ~9-fold higher exposures than aerial applicators (Knarr *et al.*, 1985; Chester *et al.*, 1987), hence the score '9', and have 3-fold higher exposure than ground boom applicators (Rutz and Krieger, 1992; Brouwer *et al.*, 1994), who were assigned a score of '3'. The level of exposure for mixing/loaders was almost the same as the exposure level for hand spray applicators (Rutz and Krieger, 1992), who were assigned a score of '8'. The comparison between two application types, hand spray and ground boom, showed ~3-fold intensity differences (i.e. on average, hand spray application causes three times more exposure than ground boom application) using various monitoring results summarized in two review articles (Rutz and Krieger, 1992; Van Hemmen, 1992). In another study, both airblast and hand spray applications generated approximately three times higher intensity levels of exposure than ground boom applications (Nigg *et al.*, 1990). We also reviewed the intensity levels of exposure associated with the use of various types of protective equipment. Rubber gloves provided ~50% protection among fruit growers (De Cock *et al.*, 1995). Similarly, closed cabs on tractors provided ~50% protection, and closed cabs with air filter provided almost 90% protection compared to tractors without cabs (Carman *et al.*, 1982). To estimate intensity scores for PPEs, we also used articles providing data on exposures by parts of the body, by calculating the proportion of the particular body part, which can be protected using PPE, in the overall body exposure (Davies *et al.*, 1983a,b; Hunt *et al.*, 1985; Hussain *et al.*, 1990; Marchado *et al.*, 1992). There were almost no published data on measurements of human exposure from application of pesticides to animals. An NCI study in Iowa provided some data for estimating scores for the application techniques of hand spraying, pouring on animals and backpack, but not for other application methods (Stewart *et al.*, 1999a,b).

The second source of information used to develop exposure scores for algorithms was the Pesticide Handlers Exposure Database (PHED, 1992). The US Environmental Protection Agency, in conjunction with Health and Welfare Canada and the American Crop Protection Association, developed the Pesticide Handlers Exposure Database, a non-chemical-specific summary database for investigating pesticide exposure to hands and to other dermal surfaces of the body, and inhalation while engaged in mixing, loading and application activities.

The Pesticide Handlers Exposure Database consists of data collected from about 100 studies submitted primarily by companies that wish to register a specific pesticide. The pesticide exposure data are presented into three files:

1. Mixer/loader/applicator file (224 records)
2. Applicator file (282 records)
3. Mixer/loader file (253 records)

Even though this database contains many more records than any published study, there is some concern about its relevance to actual exposure situations because of the controlled, almost experimental, conditions under which the application occurs. However, relative comparisons between different application methods and various types of protective equipment in the Pesticide Handlers Exposure Database provided additional exposure information to refine our scoring system. For example, in the Pesticide Handlers Exposure Database gloves provided ~40–50% protection of the overall body exposure, regardless of application method, which is similar to the magnitude of protection reported in the peer-reviewed scientific literature (De Cock *et al.*, 1995).

The other source of information used to assign exposure scores for the algorithms was a pilot exposure monitoring survey conducted by the US Environmental Protection Agency at six AHS farms in Iowa and North Carolina (US EPA, 1996). For example, this monitoring survey showed that hand spray applications resulted in approximately three times more exposure to the applicator than ground boom applications, which is consistent with the literature (Rutz and Krieger, 1992; Brouwer *et al.*, 1994).

Calculating chemical-specific cumulative exposure scores for individual study applicators

To develop lifetime cumulative exposure scores, the overall exposure intensity score for each scenario is combined with chemical specific information on duration (in number of years applied) and frequency (in number of days of applications per year) of exposure obtained from the enrollment and take-home questionnaires. For example, if an applicator used 2,4-D with a daily exposure intensity level of 7.6 for an average of 10 days/yr for 5 yr, the lifetime cumulative exposure level to 2,4-D for this particular applicator was calculated as:

Cumulative exposure for 2,4-D
= Intensity level * Duration * Frequency
= 7.6 * 5 * 10
= 380

RESULTS

The results of the enrollment questionnaire showed that 4% of pesticide applicators did not personally mix pesticides, 26% personally mixed the pesticide less than half of the time, and 70% personally mixed pesticides more than 50% of the time. Three percent of the enrolled applicators did not personally apply pesticides. Twenty-two percent of licenced applicators personally applied less than half of the total applications used on the farm, and 75% personally applied more than 50% of the total applications used on the farm.

