Application of an algorithm to quantitatively estimate non-occupational pesticide exposure intensity for spouses in the Agricultural Health Study

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Motivation

- Spouses of farmers may be exposed to pesticides from direct occupational use and from **non-occupational pathways**, such as:
  - **agricultural drift** from nearby fields
  - **take-home** from skin, clothes, shoes of farmers
  - **residential** pest treatments in the home/yard
- Most previous etiologic research has focused on (male) farmers
- Previous epidemiologic analyses of (female) spouses largely used participant reported information as exposure surrogates; single pathway
- Improved quantification of pesticide exposure intensity from non-occupational pathways may **decrease exposure misclassification** in epidemiologic analyses

Agricultural Health Study

- Cohort study of pesticide applicators and spouses in Iowa and North Carolina
- 32,345 spouses, 99% women
- 60% report applying pesticides
- Indirect exposure from applicator-husband's activities
- Previous analyses:
  - Ever/never use by spouse
  - Applicator-husband's use (e.g., days of use of a specific active ingredient)
- Unique population presents opportunities:
  - Whether any observed associations similar to those in male applicators
  - Increased risk of female-specific diseases (e.g., breast, ovarian cancer)
  - Population may be relevant to high-end of general population

Objective

- To develop a pesticide-specific algorithm for cumulative, non-occupational pesticide exposure intensity for spouses of pesticide applicators

Steps of Development

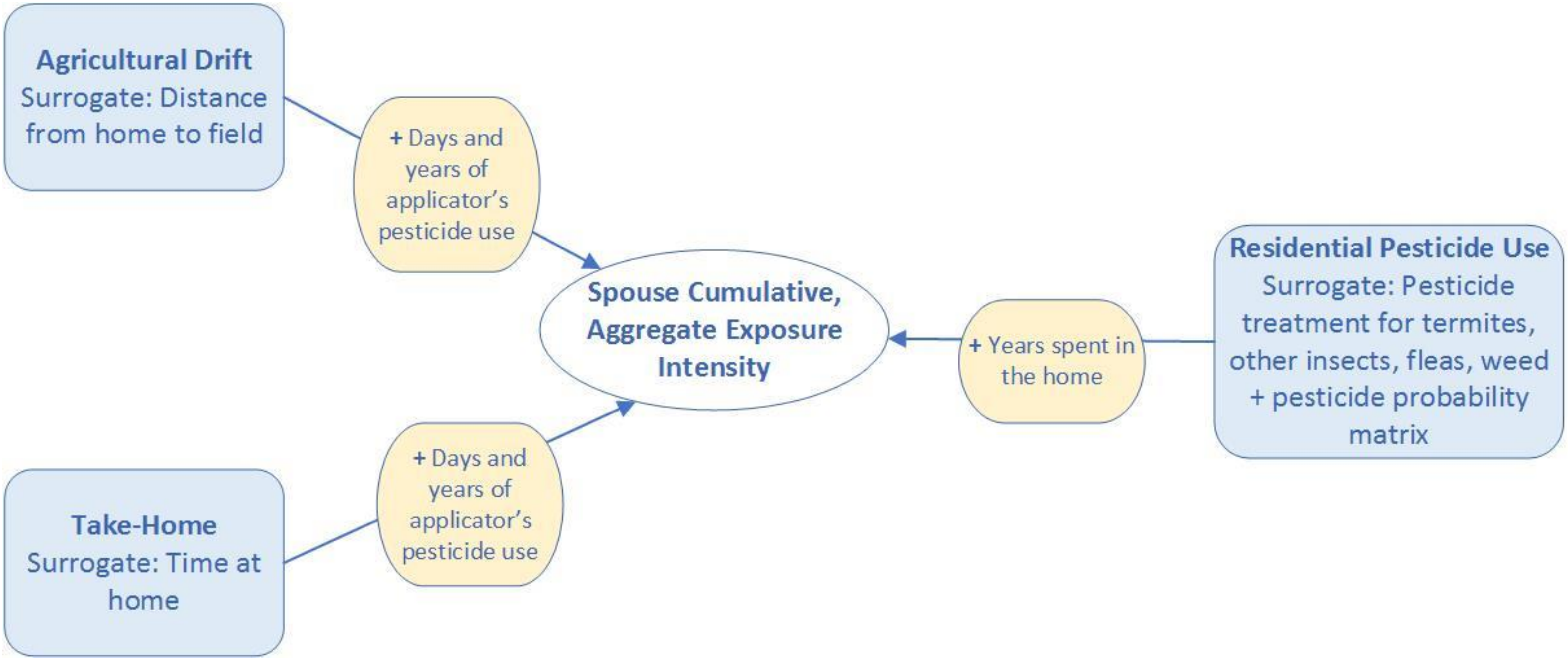
1. Literature review: identify non-occupational pesticide exposure pathways (*Deziel 2015 EHP*)
   Agricultural drift, take-home, and residential pesticide use

