

1 **Title: Clinical and Economic Impact of COVID-19 on Plantation Workers: Preliminary**
2 **Results from the Guatemala Agricultural Workers and Respiratory Illness Impact (AGRI)**
3 **Study**

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29

30 **ABSTRACT**

31 We evaluated the clinical and socioeconomic burdens of respiratory disease in a cohort of
32 Guatemalan banana plantation workers. All eligible workers were offered enrollment from June
33 15–December 30, 2020, and annually, then followed for influenza-like illnesses (ILI) through: 1)
34 self-reporting to study nurses, 2) sentinel surveillance at health posts, and 3) absenteeism.
35 Workers with ILI submitted nasopharyngeal swabs for influenza, RSV, and SARS-CoV-2
36 testing, then completed surveys at days 0, 7, and 28. Through October 10, 2021, 1,833 workers
37 developed 169 ILIs (12.0/100 person-years) and 43 (25.4%) of these ILIs were laboratory-
38 confirmed SARS-CoV-2 (3.1/100 person-years). Workers with SARS-CoV-2-positive ILI
39 reported more anosmia ($p<0.01$), dysgeusia ($p<0.01$), difficulty concentrating ($p=0.01$), and
40 irritability ($p=0.01$), and greater clinical and well-being severity scores (Flu-iiQ) than test-
41 negative ILIs; they also had greater absenteeism ($p<0.01$) and lost income (median US\$127.1,
42 $p<0.01$). These results support the prioritization of Guatemalan farm workers for COVID-19
43 vaccination.

44 INTRODUCTION

45 Essential workers have been at greater risk of COVID-19 compared to the general
46 population, but little is known about the risk to people working within the agricultural sector in
47 low- middle-income countries (LMICs) (1-3). Though limited data from the United States (U.S.)
48 have demonstrated a high SARS-CoV-2 burden in this population (1), many agricultural workers
49 continued working throughout the pandemic (4). In LMICs, agricultural workers play a critical
50 role in food security and represent a significant economic force. In Guatemala, they comprise
51 35% of the overall labor force, and agricultural products account for 45% of all exports and
52 11.3% of total gross domestic product (5). Guatemala is also a major trading partner of the U.S.,
53 exporting US\$ 2.1 billion in agricultural products annually, including nearly 50% of the U.S.
54 banana supply (6). Therefore, agricultural workers in Guatemala and similar LMICs are arguably
55 “essential” not only for local food security, but also the food security of international trading
56 partners such as the U.S.

57 In addition to increased risk of exposure to SARS-CoV-2, the virus that causes COVID-
58 19, people working in the agricultural sector may also be at increased risk of poor clinical
59 outcomes from COVID-19 because of a high prevalence of comorbidities associated with
60 environmental stress, such as chronic kidney disease of unknown origin (CKDu, “Mesoamerican
61 nephropathy”) (7-9). Economic outcomes, such as work absenteeism and decreased job
62 performance while working (“presenteeism”), are also likely significant, as is the case with
63 influenza (10-14). As agricultural workers are often the primary income earners for their
64 households, the consequences may extend to their households and communities. Despite the
65 increased clinical and economic vulnerability of agricultural workers, and their critical role in
66 global food security, little is known about the socioeconomic consequences of COVID-19 and

67 other respiratory illnesses among this essential workforce, and the subsequent impacts on their
68 households and communities.

69 The “Agricultural workers and Respiratory Illness Impact (AGRI) Study” was initially
70 designed as an influenza cohort and expanded to include other viral respiratory pathogens,
71 including SARS-CoV-2. The study has two primary aims: 1) to characterize the clinical and the
72 socioeconomic outcomes of acute respiratory viral infections among Guatemalan plantation
73 workers, and 2) to measure the effectiveness of a workplace-based vaccination program in
74 improving these outcomes. This paper provides a comprehensive description of the AGRI cohort
75 and a summary of clinical and economic outcomes from our first year of virologic surveillance.

76

77 **METHODS**

78 *Study Setting and Population*

79 The 5-year study is being conducted within a large banana plantation in the coastal
80 lowlands of southwest Guatemala. The farm workers are exposed to high temperatures and
81 humidity, and are at risk for environment-associated chronic medical conditions such as CKDu
82 (7, 15). Previous surveys (2015, 2017-18) found a predominantly young, male, and
83 economically vulnerable workforce, in which the farmworkers are typically the sole income
84 earners for their households and report high rates of food insecurity, similar to other agribusiness
85 workers in the region and migrant worker populations in the U.S. (16, 17). The regional
86 population experiences high levels of food insecurity, stunting, poverty, and communicable
87 diseases, and low access to healthcare (18, 19).

88 As is typical in many agribusinesses, field workers and packaging workers are given a
89 baseline pay, with daily bonuses based on their productivity recorded by the company. Managers

90 and workers in administrative job categories are paid by day. If a worker develops illness and is
91 provided an excused absence by their manager, they receive 2/3 of their baseline pay for the
92 duration of their excused absence, up to a maximum of US\$ 15.6 per day. Workers with
93 laboratory-confirmed SARS-CoV-2 are mandated to quarantine at home with excused absences
94 for up to two weeks duration.

95 All eligible workers within the nine banana plantation worksites were offered enrollment
96 in the study from June 15th to December 30th, 2020, and annually. Inclusion criteria include age
97 ≥ 18 years, plans to remain employed by the agribusiness ≥ 1 year, access to a telephone, and
98 agreement to allow use of company-based absenteeism and job performance records. For this
99 analysis, participant follow-up was performed through October 10, 2021, and all study
100 procedures (testing, follow-up) performed after this date were considered missing, even if the
101 associated ILI case was identified prior.

102 Following written informed consent, study nurses collected contact information as well as
103 demographic, occupational, socioeconomic, and clinical data, including risk factors for severe
104 COVID-19. Workers provided enrollment and annual blood specimens that will be screened for
105 markers of chronic kidney disease (estimated glomerular filtration rate, (20)), anti-SARS-CoV-2
106 nucleocapsid IgG (Roche Elecsys[®] immunoassay), and in some cases, anti-SARS-CoV-2
107 neutralizing antibodies (Beckham/Santiago Laboratories, University of Colorado, Aurora, CO,
108 USA). Workers leaving employment have exit interviews and are removed from the study, but
109 data collected during their employment are retained in the study database.

110 *Surveillance for Influenza-like Illness (ILI)*

111 Following enrollment, all workers began prospective active surveillance for influenza-
112 like illness (ILI), initially defined as self-reported fever/temperature $\geq 38^{\circ}\text{C}$ and cough in the last

113 10 days to focus on detection of influenza (21). In January 2021, the ILI case definition was
114 expanded to include presence of fever, cough, *or* shortness of breath in the last 10 days (COVID-
115 19-like illness (22)), to increase sensitivity of COVID-19 case detection (23).

116 The study employed three strategies for detecting ILI: 1) symptom screening through
117 workers self-reporting symptoms to a study nurse during weekly worksite visits, work
118 supervisors screening workers daily for cough and fever, and telephone contact to a study nurse
119 by workers experiencing symptoms at any time; 2) sentinel surveillance of all workers presenting
120 to worker health posts within the plantation with ILI; and 3) active monitoring and ILI screening
121 phone calls to absent workers identified on the company absenteeism registry. In February 2021,
122 absenteeism calls were discontinued because these cases of ILI were consistently identified
123 through other surveillance approaches.

