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Gender Differences in Respiratory Health Outcomes among Farming Cohorts around the Globe: Findings from the AGRICOH Consortium

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Abstract

Purpose: Respiratory hazards of farming have been identified for centuries, with little focus on gender differences. We used data from the AGRICOH consortium, a collective of prospective cohorts of agricultural workers, to assess respiratory disease prevalence among adults in 18 cohorts representing over 200,000 farmers, farm workers, and their spouses from six continents.

Methods: Cohorts collected data between 1992–2016 and ranged in size from 200 to >128,000 individuals; 44% of participants were female. Farming practices varied from subsistence farming to large scale industrial agriculture. All cohorts provided respiratory outcome information for their cohort based on their study definitions. The majority of outcomes were based on self-report using standard respiratory questionnaires; the greatest variability in assessment methods was associated with chronic obstructive pulmonary disease (COPD).

Results: For all three respiratory symptoms (cough, phlegm, and wheeze), the median prevalence in men was higher than in women, with the greatest difference for phlegm (17% vs. 10%). For asthma, women had a higher prevalence (7.8% vs 6.5%), with the difference associated with allergic asthma. The relative proportion of allergic asthma varied among cohorts. In two of eight cohorts for women and two of seven cohorts for men, allergic asthma was more common than non-allergic asthma.

Conclusions: These findings indicate that respiratory outcomes are common among farmers around the world despite differences in agricultural production. As women in the general population are at higher risk of asthma, exploring gender differences in occupational studies is critical for a deeper understanding of respiratory disease among agricultural workers.

Introduction

Agricultural work is an occupation represented by both men and women, though little formal comparison of respiratory disease prevalence by gender has been conducted. Work in agriculture has been associated with respiratory diseases as early as the mid-1500's [1]. Even as farm work becomes more industrialized, there continues to be evidence of increased respiratory risk for agricultural workers. Factors contributing to increased risk of respiratory diseases and symptoms include frequent exposure to dusts, microorganisms, toxic gases (e.g. diesel motor exhaust, welding fumes, ammonia, hydrogen sulfide, and carbon dioxide), and pesticides [2]. Agricultural activities vary by region and thus, exposures will also vary. While respiratory diseases have been a concern among farming populations for many

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centuries, recent studies have focused on differences between allergic vs. non-allergic phenotypes [3–7] due to the reduced risk of allergy associated with growing up on a farm [8].

Agricultural workers include both farmers who are owners and operators and farm workers (local and migrant). Women often have an active role in farm production activities but in some populations are not regarded as farmers, and as a result, the impact of their occupational exposures may be under-represented. Agricultural work remains an occupation that people often begin at young ages.

While many papers have been published related to the respiratory health of agricultural workers, few, if any, have attempted to integrate data from across continents and farming practices to characterize the global respiratory health implications of agricultural work. In 1998, the American Thoracic Society published a research statement on Respiratory Hazards of Agriculture [1]. In this seminal work, extensive detail was provided on the specific respiratory outcomes, as well as the range of exposures experienced by agricultural workers primarily in developed countries. However, respiratory hazards of women and agricultural work in low and middle income countries were not well represented. A limited amount of literature has been published assessing gender differences in the incidence and/or prevalence of respiratory symptoms and diseases among farming populations, and nearly all of these studies focus of populations in either the United States or Europe [9–11]. Although there has not been a multi-country study to estimate the global burden of respiratory disease among farmers, the numerous cohort studies that have been conducted around the world can help start to address this gap in knowledge.

The AGRICOH consortium was created in 2006 as a collaborative effort to assess relationships between farming exposures and health outcomes. Currently 29 cohorts are participating and they include a diverse range of types of farming from all continents [12]. To assess the prevalence of respiratory disease and symptoms among diverse farming populations and to explore differences between men and women, we focused on common respiratory endpoints from AGRICOH cohorts with respiratory outcome information.

Methods

Study Population

The AGRICOH consortium consists of 29 cohorts from around the world (http://agricoh.iarc.fr/). We focused on adults for this analysis because we were interested in occupational exposures. Fourteen cohorts were excluded from this analysis: four did not include adults, eight did not collect respiratory outcome information, and two were unable to provide data. All eligible AGRICOH cohorts agreed to participate. Additionally, three farming cohorts outside of AGRICOH, but which included AGRICOH investigators, were also identified for inclusion, resulting in 18 cohorts for this analysis [13–29]. These cohorts cumulatively represent 211,232 people. The data presented includes farming populations around the world, including those of low and middle income countries with different socioeconomic settings, spanning from 1992 to 2016.

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Data Collection

For this project, we developed a structured reporting form to collect standardized demographic and outcome information (see supplement 1). All cohorts were asked to provide summary statistics on their cohorts; raw data were not collected. All cohorts except the Agricultural Health Study (AHS) provided prevalence estimates for data collected at enrollment. For the AHS, data from the most recent AHS interview were included because this information was more complete than the enrollment information.

Cohort Demographic Information

The data collection form requested information on cohort: sample size and calendar year of data collection, as well as summary statistics regarding age distribution, gender, smoking status (current/past/never), and body mass index (BMI, <20, 20-<25, 25 - <30, and ≥30). We also collected data on the participant types (farmer, farm worker, subsistence farmer), role of women in cohort (full time farmers, help on farm, spouses), type of livestock raised (poultry, beef cattle, dairy cattle, pork, other), type of farming (row crops, vegetables, orchards, other), and grain handling. We applied the World Bank Atlas method to determine country economy classifications, categorized by gross national income (GNI) per capita: low-income (≤$1,025), lower-middle-income ($1,026-$4,035), upper-middle-income ($4,036–12,475), and high income (≥$12,476) [30].

