Asthma, respiratory symptoms and lung function across age groups in an indigenous Mayan population in Guatemala, and relation to work in the traditional textile industry: a cross-sectional pilot study

Lake Atitlan Lung Health Study

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This thesis is submitted in partial fulfilment of the requirements for the degree of Master of Philosophy in Global Health at the University of Bergen.

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Abstract

Background: Occupational exposure to fabrics and dyes in the textile industry is associated with low lung function, higher prevalence of asthma and other respiratory symptoms. Mayan communities in Guatemala have worked in the traditional textile industry for generations, an occupation that may represent a risk factor for the development of diverse lung health problems. To our knowledge, studies in these communities that describe the respiratory health and assess the impact of their occupation in the textile industry are non-existent.

Objective: We aimed to assess asthma, respiratory symptoms and the lung function in Mayan families living in the Sololá region in Guatemala, and the possible association with working in the traditional textile industry ("weaving").

Methods: A cross-sectional pilot study was developed where participants answered to a standardized interviewer-led questionnaire that investigated demographics, work and home-related exposures and their respiratory symptomatology. Anthropometric measurements, a spirometry and bio sampling were also completed. Descriptive analyses were performed to inform on the prevalence of symptoms/conditions, and simple regression models were used to analyze possible associations between working in the textile industry and respiratory symptoms/conditions (logistic regressions) and lung function values (linear regressions).

Results: A total of 291 participants were included, with a mean age 34.2 years (range 14 to 77 years). 82% were female, and 40% of those asked about their job responded that they were weavers. Weavers, compared to non-weavers, appeared to have higher prevalence of wheezing (13% *versus* 6%) and of ever having breathing difficulty (9.2% *versus* 5%), as well as more symptoms like morning and chronic cough and phlegm. Only 1% of the study population responded "yes" to ever having had asthma, but 5% of weavers reported use of traditional medicine for asthma compared to <1% among non-weavers. Women weavers had significantly higher risk of wheezing (OR 2.91; 95%CI 0.99-7.92) and indicated higher risk of wheezing without cold (2.43; 0.25-23.9), wheezing with breathlessness (2.35; 0.46-11.9) and tightness in the chest (3.05; 0.60-15.4). Spirometric measurements were found to be of limited quality due to less explosive start to the maneuver. The FVC thus measured was indicated lower among weavers (-0.13L, 95%CI -0.72-0.46; linear regression model adjusting for age, sex and height). Reporting on specific occupation-related exposures was not feasible.

Conclusions: Based on data from the present pilot study, we were able to study the lung health of the Mayan communities in terms of lung function and respiratory symptoms, and partially assess the associations with occupation as weaver. The weavers appeared to have poorer respiratory health, with indicated higher risk for selected respiratory symptoms and lower lung function (mostly non-significant differences). This study also has generated a valuable biobank, and experience in studying a difficult to reach indigenous population. Further studies are needed on potential respiratory health effects of specific activities and exposures, and how to reduce potential risks, in the traditional textile industry in these Guatemalan communities.

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List of abbreviations

AF	Attributable Fraction
ATS	American Thoracic Society
BMI	Body Mass Index
COPD	Chronic Obstructive Pulmonary Disease
DALY	Disability Adjusted Life Years
ECRHS	European Community Respiratory Health Survey
ERS	European Respiratory Society
FEF	Forced Expiratory Flow
FEV_1	Forced Expiratory Volume in 1 second
FEV_6	Forced Expiratory Volume in 6 seconds
FVC	Forced Vital Capacity
GINA	Global Initiative for Asthma
GLI	Global Lung Function Initiative
HIC	High Income Country
IVC	Inspiratory Vital Capacity
Ig E	Immunoglobulin E
ISAAC	International Study of Asthma and Allergies in Children
LMIC	Low- and Middle-Income Country
NOK	Norwegian Kroner
PAHO	Pan American Health Organization
PEF	Peak Expiratory Flow
RAST	Radio Allergo Sorbent Test
RHINESSA	Respiratory Health In Northern Europe, Spain and Australia
RSV	Respiratory Syncytial Virus
SOP	Standard Operation Procedures