2. Developed literature-based exposure pathway weights *(Deziel 2017 EHP*)
   Abstracted dust pesticide concentrations summary statistics (e.g., geometric means (GM))
   Synthesized data using novel application of mixed-effects meta-regression models

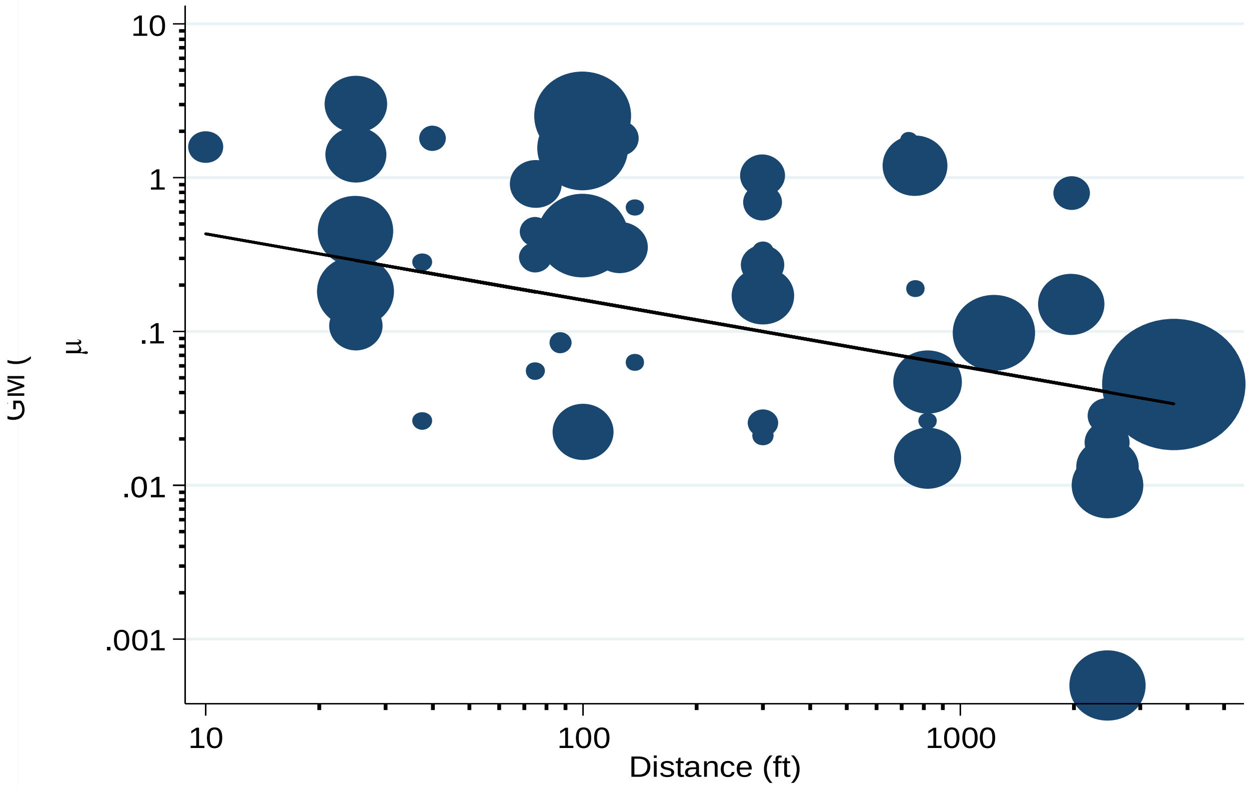
3. Used individual-level questionnaire responses from AHS spouses and applicators about pesticide use, farm characteristics, and other activities to identify subject-specific contrasts in pesticide exposure intensity (*Deziel under review JESEE*)

