

# Overview of the Agricultural Health Study [www.aghealth.org](http://www.aghealth.org)

Presented to the USDA NRCS  
Agricultural Air Quality Task Force  
August 2012



# Outline

- Who
- Why
- What
- Results
  - Non-cancer endpoints
  - Cancer endpoints
- AHS request for additional collaboration
- Importance to the Agricultural Air Quality Task Force

# Executive Committee

- National Cancer Institute
  - Dr. Michael Alavanja
  - Dr. Laura Beane-Freeman
- National Institutes of Environmental Health Sciences
  - Dr. Jane Hoppin
  - Dr. Dale Sandler
- US EPA
  - Kent Thomas, BSPH
- National Institute of Occupational Health
  - Cynthia J. Hines, MS, CIH
- Westat Coordinating Center
  - Marsha Dunn – Westat
  - Dr. Charles F. Lynch – University of Iowa

# Advisory Panel

- Clement Furlong, Ph.D. - University of Washington
- Annette G. Greer, PhD, MSN, RN - (Spouse, Representing North Carolina Spouses)
- Beate Ritz, M.D., Ph.D. - University of California at Los Angeles
- Dennis Schwab - (Farmer, Representing Farmers of Iowa)
- Bryant Worley - (Farmer, Representing Farmers of North Carolina)
- Susan Woskie, Ph.D., C.I.H. - University of Massachusetts Lowell

# Why Agricultural Health Study

- While it appears that farm populations appear healthier compared to other populations, they still may have increased rates for some diseases and specific injury.
  - Cancers such as: leukemia, lymphoma and soft tissue sarcoma, cancers of the brain, lip, prostate, skin and stomach
  - Parkinson's disease
  - Other non-cancerous diseases of the lung
    - Farmers lung, wheeze and asthma
- Long-term study of agricultural exposures and chronic diseases, injury and other lifestyle factors

# Four AHS Study Components

- Prospective cohort study - cancer and non-cancer outcomes
  - linkage with cancer registries, vital statistics, United States Renal Data System (USRDS)
  - ongoing data collection (i.e., telephone interview, food frequency questionnaire and buccal (cheek) cell collection)
- Cross-sectional studies -- including questionnaire data, functional measures, biomarkers, and GIS
- Nested case-control studies
- Exposure assessment and validation studies

# Participants and Study Timeline

- Over 89,000 participants (Iowa and North Carolina)
  - private pesticide applicators
  - spouses of pesticide applicators
  - commercial pesticide applicators
- Phase 1 - began in 1993 and concluded in 1997
- Phase 2 - follow up began in 1999 and concluded for private applicators and spouses in 2003
- Phase 2 - follow up of commercial applicators started in October 2003 and concluded in October 2005
- Phase 3 - follow up began in November 2005 and concluded in February 2010

<http://aghealth.nci.nih.gov/study.html>

# Phase and Data Collection

## Phase 1 (1993-1997)

- Telephone interview
  - Demographic information
  - Historic pesticide use
  - Current farming practices
  - Health status



# Phase and Data Collection

## Phase 2 (1997-2003)

- Computer aided telephone interview (CATI), mailed dietary questionnaire
  - To understand diet and role in cancer and other health conditions
    - Cooking practices
    - Types of foods

## Phase 2 (2003 – 2005)

- Commercial applicators

# Phase and Data Collection

## Phase 3 (2005 -2010)

- CATI
- buccal cell collection
  - To understand the possible links between genetics, chemical exposures, and disease
    - How genetic differences among people affect the body's response to chemicals
    - How diet, lifestyle, farming environment, race, ethnic background, age and other factors may be related to genetic differences

Multiple safeguards have been put into place so that test results can not be directly linked to study participants

# Composition and Progress

Table 1.	Phase 1	Phase 2		Phase 3	
	Main Qx Completed	Main Qx Admin (CATI)	Diet History Qx Admin	Main Qx Admin (CATI)	Buccal Cell Collection
Private App.	52,394	33,457	17,869	24,171	18,601
Spouses	32,345	23,796	15,385	19,959	14,255
Commercial App.	4,916	2,885	1,757	N/A	1,820
<b>Total</b>	<b>89,655</b>	<b>60,138</b>	<b>35,011</b>	<b>44,130</b>	<b>34,676</b>

Progress through May 2011

# Studies Associated with the Agricultural Health Study

# EPA Pesticide Exposure Study

- Purpose
  - to measure exposure to pesticides among private pesticide applicators and to evaluate AHS exposure algorithms
- Objectives
  - directly measures exposure to target applied pesticides among a subset of the AHS cohort
  - comparing measurements to exposure intensity estimates based on responses to questionnaires administered earlier in the study
  - identifying exposure factors
  - assessing spouse and child exposure to pesticides

# Farm Family Take-Home Pesticide Exposure Study

- Purpose
  - to evaluate pesticide contamination and exposure in farm homes and families
- Objectives
  - identify potential environmental and behavioral risk factors
  - develop recommendations to prevent pesticide exposure among farm families

# Orchard Fungicide Exposure Study

- Purpose
  - focuses on farmers who personally apply fungicides to apple and peach orchards
- Objectives
  - to measure actual exposures to the target fungicides using both environmental and biological measures of exposure
  - to identify and quantify the major determinants of exposure.