Respiratory Outcome Information

Cohorts were asked to provide prevalence and 95% confidence interval information for three respiratory symptoms (cough, phlegm, and wheeze) and two respiratory diseases (asthma and chronic obstructive pulmonary disease (COPD)). Asthma was further classified as either allergic or non-allergic, based on each cohort's definition.

Outcome definitions varied by cohort with most using standard respiratory questionnaires (e.g., American Thoracic Society Questionnaire [31] and European Community Respiratory Health Survey [32]). Some studies collected only self-reported outcome information while others incorporated clinical measurements as well. All symptom information was self-reported. Asthma was reported as either ever asthma or asthma in the past 12 months. All but one study relied on self-reported doctor's diagnosis of asthma, while the remaining study included a broader definition of having had an history in the past year of an attack of shortness of breath, an asthma attack, using asthma medication or having a positive bronchodilator test conducted by study staff [16].

COPD definition was most variable among the cohorts (supplement 1). Fifteen cohorts provided information on COPD prevalence. This information was based on self-report (67%, 10/15 cohorts), spirometry (27%, 4/15 cohorts), or an inclusive definition of either spirometry or self-report (7%, 1/15 cohorts). Among the 11 studies that used self-report to ascertain COPD status, definitions for COPD included: doctor diagnosis of COPD alone (27%); doctor diagnosis of chronic bronchitis alone (45%); the combination of doctor diagnosis of COPD, chronic bronchitis, or emphysema (18%); or self-reported history of COPD alone (9%).

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Among seven cohorts reporting both allergic and non-allergic asthma, definitions for allergic asthma were asthma with hay fever (29%), asthma with hay fever and/or eczema (14%), asthma with rhinitis and other allergic diseases (14%), asthma with positive Phadiatop test (14%), asthma with atopy or fractional exhaled nitric oxide (FeNO) >50 ppb (14%), or asthma with three or more positive responses to a skin-prick test (14%).

Statistical Analysis

Our statistical analysis focused on descriptive statistics of health outcomes. We integrated the summary statistics from all cohorts to create summary tables. To describe the distribution of respiratory outcomes among the cohorts, we calculated the median, interquartile range (IQR), and total range for prevalence of respiratory symptoms and diseases, for cohorts as a whole and then by gender. Reported medians were not weighted by cohort size, and reflect the 50^{th} percentile of individual cohort prevalence estimates. To assess the relative prevalence of allergic to non-allergic asthma, gender-stratified prevalence ratios and corresponding 95% confidence intervals were calculated for each cohort. Analysis was completed in SAS 9.4 and figures developed in R.

Results

Cohort Characteristics

A total of 18 cohorts from 11 countries participated, including 118,520 men and 92,712 women (N=211,232) from both crop and livestock farming populations. Cohorts had a wide geographic spread, including populations from six continents (Figure 1). Participants include farmers, farm workers, subsistence farmers, and rural residents. Agricultural activities range from large scale industrial agriculture to rural fruit and farmworkers in Africa (supplement 2). The majority of the cohorts were based in high-income countries (14/18, 78%), while three (17%) were based in upper-middle-income, and one (6%) in a low-income country.

The cohorts ranged in size from 206 to 128,388 participants: six (33%) included fewer than 1,000 participants; ten studies (56%) included 1,000–10,000 participants; and two (11%) included greater than 10,000 participants (Table 1). The majority of cohorts featured a greater proportion of males; however, two cohorts (KwaZulu-Natal Crop Farmers [14] and Western Cape Fruit Farm Workers [15]) included only female farm workers. The median proportion of males among cohorts was 60% (Interquartile Range (IQR): 44–78%). Among all cohorts, ages ranged from 15 to 105 years, with a median cohort-specific age of 51 years (IQR: 40.7–55.5).

Covariates

We collected data on two common risk factors for respiratory outcomes: smoking and body mass index (BMI). The prevalence of smoking varied among the cohorts. The prevalence of current smoking ranging between 5% and 50%, with a median of 15% (IQR: 9%−30%) (Table 1 and supplement 3). There were no apparent differences in smoking prevalence between industrialized and non-industrialized countries or by geographic region. Smoking varied by gender, with current smoking prevalence consistently higher among males (median = 17% [IQR: 9%−30%]) compared to females (median = 11% [IQR: 7%−22%]). For BMI,

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the proportion of obese individuals ranged from 1% to 40% (median = 17% [IQR: 13% −33%]), and overweight individuals ranged from 11% to 44% (median = 31% [IQR: 21% −44%]). Higher proportions of underweight participants were more common among KMCC [17] and African cohorts [13–16] (Table 1 and supplement 4).

Respiratory Symptoms

We collected data on cough, phlegm, and wheeze. Most cohorts collected data on all three of these outcomes (10 of 18); 72% of cohorts provided data on cough, 61% on phlegm, and 61% on wheeze. Respiratory symptoms were common in all cohorts (Supplement 5a). The median prevalence was 18.6% (IQR: 14.4–30.0%) for cough, 13.3% (IQR: 7.8–18.8%) for phlegm, and 15.0% (IQR: 8.8–16.1%) for wheeze. Farmworkers from South Africa (Western Cape Fruit Farm Workers [15] and North West Poultry Workers [16]) and France (FERMA [20]) had the highest prevalence of cough and phlegm among all cohorts. Western Cape Fruit Farm workers also had the highest prevalence of wheeze (31%), while the farmers in the AHS in the United States had the second highest prevalence of wheeze (22%). When the data were stratified by gender (Figures 2a, 2b, 2c, Supplement 5b), males were more likely to report respiratory symptoms than females, though the IQR for the median values overlapped between males and females.

Respiratory Diseases

We collected data on asthma, allergic asthma, non-allergic asthma, and COPD based on each cohort's definitions (Supplement 6a). All cohorts provided data on asthma, and 39% provided information on allergic phenotypes. 83% of cohorts provided information on COPD.