124 *Syndromic Illness Characterization*

125 Workers with ILI were interviewed by study nurses and provided clinical, epidemiologic,
126 and outcome data for themselves and general epidemiologic and socioeconomic outcome data for
127 their households. Study nurses also collected a nasopharyngeal (NP) swab, which was placed in
128 viral transport media and tested within 24 hours of specimen collection for SARS-CoV-2 using
129 the Q COVID rapid antigen test (Q-NCOV-01G, SD Biosensor[®], Republic of Korea) (24).
130 Aliquots were also tested for influenza A/B and respiratory syncytial virus (RSV) using the
131 Roche cobas[®] Liat Influenza A/B (& RSV) real-time polymerase chain reaction (rtRT-PCR)
132 instrument (25). ILI cases who tested positive for SARS-CoV-2, influenza, or RSV are hereafter
133 referred to as SARS-CoV-2-positive ILI, influenza-positive ILI, and RSV-positive ILI,
134 respectively. A subset of available ILI specimens collected through April 2021 (n=40) were also

135 tested for an additional 15 respiratory pathogens using the multiplex BioFire FilmArray RP2.1
136 assay (26).

137 Viral testing results were shared with participants when available (usually within 24
138 hours) and weekly with the Guatemala Ministry of Health.

139 *Clinical and Socioeconomic Outcome Assessments*

140 The study relied on a case-cohort study design to measure self-reported clinical and
141 socioeconomic outcomes. All subjects in the overall cohort with ILI were considered “cases.”
142 Each week, a sub-cohort of 15 enrolled workers without ILI in the preceding 28 days were
143 selected at random (~5% of the cohort per month) and considered “controls.” Follow-up surveys
144 were administered by study nurses over the phone to cases at 1 and 4 weeks following their ILI
145 visit. Controls were notified that they had been selected (day 0) and were then provided the same
146 surveys 1 and 4 weeks later; controls did not undergo diagnostic testing, and a control who
147 developed ILI during the 4-week follow-up was considered a case at the time of illness.

148 Clinical and well-being outcomes were collected using the Flu-iiQ™ inventory (27),
149 which is a validated Spanish-language outcome measure designed for clinical and epidemiologic
150 outpatient studies of influenza and RSV. The inventory includes 13 items for symptom severity,
151 which comprise a combined “systemic score” (7 items) and “respiratory score” (6 items). The
152 well-being scores include an “impact on daily activities score” (7 items), “impact on emotions
153 score” (4 items), and “impact on others score” (5 items). Each combined score is averaged by the
154 number of individual items such that all scores are between 0 and 3, with a higher score
155 indicating greater severity or negative impact on well-being. The follow-up surveys also
156 collected health-seeking behavior (e.g., hospitalization, medication usage, etc.).

157 During the follow-up surveys, economic outcomes were assessed using questions adapted
158 from the 2016 WHO Manual for Estimating the Economic Burden of Seasonal Influenza (28)
159 and supplemented with the World Bank National Survey of Living Conditions (29), which
160 includes a Spanish translation (ENCOVI) previously used in Guatemala (30), and compared to
161 the basic food basket price in Guatemala, which reflects the minimum kilocalorie (2,262
162 kilocalorie) intake for a 4.77-member household for one month (US\$ 386.3 in March 2021
163 (31)).The survey collected data on direct medical costs, direct non-medical costs (i.e.,
164 transportation), and indirect costs related to loss of productivity (i.e., absenteeism) for both the
165 worker and household. Though not included in this analysis, company reported individual-level
166 data will be linked to workers, including absenteeism, productivity metrics (task-specific units of
167 production such as tons of bananas harvested/day), and wages.

168 *Statistical Analysis*

169 Incidence density (number of cases per person-time of follow-up) of ILI and pathogen-
170 specific ILI were calculated. Descriptive statistics were used to calculate the differences between
171 clinical and socioeconomic outcomes between groups. For normally distributed continuous
172 variables, means and standard deviations were calculated, and Student's T-tests were used to
173 determine significant differences between groups. For non-normally distributed continuous
174 variables, medians and interquartile ranges were calculated, and the Wilcoxon Rank-Sum test
175 was used to determine significant differences between groups. For categorical variables, chi-
176 square and Fischer's exact tests were used to determine significant differences in distribution of
177 categories between groups. For all analyses, a p-value <0.05 was considered statistically
178 significant.

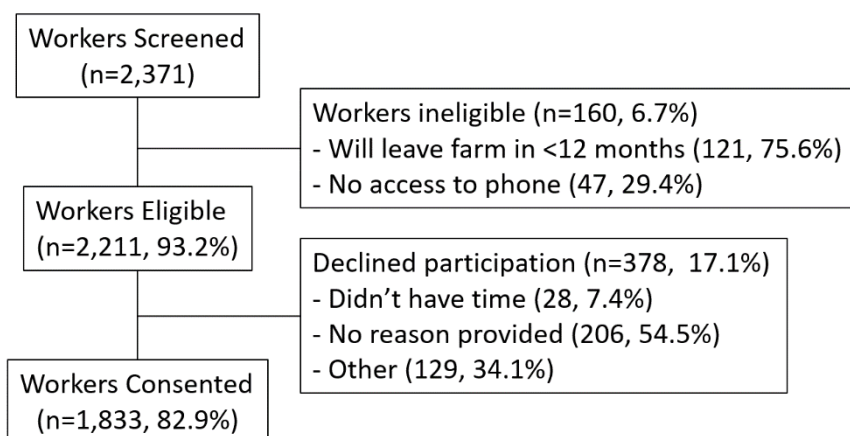
179 *Ethical Oversight*

180 The study was approved by the Colorado Multiple Institutional Review Board (COMIRB
181 protocol #19-1836) and the Guatemala Ministry of Health National Ethics Committee (HRMC-
182 560-2020). The local Southwest Trifinio Community Advisory Board for Research agreed to the
183 study. Workers receive no compensation for study participation.

184

185 RESULTS

186 Between June 15, 2020 and October 10, 2021, 2,371 workers were screened for
187 enrollment; 160 (6.7%) were ineligible and 378 (17.1%) declined participation (**Figure 1**). Of the
188 1,833 enrolled participants, 1,590 (86.7%) remained active in the study as of October 10, 2021,
189 representing 1,402.9 person-years of surveillance. Workers who declined participation were
190 slightly younger (29.6 vs 30.9 years, $p < 0.01$) than participants but had similar sex distribution
191 and ethnicity.



192

193 **Figure 1.** CONSORT Diagram. Summary of cohort enrolled in the AGRI Study in SW
194 Guatemala from June 2020 to October 2021, and followed up through October 10, 2021.
195 Ineligible and non-consenting workers were able to provide multiple reasons for not
196 participating. Only workers who completed the Day 0 (diagnosis) visit were called on Day 7 and
197 Day 28. Follow up visits scheduled for after October 10th, 2021 were considered missing.

198

199 The enrolled cohort characteristics are summarized in **Table 1**. Most workers were male
200 (84.1%) and worked in the fields (69.0%). Self-reported chronic medical conditions were
201 uncommon except for obesity (body mass index [BMI] ≥ 30 kg/m², 11.3%) and kidney disease
202 (3.2%); 12.8% of workers (n=234) took medications, the majority of whom (n=122, 52%) took
203 vitamins, followed by pain relievers/anti-inflammatories (14%), antibiotics (7%), diabetes-
204 related medication (7%), and proton pump inhibitors (6%). Only 5.9% reported ever having
205 received an influenza vaccination, including 17 (6.4%) of the 267 workers who self-reported
206 chronic diseases. Workers began to receive COVID-19 vaccination through the workplace in
207 August 2021 (ChAdOx1, AstraZeneca, England; and mRNA-1273, Moderna, USA). Of 1,334
208 workers enrolled in 2020 with samples available, 616 (46.2%) were SARS-CoV-2 anti-
209 nucleocapsid IgG reactive.

210 Household size averaged 5.7 individuals (3.3 adults, 2.3 children) with nearly half the
211 workers (n=877; 48.2%) living in the urban municipality of Coatepeque; the study catchment
212 area is approximately 2,600 km² (**Figure 2**). Median self-reported monthly income for the
213 individual worker was US\$ 337.2 (interquartile range [IQR]=311.3, 389.1) and for the household
214 was US\$ 363.2 (IQR=324.3, 505.8); 58.0% of workers reported being worried about the inability
215 to purchase food in the preceding 12 months.