Acknowledgments

Many challenges have come to my life in the past two years. Leaving my loved ones in Mexico, quitting my job as a pediatrician, living again as a student in a foreign country and, on the top of that, taking a master in one of the most renown and competitive international centers in Europe during a pandemic. These challenges have forced me to grow and work harder than I expected, as well as to overcome difficulties that I was not sure I could properly face. Today, after more than two years of positive changes and good experiences, I am finally culminating this period in my life with a smile in my face, more goals set in mind and my heart full of satisfaction.

I want to show my gratitude to everyone that was present and contributed, in a way or another, during my work during these two years. First and foremost, I want to deeply thank my supervisor Cecilie Svanes, because you have been an angel for me during this time. Thank you for inviting me to participate in this project in Guatemala, for sharing with me part of your immense knowledge, for supporting my job, for your kind words in every single step, for your patience when I was late or lost and for being the best supervisor that I could have ever asked for. I am grateful and proud to be your student, and to be part of the RHINESSA research group and its amazing members. I hope I can make you proud with my work.

Special thanks to Lore Ruano, my amazing co-supervisor and first Guatemalan friend. Thank you for introducing me to the Guatemalan culture and for showing me your support during this master through unimaginable ways. It has been a pleasure to have you as a supervisor and as a friend in this adventure with ups and downs. Thank you for understanding my worries, for teaching me what I should and should not do or say, for keeping me well fed and for reminding me where I come from. I hope one day we can have that amazing trip to Guatemala, as we originally planned.

I want to deeply thank my dear friend and partner in crime in this journey, Shokouh. You have been a real big sister for me in this “labyrinth” called thesis. Thank you for thinking about me to start with you this project in Guatemala, for your support in every step of the way, for your words of wisdom and for not giving up on me and the project, even when we both thought everything was lost. Big thanks for continuously offering me your advice and help for life, I really appreciate everything.

Very special thanks to Fernando Jerez, our great Guatemalan project coordinator, who helped us plan and execute this amazing project. Thank you for your unconditional long-distance support and your hard work, we know this study could not have happened without you. To the communities that participated and to our team of health and social workers, this study was made thanks to you all. Moreover, my gratitude to Vilde Svanes Sørbye, Benedikte Svanes Sørbye and Hilda Azevedo Andersen, you contributed enormously with your knowledge, dedication, and time. To the RHINESSA group, thank you all for providing us with your experience performing these types of studies and for your economic contributions.

Further, I want to thank the Center for International Health and the University of Bergen for giving me this opportunity by accepting me in this program and for providing an important part of the much-needed funds to develop this study. Big thanks to every single professor and member of the administrative staff that I had the chance to meet. Thank you for your help, support, your lessons and for making this experience a memorable one. Special thanks to Linda for your unconditional help.

To my friends in Mexico, thank you for your support during these two years and for encouraging me to continue and never give up, even when that meant we were going to be away from each other. Thank you my "Global Health friends" for sharing your life and your knowledge during these two years. And Pieri, my dear Peruvian friend, you know how much I enjoy sharing my life with you. You are amazing in every sense of the word. Thank you for your guidance and for helping me overcome my fears and insecurities. I finally did it!

Finally, with all the love of my heart, I want to thank my family and Esteban for all the love, support, kind words, advice, warnings, cheerful conversations and videocalls. Many unfortunate events happened during these two years, but with your help, we were able to overcome them. Remember that this achievement has been possible because of you and dedicated with love to all of you. It has been hard not having you close to share firsthand this

experience, but I am immensely grateful for having you in my life. Thank you, a thousand times.

Bergen, January 2022

1 Literature review

1.1 Lung development

Human lungs start developing between week 3 and 4 of gestation, with the formation of the tracheal outgrowth and continues up to early adulthood. Five stages have been described in this process, and any abnormalities during any stage could lead to poor development of the respiratory tract and to death (1, 2).