Figure 1 shows the prevalence of selected pesticides in both the enrollment and the take-home questionnaires. Glyphosphate, 2,4-D and atrazine were among the most commonly used herbicides in both the enrollment and take-home populations. Among insecticides, chlorpyrifos, terbufos and carbofuran were the most commonly used chemicals in both the enrollment and the take-home populations.

The use of ground booms on a tractor and hand spraying were the most common crop pesticide application techniques in both Iowa and North Carolina (Fig. 2). The furrow/banded type of application was a major technique in Iowa (63%), but less so in North Carolina (29%). Spraying and pouring pesticides were the most commonly used application techniques on animal farms in North Carolina (Fig. 3). In general, applicators in Iowa reported using more PPE than those in North Carolina (Fig. 4). The most commonly used PPE were rubber/chemically resistant gloves.

We calculated intensity, duration (lifetime total number of exposed days) and cumulative exposure to 2,4-D and chlorpyrifos for applicators based on the enrollment and take-home questionnaire responses. Use of both chemicals was more common among younger (<40 yr old) male farmers in Iowa than North Carolina. Women applicators contributed ~1% of the overall application of these chemicals in the cohort. The distribution of intensity levels, duration of exposure and lifetime cumulative exposures for the applicators from the enrollment questionnaire only (Tables 1a and 1b) and from the take-home questionnaire (Tables 2a and 3b) are presented by state, gender, age group and applicator type (private versus commercial) for both chemicals.

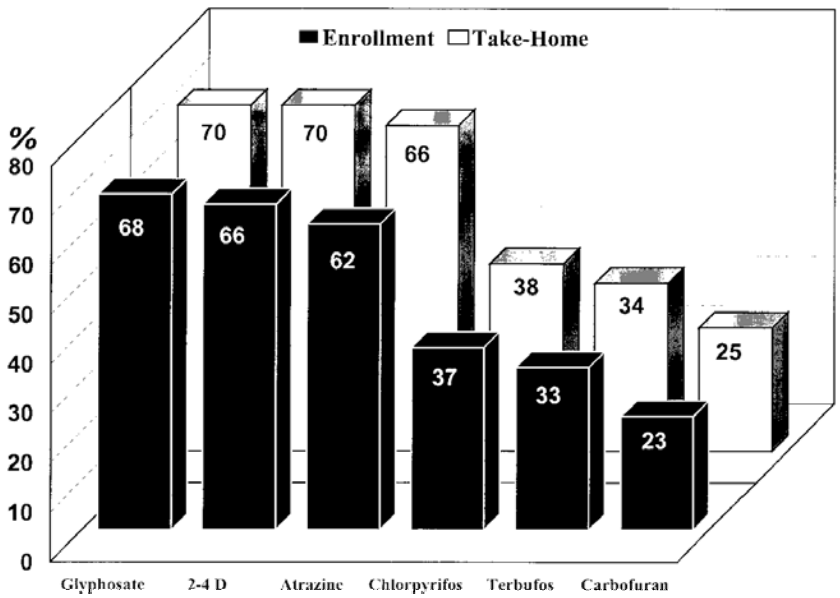

Fig. 1. Percent use of selected pesticides.

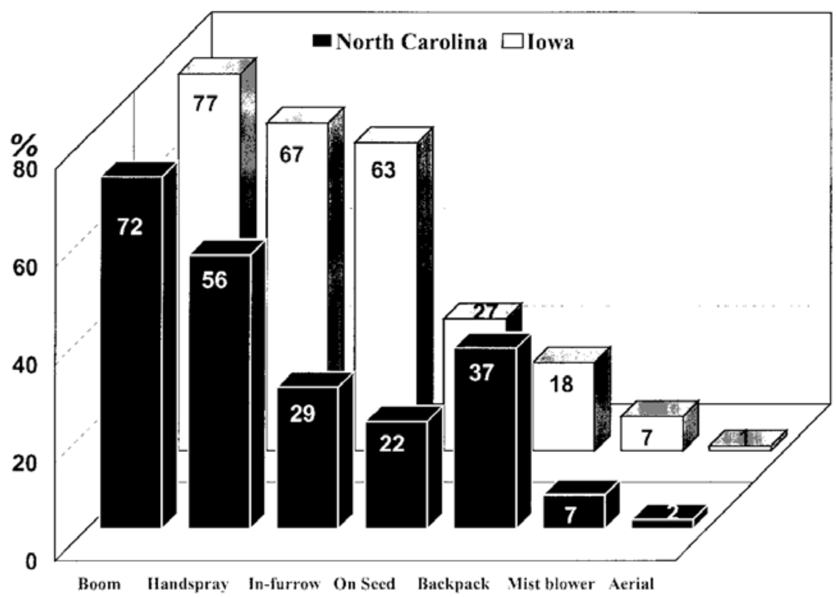

Fig. 2. Distributions of pesticide application techniques on crops by state.