4. Applied the algorithm to subset of spouses with complete data on key input variables for atrazine and chlorpyrifos (*Deziel under review JESEE)*

Conceptual Framework



Agricultural Drift Pathway



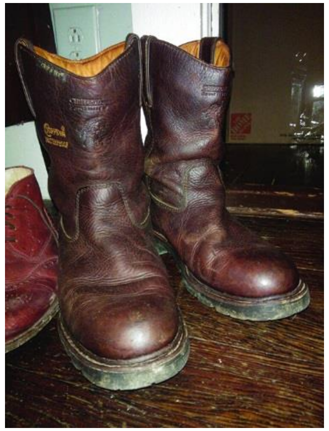
Predicted GM pesticide dust concentrations in relation to **distance between home and treated fields** (52 statistics from 7 studies).

Distance (ft)	Proximity-based Weight (95% CI)
25	6.6 (2.5, 17.1)
75	4.1 (2.0, 8.4)
150	3.0 (1.7, 5.4)
450	1.9 (1.4, 2.6)
560	1.7 (1.3, 2.3)
750	1.5 (1.2, 1.9)
1350	1.2 (1.1, 1.3)
1980 (Ref)	1.0

Proximity weights with confidence intervals (CI) for various distances between homes and treated fields.

1980 ft = 0.6 km

Take-Home Pathway



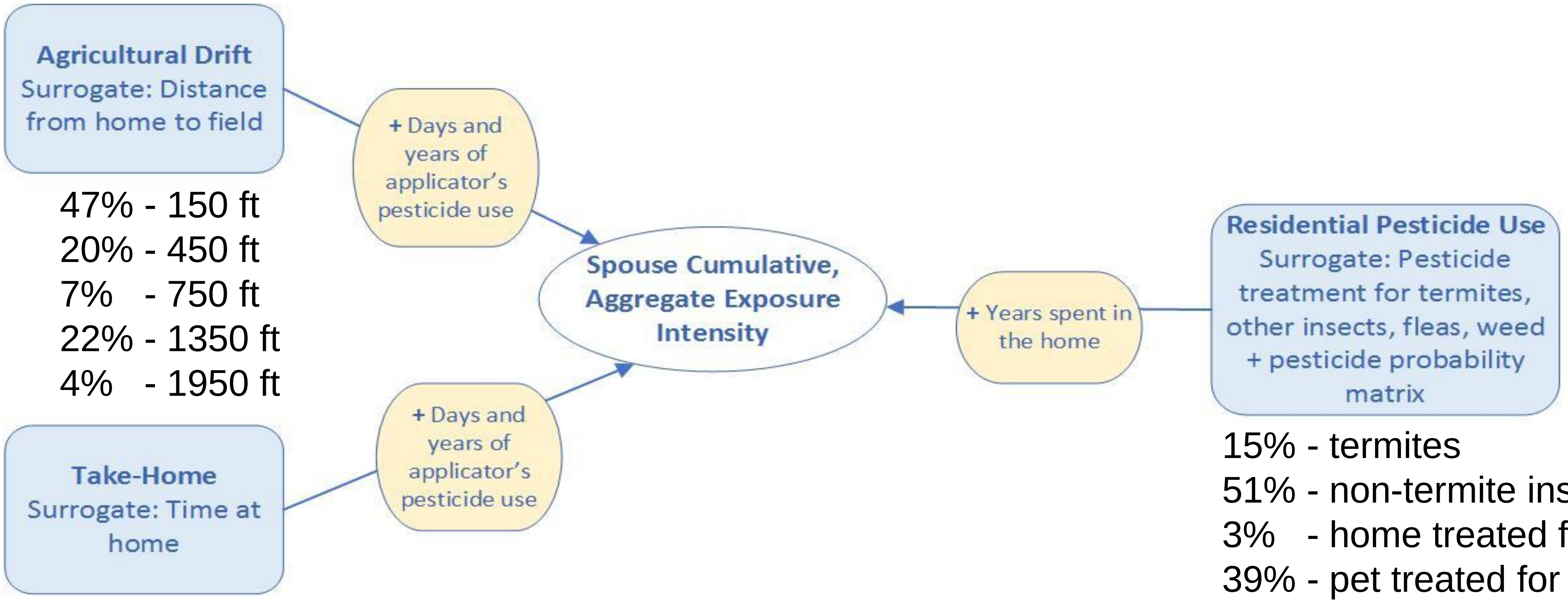
- Meta-regression yielded 2.3 (95% CI: 1.5, 3.3) times higher house dust pesticide concentrations in homes of farmers with high vs. low pesticide use
- **Time spouse spent at home** based on self-reported information about their off-farm employment
- AHS applicators reported the **days & years of use of specific pesticides**