First is the **embryonic stage** (3-7 weeks of gestation), when the trachea branches into the two main bronchi and subsequently into lobar and segmental bronchi, with 18 major lobules formed at the end of this stage. Second, the **pseudoglandular stage** (7-17 weeks of gestation), characterized by progressive branching, with formation of about 70% of the total airway by week 14. Tissues start to differentiate, and vascular formation progresses. Next, the **canalicular stage** (17-27 weeks), with the formation of bronchioles, alveolar ducts and primitive alveoli. Initial differentiation of type 1 and type 2 pneumocytes, and the formation of the alveolar capillary barrier are hallmarks in this stage. Fourth, the **saccular stage** (28-36 weeks), when dilation of acinar tubules forming saccules, septation and multiplication of alveoli and further differentiation of pneumocytes occur. And finally, the **alveolar stage** (36 weeks of gestation up to two years of age), with further maturation of the alveolar tree to enhance gas exchange (2-5).

1.2 Spirometry

Spirometry is an important tool used to measure lung function or, in other words, the individual's process of inhaling and exhaling in specific ways as a function of time. Data obtained from the spirometry can vary according to the purpose of this, however, there are three measurements that are most used to assess the lung health: the Forced Vital Capacity (FVC), which represents the volume of air exhaled in a forced expiration after a full inspiration; and the Forced Expiratory Volume in one second and in six seconds (FEV_1 and FEV_6), which refers to the fraction of air exhaled in the first and sixth second of the forced expiration, respectively; and the ratio between these two volumes, the FEV_1/FVC ratio, which is calculated and is useful to detect airflow limitation. Other information available from the spirogram can be the Peak Expiratory Flow (PEF), Forced Expiratory Flow (FEF- with rates at 25%, 50% and 75% FVC usually given) and the Inspiratory Vital Capacity (IVC) (6, 7).

To undertake a spirometry, special equipment and cooperation from patients are needed. Diverse spirometers are available in the market which meet standardization criteria according to the American Thoracic Society (ATS) and the European Respiratory Society (ERS) (6). Specific international guidelines for the procedure (including equipment, calibration and quality control aspects) and the systematic evaluation of the maneuver are available (6, 7).

The interpretation of a spirogram requires the consideration of a range of factors. For several years, efforts have been made to develop systems to predict normal lung function values for different populations and age ranges. However, defining "normal" lung function is a challenging task, and the generalizability across factors such as age, sex, ethnicity, etc. can be discussed (8). Reference values are ideally obtained from representative samples of healthy persons, and the equations are derived from their spirometric measurements and account for age, sex, height or height squared, and, often, ethnicity. There are different sets of reference values and equations obtained from different populations around the world, with variation in the selection of the sample, the definition of "healthy", the age range, and the variables included in the equations (7).

Among commonly used reference equations, we can name those obtained from the third National Health and Nutrition Examination Survey (NHANES III), which were based on a population sample from the United States of America, aged 8-80 years (9); the predictions for Norwegian adults, including those from the HUNT study of Nord-Trøndelag in 2001 (10); and finally, the reference equations proposed by the Global Lung Initiative (GLI), led by six international societies, which described normal spirometry values in people 3 to 95 years old in 26 countries (11). These are based on extensive data from Caucasians but have much less data from other ethnicities.

1.3 Lung function

Normal pulmonary function is defined as the expected lung function and capacity in a healthy individual. Adult lung function is the result of a complex development that includes the previously commented five embryonic and early life stages, the development and growth of the respiratory system until it reaches a maximal lung function in early adulthood, a plateau phase, and subsequent decline with ageing of the lungs (1, 3).