The mean intensity level of exposure to 2,4-D for the applicators from the enrollment questionnaire resulted in a score of 6.4, while the average lifetime application was 179 days. The mean intensity score for 2,4-D exposure was higher in North Carolina (7.6) than Iowa (6.0) and among farmers (6.5) compared with commercial applicators (5.1) (Table 1a). The mean intensity scores did not differ by gender or applicators' age. Female applicators had shorter mean duration of exposure (100 days) than the male applicators (180 days). The mean duration of exposure to 2,4-D was longer in Iowa (184 days) than North Carolina (161 days). Duration of lifetime exposure increased with increasing age group, ranging from 137 days for the age group <40 yr old to 211 days for applicators 60 yr and older. Dramatic differences in duration of exposure occurred between farmers (164 days) and commercial applicators (327 days). Although applicators in North Carolina had fewer days of exposure to 2,4-D than applicators in Iowa, they had higher overall lifetime cumulative exposure (1249 scores) than Iowa applicators (1116 scores), due to their higher intensity levels. Female applicators had lower cumulative exposure level (593 scores) than male applicators (1155 scores) due to the shorter duration of exposure. Increased cumulative

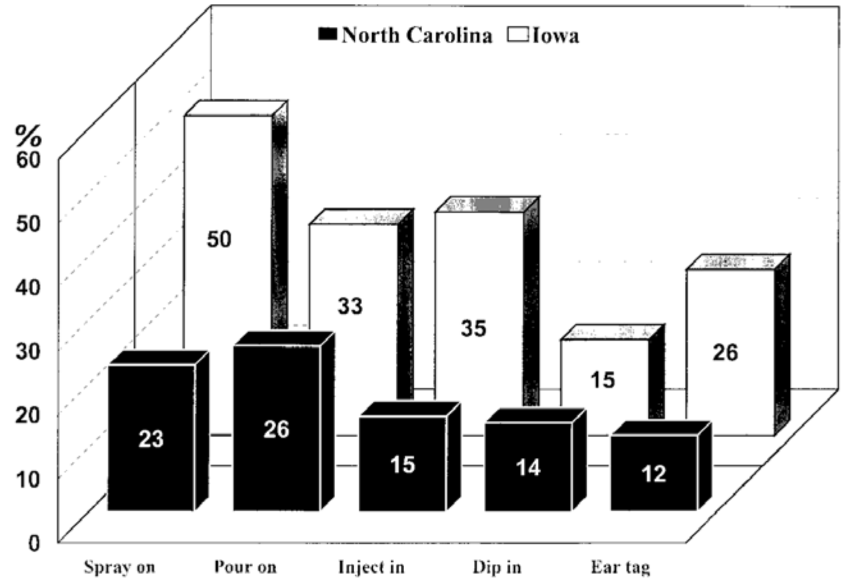

Fig. 3. Percent use of application techniques for animal pesticides by state.

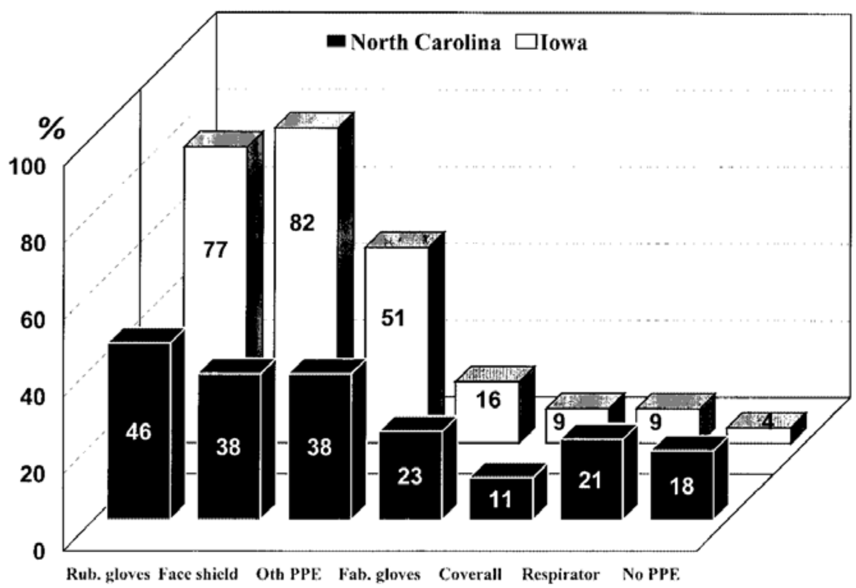

Fig. 4. Percent use of selected PPEs by state.

exposure was observed with increasing age group, ranging from 874 scores for the younger age group (<40 yr old) to 1408 for the oldest age group (60+ yr old). Although the mean intensity level for commercial applicators was much lower than for farmers, the commercial applicators had higher mean cumulative exposures (1692 scores) than farmers (1096 scores), due to the long duration of exposure.