Residential Use Pathway

- Reported home and yard pest treatment types: termites, insects, fleas/ticks in home, fleas/ticks on pets, weeds
- Probability matrix documenting likelihood that active ingredients were used in home pest treatment products (*https://dceg.cancer.gov/tools/design/pesticide*)

Probability of Active Ingredient Use in Pest Treatment	Weight (95% CI)
0	0
≥1% to <20%	1.3 (1.1-1.6)
≥20%	1.5 (1.2-1.9)

Application to AHS Spouses



47% - 150 ft
20% - 450 ft
7% - 750 ft
22% - 1350 ft
4% - 1950 ft

15% - termites
51% - non-termite insects
3% - home treated for fleas
39% - pet treated for fleas
37% - weed treatment

73% had a full-time off-farm job
18% part-time off-farm job
9% no off-farm job

Application to AHS Spouses (n=19,064)

	Chlorpyrifos		Atrazine	
Applied by applicator-husband	44%		76%	
Exposed via residential use pathway	63%		5%	
Exposure metrics if pesticide applied	**Median (IQR)**	**Ratio 75/25**		**Ratio 75/25**
Days applied	3.5 (3.5-8.0)	2.3	8.0 (3.5-25.5)	7.3
Years applied	7.0 (2.5-7.0)	2.8	7.0 (2.5-14.5)	5.8
Take-home exposure	2.5 (0.9-6.6)	7.3	5.8 (2.1-15)	7.1
Agricultural drift exposure	4.1 (1.7-11)	6.5	8.0 (2.6-22)	8.5
Residential use exposure	40 (27-75)	2.8	33 (19-45)	2.4
Summed exposure	39 (19-73)	3.8	16 (5.4-38)	7.0

Correlation between Pathways

	Spearman Correlation Coefficients			
	Take-home	Agricultural Drift	Residential Use	Total Non-Occupational
Chlorpyrifos, spouses with $E_{non\text{-}occ}$ >0				
Take-home	1	0.99	0.02	0.31
Agricultural Drift		1	0.01	0.31
Residential Use			1	0.90
Atrazine, spouses with $E_{non\text{-}occ}$ >0				
Take-home	1	0.98	0.02	0.96
Agricultural Drift		1	0.02	0.96
Residential Use			1	0.24

Limitations: Exposure Misclassification

- Data too sparse to characterize exposure differences
  - E.g., by active ingredient, pesticide type, crop type, region, application type
- Data too sparse to model certain pathways
  - E.g., dietary ingestion, bystander
- Distance to nearest field was commonly reported
  - Insufficient data on more specific and detailed approaches, e.g., crop maps, GIS
- Omitted modifiers
  - Personal behaviors (limited evidence)
  - Pesticide usage of neighbors and other house residents

Strengths

- Data-driven, transparent framework that can be modified when new data become available
- Aims to reduces misclassification
- Demonstrated active ingredient-specific exposure contrast
- Facilitates etiologic analyses in a novel population

Current and Future Efforts

- Application of the algorithm for other pesticide active ingredients, e.g, 7 organochlorine insecticides (n=30,552 spouses) (*Louis in prep*)
- Algorithm evaluation/validation – direct and indirect
- Etiologic analyses

Conclusions

- This transparent, data-driven algorithm of cumulative pesticide exposure will facilitate etiologic analyses within the AHS
- Some exposure misclassification will remain due to limitations in data available from the literature and the AHS
- Updates can be made when new information becomes available, and the equations could be adapted to other studies with similar information

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