216 *Asymptomatic controls*

217 Of the 915 asymptomatic controls that were randomly selected (August 10, 2020–
218 October 10, 2021), the study team was able to contact 696 (76.0%) by phone. There were no
219 significant differences in enrollment characteristics between those contacted and not contacted.
220 Of the 696 controls who were contacted initially, 623 (89.5%) and 588 (84.4%) were
221 successfully contacted at 1 and 4 weeks, respectively.

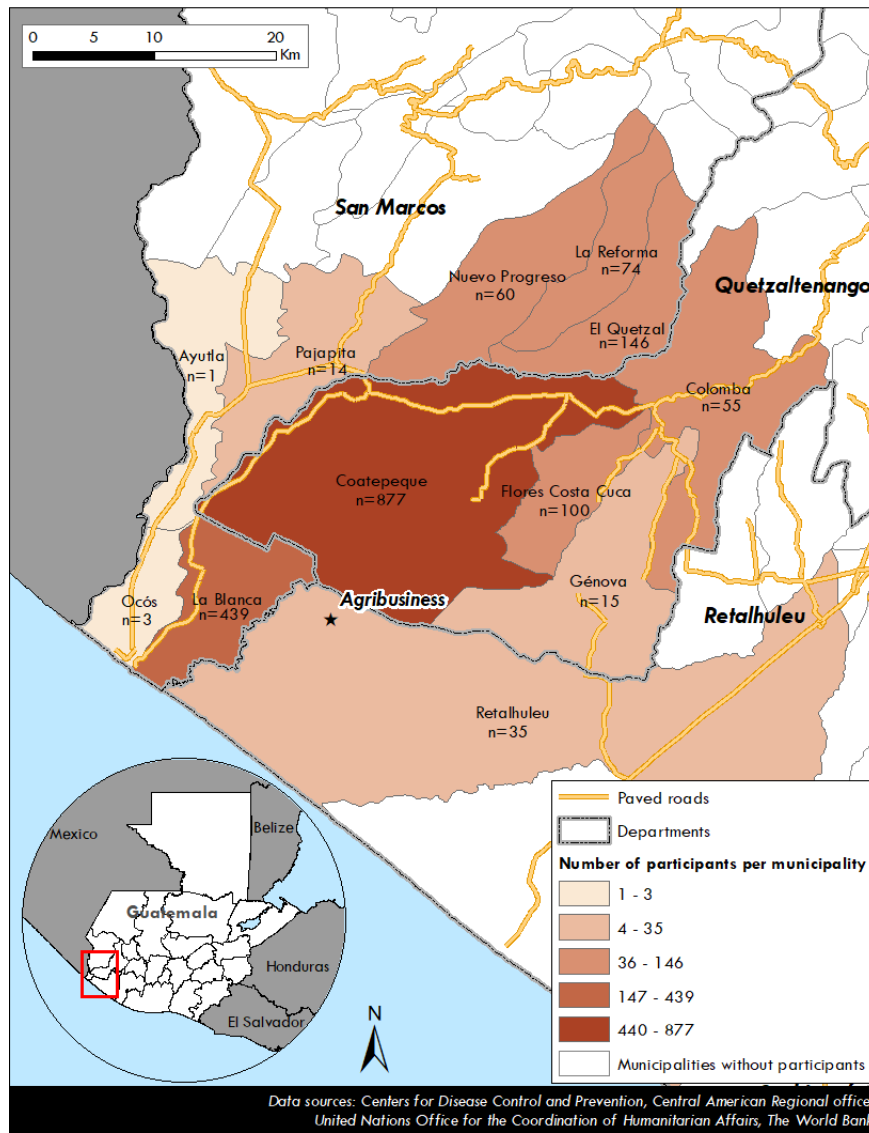
Table 1. Characteristics of cohort participants, Guatemala (n=1,833)

Worker Demographics	
Age in years (mean, SD)	30.9 (8.7)
Male sex, n (%)	1541 (84.1)
Ethnicity, n (%): Ladino	801 (43.7)
Indigenous	113 (6.2)
Other	3 (0.2)
Don't know	916 (43.7)
Worker Health, n (%)	
Obesity (measured BMI > 30 kg/m ²), n= 1159 with data	131 (11.3)
Class 1 (BMI 30-<35 kg/m ²)	103
Class 2 (BMI 35-<40 kg/m ²)	24
Class 3 (BMI ≥40 kg/m ²)	4
Kidney disease	58 (3.2)
Blood disorder (e.g., sickle cell disease)	25 (1.4)
Cardiovascular disease (e.g., heart failure, CAD)	29 (1.6)
Diabetes	27 (1.5)
Liver disease	19 (1.0)
Asthma	10 (0.6)
Pulmonary Disease (e.g., COPD)	10 (0.6)
Neurologic disease (e.g., stroke)	10 (0.6)
Taking medications	234 (12.8)
Received influenza vaccine	108 (5.9)
Work Conditions	
Type of Work, n (%)	
Administration	60 (3.3)
Field worker	1264 (69.0)
Field manager	77 (4.2)
Packer (plant worker)	413 (22.5)
Plant manager	19 (1.0)
Duration of employment, n (%)	
≤2 years	1115 (60.9)
3-4 years	242 (13.2)
≥5 years	475 (25.9)
Monthly income, \$USD, median (IQR)	337.2 (311.3, 389.1)
Household Conditions	
# adults in house, median (IQR)	3 (2–4)
# children in house, median (IQR)	2 (1–3)
Concern about food insecurity in last year, n (%)	1063 (58.0)
Household monthly income, \$USD, median (IQR)	363.2 (324.3–505.8)
\$USD spent in the last 7 days, median (IQR):	
Meat, fish, and seafood	25.9 (13.0–38.9)
Milk, eggs, and dairy products	15.6 (9.7–25.9)
Greens, vegetables, and fruit	13.0 (6.8–19.5)
Alcoholic drinks and tobacco	0 (0–0)

Abbreviations: SD=standard deviation, BMI=body mass index, CAD=coronary artery disease, IQR=interquartile range, USD=US dollars

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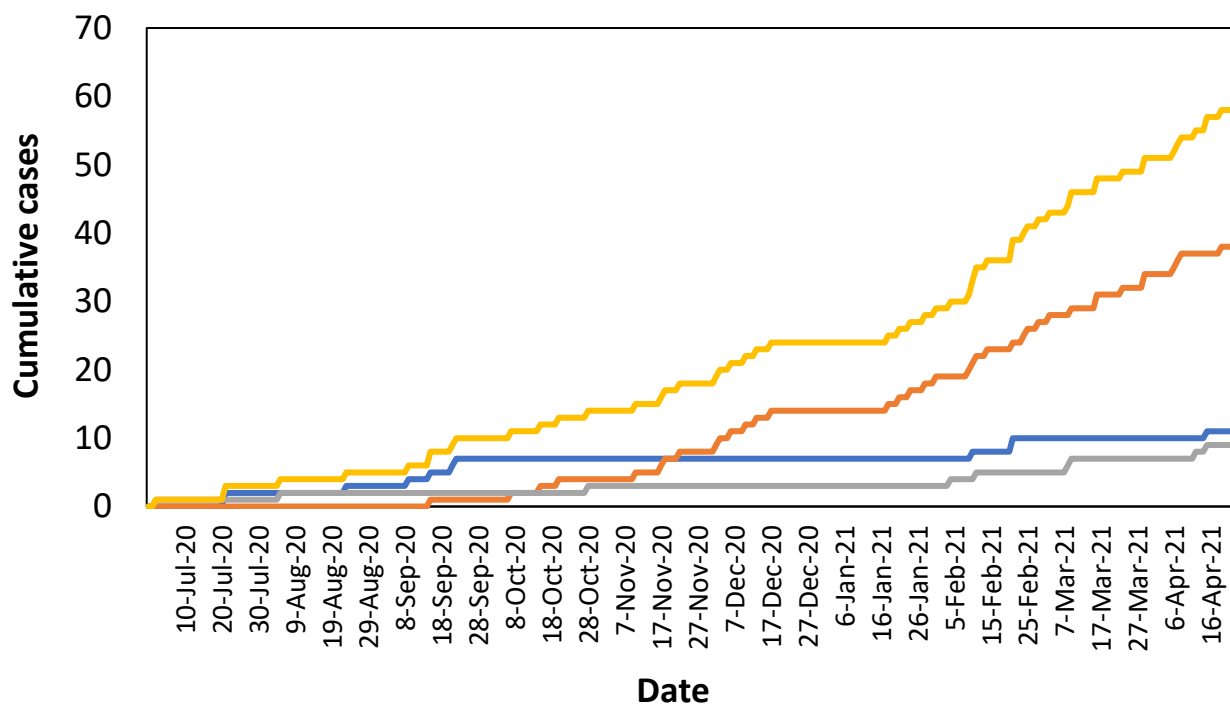
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225 **Figure 2.** Map of the study region (2,600 km²) showing number of enrolled subjects living in
226 each municipality, n=1,819 with reported data.