Although the distribution of intensity of chlorpyrifos by demographic characteristics was similar to that observed for 2,4-D, there was quite a difference in terms of duration of exposure between the two chemicals (Tables 1a and 1b). The mean lifetime duration of exposure to chlorpyrifos (79 days) was much lower than the mean duration of exposure to 2,4-D (179 days). The duration of exposure to chlorpyrifos was longer in North Carolina (87 days) than Iowa (75 days). Although the mean intensity level for female applicators (6.4 scores) was slightly higher compared to male applicators (6.2 scores), there were very few differences between the genders for duration and cumulative exposure, suggesting that intensity had the strongest role in determining cumulative exposures. Similar to the 2,4-D exposure pattern, there was no difference in mean intensity scores by the age groups; however, lifetime duration and cumulative exposure showed some variation between the four age groups. Similar to 2,4-D patterns, commercial applicators showed lower mean intensity levels, longer mean durations and higher

Table 1a. The mean intensity calculated from the enrollment algorithm, duration and cumulative exposure levels of 2,4-D exposure among applicators from the enrollment questionnaire by state, gender, age group and applicator type

Stratified by	No. of 2,4-D users (%)	Mean intensity level [score] (SD)	Mean lifetime duration [days] (SD)	Mean cumulative exposure [score-days] (SD)
State				
Iowa	28550 (75)	6.0 (3.4)	184 (317)	1116 (2348)
North Carolina	9609 (25)	7.6 (4.6)	161 (320)	1249 (2936)
Gender				
Male	37717 (99)	6.4 (3.8)	180 (320)	1155 (2516)
Female	442 (1)	6.4 (4.0)	100 (228)	593 (1362)
Age group				
<40	12087 (32)	6.3 (3.6)	137 (236)	874 (1880)
40–49	11096 (29)	6.4 (3.8)	182 (301)	1170 (2258)
50–59	8043 (21)	6.5 (3.9)	208 (368)	1322 (2770)
60+	6931 (18)	6.4 (4.0)	211 (395)	1408 (3374)
Type				
Private (farmer)	34428 (90)	6.5 (3.8)	164 (287)	1096 (2397)
Commercial	3731 (10)	5.1 (3.4)	327 (522)	1692 (3435)
All applicators	38159 (100)	6.4 (3.8)	179 (319)	1149 (2507)

Table 1b. The mean intensity calculated from the enrollment algorithm, duration and cumulative exposure levels of chlorpyrifos exposure among applicators with the enrollment questionnaire by state, gender, age group and applicator type

Stratified by	No. of chlorpyrifos users (%)	Mean intensity level [score] (SD)	Mean lifetime duration [days] (SD)	Mean cumulative exposure [score-days] (SD)
State				
Iowa	14518 (69)	5.8 (3.3)	75 (163)	424 (1079)
North Carolina	6458 (31)	7.1 (4.4)	87 (203)	608 (1638)
Gender				
Male	20654 (99)	6.2 (3.7)	79 (176)	480 (1269)
Female	295 (1)	6.4 (4.2)	77 (191)	492 (1760)
Age group				
<40	7170 (34)	6.2 (3.6)	77 (150)	465 (1039)
40–49	6419 (31)	6.2 (3.7)	79 (178)	491 (1375)
50–59	4234 (20)	6.1 (3.9)	85 (211)	508 (1467)
60+	3152 (15)	6.2 (3.6)	72 (178)	452 (1295)
Type				
Private (farmer)	19288 (92)	6.3 (3.7)	71 (148)	450 (1112)
Commercial	1688 (8)	4.9 (3.4)	164 (360)	820 (2416)
All applicators	20976 (100)	6.2 (3.7)	79 (176)	480 (1277)

lifetime cumulative exposures to chlorpyrifos than farmers.