# Factors Associated with Self-reported Parkinson's Disease

- Purpose
  - to focus on the environmental and genetic causes of Parkinson's Disease in participants with self-reported Parkinson's disease by comparing to participants without PD



# Iowa Corn Farmers Study

- Purpose
  - to evaluate exposures to farmers who plant field corn and apply atrazine and chlorpyrifos to their crop and non-farmers serving as controls for the study
- Objectives
  - to look for biologic changes associated with farming practices and exposures over the course of the growing season
    - periodic collection of questionnaires
    - samples of urine and blood

# Rheumatoid Arthritis Study

- Purpose
  - confirm self-reported diagnosis of rheumatoid arthritis (RA) and other autoimmune diseases
- Objectives
  - identify screening questions that increase the likelihood that a self-reported diagnosis is true
  - assess risk factors for RA and other autoimmune diseases in the AHS cohort

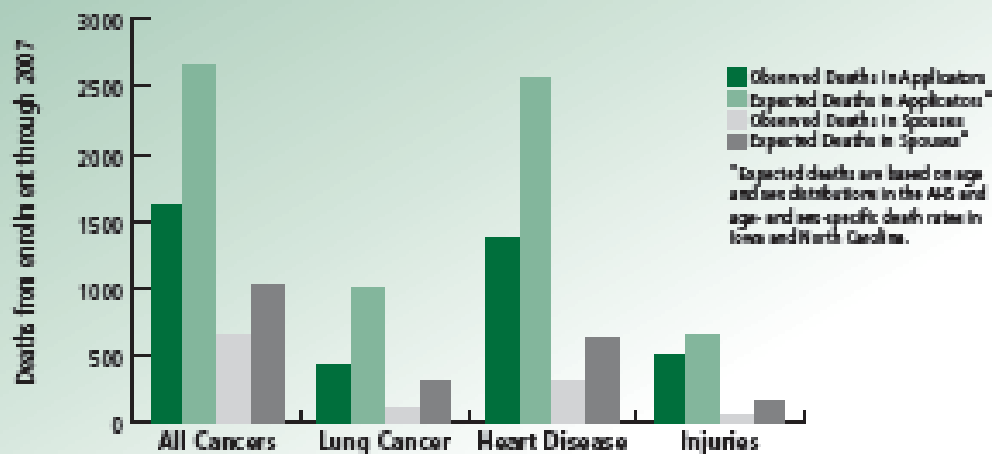
# Research Findings

Associated Health Outcomes

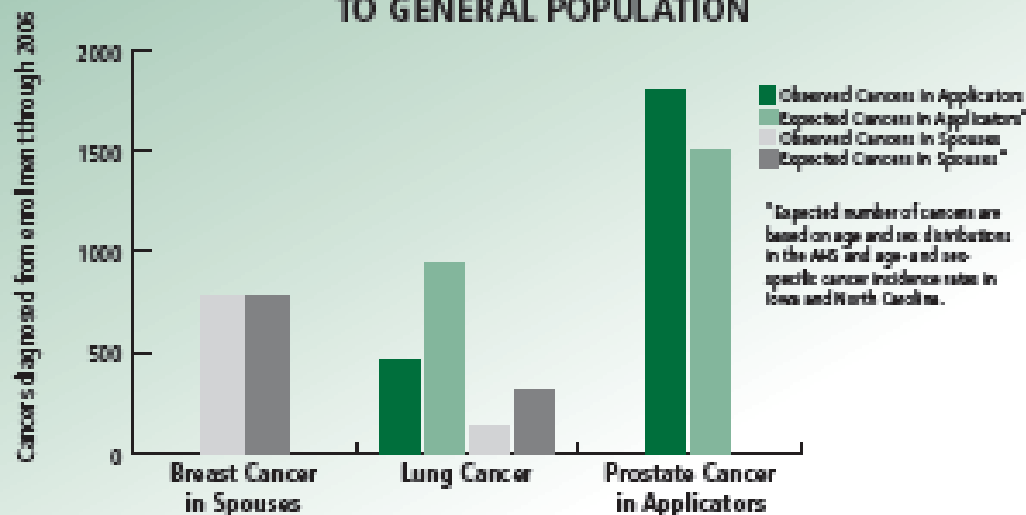
# General Health of AHS

- Less likely than the general public to die from heart disease, cancer, diabetes, lung disease and liver disease
- Lower or similar rates of smoking-related cancers such as oral, esophageal, lung and bladder, when compared to the general population
- Overall injury death rates were lower, but deaths related to machinery are higher among AHS farmers compared to non-farmers

## DEATHS IN THE AHS LOWER THAN GENERAL POPULATION



## CANCERS DIAGNOSED IN THE AHS COMPARED TO GENERAL POPULATION



Waggoner, et al. *American Journal of Epidemiology*. 2011; 173: 71-83.

Kouros, et al. *Journal of Occupational Environmental Hygiene*. 2010; 52(11): 1090-1105.