The median prevalence of asthma was 7.2% (IQR 5.7%−10.1%) with individual study values ranging from 0.5% in the Ethiopian [13] cohort to 16.0% among Victorian Grain Farmers [28] in Australia. Differences in asthma prevalence by gender did not follow the same trend as observed for symptoms (Figures 3a and 3b). The median prevalence was slightly higher among females (7.8% [IQR:6.5%−10.5%]) compared with males (6.5% [IQR: 4.0% −11.3%]).

In the seven cohorts with data on allergic and non-allergic asthma, allergic asthma (5.0% [IQR:3.0%−5.1%]) was more common than non-allergic asthma (2.0% [IQR:1.9%−7.0%]). This trend persisted after stratifying by gender; the median prevalence of allergic and non-allergic asthma among females was 5.5% and 3.5%, respectively, while among men, the median prevalence was 3.6% for both allergic and non-allergic asthma. Among the gender-stratified results, we also observed that women had higher prevalence ratios (PRs) than men, comparing allergic to non-allergic asthma (Figure 4). Upon aggregating data across all cohorts, women (PR: 1.01 [95% CI: 0.95–1.06]) had a significantly higher prevalence ratio of allergic to non-allergic asthma compared to men (PR: 0.76 [95% CI: 0.72–0.82]), indicating that allergic asthma and non-allergic asthma prevalence were similar in women, but that men were less likely to have allergic asthma.

Information on COPD was provided by 14 of 18 cohorts. One third of the cohorts used spirometry to classify COPD; the remaining two thirds used self-reported doctor diagnosis

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of at least one of these three outcomes (chronic bronchitis, emphysema, or COPD). The median prevalence of COPD among all cohorts was 4.5% [IQR: 2.8%−10.0%]) with COPD prevalence ranging from 0.5% in the MAUCO [29] cohort to 14.6% among Norwegian [22] farmers. The studies that reported using spirometry to estimate COPD prevalence had values ranging from 1.9% to 14.6% [median = 10.0% [IQR: 4.5%−11.1%]; studies that used self-reported prevalence had values ranging from 0.5 to 11.9% for COPD [median = 3.7% [IQR: 2.8%−10.0%]. When we stratified the COPD data by gender, the median prevalence for males was 5.5% (IQR: 1.9%−12.2%) and for females was 4.0% (IQR: 2.0%−7.9%) (Supplement 6b).

Discussion

Using the data from 18 agricultural cohorts from around the world, we sought to characterize the prevalence of respiratory symptoms and diseases among the AGRICOH consortium as indicators of respiratory health among farmers worldwide with particular focus on differences by gender. In this analysis, respiratory symptoms were common and higher among men than women; while respiratory diseases were less common and women had a higher prevalence of asthma and men had higher prevalence of COPD. Although farming practices differ around the world, we found that the prevalence of these respiratory outcomes did not vary substantially between cohorts with any notable trends by region.

The 18 cohorts included here represent a small subset of agricultural workers worldwide. No comprehensive study of agricultural workers using a common protocol around the world has been conducted. While large, our sample is by no means comprehensive and the representation between developed and developing countries is uneven. Some cohorts included a relatively small number of farmers and focused only on specific types of farming, such as the all-female Western Cape Fruit Farmers [15] cohort in South Africa, while others featured much larger populations that included a wide variety of types of farming activities as well as spouses of farmers (e.g., AHS, AGRICAN, and Norwegian Farmers). Overall, the average age among our cohort members (56.8 years) is similar to the average age of farmers in both developed countries and across Africa (60 years), as reported by the Food and Agriculture Organization of the United Nations in 2014 [33].

Overall, males reported more respiratory symptoms than women, but this was not true for every cohort. In general population samples, such as the National Health and Nutrition Examination Survey (NHANES) in the United States, the prevalence of wheeze and cough is similar in men and women while the prevalence of phlegm is much more common in men [34]. Here we observe greater differences between men and women in cohorts limited to specific farm activities, such as poultry work, with a high potential for exposure to respiratory irritants (e.g., Northwest Poultry Workers). We were unable to evaluate specific farming practices due to both the small number of cohorts and the complex exposure experience of individuals within the larger cohorts (e.g., AHS, AGRICAN). Occupational exposures and the types of tasks that men are more likely to engage in may contribute to this higher outcome prevalence [3]. Smoking is more common in men, and that may also contribute to some of the observed differences. However, in our study sample, there is more variability in the prevalence of symptoms by cohort rather than between men and women,

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suggesting different baseline rates of symptoms in different populations as well as differences in type of farming and related exposures.

Asthma prevalence was higher in women agricultural workers, likely due to the higher prevalence of allergic asthma in women. Similarly, women around the world have a higher prevalence of asthma than men. In an earlier analysis of AHS data from 2005–2010, women in the AHS had more asthma than men in the AHS, but lower prevalence of asthma compared to the US population [35]. This may be due to factors associated with who becomes a farmer (for example, people with a history of asthma may choose a different profession) as well as agricultural exposures that appear to reduce allergic outcomes in farmers and their families [3,8,36]. The prevalence of asthma among our cohorts ranged from <1% to 16% with a median prevalence of 7.2%. Globally, asthma prevalence in adults aged 18–45 from 70 countries in 2002–2003 ranged from 0.2 (China) to 21% (Australia) with an overall prevalence of 4.3% [37]. While that study did not include all the same countries included here, it suggests that farmers may have a higher prevalence of asthma than the general population. Surprisingly, we observed a higher prevalence of allergic asthma than non-allergic asthma in the cohorts with data on this outcome (5.0% vs. 2.0%); this difference may have been due to higher prevalence of asthma in women and that women had a higher prevalence of allergic asthma. There is an extensive literature suggesting that farmers have a lower prevalence of allergic asthma [3,4,38]. We cannot evaluate whether our findings are due to the diversity of our cohorts over continents and agricultural practices, or due the primarily cross-sectional data used, or the fact that allergy may have been assigned based on questionnaire information. Future studies should focus on better characterization of allergic asthma.