227
228 **Absenteeism**

229 From August 31, 2020 to February 19, 2021, 736 workers (51.4%) had ≥ 1 day of work
230 absence. Study personnel contacted 504 (68.5%) after three attempts, and there were no
231 differences between contacted and uncontacted workers other than number of children (2.7 vs
232 2.2, respectively, $p < 0.01$). Risk associations for absenteeism are shown in **Supplemental Table**
233 **1.**

234 **Respiratory Illnesses**

235 Between June 15, 2020 and October 10, 2021, the study identified 169 ILI episodes
236 occurring among 145 unique persons; of those, 136 (93.8%) persons (for 157 ILI episodes) and
237 129 (89.0%) persons (for 149 ILI episodes) completed the 7- and 28-day follow up surveys by
238 analysis closeout (**Supplemental Table 2**). Of the 153 ILI episodes (among 132 unique persons)
239 with completed SARS-CoV-2 antigen testing by analysis closeout, 43 (28.1%) were positive for
240 SARS-CoV-2. Of 151 ILI episodes (among 131 unique persons) with complete influenza and
241 RSV RT-PCR testing, 6 (3.7%) were RSV-positive, and 0 were influenza-positive. The incidence
242 density of ILI was 12.0 person-years (P-Y) and of SARS-CoV-2 was 3.1/100 P-Y (**Figure 3**).



243 **Figure 3.** Cumulative ILI Events in the AGRI Cohort, June 15, 2020 to October 10, 2021. From
244 June 2020–October 2021, ILI was defined as “cough and fever”; in January 2021, the ILI case
245 definition was expanded to “cough or fever or shortness of breath”. Includes all-cause ILI
246 (yellow), SARS-CoV-2-positive ILI (blue), SARS-CoV-2 negative ILI (orange), and ILI without
247 test obtained (gray).

248

249 BioFire FilmArray RP2.1 testing (n=40) on available specimens confirmed 9 of 9 SARS-
250 CoV-2 infections tested, 1 of 1 RSV infection, and identified an additional 8 picornaviruses
251 (rhino/enterovirus target on FilmArray) and 6 seasonal coronavirus (3 NL63, 1 OC43, and 2
252 N229E) ILI cases. The adult worker was usually the index case within the household for both
253 SARS-CoV-2 ILI (>80%) infections (**Table 2**) and ILI (>85%) (**Supplemental Table 2**).

254 Workers with SARS-CoV-2 had longer fever duration at the time of diagnosis (day 0; 3.3
255 vs 2.3 days; $p<0.01$) and increased frequency of anosmia (44.2% vs 17.3%; $p<0.01$) and
256 dysgeusia (48.8% vs 24.6%; $p<0.01$), compared to SARS-CoV-2-negative workers with ILI
257 (**Table 2**). SARS-CoV-2 cases were also more likely to have difficulty concentrating (41.9% vs
258 20.9%, $p=0.01$), irritability (58.1% vs 33.6%, $p=0.01$), and dependence on others (37.2% vs
259 20.9%, $p=0.04$). SARS-CoV-2-positive workers had higher systemic Flu-iiQ severity scores
260 (indicating greater disease severity) at diagnosis than SARS-CoV-2-negative workers, but other
261 clinical scores remained non-significant. SARS-CoV-2-positive workers reported worse impact
262 on “daily activities” (0.50 vs 0.22, $p=0.01$) and “emotions” (0.62 vs 0.31, $p<0.01$) scores than
263 SARS-CoV-2-negative workers at diagnosis, and worse “impact on others” score at day 7 (0.37
264 vs 0.16, $p=0.03$), with all other Flu-iiQ well-being scores showing a similar non-significant trend
265 (**Table 2, Figure 4**). Clinical outcomes of workers with ILI episodes versus asymptomatic
266 controls are shown in **Supplementary Table 2**.

267 *Economic Outcomes*

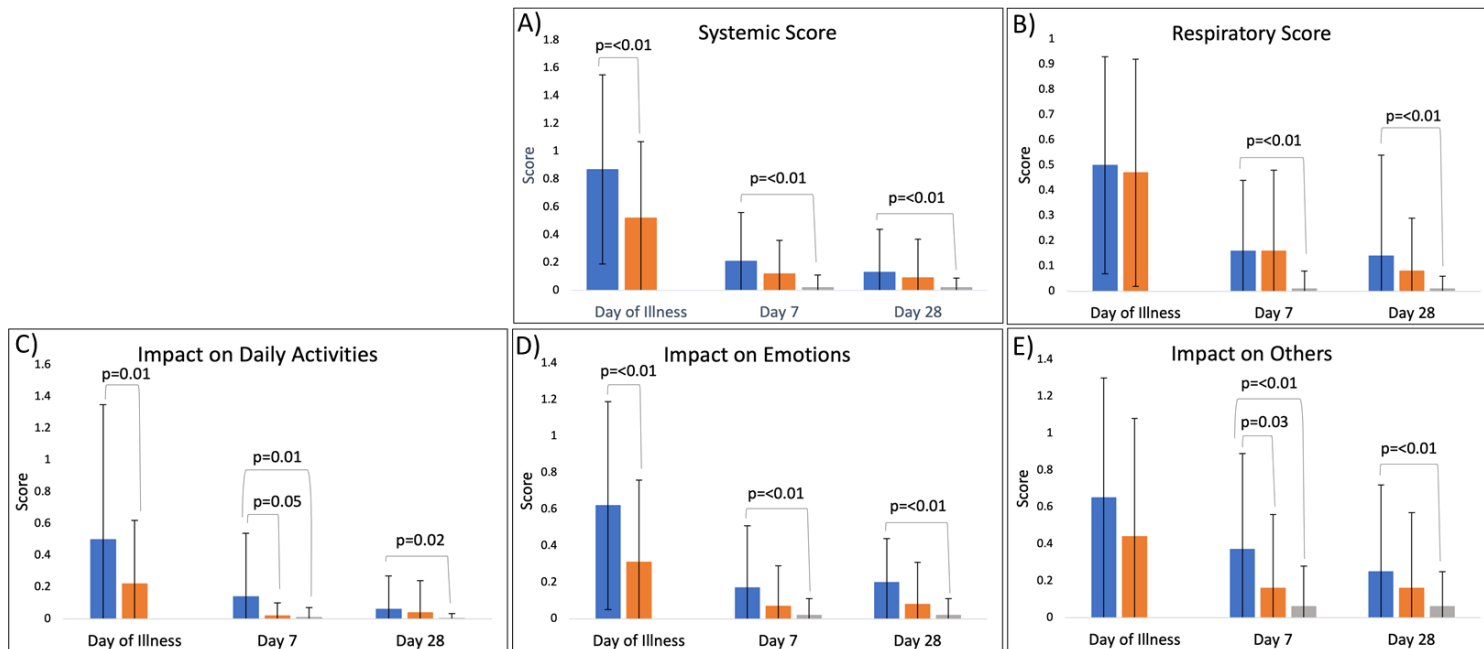
268 Compared to SARS-CoV-2-negative workers with ILI, SARS-CoV-2 positive workers
269 had greater self-reported lost income (median US\$ 127.1 vs \$0, $p<0.01$), and combined
270 (healthcare, transportation, lost wages) total cost (US\$ 147.9 vs \$12.7, $p<0.01$) at day 7 (reported
271 over the preceding 2 weeks) (**Figure 5**); workers with SARS-CoV-2 also had more days of work