# Retinal Degeneration

- 2 times more common in applicators who had used fungicides and chemicals to control fungus and prevent crop rot
- 1.5 times more common in applicators of organochlorine pesticides – aldrin, DDT - NOT clearly related to other pesticides
- More than twice as common in applicators who raised orchard fruits (apples/peaches)
- Also associated with Christmas tree and peanut farming
- Similar in both Iowa and North Carolina cohorts
- Associated with application over more days over lifetime
- Associated with method of application – handspray, backpack, mist blower vs boom sprayer
- Unassociated with use of whole body PPE, goggles or facemask

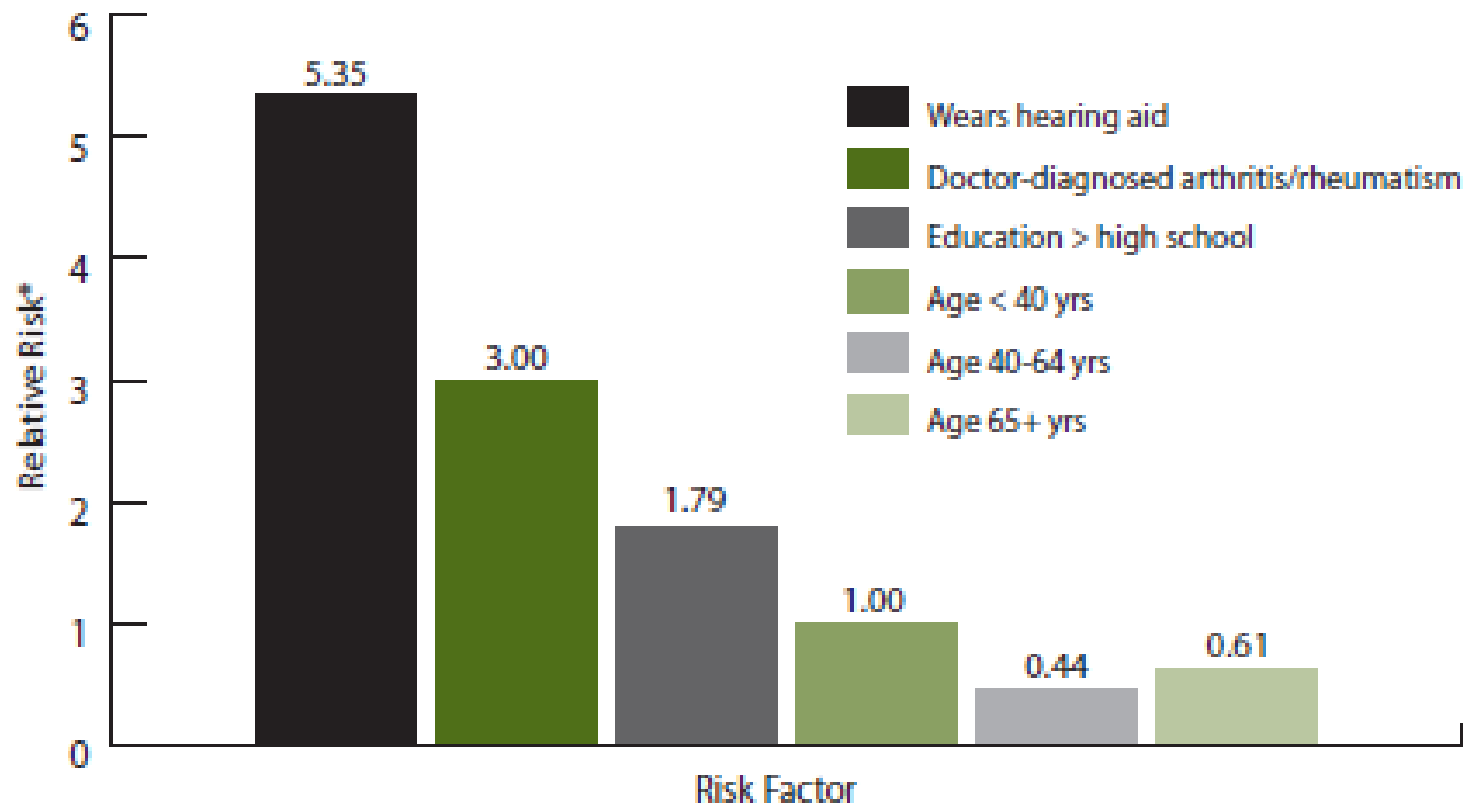
# Risk Factors for Agricultural Injury

Iowa – 6,999 farmers, last 12 months 1997, 431 with injury compared to 473 without

- Long work hours (>50 hrs / week)
- Better education (recall/report)
- Younger age (<25 years of farming, 1.8 Xs increased risk)
- Large livestock on the farm (1.7Xs hog, 1.69 Xs cattle)
- Medication (potential side effects)
- Hearing-aid use (5.4 Xs higher livestock, 4.4 machinery-related)
- Problem drinking (2.5 Xs greater risk)
- Arthritis (animal-related injury)