The COPD results highlight the challenge of combining data across cohorts when disease definitions vary greatly, as has been reported by others [39]. Among the 15 cohorts that evaluated COPD prevalence, six different definitions of COPD were employed. COPD is classified based both on symptoms (chronic cough and phlegm) as well as airway obstruction as assessed through spirometry [40]. COPD encompasses the spectrum of obstructive diseases and includes chronic bronchitis and emphysema. Not all cohorts used spirometry to diagnose COPD, but rather relied on doctor diagnosis of COPD. This will capture individuals who have been diagnosed accurately by their physician, but will miss those who have not had this detailed clinical work up; suggesting a sensitive, but not specific outcome. Additionally, it will capture those who received a diagnosis but did not meet the clinical criteria, creating false positives [41]. Within an individual cohort, these biases may behave in the same manner, but between cohorts the factors that influence diagnosis and over reporting may differ making it almost impossible to combine across these studies.

Although this study importantly characterizes farming cohorts around the world, it does feature some limitations. Comparability between cohorts may be limited due to differences in study year, ranging from 1992 to 2016. Cohorts ranged from small, focused cohorts with detailed information on a specific type of agriculture to large studies that include farmers engaged in a wide variety of activities. In choosing to include as many cohorts as possible, we forfeit the ability to focus on specific types of agriculture or agricultural practices. Participating cohorts provided demographic and symptom and disease metadata, but did not

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share participant-level data. As a result, the prevalence estimates reported are not adjusted or standardized to account for important confounding variables such as smoking, age, status, income, education, and farming practices. While the AGRICOH consortium includes cohorts from around the world, the analysis was limited to those 15 cohorts, and three additional ones that evaluated respiratory symptoms and diseases around the world. Consequently, our descriptive analysis only features study populations from 11 countries, and more work is needed to truly characterize the global burden of respiratory outcomes in agricultural workers. Given that this study included only farmers, we were unable to make direct comparisons to the general public and assess the impact of agricultural production on respiratory health. The lack of national data on asthma prevalence makes it difficult to compare both within countries by occupation and between countries with regard to national prevalence. Global data on asthma prevalence will allow more rigorous analysis of variability by occupation and country.

International collaborative research provides valuable opportunities to investigate symptom and disease burden across many regions and geographic settings and diverse study populations. Future research would greatly benefit from sharing of participant-level data, allowing estimates to be standardized or adjusted for important confounders such as what is being done by the OMEGA NET consortium [42], and improving comparability between cohorts by applying common protocols like the ISAAC study for children [43] and the new DEGREE study for epidemiologic studies in low and middle income populations [44]. Data harmonization and standardization are not trivial tasks and we were unable to perform these at this time.

Asthma and COPD are important contributors to morbidity and mortality worldwide [39]. Our analysis shows that farmers and agricultural workers are impacted by these health outcomes. Agriculture represents a complex exposure environment and respiratory diseases are multi-factorial in nature. As a result, it is difficult to identify specific etiologic factors that contribute to or protect against respiratory disease. However, in these diverse cohorts, adult respiratory disease and symptoms were common and, it is likely that occupation contributed to these outcomes. The United Nation’s International Labour Organization estimated in 2009 that there were about 1.07 billion people employed in agriculture around the world, accounting for nearly 35% of the global workforce [45]. Therefore, understanding the global impacts of agricultural production on respiratory health is critical.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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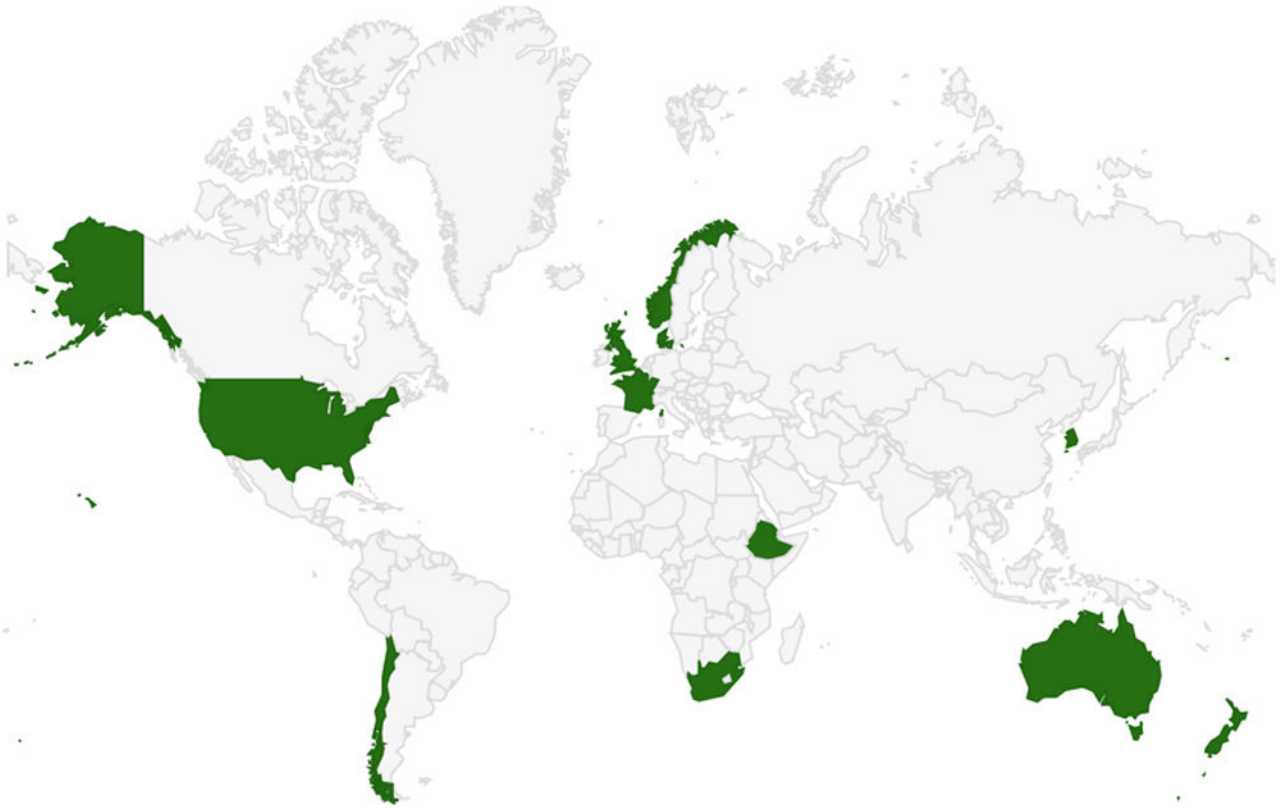

