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## Dairy Farm Work and Protection from Gastrointestinal Illness

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### Abstract

Gastrointestinal (GI) disorders are a major public health burden in the United States. Due to close contact with animals, farmers may be a high risk subgroup for acute GI infections, though some studies suggest farm work is actually protective against GI illness. The purpose of this study was to examine associations between dairy farm work and GI symptoms over 3 years. A prospective, matched cohort study was used that included 70 adult dairy farm workers and 74 matched (age, gender, ZIP code) non-farm participants from central Wisconsin. The outcome was mean GI symptom scores for abdominal pain, diarrhea, constipation, dyspepsia, nausea, and reflux, per the 23-item Gastrointestinal Symptoms Severity Index (GISSI). After adjustment for potential confounding variables, linear regression results indicated dairy farm workers had significantly lower GISSI scores for abdominal pain (mean±SE = 4.3 ± 1.1 dairy vs. 7.6 ± 1.1 non-farm,  $p = .047$ ), diarrhea (3.2 ± 1.0 dairy vs. 7.0 ± 1.0 non-farm,  $p = .010$ ), constipation (2.0 ± 0.8 dairy vs. 6.6 ± 0.8 non-farm,  $p < .001$ ), and dyspepsia (2.0 ± 0.6 dairy vs. 3.9 ± 0.5 non-farm,  $p = .026$ ). Working on a dairy farm was associated with significantly less frequent and severe GI illness symptoms in adults. Future research should identify underlying causal pathways, including possible farm animal exposures, that influence beneficial gut microbiota that could inform therapeutic remedies to help prevent clinical GI disorders.

### Keywords

Farm; adults; gastrointestinal; symptoms; cohort

### Introduction

With estimated costs exceeding 140 billion dollars annually, the burden of gastrointestinal (GI) disorders is considerable in the United States.<sup>1</sup> Affecting ~60% of adults in any given

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week, GI illness symptoms are common.<sup>2</sup> White females, as well as younger and more educated individuals, are more likely to report GI symptoms.<sup>2</sup>

Farmers are also considered to be at higher risk of some GI disorders. Prior studies have shown farm workers and residents of watersheds with high concentrations of farm animals are more susceptible to severe GI infections.<sup>3–7</sup> For dairy farm workers, this is probably related to contact with animal excreta secondary to livestock management, manure handling, and related exposures to antimicrobial-resistant microorganisms.<sup>8</sup> These observations are not uniform, however, as a survey in Quebec found residents of the most intense farming regions had 30% lower odds of acute GI illness.<sup>9</sup> Few studies have examined associations between dairy farm work and general GI illness symptoms, which are precursors to clinical GI disorders.

## Methods

### Design and setting

Utilizing a prospective matched cohort design, the Dairy Microbiome (DOME) study examined seasonal changes in nasal and gut microbiota exchange between dairy farm workers and cows. The source population included residents of the Marshfield Epidemiologic Study Area (MESA)<sup>10</sup> and adjacent ZIP codes. MESA is a population-based research resource that captures information from individuals who receive care from the Marshfield Clinic Health System (MCHS) and reside in the 14 ZIP codes surrounding Marshfield, Wisconsin (USA). Residents of MESA receive over 90% of their healthcare from MCHS providers.<sup>11</sup>

### Participants

Two groups were enrolled, including dairy farm workers and a matched comparison group of non-farm individuals. All participants were age ≥18 years. Dairy farm workers had 4 hours per week of close contact with farm animals. For each dairy farm worker, an adult who was unexposed to farm environments, and matched on age ( $\pm 2$  years), gender, and residential ZIP code, was also enrolled. Procedures were approved by the MCHS Institutional Review Board and included written informed consent and HIPAA authorization.

### Recruitment

Recruitment was conducted over one year beginning in spring 2019. Dairy farm workers were recruited from dairy operations, as identified by the Wisconsin register of licensed dairy producers.<sup>12</sup> Dairy operation addresses were linked to MCHS patient records and dairy operation proprietors were invited to participate in DOME. An initial mailed outreach, along with several phone follow-ups, were made to describe the study and invite all farm workers at each dairy operation. After phone screening, an enrollment visit was setup for interested individuals. Dairy operations within MESA were invited first, followed by operations in ZIP codes adjacent to MESA. Once a dairy farm worker was enrolled, those unexposed to farm work were contacted similarly until an age/gender/ZIP matched individual was enrolled.