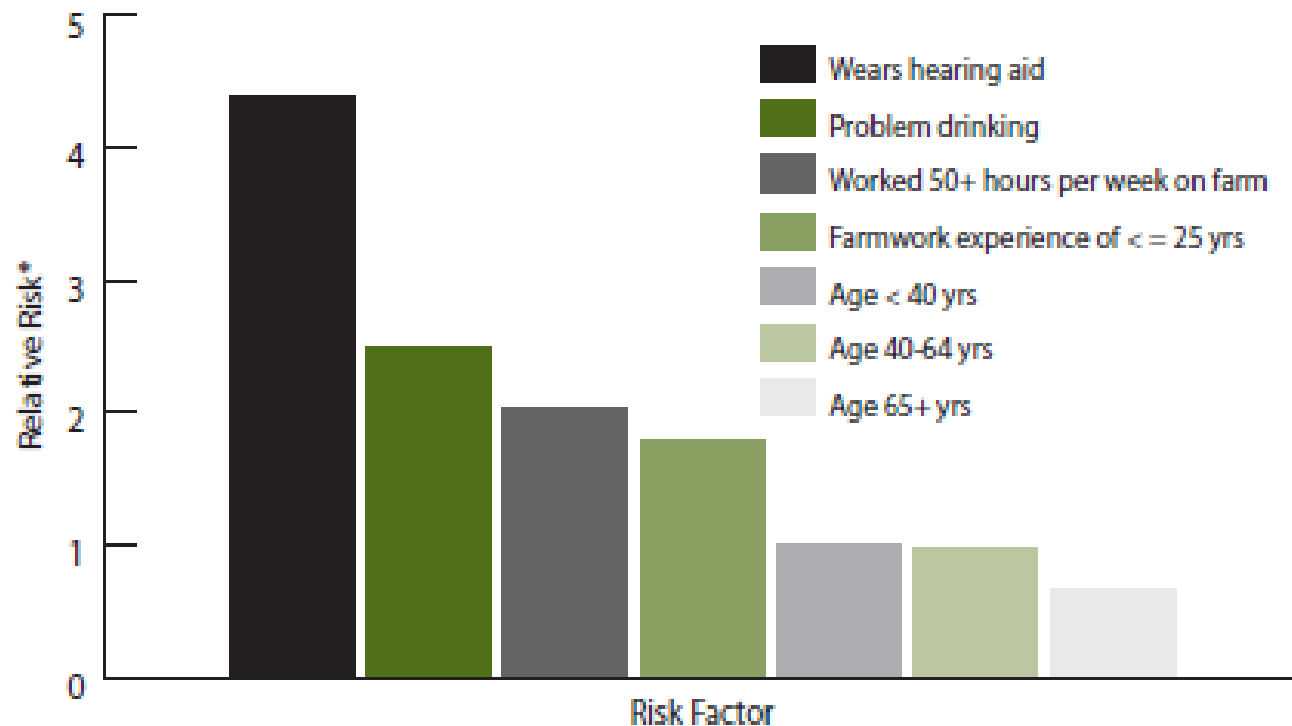
AHS Report 2004

Figure 1. Factors significantly associated with animal-related injury among 116 farmers and 342 uninjured farmers, all with large animals on the farm, Iowa, 1997





**Figure 2. Factors significantly associated with machinery-related injury among 205 farmers and 473 uninjured farmers, Iowa, 1998**



\*Each relative risk has been adjusted for all other factors in each figure. If the relative risk is greater than 1.00, it indicates the factor is harmful or increases risk of injury. If the risk factor is less than 1.00, it indicates the factor is protective or decreases risk of injury. For example, the relative risk of 4.37 for wearing a hearing aid means that those farmers with this factor had 4.37 times higher risk of machinery-related injury than farmers who did not wear a hearing aid.

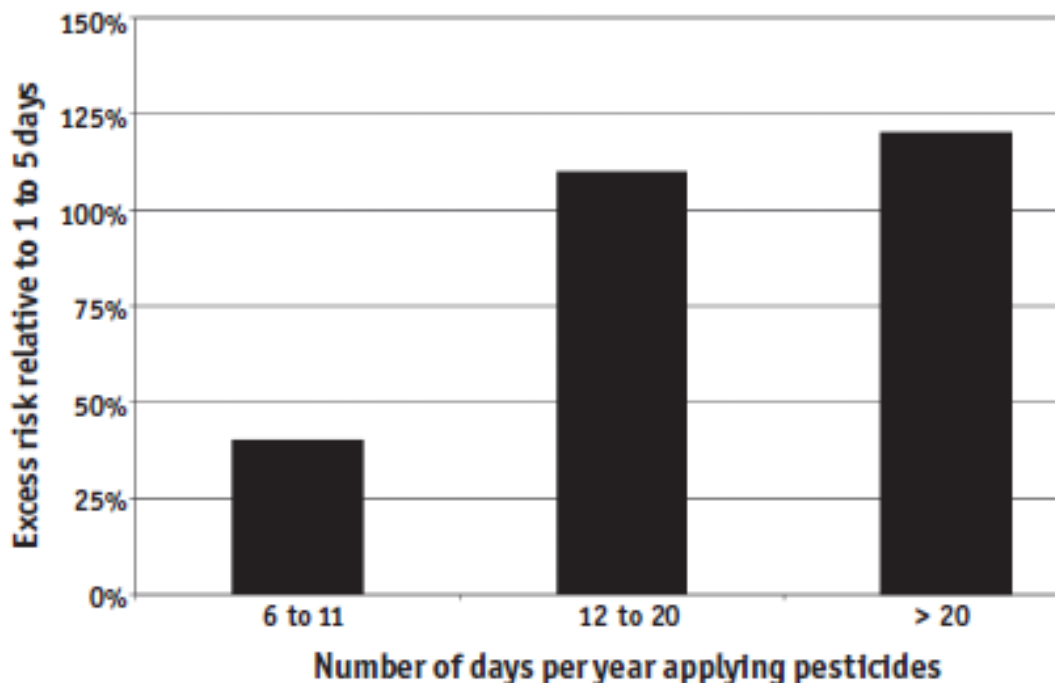
# High pesticide exposure events

- Enrollment questionnaire - 14 of 100 AHS applicators have experienced a high exposure event during their lifetime
- Linked to 7 factors
  - 1) delay in changing clothing or washing after pesticide application
  - 2) mixing pesticide application clothing with the family wash
  - 3) washing pesticide-contaminated hands inside the home after application
  - 4) applying pesticides within 50 yards of their well
  - 5) storing pesticides in the home
  - 6) self-repairing application equipment
  - 7) using pesticides for more than 10 years