Figure 1:
World map of included AGRICOH Countries

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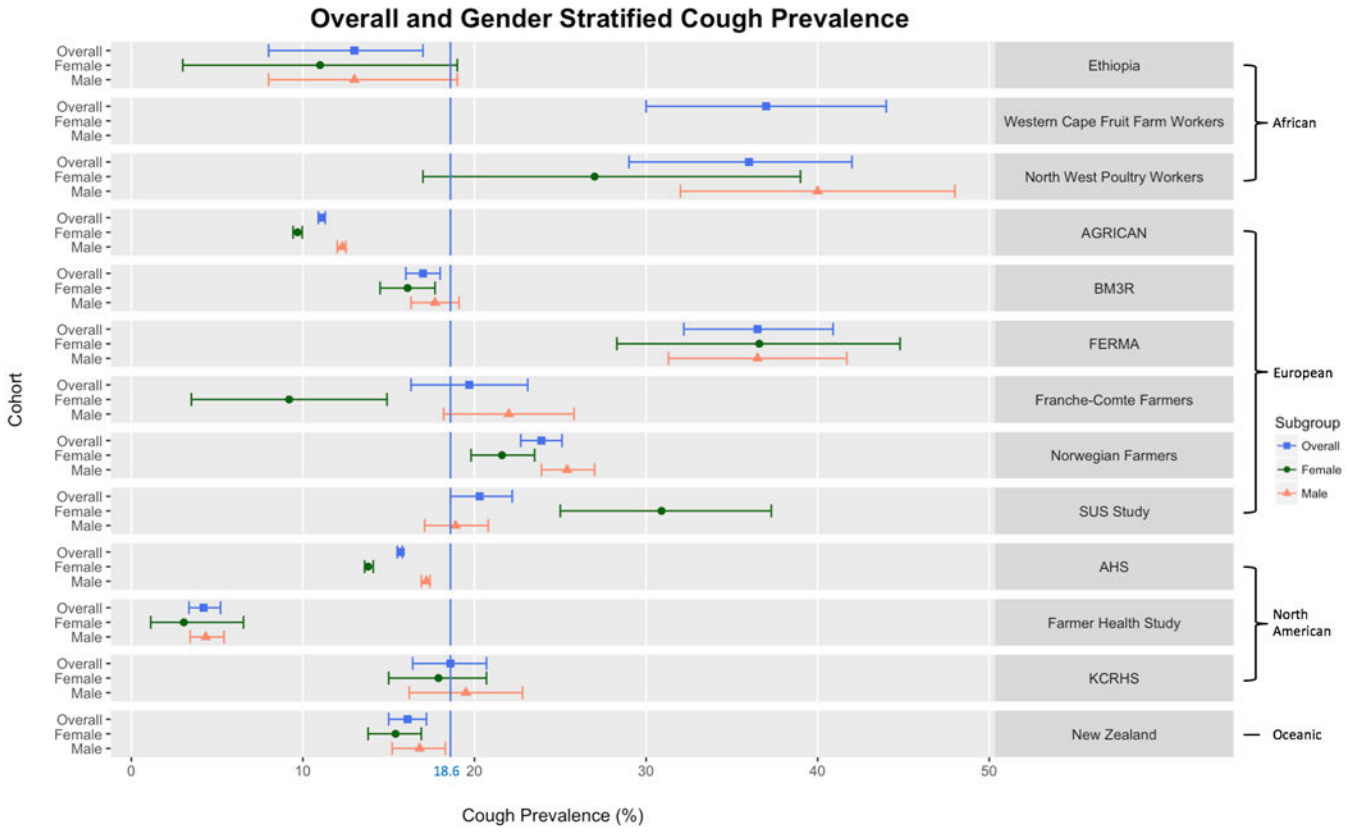