Table 2. Comparison of Self-Reported Outcomes in SARS-CoV-2-positive ILI vs SARS-CoV-2-negative ILI

	Day 0 SARS-CoV-2 positive (n=43)	Day 0 SARS-CoV-2 negative (n=110)	p-value*	Day 7 SARS-CoV-2 positive (n=41)	Day 7 SARS-CoV-2 negative (n=103)	p-value*	Day 28 SARS-CoV-2 positive (n=38)	Day 28 SARS-CoV-2 negative (n=97)	p-value*
Clinical Symptoms									
# days of fever (if fever), mean (SD)	3.3 (2.0)	2.3 (1.5)	<0.01	4.4 (2.8)	3.3 (2.5)	0.08	0.5 (0.0)	3.4(2.2)	0.04
# days of cough (if cough), mean (SD)	3.3 (1.9)	3.6 (2.1)	0.45	6.1 (2.3)	5.1 (2.6)	0.07	4.5 (4.9)	5.1 (3.5)	0.84
Have you felt the following (last 24 hours), n (%):									
Fever	32 (74.4)	60 (54.6)	0.02	2 (4.9)	11 (10.8)	0.35	4 (10.5)	4 (4.2)	0.22
Nasal Congestion	18 (41.9)	39 (35.5)	0.46	5 (12.2)	17 (16.7)	0.50	2 (5.3)	6 (6.3)	1.00
Myalgia	23 (53.5)	46 (41.8)	0.19	3 (7.3)	10 (9.8)	0.76	5 (13.2)	6 (6.3)	0.19
Headache	30 (69.8)	55 (50.0)	0.03	13 (31.7)	21 (20.6)	0.16	8 (21.1)	14 (14.6)	0.36
Cough	24 (55.8)	39 (35.5)	0.02	7 (17.5)	14 (13.7)	0.57	3 (7.9)	7 (7.3)	1.00
Sore Throat	15 (34.9)	50 (45.5)	0.23	6 (14.6)	14 (13.7)	0.89	4 (10.5)	7 (7.3)	0.51
Dysgeusia	21 (48.8)	27 (24.6)	<0.01	8 (19.5)	6 (5.9)	0.01	3 (7.9)	2 (2.1)	0.14
Expectoration	16 (37.2)	45 (40.9)	0.67	12 (29.3)	18 (17.7)	0.12	7 (10.5)	8 (8.3)	0.74
Fatigue	24 (55.8)	30 (27.3)	<0.01	7 (17.1)	11 (10.8)	0.31	6 (15.8)	5 (5.2)	0.04
Anosmia	19 (44.2)	19 (17.3)	<0.01	9 (22.0)	3 (2.9)	<0.01	3 (7.9)	2 (2.1)	0.14
Loss of Appetite	17 (39.5)	31 (28.2)	0.17	4 (9.8)	5 (4.9)	0.28	1 (2.6)	2 (2.1)	1.00
Dyspnea	13 (30.2)	25 (22.9)	0.35	4 (9.8)	5 (4.9)	0.28	4 (10.8)	1 (1.0)	0.02
Neck Pain	14 (33.3)	18 (16.4)	0.02	6 (14.6)	5 (4.9)	0.05	4 (10.5)	4 (4.2)	0.22
Interrupted Sleep	11 (25.6)	19 (17.3)	0.24	8 (19.5)	6 (5.9)	0.01	3 (7.9)	4 (4.2)	0.40
Wheezing	4 (9.5)	14 (12.7)	0.78	1 (2.4)	5 (4.9)	0.67	4 (10.5)	1 (1.0)	0.02
Well-Being**									
Have you had difficulty with (last 24 hrs), n (%):									
Getting out of bed	16 (37.2)	26 (23.6)	0.09	5 (12.2)	4 (3.9)	0.12	2 (5.3)	4 (4.2)	1.00
Preparing meals...	8 (18.6)	10 (9.1)	0.10	3 (7.3)	1 (1.0)	0.07	2 (5.3)	2 (2.1)	0.32
Performing usual...	16 (37.2)	27 (24.6)	0.12	4 (9.8)	3 (2.9)	0.10	3 (7.9)	3 (3.1)	0.35
Leaving the home...	13 (30.2)	14 (12.7)	0.01	6 (14.6)	0 (0)	<0.01	2 (5.3)	2 (2.1)	0.32
Concentrating on...	18 (41.9)	23 (20.9)	0.01	4 (9.8)	2 (2.0)	0.06	2 (5.3)	5 (5.2)	1.00
Taking care of...	16 (37.2)	13 (11.7)	<0.01	4 (9.8)	0 (0)	0.01	2 (5.3)	4 (4.2)	1.00
Leave the room	9 (20.9)	14 (12.7)	0.20	4 (9.7)	0 (0)	0.01	2 (5.3)	2 (2.1)	0.32
Have you felt the following (last 24 hours), n (%):									
Irritable	25 (58.1)	37 (33.6)	0.01	4 (9.8)	8 (7.8)	0.74	4 (10.5)	6 (6.3)	0.47
Defenseless	18 (41.9)	20 (18.2)	<0.01	5 (12.2)	5 (4.9)	0.12	3 (7.9)	3 (3.1)	0.35
Worried	19 (44.2)	35 (31.8)	0.15	13 (31.7)	8 (7.8)	<0.01	5 (13.2)	10 (10.4)	0.65
Frustrated	15 (34.9)	16 (14.6)	<0.01	3 (7.3)	6 (5.9)	0.72	2 (5.3)	5 (5.2)	1.00
People worrying...	30 (69.8)	57 (51.8)	0.04	18 (43.9)	21 (20.6)	<0.01	11 (29.0)	18 (18.8)	0.20
Being a burden	13 (30.2)	30 (27.3)	0.71	9 (22.0)	10 (9.8)	0.05	5 (13.2)	9 (9.4)	0.52
People being...	13 (30.2)	24 (21.8)	0.27	8 (19.5)	8 (7.8)	0.05	7 (18.4)	7 (8.3)	0.10
Needing to depend...	16 (37.2)	23 (20.9)	0.04	10 (24.4)	9 (8.8)	0.01	6 (15.8)	10 (10.4)	0.39
People having to do extra...	15 (34.9)	21 (19.1)	0.04	10 (24.4)	10 (9.8)	0.02	8 (21.1)	8 (8.3)	0.04
Flu-iiQ Severity Scores***									