# High pesticide exposure events

- 5 year follow up 6.5 of 1000 experienced a high exposure event
- factors associated with exposure during follow up
  - Types of chemicals – form liquid vs solid
  - Previous high exposure incident – 3.8Xs more likely
  - Storing pesticides in the home – 40% increased risk
  - Younger age (<45 yoa) – 2Xs more likely to report an event
  - Washing work clothes with family clothes
  - State of residence – Iowa 2xs more likely than NC
  - Risk acceptance score – five questions to evaluate person's attitudes towards risk

## Risk of Extreme Exposure Event and Number of Pesticide Applications (days per year)



## Symptoms

- 50% reported multiple symptoms
  - Of the 50%, 96% reported multiple symptoms
  - More likely to report symptoms if head and neck were exposed 32% vs 10%
  - 13% reported initiating a health care visit related to the event
  - 1 person was hospitalized
- Skin irritation ..... 21%
  - Eye irritation ..... 17%
  - Headache or dizziness .... 16%
  - Nausea ..... 10%
  - Tearing or drooling ..... 9%
  - Chest discomfort ..... 9%

Concern that farmers may not recognize the symptoms of pesticide exposure 28

# Neurological Symptoms and Pesticide Use

- Neurological symptoms associated with
  - Length of pesticide use
  - History of high personal exposure event (14/100)
  - History of pesticide poisoning
  - Contact with livestock

Neurological symptoms that may sometimes be related to pesticide exposure:

- absentmindedness
- blurred or double vision
- changes in smell or taste
- depression
- difficulty concentrating
- difficulty speaking
- dizziness
- excessive sweating
- fast heart rate
- fatigue
- headache
- insomnia
- irritability
- loss of appetite
- loss of consciousness
- nausea
- numbness in hands or feet
- poor balance
- poor night vision
- tension
- tremor in hands
- twitches in arms or legs
- weakness in arms or legs

# Hearing Loss

- Increased self-reported hearing loss with several measures of pesticide exposures
  - Reported high exposure events
  - Sickened by pesticide poisoning
  - Sought medical treatment for pesticide exposure
- More study is needed to address additional factors which may also impact hearing loss
  - Loud noises such as tractors and machinery
  - Exposures to heavy metals and solvents

# Depression

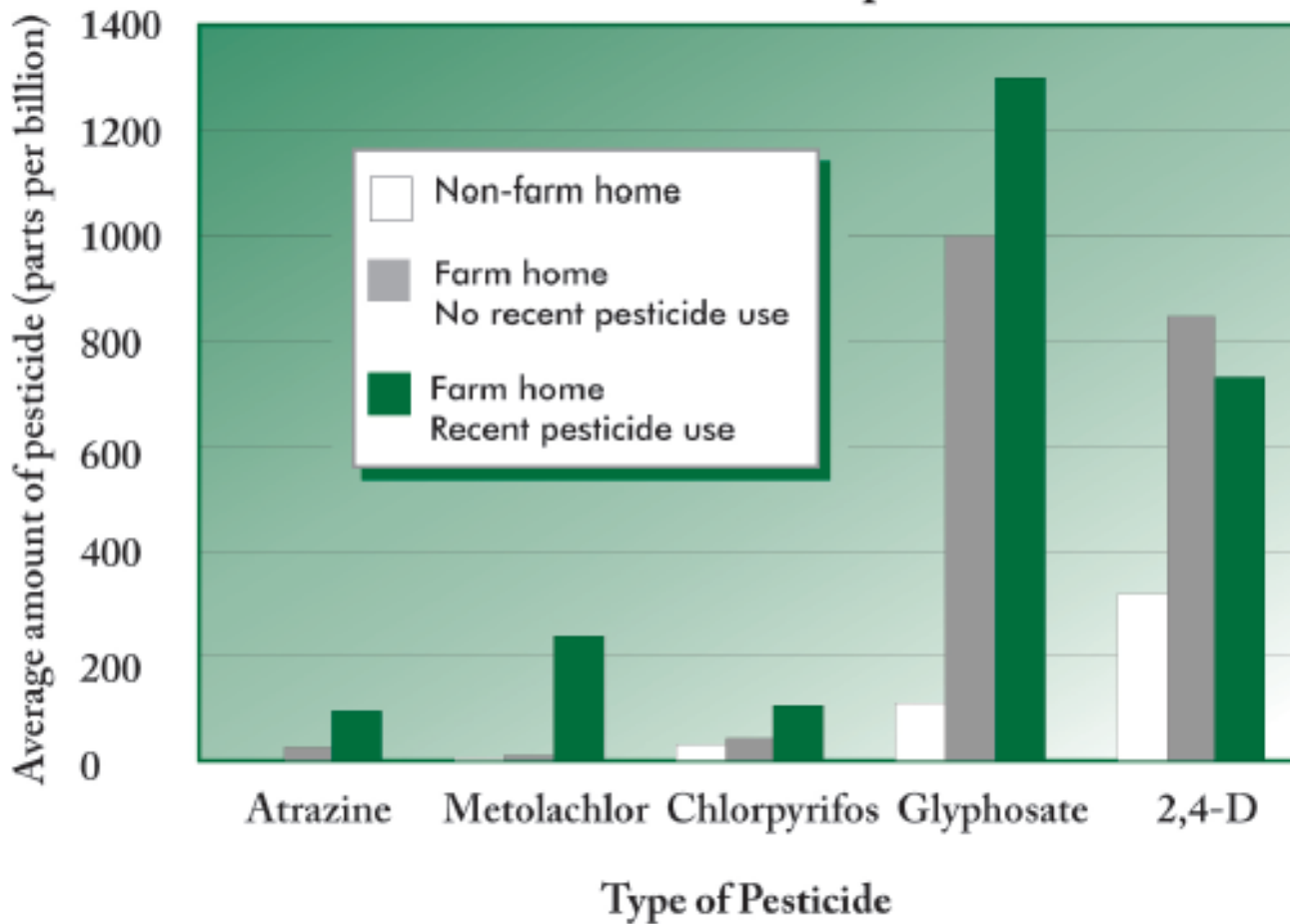
- Has been associated with pesticide poisoning
- In male pesticide applicators, Doctor diagnosed depression was linked to
  - Pesticide poisoning
  - High exposure events, pesticide spills
  - Use of organochlorines and organophosphates
  - Many days of pesticide application over a lifetime
- Even without Doctor confirmed poisoning experiencing depression more likely with greater pesticide use
- Farm women pesticide poisoning linked to depression
- No relationship found in spouses without pesticide poisoning