## Measures

The outcome was GI illness symptoms. Six GI component scores were calculated from the Gastrointestinal Symptoms Severity Index (GISSI),<sup>13</sup> which captures abdominal pain, diarrhea, constipation, dyspepsia, nausea, and reflux. The instrument has shown good test-retest reliability across component scores (range 0.70–0.93), as well as discriminant validity via significant prediction of patients presenting with primary diagnoses of each condition represented by the component scores. GISSI items assess self-reported frequency, severity, and bothersomeness across 23 different symptoms over the prior 30 days. Symptom features are combined to create each component score, which is standardized to 0–100 points (higher scores = more frequent/severe GI symptoms). The GISSI was administered quarterly and, to summarize the breadth and variability of GI symptoms, component scores were averaged across participants' enrollment periods (up to 3 years).

## Covariates

Based on their potential to confound GI associations, several sociodemographic and clinical covariates were selected *a priori* from enrollment surveys and linked MCHS electronic health records. Covariates included age, gender, education, season of enrollment, smoking, body mass index (normal weight, overweight, obese),<sup>14</sup> and number of GISSI assessments available during the study.

## Analyses

Linear regression was used to compare GISSI component scores (separately) between groups. Univariate models were initially created, followed by multivariable models that included all covariates simultaneously. To assess potential confounding, differences were noted between the univariate vs. multivariable modeled estimates for dairy farm workers.

## Results

The sample included 70 individuals in the dairy farm group and 74 in the matched, non-farm group (4 replacements in this group were retained in analyses). The two groups were similar on most baseline characteristics, but the non-farm group had a significantly greater percentage of individuals with a college degree, obesity, and were current smokers (Table 1). Overall, 77% of participants reported at least one GI symptom during their enrollment period, with diarrhea (46%) the most common, followed by constipation (40%), abdominal pain (40%), reflux (40%), dyspepsia (32%), and nausea (20%).

In univariate models, dairy farm workers had significantly lower GISSI scores for abdominal pain (mean±SE = 3.9 ± 0.8 dairy vs. 7.9 ± 1.2 non-farm,  $p = .007$ ), diarrhea (3.1 ± 0.6 dairy vs. 7.1 ± 1.1 non-farm,  $p = .002$ ), constipation (2.1 ± 0.4 dairy vs. 6.5 ± 1.0 non-farm,  $p < .001$ ), and dyspepsia (1.8 ± 0.4 dairy vs. 4.0 ± 0.6 non-farm,  $p = .004$ ). Nausea (2.1 ± 0.4 dairy vs. 3.6 ± 0.8 non-farm,  $p = .091$ ) and reflux (3.3 ± 0.6 dairy vs. 4.6 ± 0.6 non-farm,  $p = .144$ ), while trending lower in dairy farm workers, were not significantly different. In the covariate adjusted models summarized in Table 2 and Figure 1, the magnitude and significance of these associations were slightly attenuated, but remained similar. With the exceptions of smoking and gender in the dyspepsia and nausea models, no covariates

were significant predictors of GISSI component scores, nor did they appreciably shift any univariate estimates of differences between groups (indicating no confounding).

## Discussion

As expected,<sup>2</sup> GI illness symptoms impacted most participants at some point during the 3-year DOME study. The overall burden of GI symptoms, however, was consistently lower in dairy farm workers. In particular, constipation and diarrhea scores were 2–3 times greater in the non-farm group. This was intriguing given that prior research suggests farm workers, as well as those who live in watersheds with high concentrations of livestock, are more apt to develop severe GI infections.<sup>3–7</sup>

Dairy farm workers are in regular, close contact with cows (e.g., milking, cleaning animals and facilities) and handling of antimicrobial saturated manure (shedding up to  $10^7$  *Escherichia coli* bacteria per gram<sup>15</sup> is an occupational hazard that can, for example, double the risk of *Cryptosporidium* infection, which can trigger life threatening diarrhea.<sup>16</sup> Our study findings, however, were actually more consistent with a survey by Febriani and colleagues,<sup>9</sup> who found residents of the most intense farming regions of Quebec reported persistent vomiting and diarrhea less often than residents of other watersheds. Discrepant findings in this body of literature are likely a function of methodological differences in GI distress measures and target samples/regions, including animal mixes and watersheds with varying diversity of bacterial and protozoal pathogens. It could be that farm workers are both more susceptible to acute GI infection resulting in hospitalization, yet experience sub-clinical GI symptoms less often.