Systemic Score	0.87 (0.68)	0.52 (0.55)	<0.01	0.21 (0.35)	0.12 (0.24)	0.19	0.13 (0.31)	0.09 (0.28)	0.41
Respiratory Score	0.50 (0.43)	0.47 (0.45)	0.64	0.16 (0.28)	0.16 (0.32)	0.99	0.14 (0.4)	0.08 (0.21)	0.41
Impact on Daily Activities	0.50 (0.85)	0.22 (0.40)	0.01	0.14 (0.40)	0.02 (0.08)	0.05	0.06 (0.21)	0.04 (0.20)	0.71
Impact on Emotions Score	0.62 (0.57)	0.31 (0.45)	<0.01	0.17 (0.34)	0.07 (0.22)	0.09	0.20 (0.24)	0.08 (0.23)	0.60
Impact on Others Score	0.65 (0.65)	0.44 (0.64)	0.08	0.37 (0.52)	0.16 (0.40)	0.03	0.25 (0.47)	0.16 (0.41)	0.27
Epidemiology									
# in house w/ similar illness (last 2 weeks)	0.30 (0.64)	0.13 (0.36)	0.10	0.34 (0.62)	0.17 (0.49)	0.09	0.11 (0.39)	0.14 (0.41)	0.61
Index case in house, n (%)									
Self	35 (81.4)	97 (88.2)		34 (82.9)	96 (94.1)		33 (86.8)	90 (93.8)	
Spouse	2 (4.7)	3 (2.7)		1 (2.4)	1 (1.0)		1 (2.6)	1 (1.0)	
Parent	0 (0)	2 (1.8)	0.13	1 (2.4)	1 (1.0)	0.10	0 (0)	0 (0)	0.24
Sibling	3 (7.0)	3 (2.7)		3 (7.3)	2 (2.0)		3 (7.9)	3 (3.1)	
Cousin	1 (2.3)	0 (0)		1 (2.4)	0 (0)		0 (0)	0 (0)	
Child	0 (0)	4 (3.6)		0 (0)	1 (1.0)		0 (0)	2 (2.1)	
*p-values are from t-tests for continuous variables, and chi-square test for categorical variables.									
**Items truncated per Flu-iiQ licensing agreement; full items available from the author.									
***Higher scores indicate worse outcomes									

272



273 **Figure 4.** Flu-iiQ severity scores (range: 0-3), by subdomain, for workers with SARS-CoV-2-
 274 positive influenza-like illness (ILI), SARS-CoV-2-negative ILI, and asymptomatic controls.
 275 Higher score indicates greater clinical severity (Panels A and B) or greater negative impact on
 276 well-being (Panels C-E). Significant differences ($p < 0.05$) are identified within each group.
 277 Blue=SARS-CoV-2-positive ILI, orange=SARS-CoV-2-negative ILI, gray=asymptomatic
 278 controls.

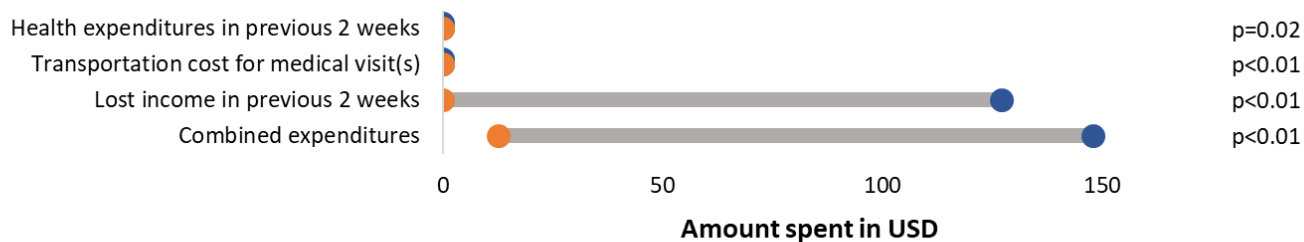
280 absence ($p < 0.01$), with most (81.8%) having >5 days of work absence. Household expenditures
 281 on fruits/vegetables were higher at day 7 for SARS-CoV-2-positive workers vs test-negatives
 282 with ILI (US\$ 19.5 vs \$13.0, $p < 0.01$); differences in all other household expenditures between
 283 SARS-CoV-2 test-positive and test-negative workers were not statistically significant.

284 DISCUSSION

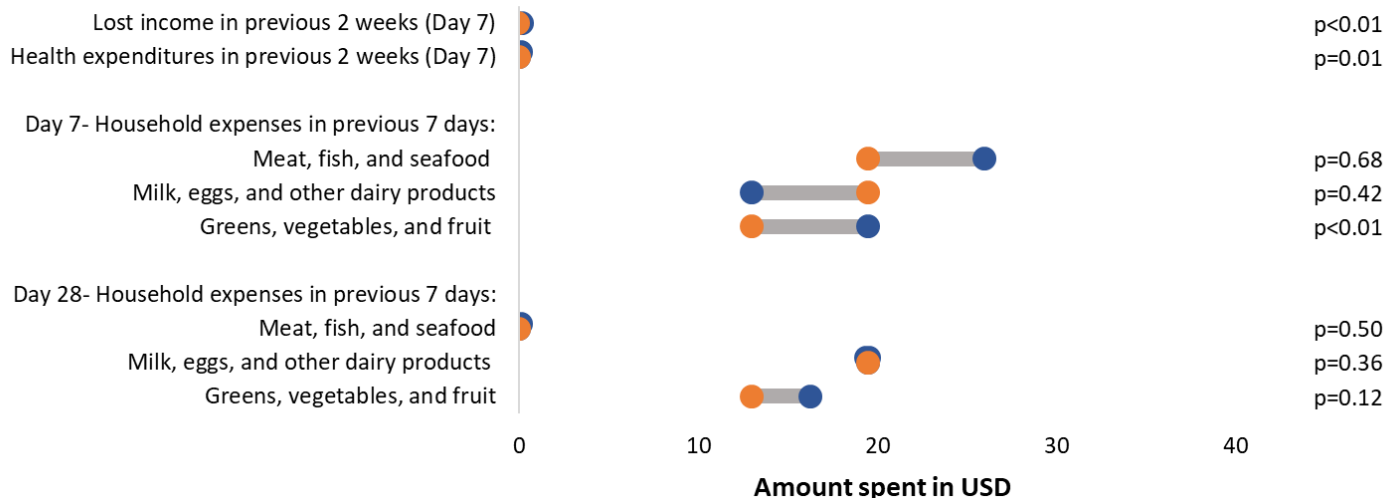
285 As of October 10 2021, Guatemalan plantation workers in this prospective cohort study
 286 experienced a substantial burden of acute respiratory illness during the COVID-19 pandemic, of
 287 which one in four tested positive for SARS-CoV-2; those with COVID-19 had greater disease
 288 severity, absenteeism, and economic losses than workers with SARS-CoV-2-negative ILI.

289 Similar to limited data from the U.S. (1), plantation workers in Guatemala were at risk for
 290 SARS-CoV-2 infection (3.1 cases/100 P-Y) throughout the 2020-21 season. Compared to other

Worker Impact at Day 7



Household Impact at Days 7 and 28



291 **Figure 5.** Differences in expenditures between SARS-CoV-2-positive and -negative workers
 292 with influenza-like illness (ILI). Workers with SARS-CoV-2-positive ILI (dark blue circle)
 293 reported significantly greater lost income and combined expenditures related to their illnesses in
 294 the week following their illness than SARS-CoV-2-negative workers with ILI (orange circle).

295

296 members of their households, the plantation workers were nearly always the index symptomatic
 297 case. These findings, along with the critical role agricultural workers play in Guatemalan and
 298 global food security (4, 6), lend support to the prioritization of vaccinating plantation workers
 299 against COVID-19.

300 Although preliminary, our findings suggest COVID-19 illness was associated with
 301 greater overall clinical severity and impairment, which persisted at 7- and 28-days post-illness
 302 compared to non-SARS-CoV-2 ILI cases. COVID-19 symptoms were consistent with those

303 reported elsewhere, with higher frequencies of anosmia and dysgeusia and prolonged fever
304 differentiating COVID-19 from other ILI cases. Interestingly, COVID-19 was significantly
305 associated with irritability and difficulty concentrating, consistent with post-acute sequelae of
306 SARS-CoV-2 (PASC, or “long COVID”) (32, 33). The irritability and inability to concentrate,
307 which persisted in some workers at both 7 and 28 days, may place workers at risk, for example,
308 when using machetes to harvest bananas and when operating heavy equipment. The Flu-iiQ well-
309 being scores, which include socio-emotional and functional activities, generally indicated more
310 severe illness among workers with COVID-19 compared to workers with other ILI at the time of
311 diagnosis and day 7, with a non-significant trend at 28 days. It is unknown to what extent
312 symptoms or sequelae persist beyond 28 days in this population.