# Pesticide Residues in the Homes of Farm Families

- To determine if pesticides find their way into homes from the clothes and shoes of family member who work with the chemicals.
- Dust collected from 25 farm homes and 25 non-farm homes in 2 counties in Iowa
  - Farm homes had higher pesticides than non-farm homes
  - Higher concentrations of atrazine and metochlor found in homes of applicators from tracked dirt in and work clothes
  - Glyphosate and 2,4-D found in both farm and non-farm homes (used in both agriculture and residential settings)
  - Chlorpyrifos also found in most homes



## How much pesticide residue was found in the carpet dust?



# Diabetes

- 1,200 AHS participants who developed diabetes during the study period (1993 - 2003)
- Link with diabetes and 7 pesticides
  - Aldrin, chlordane, heptachlor, dichlorvos, trichlorfon, alachlor, and cyanazine (organochlorines and organophosphates)
- Participants who had used herbicides alachlor and cyanazine had higher risk for developing the disease, particularly with repeated use
- Participants who used aldrin, chlordane, and heptachlor more than 100 lifetime days had 51%, 63%, and 94% increased odds of developing the disease
- Confirmed the link between diabetes and overweight and obese, potentially more storage of pesticides/pollutants in fat

# Parkinson's Disease (PD)

- Male AHS applicators and female spouses who used pesticides > 400 days/lifetime had increased risk for PD
- Participants who used paraquat, cyanazine, trifluralin, or 2,4,5,-T had an increased risk
- Participants who used Rotenone and paraquat developed PD 2.5 times more often than those who did not
- Related to high pesticide exposure events
- Using PPE was associated with reduced risk of PD
- Supports the evidence that some pesticide exposure may increase the risk of developing PD
  - Add-on study Farming and Movement Evaluation (FAME) to investigate disease, exposure and genetics and PD
  - evaluate the role of pesticides and other farm-related exposures in PD

# Farmers Lung

- Rare disease, generally associated with dairy farming and handling moldy hay and grain
- Reported by 2% of AHS farmers and 0.2% of spouses
- Most cases in Iowa
- Highest risk associated with dairy and poultry farmers
- Participants who used lindane and DDT more likely to report the disease
- Farmers and spouses who had applied pesticides for more than 30 years had 50% higher chance of reporting the disease

# Rhinitis

- 67% of farmers polled had current rhinitis (1993-1997)
  - 39% had 3 or more individual episodes
- Glyphosate and petroleum oil associated with current rhinitis and increased episodes
- 4 organophosphates, chloropyrifos, diazinon, dichorvos, malathion
- Carbaryl and permetherin use on animals were predictors of current rhinitis
- Fungicide, captan also a predictor of rhinitis
- Specific pesticides may contribute to rhinitis and agricultural activities did not explain this

# Wheeze

- Farmers have more respiratory disease and symptoms than other occupational groups
- 20, 468 answered questions about wheeze, 18% reported wheeze
- 40% more likely to wheeze if you drive a diesel tractor,
- Driving a gasoline tractors was associated with less wheeze

# Wheeze

- Animal and animal-related exposures can trigger wheeze
- Increased animal contact more likely to wheeze
- Increase in the number of animals more wheeze than farmers with fewer animals (>500 poultry, >1000 livestock)
- Contact with manure as well as synthetic fertilizers associated with wheeze
- Parathion increases association with wheeze , chloropyrifos, malathion also associated
- Paraquat, atrazene, alachlor, chorimoron ethyl, EPTC
- Using pesticides more often increases wheeze, no difference noted by application method