For both 2,4-D and chlorpyrifos, we also calculated mean intensity, duration and cumulative exposure for applicators who filled out the take-home questionnaire (n = 22904), using the exposure information from the enrollment questionnaire only (Tables 2a and 2b). The main purpose of this exercise was to evaluate the differences in two study populations (i.e. the whole cohort with the basic information and the sub-cohort with detailed information). The distribution patterns of all basic exposure indices (i.e. intensity, duration and cumulative exposure to 2,4-D and chlorpyrifos) by state, gender, age and applicator type were almost identical in the two study populations (Tables 1a and 2b), indicating that the sub-cohort of applicators from the take-home questionnaire are representative of the entire cohort in terms of exposure.

For individuals who completed the take-home questionnaire, we calculated the same exposure measures (i.e. intensity and cumulative exposure), using the detailed algorithm based on variables in the questionnaire (Tables 3a and 3b). The average intensity

Table 2a. The mean intensity calculated from the general algorithm, duration and cumulative exposure levels of 2,4-D exposure using enrollment questionnaire information among applicators with the take-home questionnaire by state, gender, age group and applicator type

Stratified by	No. of 2,4-D users (%)	Mean intensity levels [score] (SD)	Mean duration [days] (SD)	Mean cumulative exposure [score-days] (SD)
State				
Iowa	12001 (74)	6.0 (3.4)	170 (281)	1050 (2125)
North Carolina	4076 (26)	7.7 (4.6)	147 (291)	1179 (2892)
Gender				
Male	15891 (98)	6.5 (3.8)	165 (284)	1089 (2350)
Female	186 (2)	6.7 (4.3)	99 (253)	537 (1192)
Age group				
<40	3848 (23)	6.5 (3.5)	114 (176)	766 (1859)
40–49	4402 (27)	6.4 (3.7)	156 (248)	1025 (1902)
50–59	3804 (23)	6.5 (3.8)	190 (329)	1235 (2652)
60+	4023 (26)	6.5 (4.0)	196 (345)	1317 (2819)
Type				
Private (farmer)	15909 (99)	6.5 (3.8)	164 (284)	1084 (2344)
Commercial	168 (1)	5.6 (3.8)	288 (409)	1711 (4004)
All applicators	16077 (100)	6.5 (3.8)	164 (284)	1082 (2341)

Table 2b. The mean intensity calculated from the general algorithm, duration and cumulative exposure levels of chlorpyrifos exposure using enrollment questionnaire information among applicators with the take-home questionnaire by state, gender, age group and applicator type

Stratified by	No. of chlorpyrifos users (%)	Mean intensity level [score] (SD)	Mean lifetime duration [days] (SD)	Mean cumulative exposure [score-days] (SD)
State				
Iowa	6090 (71)	5.8 (3.2)	61 (113)	356 (737)
North Carolina	2475 (29)	7.1 (4.4)	72 (146)	493 (1084)
Gender				
Male	8455 (99)	6.2 (3.6)	65 (123)	396 (855)
Female	110 (01)	6.6 (4.2)	74 (186)	356 (693)
Age group				
<40	2265 (26)	6.4 (3.6)	63 (101)	406 (816)
40–49	2534 (30)	6.2 (3.6)	64 (145)	385 (917)
50–59	1955 (23)	6.0 (3.6)	68 (114)	402 (752)
60+	1739 (21)	6.3 (3.8)	63 (127)	388 (911)
Type				
Private (farmer)	8467 (99)	6.2 (3.6)	65 (123)	395 (853)
Commercial	98 (01)	5.3 (3.9)	86 (117)	383 (559)
All applicators	8565 (100)	6.2 (3.6)	65 (124)	395 (853)

level obtained from the detailed algorithm (5.9 scores) was lower than the intensity level (6.4 scores) obtained from the general algorithm, due to the availability of information on various exposure-reducing factors in the more comprehensive detailed algorithm (Table 3a). Similar to the entire cohort, average intensity and cumulative exposure to 2,4-D were higher in Iowa than in North Carolina. In contrast to the general algorithm, the detailed algorithm generated a lower level of intensity for women applicators (5.2 scores) compared with male applicators (5.9 scores). The cumulative exposure pattern obtained from the detailed algorithm; however, was similar to that obtained from the general algorithm. The oldest age group (60+ yr old) showed a much lower intensity level (5.2 scores), while the youngest age group (<40 yr old) had the highest intensity scores (6.3 scores). Cumulative exposure among the youngest group was much lower than the other age groups, due to the lower duration of exposure to 2,4-D (114 days) in this age group. Among farmers and commercial applicators, exposure measures obtained using the

Table 3a. The mean intensity calculated from the detailed algorithm, duration and cumulative exposure levels of 2,4-D exposure using the take-home questionnaire by state, gender, age group and applicator type