Causal mechanisms for the GI illness symptom protection observed in dairy workers in DOME are unknown. The associations were robust in multivariable models that accounted for some typical GI risk factors such as age, gender, smoking, and obesity, but other potential confounding variables like antibiotic use were not measured. Superior diet quality in farm workers seems an unlikely explanation,<sup>17</sup> but greater abundance of beneficial microbes in dairy farmer workers' GI tract could be a contributor.<sup>18</sup> As observed in farm children, regular exposure to animals primes immune-protective pathways that result in fewer cases of asthma and atopic diseases,<sup>19,20</sup> and perhaps prevention of other pro-inflammatory conditions.<sup>21</sup> Additionally, farm workers have greater microbial diversity in their nasal cavity, which is hypothesized to protect against staphylococcal infection.<sup>22</sup> As microbiomes and resistomes can readily shift for people exposed to farm environments (including non-farmers),<sup>23</sup> future analyses should consider bacterial enterotype comparisons between individuals with and without GI disorders to examine how protective gut microbiota may differ in dairy farm workers, analogous to studies by Costea and colleagues.<sup>24</sup>

Strengths of this study included the prospective cohort design, matched analyses, and defined source population. The chief limitations were the small sample size and self-reported GI outcomes. This precluded examination of important subgroups and increased risks of recall and self presentation biases (e.g., farmer stoicism) of symptom severity. The degree to which increased GISSI scores translate into clinical GI disorders remains unknown, as less than 20% of adults seek medical care following GI symptom onset,<sup>25</sup>

and some potential confounders (e.g., antibiotic use, dietary habits) were unavailable. In addition, the source population was racially homogenous and focused on dairy farming, thereby limiting generalizability to more diverse groups or other agricultural specialties. Future research should target broader populations, along with more robust control matching, assessments of nutrition and health attitudes, and detailed information on animal exposures.

Working on a dairy farm was associated with significantly less frequent/severe GI illness symptoms in adults. Causal factors underlying this observation remain unknown, but highlight the need for more research into potentially beneficial environmental exposures where interactions with farm animals (and associated microbiota) are routine. This could eventually guide therapeutic remedies to help prevent clinical GI disorders.

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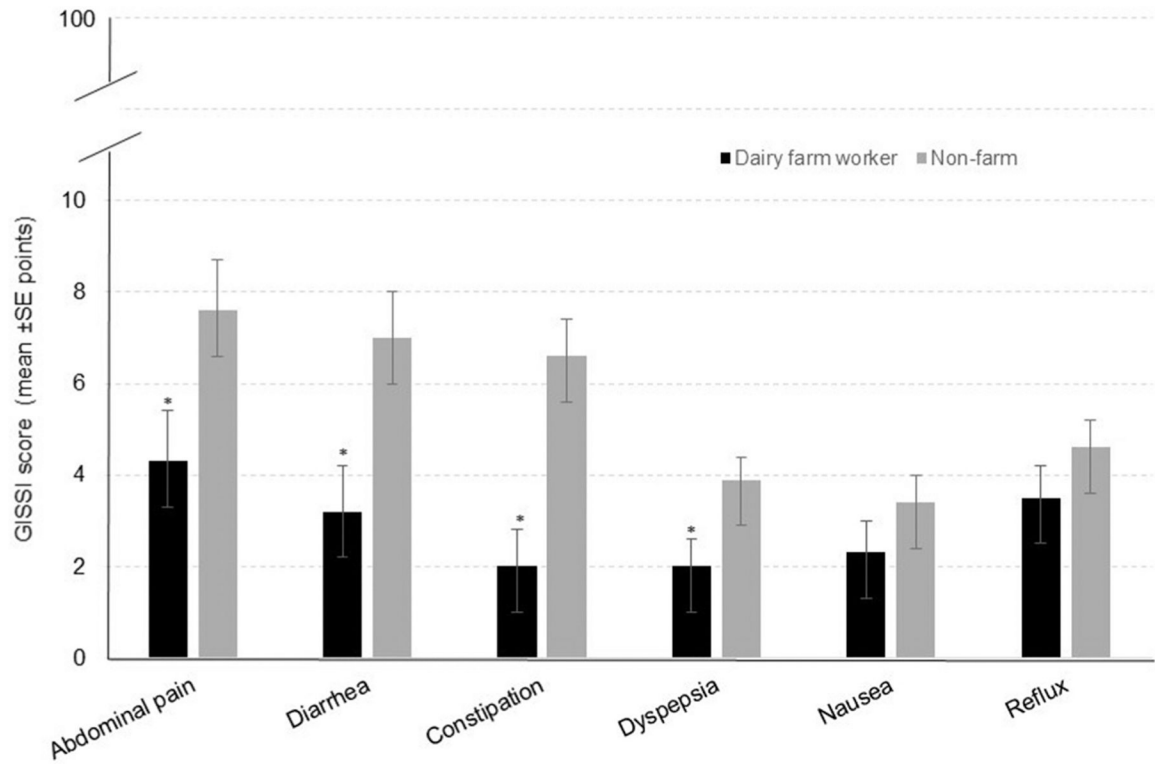
## Data availability statement

The data that support the study conclusions are unavailable for public access because informed consent to share said data (beyond the research team) was not obtained from study participants.