# Adult Onset Asthma

- Asthma diagnosed at >20 yrs
  - Of 19,704, 127 allergic, 314 non-allergic
- Evaluated 48 pesticides and other farming activities
- 12 pesticides associated to allergic asthma
  - 2Xs OR for coumophos, heptachlor, parathion, 80/20 carbon tetrachloride/carbon disulfide, ethylene dibromide
- Pesticides also associated with non-allergic asthma
- Current animal handling and other forms of farm activities did not confound these associations
- Pesticides may be overlooked as a contributor to asthma



# Cancer Related Study Results

# Prostate Cancer

- Iowa and North Carolina n = 55,332 (1994-1999)
  - evaluated association of 45 agricultural pesticides
  - 566 cases of prostate cancer
- Commercial applicators 41% excess risk
- Private applicators 27% excess risk
- Family history of prostate cancer (19% vs 8.9%)
- Pesticides of interest
  - Chlorpyrifos, coumaphos, fonofos, phorate, permethrin
  - Methyl bromide – dose-response association (# of days)
- Herbicides
  - Butylate

AHS Report 2003

# Methyl bromide update 2012

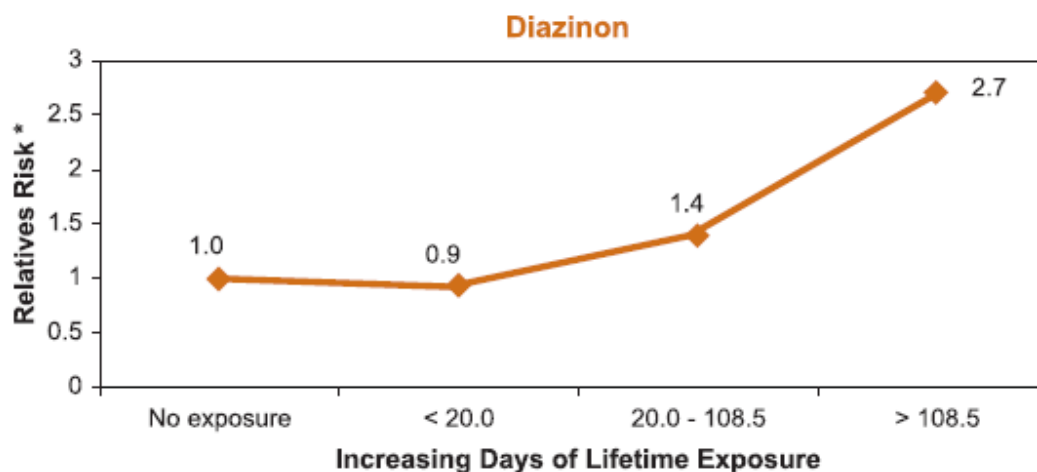
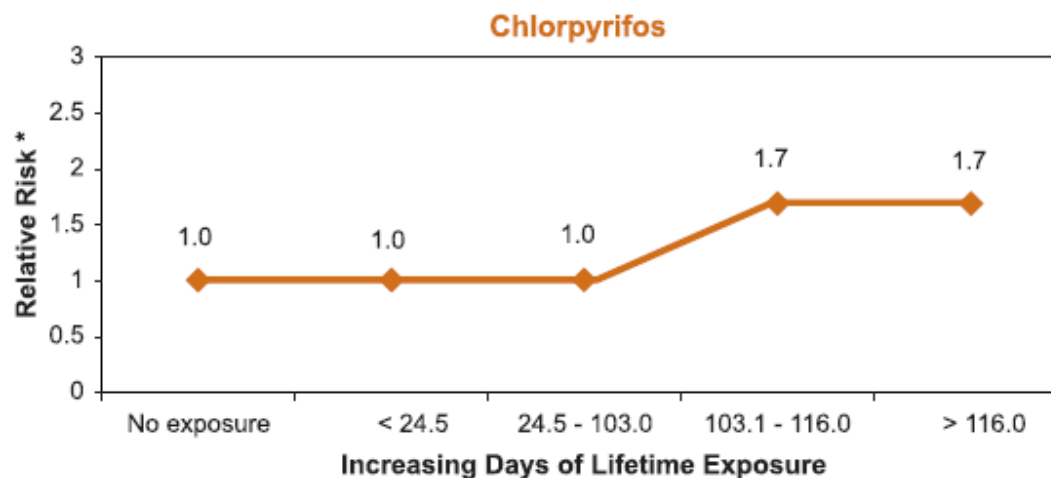
- Previously reported association with prostate cancer was not supported upon further follow up
  - However an elevated risk associated with methyl bromide was observed, not statistically significant
- New study of 53,588 AHS pesticide applicators, 1993-2007, found that methyl bromide was associated with risk of stomach cancer specifically with increased use, low, high vs no use
- Little association with other site cancers such as lung, colon, lymphohemopoietic

Barry et al., Cancer Causes Control, 2012

# Lung Cancer

- AHS pop, 50% less likely to have lung cancer
  - 14% smoke vs 23% general population
  - 20 Xs increased risk for smokers 20yrs or more
- Associated factors
  - Age
  - History pneumonia, chronic lung diseases (bronchitis, emphysema)
  - Off farm exposures, asbestos and lead
  - Evidence not clear, association between chemical use and lung cancer are very complex
  - Pesticides and herbicides associated, further study required
    - Chlorpyrifos and diazinon
    - Metolachlor and pendimethalin (days of use)

**Figures 1-2. Pesticides significantly associated with lung cancer among AHS pesticide applicators, 1993-2001.**



\* All relative risks are computed with non-users of the chemical as a comparison group. They are adjusted for age, cigarette smoking, and other potential confounding factors. The relative risk is the ratio between the risk of lung cancer among users of the chemical and the risk of lung cancer among nonusers. A relative risk of 1 indicates no excess risk with exposure. A relative risk of 4 indicates a four-fold excess.