Stratified by	No. of 2,4-D users (%)	Mean intensity level [score] (SD)	mean lifetime duration [days] (SD)	Mean cumulative exposure [score-days] (SD)
State				
Iowa	12001 (74)	6.1 (4.1)	170 (281)	1160 (2373)
North Carolina	4076 (26)	5.5 (3.7)	147 (291)	950 (2064)
Gender				
Male	15891 (98)	5.9 (4.0)	165 (284)	1113 (2305)
Female	186 (2)	5.2 (4.5)	100 (253)	576 (1874)
Age group				
<40	3848 (23)	6.3 (3.8)	114 (175)	855 (1551)
40–49	4402 (27)	6.2 (4.0)	156 (248)	1071 (2014)
50–59	3804 (23)	6.0 (4.1)	190 (329)	1264 (2540)
60+	4023 (26)	5.2 (4.0)	196 (345)	1211 (2830)
Type				
Private (farmer)	15909 (99)	5.9 (4.0)	163 (283)	1110 (2305)
Commercial	168 (1)	5.3 (3.7)	288 (409)	2215 (4007)
All applicators	16077 (100)	5.9 (4.0)	164 (284)	1108 (2303)

Table 3b. The mean intensity calculated from the detailed algorithm, duration and cumulative exposure levels of chlorpyrifos exposure using the take-home questionnaire by state, gender, age group and applicator type

Stratified by	No. of chlorpyrifos users (%)	Mean intensity level [score] (SD)	Mean lifetime duration [days] (SD)	Mean cumulative exposure [score-days] (SD)
State				
Iowa	6090 (71)	7.1 (5.8)	61 (113)	452 (1022)
North Carolina	2475 (29)	7.9 (5.8)	72 (146)	596 (1746)
Gender				
Male	8455 (99)	7.4 (3.9)	65 (122)	490 (1266)
Female	110 (01)	7.8 (6.2)	74 (186)	598 (1076)
Age group				
<40	2265 (26)	7.8 (5.8)	63 (101)	528 (932)
40–49	2534 (30)	7.6 (6.0)	64 (145)	512 (1734)
50–59	1955 (23)	7.2 (5.8)	68 (114)	486 (954)
60+	1739 (21)	6.2 (5.4)	63 (127)	420 (1032)
Type				
Private (farmer)	8467 (99)	7.3 (5.8)	65 (123)	490 (1266)
Commercial	98 (1)	7.4 (6.0)	86 (117)	772 (1252)
All applicators	8565 (100)	7.3 (5.7)	65 (124)	492 (1272)

detailed algorithm showed patterns similar to the measures obtained from the general algorithm. Intensity and cumulative exposure to chlorpyrifos showed patterns similar to those obtained by the general algorithm, except mean intensity level for farmers (7.3 scores) and commercial applicators (7.4 scores) are almost the same when they are calculated using the detailed algorithm; however, the mean value of intensity level for commercial applicators was only based on 98 subjects from Iowa only (Table 3b). There were no commercial applicators who participated to the take-home questionnaire part of the study in North Carolina.

We compared both intensity and cumulative exposure levels obtained from the general and detailed algorithms by quintiles to measure the percent agreement between the two algorithms (Table 4a–d). For the 2,4-D intensity level there was 28% exact agreement, and 57% ± one or two category differences (Table 4a). Similar patterns were observed for chlorpyrifos with 28% exact agreement, and 55% ± one or two category differences (Table 4b). Agreements for cumulative exposure were much higher than the intensity measures for both 2,4-D and chlorpyrifos. We found 57% exact agreement, and 42% ± one or two category difference(s) for 2,4-D

Table 4a. Percent agreements between intensity level obtained from the general and detailed algorithms for exposure to 2,4-D

	Detailed, *n* (%)					
General	1–20 percentile	21–40 percentile	41–60 percentile	61–80 percentile	81–100 percentile	Total
1–20 percentile	915 (0.08)	487 (0.04)	376 (0.03)	263 (0.02)	242 (0.02)	2283 (0.20)
21–40 percentile	537 (0.05)	585 (0.05)	543 (0.05)	373 (0.03)	287 (0.02)	2325 (0.20)
41–60 percentile	269 (0.02)	434 (0.04)	479 (0.04)	508 (0.05)	539 (0.05)	2229 (0.20)
61–80 percentile	325 (0.02)	449 (0.04)	516 (0.05)	548 (0.05)	537 (0.05)	2375 (0.20)
81–100 percentile	233 (0.02)	325 (0.02)	362 (0.03)	593 (0.05)	671 (0.06)	2184 (0.20)
Total	2279 (0.20)	2280 (0.20)	2276 (0.20)	2285 (0.20)	2276 (0.20)	11396 (1.00)