313 Plantation workers in this cohort experienced a significant economic impact from
314 COVID-19. Self-reported data suggest a significant difference in absenteeism, lost earnings, and
315 total costs between COVID-19 and other ILI cases. Median monthly household income (US\$
316 363.2), already just below the mean basic monthly food basket price in Guatemala (US\$ 386.3),
317 was reduced significantly in workers with COVID-19 (median lost income: US\$ 127.1, median
318 total cost of illness: \$147.9), placing these households at increased risk for food insecurity and
319 economic hardship. Notably, economic insecurity is one of the primary drivers of emigration
320 from Guatemala (34, 35), and thus the economic impact and policy implications of COVID-19
321 on these plantation workers and their households, as well as others in similar settings, may
322 extend beyond the Guatemalan border.

323 While SARS-CoV-2 was the most frequently detected respiratory pathogen among
324 workers with ILI, we detected no cases of influenza and only 6 cases of RSV. Influenza and RSV
325 both circulate year-round in Guatemala and comprise a substantial proportion of ILI cases in

326 population-based studies in Central and South America (36-39). The lower incidence observed in
327 our cohort suggests mitigation strategies—primarily the closing of schools, mask use, and some
328 level of physical distancing—may have been effective in limiting some transmission of influenza
329 and RSV. The observation of rhino/enterovirus and seasonal coronaviruses (NL63, OC43, and
330 N229E) cases in a subset of our cohort is consistent with other reports, (40, 41) though the
331 reasons for these detections despite physical distancing measures merit further study. The AGRI
332 cohort and similar studies will provide important observations on the effectiveness of population-
333 based preventive measures such as vaccines on the burden of respiratory pathogens. Also
334 important, our data demonstrate that syndromic surveillance in the workplace is a feasible
335 population-based approach to rapidly characterize an emerging pathogen.

336 The AGRI study design has some inherent strengths and limitations. Though the study
337 includes weekly visits to worksites to identify symptomatic ILI cases, it still requires some level
338 of self-reporting to study personnel, and therefore may underestimate incidence. Workers with
339 laboratory-confirmed SARS-CoV-2 are required to isolate and may be incentivized to under-
340 report illness to avoid lost wages, thus providing a bias towards lower incidence and more severe
341 cases of disease being reported. Required isolation likely increases duration of absenteeism in
342 workers who are SARS-CoV-2-positive, though it still reflects the consequences of COVID-19
343 in this population. Self-reported study outcomes are also subject to recall bias, which we aimed
344 to minimize by including controls with similar follow-up. Laboratory test results are provided to
345 the worker when available, and thus self-reported outcomes may be impacted by diagnostic bias.
346 We did not perform pathogen testing on controls. We relied on an antigen test for detection of
347 SARS-CoV-2 infection and an ELISA assay for anti-nucleocapsid IgG, which may have
348 decreased performance compared to PCR and virus neutralization assays, respectively; future

349 studies will compare these approaches. Future studies will also include company-reported data,
350 which will provide a more objective assessment of wages, allowing us to compare self- and
351 company-reported metrics. Finally, to decrease the risk of healthy worker bias (42), the study
352 collects post-acute (28-day) outcomes on all ILI cases and will ultimately measure loss of
353 employment (using company data) as an outcome measure of ILI.

354 In conclusion, preliminary data from the AGRI cohort suggest a significant clinical and
355 socioeconomic impact of respiratory illnesses, especially COVID-19, on plantation workers in
356 Guatemala. The study demonstrates the feasibility and value of conducting workforce-based
357 syndromic surveillance during epidemic activity and uses several innovative approaches to
358 measure disease outcomes in the acute and post-acute setting, such as the implementation of
359 active surveillance and molecular diagnostics within a large banana plantation and the inclusion
360 of company-reported economic measures. It also provides a more comprehensive assessment of
361 how communicable diseases economically impact an essential, yet vulnerable, workforce
362 population and their households. Given the high clinical and economic burden of COVID-19
363 disease among plantation workers in our cohort, and their likely role in household transmission,
364 our results support the prioritization of people working in the agricultural sector for vaccination
365 against COVID-19, potentially through the workplace.

366 **FOOTNOTES**

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390 **Author Roles:** DO, MC, ML, FH, HM, KE, LSN, EJA: conceptualization, methodology,

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392 investigation, administration. ML, MG, JM, ANC, CI, LMD, EZ, EAB: analysis, visualization,

393 writing. DO, MC, EJA: supervision, administration.

394 **|Conference Presentation:** Abstracts was presented at ISIRV 2021 Oct 19-21, 2021 and

395 ASTMH, Nov 17-21, 2021.

396 **Supplementary Tables**

Supplementary Table 1: Absenteeism Characteristics, August 31 2020-February 19 2021

Characteristics	Workers with no absence (n=695)	Workers with any absence (n=736)	p-value*
Worker Demographics			
Age: mean (SD)	32.7 (9.1)	30.0 (8.0)	<0.01
Male sex, n (%)	611 (87.9)	593 (80.6)	<0.01
Ethnicity: Ladino	312 (44.9)	315 (42.8)	
Indigenous	47 (6.8)	50 (6.8)	0.82
other	1 (0.1)	2 (0.3)	
don't know	335 (48.2)	369 (50.1)	
Worker Health, n (%)			
Asthma	1 (0.1)	7 (1.0)	0.04
Pulmonary disease	4 (0.6)	5 (0.7)	0.80
Kidney disease	27 (3.9)	22 (3.0)	0.35
Cardiovascular disease	10 (1.4)	10 (1.4)	0.90
Diabetes	13 (1.9)	7 (1.0)	0.14
Blood disorder (sickle cell)	8 (1.2)	14 (1.9)	0.25
Neurologic disease (stroke)	3 (0.4)	5 (0.7)	0.53
Liver disease	5 (0.7)	10 (1.4)	0.24
Obesity (BMI \geq 30 kg/m ²), n=773	67 (15.6)	15 (4.4)	<0.01
Taking medications?	83 (11.9)	95 (12.9)	0.57
Ever received influenza vaccine	50 (7.2)	41 (5.6)	0.21
Work Conditions			
# of absences/person, median (IQR)	0 (0, 0)	5.3 (2, 7)	<0.01
Type of Work, n (%)			
Administration	43 (6.2)	0 (0)	
Field worker	42 (66.5)	528 (71.7)	<0.01
Field manager	54 (7.8)	3 (0.4)	
Packer (factory worker)	120 (17.3)	205 (27.9)	
Factory manager	16 (2.3)	0 (0)	
How long worked at farm, n (%)			
\leq 2 years	346 (49.8)	453 (61.5)	<0.01
3-4 years	104 (14.9)	113 (15.4)	
\geq 5 years	245 (35.3)	170 (23.1)	
Monthly income, \$USD, median (IQR)	337.2 (311.3, 389.1)	337.2 (311.3, 363.2)	<0.01
Household Conditions			
# adults in house, mean (SD)	3.2 (1.6)	3.4 (1.8)	0.01
# children in house, mean (SD)	2.3 (1.6)	2.5 (1.7)	<0.01
Concern about food insecurity in last year, n (%)	401 (57.7)	464 (63.0)	0.04
Lacked money for food in the last 12 months, n (%)	506 (72.8)	505 (68.6)	0.08
Household monthly income, \$USD, median (IQR)	363.2 (324.3, 466.9)	376.1 (324.3, 466.9)	0.06
\$USD spent in the last 7 days, median (IQR):			
Meat, fish, and seafood	22.7 (13.0, 32.4)	19.5 (13.0, 38.9)	0.68
Milk, eggs, and other dairy products	13.0 (9.1, 24.9)	15.6 (9.7, 25.9)	0.07
Greens, vegetables, and fruit	13.0 (6.5, 19.5)	13.0 (6.5, 19.5)	0.83
Alcoholic drinks and tobacco	0 (0, 0)	0 (0, 0)	0.16

*p-values are from t-tests for continuous variables, and chi-square test for categorical variables.