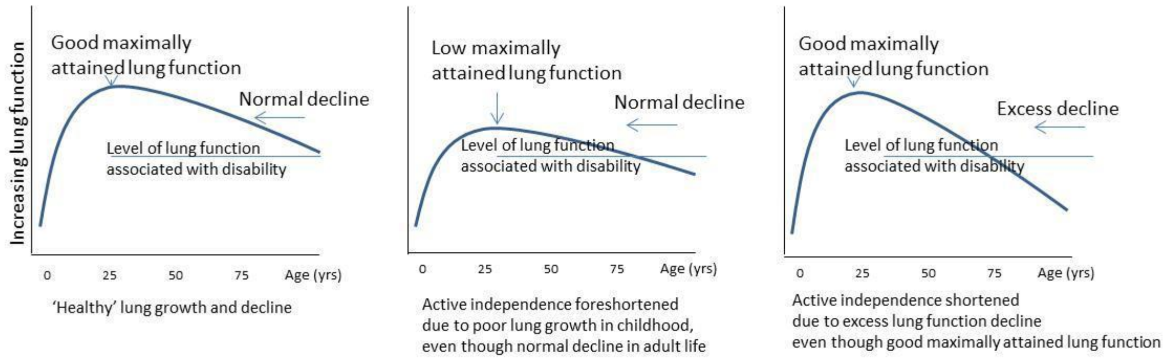


Figure 1. Normal lung function and lung function decline due to different abnormalities in lung growth. From: <https://brn.cat/wp-content/uploads/2018/10/6.-BRN-Seminar-ALEC.pdf>. (Accessed January 10, 2022).

As depicted in Figure 1, normal lung function and lung function decline may be influenced by intrinsic and extrinsic factors at different life stages and even across generations (1, 12, 13). The resulting lung function will vary according to height (standing height is the most commonly used as a proxy to the size of the thorax), age, weight, sex and ethnicity (11). Fletcher and Peto, in 1977, first described a normal development of lung function attained at age 25 years, and further decline of the same, mainly associated with smoking behavior (14). Several studies have described normal physiological decline of lung function, as well as other factors influencing it at several stages of life, including infections (1). An age-related decline in lung function was estimated to start after age 25 years, with an average loss of 20 ml/year in FEV1 and a decline in FVC to approximately 75% of the best value (15). Similarly, a large multicenter study found strong associations between early life factors or "disadvantage factors" (maternal asthma, paternal asthma, maternal smoking, childhood asthma and childhood respiratory infections) and both level and decline in lung function, importantly describing that with an increasing number of childhood disadvantage factors, a greater decline in function was found (13). The concept that processes initiated early in life may give persistent physiological impact with impact on ageing was also supported by an analysis specifically targeting early life risks and lung function decline (16) . Another study evidenced that a relationship may exist between single exposures (low birth weight, tobacco in utero and asthma in childhood) and changes in lung function or COPD later in life (17). Finally, occupational and home exposures (i.e., cleaning) later in life have been considered a risk factor for decline in lung health (18).

1.4 Asthma

1.4.1 Asthma definition

Asthma is defined by the Global Initiative for Asthma (GINA) as “a heterogeneous disease, characterized by chronic airway inflammation” (19). As a global consensus, the definition of asthma includes the presence of respiratory symptoms such as wheezing, chest tightness, shortness of breath and cough, accompanied by measurable expiratory airflow limitation (19, 20) Symptoms and variable airflow limitations can vary in time and severity, with numerous triggers such as respiratory infections, cold, exercise and allergens among others (19, 21).

1.4.2 Asthma prevalence around the world

Asthma is one of the most common non-communicable diseases worldwide (22). It is estimated that 300 million people around the world are affected, with 10-12% of adults and almost 15% of children affected (21, 23, 24). Both the prevalence and the mortality vary across countries and regions within countries. High-income countries (HIC) have higher prevalence in general, while the mortality is higher in resource-poor countries, where access to efficient medication is still a problem (25, 26). The data must be considered with some caution since there are generally much less data from low and middle-income countries (LMICs) than from the HIC.

According to the Global Burden of Asthma report from 2004, the highest prevalence around the world in HIC was in United Kingdom (15%), New Zealand (15.1%), Australia (14.7%), Ireland (14.6%), Canada (14.1%), and the United States (10.9%) (27).