Table 4b. Percent agreements between intensity levels obtained from the general and detailed algorithms for exposure to chlorpyrifos

	Detailed, *n* (%)					
General	1–20 percentile	21–40 percentile	41–60 percentile	61–80 percentile	81–100 percentile	Total
1–20 percentile	469 (0.07)	271 (0.04)	225 (0.04)	181 (0.03)	154 (0.02)	1300 (0.20)
21–40 percentile	263 (0.04)	335 (0.05)	263 (0.04)	229 (0.04)	142 (0.02)	1232 (0.20)
41–60 percentile	217 (0.03)	262 (0.04)	291 (0.05)	275 (0.04)	282 (0.04)	1327 (0.21)
61–80 percentile	202 (0.03)	220 (0.03)	253 (0.04)	273 (0.04)	274 (0.04)	1222 (0.19)
81–100 percentile	117 (0.02)	181 (0.03)	240 (0.04)	311 (0.05)	413 (0.07)	1262 (0.20)
Total	1268 (0.20)	1269 (0.20)	1272 (0.20)	1269 (0.20)	1265 (0.20)	6343 (1.00)

Table 4c. Percent agreements between cumulative exposure measures obtained from the general and detailed algorithms for exposure to 2,4-D

	Detailed, *n* (%)					
General	1–20 percentile	21–40 percentile	41–60 percentile	61–80 percentile	81–100 percentile	Total
1–20 percentile	1514 (0.16)	527 (0.04)	149 (0.01)	40 (0.004)	2 (0.0001)	2232 (0.20)
21–40 percentile	534 (0.04)	944 (0.08)	537 (0.05)	184 (0.01)	45 (0.004)	2244 (0.20)
41–60 percentile	135 (0.01)	541 (0.05)	923 (0.08)	528 (0.05)	146 (0.01)	2273 (0.20)
61–80 percentile	40 (0.004)	182 (0.02)	511 (0.04)	988 (0.09)	469 (0.04)	2190 (0.20)
81–100 percentile	13 (0.001)	40 (0.004)	116 (0.01)	492 (0.04)	1573 (0.16)	2234 (0.20)
Total	2235 (0.20)	2234 (0.20)	2236 (0.20)	2232 (0.20)	2235 (0.20)	11172 (1.00)

Table 4d. Percent agreements between cumulative exposure measures obtained from the general and detailed algorithms for exposure to chlorpyrifos

	Detailed, *n* (%)					
General	1–20 percentile	21–40 percentile	41–60 percentile	61–80 percentile	81–100 percentile	Total
1–20 percentile	738 (0.12)	317 (0.05)	142 (0.02)	48 (0.008)	4 (0.0008)	1249 (0.20)
21–40 percentile	332 (0.05)	479 (0.08)	295 (0.04)	100 (0.02)	35 (0.006)	1241 (0.20)
41–60 percentile	122 (0.02)	293 (0.04)	438 (0.08)	316 (0.05)	83 (0.01)	1252 (0.20)
61–80 percentile	53 (0.008)	138 (0.02)	299 (0.04)	496 (0.08)	254 (0.04)	1240 (0.20)
81–100 percentile	1 (0.0008)	17 (0.001)	74 (0.01)	284 (0.04)	869 (0.14)	1245 (0.20)
Total	1246 (0.20)	1244 (0.20)	1248 (0.20)	1244 (0.20)	1245 (0.20)	6227 (1.00)

(Table 4c) and 50% exact agreement, and 46% ± one or two category for chlorpyrifos (Table 4d).

DISCUSSION

We present a chemical-specific quantitative pesticide exposure assessment method for use in epidemiological studies conducted in an agricultural environment. We developed and compared pesticide-specific mean exposure scores using the exposure information from the enrollment and the take-home questionnaires to evaluate potential selection bias for the sub-cohort (i.e. the take-home population) in terms of differences in pesticide exposure levels. Although the entire cohort (i.e. the enrollment population) showed slightly more application days for 2,4-D and chlorpyrifos than among the sub-cohort members, both populations showed a similar intensity of exposure and a similar distribution of exposure levels by demographic variables, suggesting that the sub-cohort population is representative of the entire cohort population in terms of evaluation of health risk by information limited to the take-home questionnaire. We also compared the mean exposure levels for the same sub-cohort population (take-home population), using the results from two different algorithms (general and detailed) in terms of percent agreement and correlations. Although we used different scales in two different algorithms because of the different variables involved in the algorithms, high concordance was observed between the two different algorithms in terms of percent agreement and correlation. This relatively high concordance, especially in cumulative exposure measures, suggests that the results of the general algorithm can be used in the evaluation of disease risks, even though it is based on less exposure information.