Abbreviations: SD=standard deviation, BMI=body mass index, IQR=interquartile range, USD=US dollars

Supplementary Table 2. Comparing Self-Reported Outcomes in ILI vs Asymptomatic Controls							
	Day 0 ILI (n=169)	D7 ILI (n=157)	D7 Control (n=623)	p-value*	D28 ILI (n=149)	D28 Control (n=588)	p-value*
<i>Clinical Symptom</i>							
# days of cough (if cough), mean (SD)	3.5 (2.1)	5.3 (2.6)	3.4 (2.6)	0.05	5.0 (3.5)	3.7 (2.0)	0.32
# days of fever (if fever), mean (SD)	2.6 (1.8)	3.6 (2.6)	1.5 (0.6)	<0.01	2.6 (2.3)	3.5 (3.0)	0.55
Have you felt the following (last 24 hours), n (%):							
Fever	96 (57.5)	14 (9.0)	4 (0.7)	<0.01	8 (5.4)	3 (0.5)	<0.01
Nasal Congestion	60 (35.9)	23 (14.7)	16 (2.7)	<0.01	9 (6.1)	6 (1.1)	<0.01
Myalgia	73 (43.7)	14 (9.0)	23 (3.9)	0.01	11 (7.5)	11 (2.0)	<0.01
Headache	89 (53.3)	37 (23.7)	22 (3.7)	<0.01	25 (17.0)	14 (2.5)	<0.01
Cough	69 (41.3)	22 (14.2)	2 (0.34)	<0.01	10 (6.8)	1 (0.2)	<0.01
Sore Throat	66 (39.5)	20 (12.8)	7 (1.2)	<0.01	12 (8.2)	10 (1.8)	<0.01
Dysgeusia	51 (30.5)	15 (9.6)	2 (0.3)	<0.01	6 (4.1)	2 (0.4)	<0.01
Expectoration	62 (37.1)	30 (19.2)	4 (0.7)	<0.01	12 (8.2)	2 (0.4)	<0.01
Fatigue	58 (34.7)	19 (12.2)	18 (3.0)	<0.01	11 (7.5)	19 (3.4)	0.03
Anosmia	40 (24.0)	13 (8.3)	1 (0.2)	<0.01	6 (4.1)	2 (0.4)	<0.01
Loss of Appetite	49 (29.3)	10 (6.4)	6 (1.0)	<0.01	3 (2.0)	7 (1.3)	0.44
Dyspnea	41 (24.7)	10 (6.4)	1 (0.2)	<0.01	5 (3.4)	1 (0.2)	<0.01
Neck Pain	34 (20.5)	11 (7.1)	8 (1.3)	<0.01	8 (5.4)	8 (1.4)	<0.01
Interrupted Sleep	33 (19.8)	15 (9.6)	7 (1.2)	<0.01	7 (4.8)	6 (1.1)	<0.01
Wheezing	19 (11.5)	6 (3.9)	1 (0.2)	<0.01	5 (3.4)	0 (0)	<0.01
<i>Well-Being**</i>							
Have you had difficulty with (last 24 hrs), n (%):							
Getting out of bed	44 (26.4)	10 (6.4)	7 (1.2)	<0.01	7 (4.8)	6 (1.1)	<0.01
Preparing meals...	18 (10.8)	4 (2.6)	3 (0.5)	0.04	4 (2.7)	1 (0.2)	0.01
Performing usual...	45 (27.0)	9 (5.8)	4 (0.7)	<0.01	6 (4.1)	2 (0.4)	<0.01
Leaving the home...	27 (16.2)	6 (3.9)	2 (0.3)	<0.01	4 (2.7)	1 (0.2)	0.01
Concentrating on...	43 (25.8)	9 (5.8)	7 (1.2)	<0.01	7 (4.8)	1 (0.2)	<0.01
Taking care of...	31 (18.6)	4 (2.6)	3 (0.5)	0.04	6 (4.1)	1 (0.2)	<0.01
Leave the room	23 (13.8)	4 (2.6)	2 (0.3)	0.02	4 (2.7)	0 (0)	<0.01
Have you felt the following (last 24 hours), n (%):							
Irritable	66 (39.5)	13 (8.3)	10 (1.7)	<0.01	10 (6.8)	5 (0.9)	<0.01
Defenseless	40 (24.0)	12 (7.7)	9 (1.5)	<0.01	6 (4.1)	4 (0.7)	0.01
Worried	59 (35.3)	23 (14.7)	13 (2.2)	<0.01	15 (10.2)	20 (3.6)	<0.01
Frustrated	34 (20.4)	10 (6.4)	7 (1.2)	<0.01	7 (4.8)	8 (1.4)	0.01
People worrying...	93 (55.7)	40 (25.6)	56 (9.4)	<0.01	29 (19.7)	69 (12.4)	0.02
Being a burden	47 (28.1)	20 (12.8)	12 (2.0)	<0.01	14 (9.5)	15 (2.7)	<0.01
People being...	38 (22.8)	16 (10.3)	16 (2.7)	<0.01	15 (10.2)	15 (2.7)	<0.01
Needing to depend...	42 (25.2)	19 (12.2)	20 (3.4)	<0.01	16 (10.9)	19 (3.4)	<0.01
People having to do extra...	37 (22.2)	21 (13.5)	22 (3.7)	<0.01	16 (10.9)	20 (3.6)	<0.01
<i>Flu-iiQ Severity Scores</i>							

Systemic Score	0.60 (0.47)	0.14 (0.28)	0.02 (0.09)	<0.01	0.10 (0.28)	0.02 (0.07)	<0.01
Respiratory Score	0.46 (0.44)	0.15 (0.11)	0.01 (0.07)	<0.01	0.09 (0.27)	0.01 (0.05)	<0.01
Impact on daily activities	0.28 (0.49)	0.05 (0.22)	0.01 (0.06)	0.01	0.04 (0.19)	0.004 (0.03)	0.02
Impact on Emotions Score	0.39 (0.51)	0.11 (0.28)	0.02 (0.09)	<0.01	0.07 (0.22)	0.02 (0.09)	<0.01
Impact on Others Score	0.49 (0.65)	0.21 (0.43)	0.06 (0.22)	<0.01	0.17 (0.41)	0.06 (0.19)	<0.01
Epidemiology							
# in house w/ similar illness (last 2 weeks)	0.17 (0.45)	0.21 (0.52)	0.01 (0.10)	<0.01	0.12 (0.38)	0.01 (0.15)	<0.01
Index case in house, n (%)							
Self	145 (86.8)	142 (91.0)	1 (14.3)		135 (91.8)	3 (42.9)	
Spouse	5 (3.0)	2 (1.3)	2 (28.6)		2 (1.4)	1 (14.3)	
Parent	2 (1.2)	2 (1.3)	1 (14.3)	<0.01	1 (0.7)	0 (0)	<0.01
Sibling	6 (3.6)	5 (3.2)	0 (0)		6 (4.1)	0 (0)	
Cousin	1 (0.6)	1 (0.6)	0 (0)		0 (0)	0 (0)	
Child	4 (2.4)	1 (0.6)	3 (42.9)		2 (1.4)	2 (28.6)	
*p-values are from t-tests for continuous variables, and chi-square test for categorical variables.							
** Items truncated per Flu-iiQ licensing agreement; full items available from the author.							
Abbreviations: ILI = influenza-like illness case, D7 = day 7, D28 = day 28.							

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