It is estimated that more than 40 million people in Latin America have the disease, and that approximately 50 million persons in Africa are affected (28). However, few sources give an estimate of the prevalence of the disease in the Latin American region. According to GINA in 2004, the highest asthma prevalence was found in Peru (13%) and the lowest in Mexico (3.3%) among Latin American countries (27). In children, the International Study of Asthma and Allergies in Childhood (ISAAC) phase III, found that the prevalence of asthma in children aged 13-14 years old was the highest in Peru and then in Cuba (33.1% and 30.9%, respectively) and the lowest in Mexico and Guatemala (6.9% and 2.6%, respectively) (29, 30).

1.4.3 The global burden of asthma

According to the Global Asthma Report, in 2016, asthma contributed to 23.7 million Disability Adjusted Life Years (DALYs), across all ages (31). The Institute for Health Metrics and Evaluation (IHME), in 2017, reported that asthma represented 0.91% of total DALYs worldwide (32). Globally, asthma is ranked 16th among the leading causes of years lived with disability and represents the number 28th among the leading causes of burden of disease (33). It is predicted that by 2025, 100 million more patients will have asthma (27).

The percentage of DALYs attributed to asthma varies with age groups. According to IHME, among children aged 5-14 years, 2.16% of total DALYs are due to asthma. This percentage is lower for persons 15-49 years old, at 0.9% of DALYS (33). The change could be explained because of the share of the burden with other chronic respiratory symptoms affecting older people, like Chronic Obstructive Pulmonary Disease (COPD), as well as remission of the asthmatic syndrome when reaching adulthood (17, 34). There is an estimation that asthma is responsible for 397,000 deaths worldwide every year (22)**.** Again, we emphasize that these results must be considered with some caution due to limited data from LMIC**.**

1.4.4 Asthma phenotypes

Several studies have tried to identify specific asthma phenotypes (35). These phenotypes represent “groups” of characteristics according to clinical presentation, mechanisms of disease, inflammatory profile and demography (35-37). They could be used as an organized manner in which asthmatic patients can be categorized and treated (19, 21). Some of the most common phenotypes described are allergic asthma, non-allergic, adult-onset, asthma with persistent airflow limitation and asthma with obesity. Each of these phenotypes has its own distinguishing features (19, 37)**.**

1.4.5 Pathophysiology of asthma

Different mechanisms are involved in the pathophysiology of asthma and uniform across phenotypes (Figure 2). According to the definition provided before, inflammation of the airways is the main characteristic in this disease, involving the trachea and going down to terminal bronchioles (21, 36, 38).

In asthma, the airway mucosa is infiltrated with distinct types of inflammatory cells, specially eosinophils and T lymphocytes (21). Other inflammatory cells might be involved in the process, such as activated mast cells, macrophages, dendritic cells and neutrophils (39). Changes are also seen in some structural cells (epithelial, endothelial, nerve cells, etc.) (38). In addition to cells acting directly, there is a range of mediators for this inflammation. Cytokines, chemokines, oxidative stress, nitric oxide and transcription factors are among such mediators (20, 21). This chronic inflammation leads to structural changes or remodeling, that further leads to narrowing of the airways (38). Mucus accumulation, edema and thickening of the airway walls are seen in advanced, and sometimes irreversible, stages of the disease (21). Apart from this inflammatory response, airway hyperresponsiveness plays an important role and results in airway narrowing in response to triggers (20). The various mechanisms for this dynamic abnormality can be related to an excessive contraction of the smooth muscle, thickening of the airway wall and sensory nerves action (38, 40).