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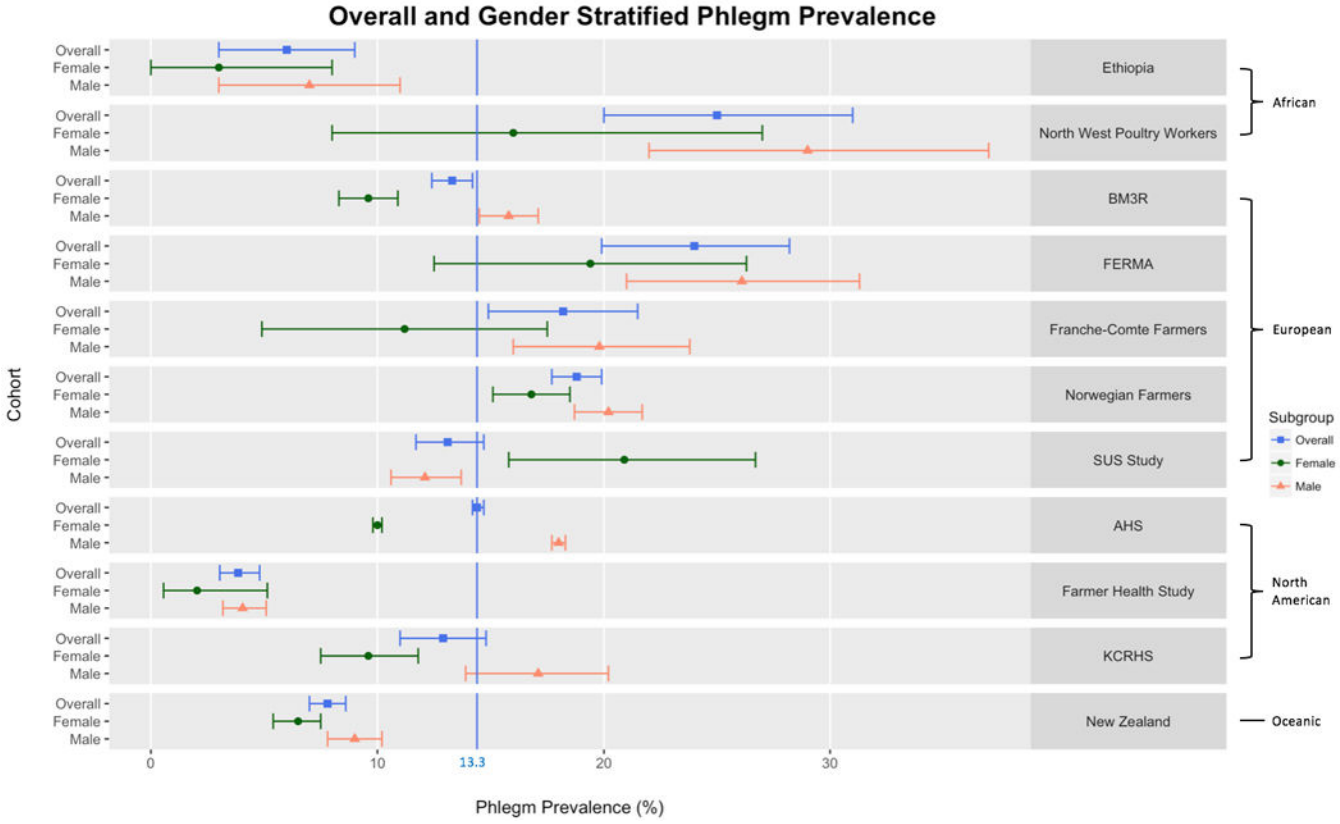

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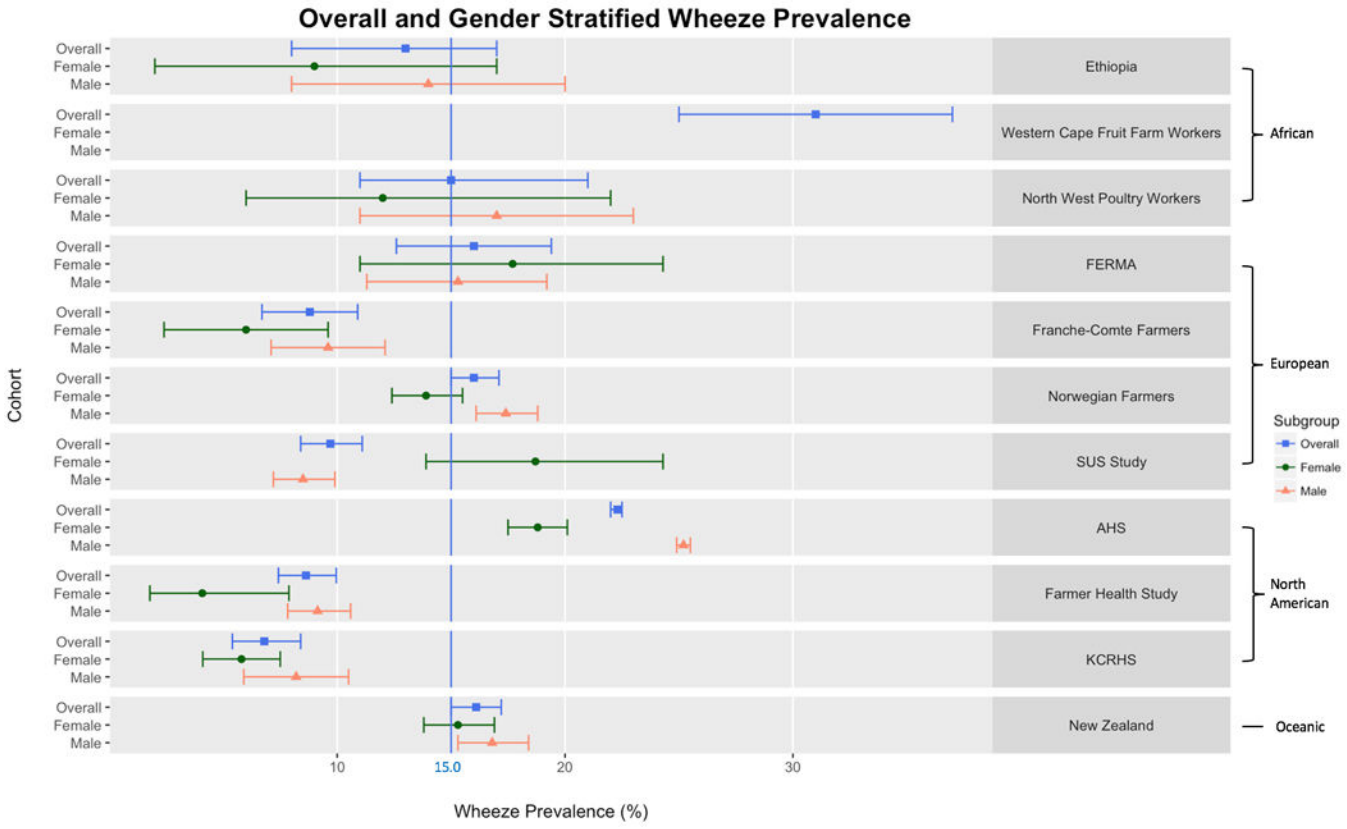

Figure 2:

Overall and gender-stratified (a) cough prevalence, phlegm prevalence (b), and wheeze prevalence (c) among AGRICOH cohorts.