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Adjusted for age, gender, education, season of enrollment, body mass index, smoking, and number of GISSI scores available.  
 \*  $p < 0.05$  difference between groups.

**Figure 1.** Multivariable model-based estimates of Gastrointestinal Symptoms Severity Index (GISSI) component scores between.

**Table 1.** Characteristics of adults who do vs. do not work on dairy farms in central Wisconsin.

	Dairy farm worker <i>n</i> = 70	Non-farm <i>n</i> = 74	<i>P</i>
Age (y)	42.3 ± 14.2	43.1 ± 14.3	0.735
Gender			
Female	22 (31%)	22 (30%)	
Male	48 (69%)	52 (70%)	0.825
Race/Ethnicity			
White, non-Hispanic	67 (96%)	73 (99%)	
Non-White or Hispanic	3 (4%)	1 (1%)	0.284
Education			
Less than high school	10 (14%)	2 (3%)	
High school	15 (21%)	19 (26%)	
Associate degree or some college	30 (43%)	33 (46%)	
College degree	11 (16%)	20 (27%)	
Unknown	4 (6%)	0 (6%)	0.014
Season of enrollment			
Spring	18 (26%)	21 (28%)	
Summer	15 (24%)	18 (24%)	
Fall	17 (21%)	18 (24%)	
Winter	20 (29%)	17 (23%)	0.882
Body mass index			
Obese	23 (33%)	36 (49%)	
Overweight	25 (36%)	23 (31%)	
Normal weight	13 (19%)	15 (20%)	
Unknown	9 (13%)	0 (0%)	0.007
Smoker			
Current	5 (7%)	12 (16%)	
Former	3 (4%)	15 (20%)	
Never	51 (73%)	44 (59%)	
Unknown	11 (16%)	3 (4%)	0.001

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	<b>Dairy farm worker n = 70</b>	<b>Non-farm n = 74</b>	<b>P</b>
Number of GISSI's available (over 3 years)	9.1 ± 4.1	8.6 ± 3.4	0.440

Values are reported as mean ±SD or frequency (% of total). GISSI = Gastrointestinal Symptoms Severity Index.

Multivariable linear regression models of Gastrointestinal Symptoms Severity Index (GISSI) component scores between adults who do vs. do not work on dairy farms in central Wisconsin.