Most previous epidemiological studies have considered pesticides as a group without further characterization of chemical-specific exposures (Zahm *et al.*, 1997). Some epidemiological studies have evaluated risk of cancers by chemical-specific exposures, and frequency or duration (Brown *et al.*, 1990; Zahm *et al.*, 1990; Blair *et al.*, 1998; Baris *et al.*, 1998), but intensity of exposure to individual pesticides has been largely ignored. Most studies were limited to use of surrogate measures of intensity, such as number of acres or animals, days of pesticide application, crop type or information on PPE use. The Agricultural Health Study (Alavanja *et al.*, 1996) was designed to capture chemical-specific intensity- and duration-related pesticide exposure information. The enrollment and take-home questionnaires provided detailed information on mixing status, application techniques, types of PPE used, work-practices and personal hygiene, which are known to be the major determinants of exposure to pesticide in agricultural settings. These exposure data allowed us to develop quantitative exposure scores, including daily intensity or lifetime cumulative exposure to a specific pesticide, for use in analyses of disease risk and pesticide exposure.

To develop a weighting factor for each of the exposure variables, we relied mostly on the results of the different exposure measurements from monitoring studies that used different individual pesticides for the same variables. Pesticide monitoring surveys suggest that the intensity of exposure variables, such as mixing status, application technique or PPE type, is largely independent of the pesticide used (Stamper *et al.*, 1989; Krieger *et al.*, 1990; Byers *et al.*, 1992). For example, studies indicated that the ratio of exposure levels between two application techniques or between mixing and a particular application technique was similar for different pesticides. These findings provided some additional confidence that the use of the non-chemical-specific Pesticide Handlers Exposure Database to estimate relative intensity weight factors might be a reasonable approximation of actual chemical-specific weight factors.

There were some limitations to the data collection procedures that we used in this study. Although we collected chemical-specific information on duration and frequency-related exposure variables, the intensity-related information, such as mixing status, application technique, PPE used, repair status and personal hygiene, was collected for pesticides in general (in the enrollment questionnaire) or in classes of pesticides, such as in herbicides, crop insecticides, animal insecticides, fungicides or fumigants (in the take-home questionnaire). However, various literature resources, particularly pesticide reference manuals (Royal Society of Chemistry, 1991; American Crop Protection Association, 1996), provided considerable information to link these intensity-related exposure variables to specific pesticides. The manuals recommend only selected application types for individual pesticides. For example, airblast application is suggested for crop insecticide and fungicide use only. Similarly, ear tags or other animal-specific application methods, such as pour on, spray on or injection, are techniques specific to animal insecticides only; gas canisters, pouring fumigants from buckets or row fumigants are specific to fumigants only.

The other limitation was related to the question that asked applicators to check 'All that apply'. There were multiple application methods marked for the same group of pesticides. If more than one application technique was reported and more than one application technique was recommended for a specific pesticide in reference manuals, then all recommended and reported application techniques were used in the calculation of the mean application score for that particular pesticide. Similarly, the question on the PPE assumes that farmers were using the same PPE for mixing, applying and repairing activities, which may not be the case in real life situations. We will be obtaining more information for each activity and chemical in a follow-up questionnaire, from which we will be able to test the validity of these assumptions. These assumptions introduce some misclassification into our exposure data that make it difficult to observe associations between pesticide exposure and disease outcomes.

Despite these limitations, the exposure assessment approach proposed here represents a step forward in the estimation of pesticide exposure in an epidemiological cohort. The approach utilizes a mixture of professional judgment and the existing literature data to quantify potential pesticide exposure in a more detailed manner than has been attempted before. The intensity scores derived in these algorithms require further validation. The literature suggests that there is substantial interapplicator variability of exposure even for the same type of application procedure (Lavy *et al.*, 1982; Frank *et al.*, 1985; Chester and

Hart, 1986). Even with the many complexities in estimating exposures, a recent study has suggested that pesticides experts, industrial hygienists and crop-growing experts can identify the most important determinants of external exposures (De Cock *et al.*, 1996). We are in the process of developing a series of validation studies to evaluate the effects of each exposure variable in our algorithms. In these validation studies, we will monitor the most commonly used exposure scenarios observed in our cohort study and compare the algorithm-based intensity estimates with the results of the monitoring data for that particular scenario. Further refinement of the individual exposure score will be carried out by using its predictive value obtained from a regression modeling based on the exposure variables used in our algorithms and the actual monitoring results for the given exposure scenario.

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