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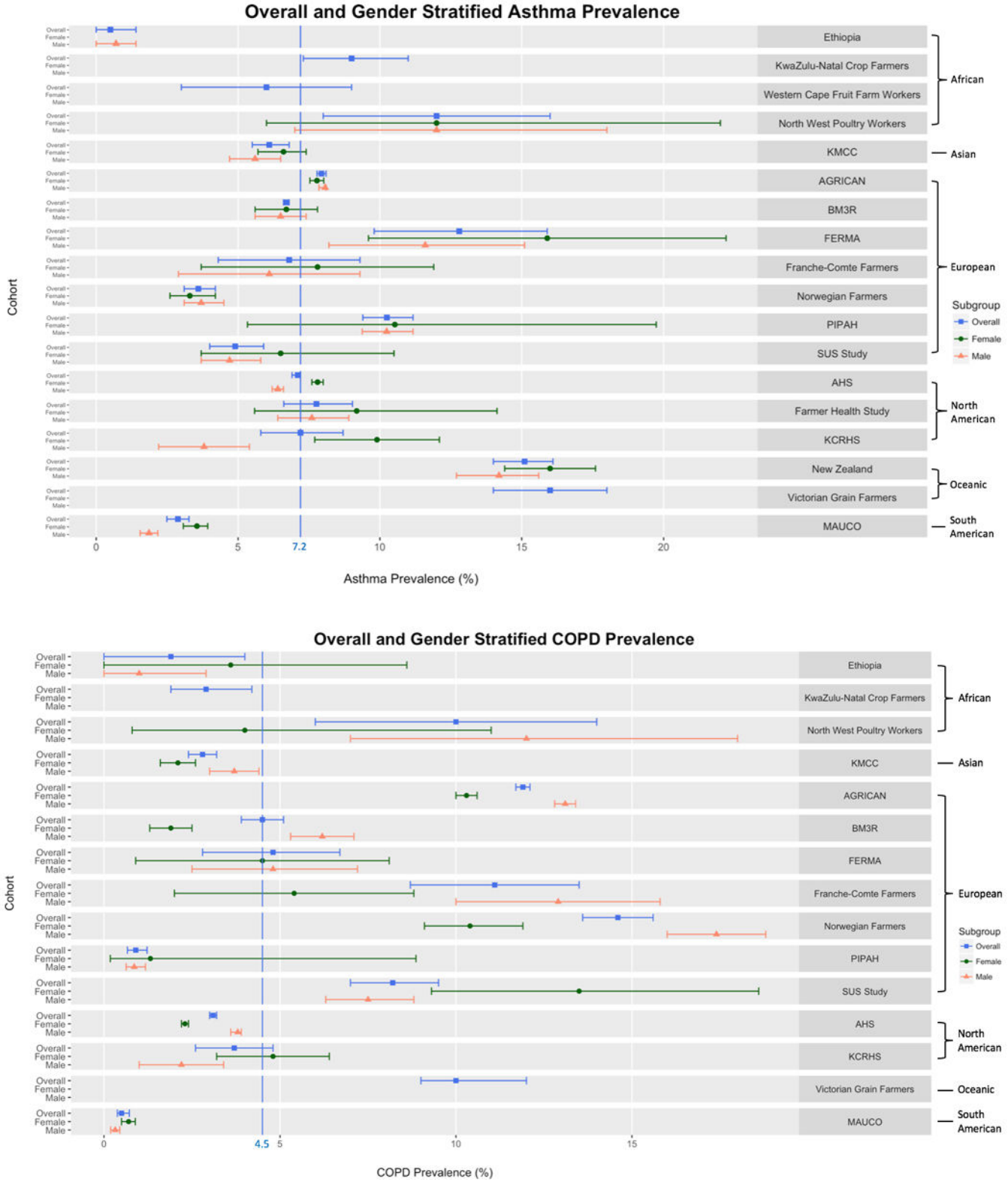

Figure 3:

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Overall and gender-stratified asthma prevalence (a) and COPD prevalence (b) among AGRICOH cohorts.