**Table 2.**

Group	GISSI scores (mean $\pm$ SE points difference), p					
	Abdominal pain	Diarrhea	Constipation	Dyspepsia	Nausea	Reflux
Dairy farm vs. Non-farm	<b>-3.3 <math>\pm</math> 1.7, p = .047</b>	<b>-3.8 <math>\pm</math> 1.4, p = .010</b>	<b>-4.7 <math>\pm</math> 1.2, p &lt; .001</b>	<b>-1.9 <math>\pm</math> 0.8, p = .026</b>	-1.1 $\pm$ 1.0, p = .278	-1.0 $\pm$ 1.0, p = .324
Age (yrs)	-0.1 $\pm$ 0.1, p = .360	0.0 $\pm$ 0.1, p = .509	0.0 $\pm$ 0.1, p = .369	0.0 $\pm$ 0.0, p = .814	-0.1 $\pm$ 0.0, p = .190	0.0 $\pm$ 0.0, p = .834
Gender						
Female vs. Male	2.8 $\pm$ 1.8, p = .115	0.2 $\pm$ 1.5, p = .874	1.3 $\pm$ 1.3, p = .333	0.9 $\pm$ 0.9, p = .327	<b>2.9 <math>\pm</math> 1.0, p = .006</b>	-0.3 $\pm$ 1.0, p = .758
Education						
Less than high school vs. College degree	-2.6 $\pm$ 3.6, p = .785	1.2 $\pm$ 3.1, p = .698	2.1 $\pm$ 2.7, p = .443	-0.4 $\pm$ 1.8, p = .828	-2.6 $\pm$ 2.1, p = .223	0.3 $\pm$ 2.1, p = .906
High school vs. College degree	1.6 $\pm$ 2.3, p = .492	-1.0 $\pm$ 2.0, p = .638	-2.2 $\pm$ 1.7, p = .313	1.0 $\pm$ 1.1, p = .401	0.3 $\pm$ 1.4, p = .850	1.2 $\pm$ 1.4, p = .383
Associates degree vs. College degree	-0.5 $\pm$ 2.1, p = .821	-2.1 $\pm$ 1.8, p = .251	-1.9 $\pm$ 1.5, p = .208	0.9 $\pm$ 1.0, p = .363	1.4 $\pm$ 1.2, p = .236	-0.1 $\pm$ 1.2, p = .953
Unknown vs. College degree	-2.2 $\pm$ 5.0, p = .663	-4.0 $\pm$ 4.3, p = .359	0.5 $\pm$ 3.7, p = .898	0.6 $\pm$ 2.5, p = .805	-0.3 $\pm$ 2.9, p = .917	-2.0 $\pm$ 2.6, p = .500
Season of enrollment						
Spring vs. Fall	2.2 $\pm$ 3.3, p = .330	1.6 $\pm$ 2.0, p = .415	1.5 $\pm$ 1.7, p = .365	2.0 $\pm$ 1.1, p = .069	2.0 $\pm$ 1.3, p = .131	1.5 $\pm$ 1.3, p = .261
Summer vs. Fall	0.0 $\pm$ 2.3, p = .996	-1.1 $\pm$ 2.0, p = .564	1.4 $\pm$ 1.7, p = .421	0.2 $\pm$ 1.1, p = .844	1.3 $\pm$ 1.3, p = .323	1.6 $\pm$ 1.3, p = .248
Winter vs. Fall	-2.2 $\pm$ 2.4, p = .352	-1.7 $\pm$ 2.1, p = .412	0.4 $\pm$ 1.8, p = .840	0.2 $\pm$ 1.2, p = .886	0.6 $\pm$ 1.4, p = .682	0.0 $\pm$ 1.4, p = .978
Body mass index (categories)						
Obese vs. Normal weight	-0.3 $\pm$ 2.2, p = .905	2.6 $\pm$ 1.9, p = .172	-2.0 $\pm$ 1.6, p = .223	-1.0 $\pm$ 1.1, p = .373	-1.3 $\pm$ 1.3, p = .299	0.5 $\pm$ 1.3, p = .687
Overweight vs. Normal weight	-0.4 $\pm$ 2.3, p = .844	3.4 $\pm$ 2.0, p = .091	-2.9 $\pm$ 1.7, p = .091	-1.2 $\pm$ 1.1, p = .296	-0.1 $\pm$ 1.3, p = .918	1.7 $\pm$ 1.3, p = .196
Unknown vs. Normal weight	0.7 $\pm$ 4.8, p = .887	2.7 $\pm$ 4.1, p = .522	0.6 $\pm$ 3.6, p = .877	0.7 $\pm$ 2.4, p = .771	4.4 $\pm$ 2.8, p = .119	1.7 $\pm$ 2.8, p = .538
Smoking						
Current vs. Never	3.2 $\pm$ 2.5, p = .193	3.6 $\pm$ 2.1, p = .099	2.7 $\pm$ 1.8, p = .152	<b>3.9 <math>\pm</math> 1.2, p = .002</b>	<b>3.7 <math>\pm</math> 1.4, p = .012</b>	1.9 $\pm$ 1.5, p = .201
Former vs. Never	-0.3 $\pm$ 2.6, p = .910	0.5 $\pm$ 2.3, p = .811	0.3 $\pm$ 1.9, p = .869	1.6 $\pm$ 1.3, p = .211	1.3 $\pm$ 1.5, p = .398	2.8 $\pm$ 1.5, p = .074
Unknown vs. Never	1.2 $\pm$ 3.8, p = .761	0.9 $\pm$ 3.3, p = .782	-0.9 $\pm$ 2.9, p = .748	1.9 $\pm$ 1.9, p = .312	<b>6.0 <math>\pm</math> 2.2, p = .008</b>	2.6 $\pm$ 2.2, p = .243
Number of GISSI's available (over 3 years)	-0.2 $\pm$ 0.2, p = .477	0.0 $\pm$ 0.2, p = .873	0.2 $\pm$ 0.2, p = .276	0.0 $\pm$ 0.1, p = .826	0.1 $\pm$ 0.1, p = .591	-0.1 $\pm$ 0.1, p = .649

Bold values indicate a significant association with GISSI scores.