# Breast Cancer

- AHS wives (30,454) had slightly less breast cancer risk than the general population
  - More physically active, healthier lifestyle
  - 2Xs the risk if family history of breast cancer
  - Increased risk if overweight or obese
- Suggestive increased association among women who did not apply pesticides
  - Living next to fields where pesticides were applied
  - Living on a farm that had ever used, aldrin, carbaryl, chlordane, dieldrin, heptachlor, lindane and malathion
  - Husband that used herbicide 2,4,5-TD or fungicide captan

# Colorectal Cancer

- AHS participants have lower colorectal cancer than the general population
- Evaluated pesticide exposure of 305 private applicators diagnosed during the 7 year study timeframe compared to those who did not develop the disease
- Chlorpyrifos and aldicarb were associate with the risk of developing rectal or colon cancer
- First study to associate aldicarb, while chlorpyrifos has previously been associated with rectal cancer
- More study to further evaluate these findings

# Multiple Myeloma

- Rare cancer, occurs more frequently in farmers than non-farmers
- Small sub-study of AHS investigating biomarker in blood (MGUS), monoclonal gammopathy of undetermined significance, and some with this marker go on to develop MM
- Found more MGUS in men over 50 compared to the general population
- Link between MGUS and some pesticides but study is too small to draw firm conclusions
- Further study needed to identify specific exposures related to MGUS which may help to understand multiple myeloma and prevent it's progression

Landgren, et al. *Blood*, 2009 June 18;113(25):6386-6391.

Perrotta, et al. *J Occup Med Toxicol*. 2008; 3:27.



# Other Add-on Studies

# Lung Health Study

- Purpose
  - Investigate the onset of asthma and associations with pesticide exposure and other farming exposures
  - Data collection Lung function, allergic status and genetic characteristics associated with asthma and other respiratory illnesses
  - Recruitment, 3000 participants in the AHS
- Early findings which informed the study
  - Women who grew up on farms have less reported asthma
  - Regardless of if they grew up on a farm or not, there was a higher risk of asthma with allergies if they used:
    - 2,4 –D and glyphosate (herbicides)
    - carbaryl, coumaphos, DDT, malathion, parathion, permethrin (on animals), phorate (insecticides)
    - metalaxyl (fungicides)

AHS Updates 2008, 2009, 2012

# Biomarkers of Exposure and Effects in Agriculture (BEEA)

- Purpose
  - to understand how pesticides influence disease risks and biomarkers of exposure
- Objectives
  - environmental samples to be collected
    - Blood and urine
    - House dust
    - used in coordination with questionnaire data and buccal cell collection
  - recruiting 1,600 participants

# Methicillin-resistant *Staphylococcus aureus* Study

- Current thought, MRSA infections associated with a stay in the hospital but some people can become infected with livestock-animal associated MRSA
- Purpose
  - Explore factors that may increase a person's chance of developing a MRSA infection
- Objectives
  - 1,100 AHS participants – nose and throat swabs
  - Complete surveys for possible infection and supply more nose and throat samples if participant develops and infection
- Currently recruiting

# AHS is Currently Accepting Proposals for New Studies

- STaRS – Study Tracking and Retrieval System
  - supports policies and procedures of AHS
  - reviews requests for data
  - project proposals
  - publications
- Provides staff support for investigators
  - for approval
  - to support the review
  - approval by the AHS Executive Committee

AHS Contact	Topics for Research Proposals
Michael Alavanja NCI	Cancer in Applicators and Spouses
	Biomarkers and Molecular Genetics
	Injury
	Acute Effects of Pesticide Exposure
	Diet
	Geographic Information Systems
	Statistical Methods
Laura Beane-Freeman NCI	Cancer in Applicators and Spouses
	Biomarkers
	Geographic Information Systems
	Exposure to Animals
	Mortality and Lifestyle Factors
Jane Hoppin NIEHS	Respiratory and Allergic Disease
	Statistical Methods
	Cardiovascular Outcomes
	Pesticide Exposure Assessment: Questionnaires and Biological Markers
	Biologic and Functional Effects of Chronic Pesticide Exposure
Freya Kamel - NIEHS	Neurological Disease and Function
Dale Sandler NIEHS	Reproductive Health
	Child and Adolescent Health
	Autoimmune Disease and Immune Function
	Other Non-cancer Chronic Disease
Kent Thomas - EPA	Pesticide Exposure Assessment - Field Studies
Cynthia Hines - NIOSH	Pesticide Exposure Assessment - Field Studies

# AHS Website Contact Information

- Agricultural Health Study

[www.aghealth.org](http://www.aghealth.org)

- NCI Publications Link

<http://aghealth.nci.nih.gov/publications.html>

- NIEHS Research Link

<http://www.niehs.nih.gov/research/atniehs/labs/epi/studies/ahs/index.cfm>

- NIH Results Link

<http://aghealth.nci.nih.gov/results.html>