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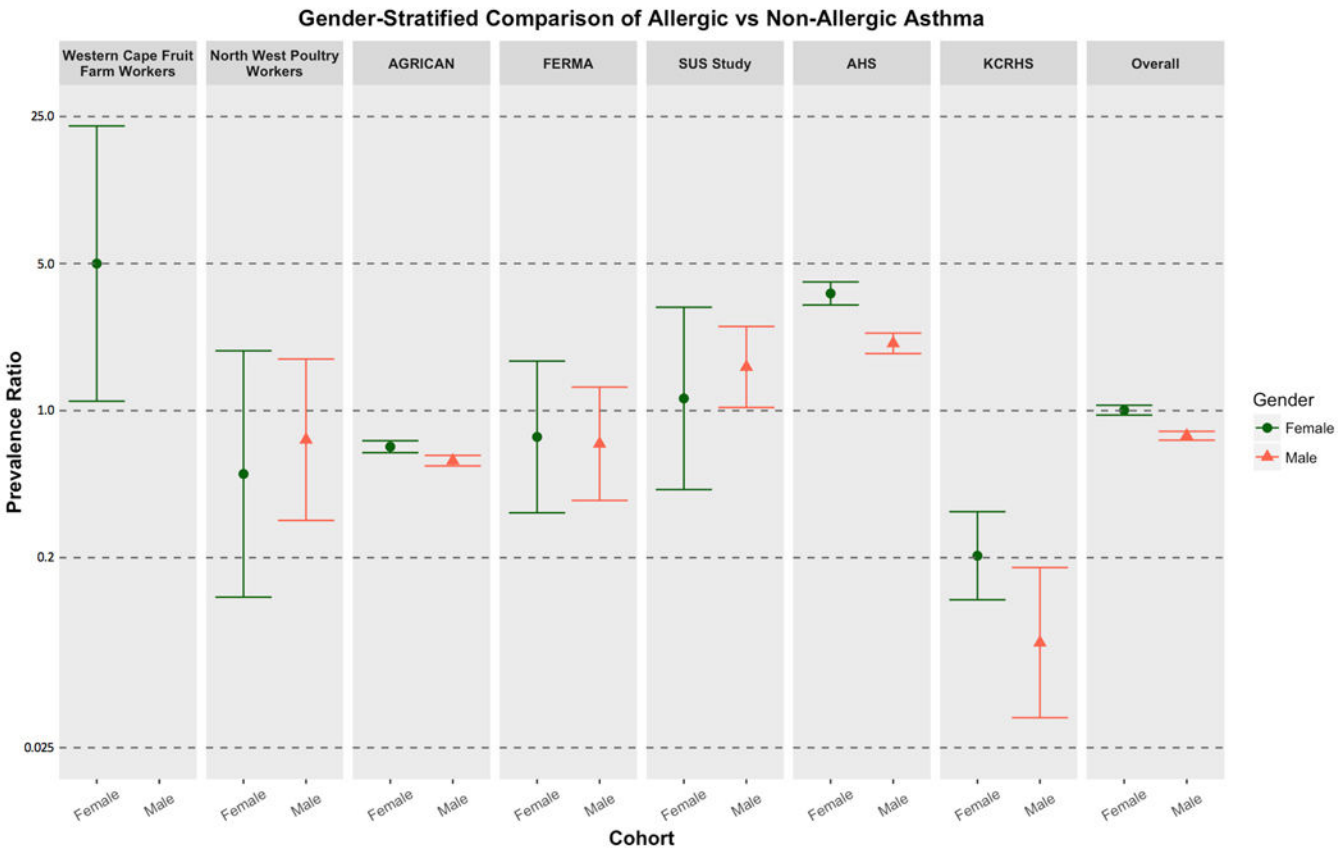

Figure 4:
Gender-stratified ratio of allergic vs. non-allergic asthma within AGRICOH cohorts.

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Table 1:

Characteristics of the AGRICOH cohorts that included respiratory outcomes

Cohort	Country	Sample Size	Year‡	Male (%)	Mean Age (std)	Age Range	Smoking (%)+			BMI (%)+			
							Never	Past	Current	<20	20 - <25	25 - <30	≥30
Africa													
Ethiopia[13]	Ethiopia	206	2014	69	27 (7)	15–57	95	0	5	32	56	11	1
KwaZulu-Natal Crop Farmers[14]	South Africa	911	2006	0	42 (13)	18–82	94	0	6	*NR*	*NR*	*NR*	*NR*
Western Cape Fruit Farm Workers[15]	South Africa	211	2009	0	37 (12)	17–73	50	0	50	17	28	22	33
North West Poultry Workers[16]	South Africa	230	2012	68	37 (9)	21–68	56	1	43	17	48	17	17
Asia													
KMCC[17]	Korea	8,431	2004	44	58 (10)	19–91	60	11	29	14	65	18	3
Europe													
AGRICAN[18]	France	128,388	2007	56	65 (15)	20–105	65	27	9	4	37	44	15
BM3R[19]	France	5,095	2013	59	57 (9)	40–75	65	22	14	4	46	31	19
FERMA[20]	France	473	2012	71	47 (12)	18–78	55	24	21	8	45	29	17
Franche-Comte Farmers[21]	France	915	2006	74	55 (11)	30–80	62	24	15	2	49	32	17
Norwegian Farmers[22]	Norway	4,735	2009	60	49 (11)	21–69	50	22	28	2	43	44	11
PIPAH[23]	United Kingdom	4,536	2014	98	54 (12)	19–88	65	26	9	2	41	44	13
SUS Study[24]	Denmark	1,964	1992	88	19 (3)	17–49	70	0	30	*NR*	*NR*	*NR*	*NR*
North America													
AHS*	USA	39,464	2016	53	65 (11)	32–104	68	27	5	3	22	40	35
Farmer Health Study[25]	USA	1,947	1993	90	54 (13)	21–90	55	32	12	*NR*	*NR*	*NR*	*NR*
KCRHS[26]	USA	1,256	1997	44	52 (16)	18–92	62	24	15	3	31	31	36
Oceania													
New Zealand[27]	New Zealand	4,288	2005	52	49 (11)	20–93	58	30	12	4	36	44	17
Victorian Grain Farmers[28]	Australia	1,102	1995	100	51 (13)	19–90	57	13	30	*NR*	*NR*	*NR*	*NR*
South America													
MAUCO[29]	Chile	7,080	2015	39	54 (10)	36–77	45	23	31	1	16	44	40

*Data not yet published

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† Percentages may not add up to 100% due to rounding

‡ If multiple years included in cohort, the last year of data collection is provided

BMI, body mass index; NR, not reported

KMCC, Korean Multi-center Cancer Cohort; AHS, Agricultural Health Study; GDMSP, Grain Dust Medical Surveillance Program; KCRHS, Keokuk County Rural Health Study