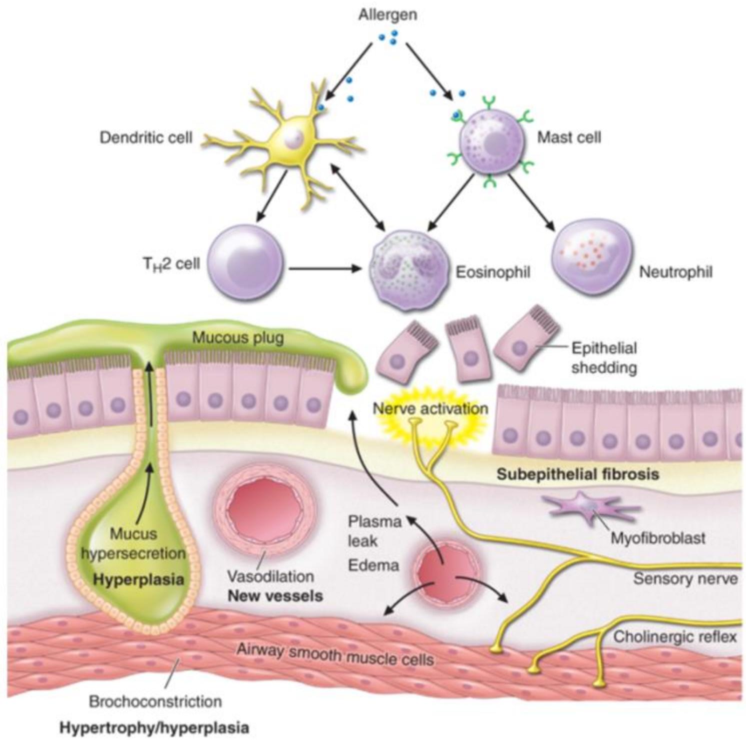


Figure 2. The pathophysiology of asthma**.** From *The pathophysiology of asthma is complex with participation of several interacting inflammatory cells, which result in acute and chronic inflammatory effects on the airway*. Harrison's Principals on Internal Medicine, 20th, by Kasper et al., 2018, www.accessmedicine.com. Copyright McGraw-Hill Education.

1.4.6 Diagnosis of asthma

There is no gold standard available for the diagnosis of asthma (20, 41). The diagnosis is principally based on a detailed history of respiratory symptoms that suggest intermittent airway obstruction and complementary measurements of lung function, with spirometry and peak expiratory flow measurements, reversibility testing with and without bronchodilator, as well as measurement of bronchial hyperreactivity upon administration of an irritant such as methacholine or mannitol (19, 20, 41).

Spirometry is the preferred method to assess airflow limitations and reversibility in patients with suspected asthma (6, 19). Measurements of FVC, FEV_1 and the FEV_1/FVC ratio can give information about obstruction of the airways (20). Normal values of these measurements have been described for age ranges and sex (7, 11). The addition of specific drugs (Beta 2-agonist or bronchodilators) to assess reversibility are also useful in the diagnosis of asthma

(6, 20). PEF is measured by a cheap device and can be used by the patient to do repeated measurements to assess variability over time (19).

Other diagnostic tests include serological tests to detect antibodies to specific allergens (e.g. Radio Allergo Sorbent Test or RAST); skin tests to common inhalant allergens; chest radiographies, principally during exacerbations or complications; and exhaled nitric oxide, used to assess eosinophilic inflammation of the airways and, in some cases, to determine changes in treatment (19-21, 42).

1.4.7 Treatment of asthma

The treatment of asthma is mainly focused on reducing symptom burden and avoiding exacerbations, as no cure is available (19, 43). Typically, the treatment is described in a stepwise approach, with pharmacological and non-pharmacological interventions included (changes in lifestyle) (20). Among the drugs used for this disease, inhaled steroids are considered the main treatment in order to diminish tissue inflammation and reduce exacerbations (19). Besides, inhaled bronchodilators, are used for relieving symptoms. Other interventions are available and in development (20, 41, 43). In general, correct treatment is costly, and oral corticosteroids may be used as a much cheaper alternative in low-income settings in spite of the severe side-effects.

1.4.8 Causes of asthma

The last decades, there has been a major effort to elucidate the causes of asthma (34, 44, 45). Several studies have given important information about the causes and mechanisms that lead to the development of this syndrome (46, 47), however, there is still not a knowledge basis that can guide efficient interventions that might prevent asthma (42). It is well documented that asthma is a heterogeneous condition (39, 48). Several risk factors could predispose to asthma (host and environmental factors), but there are also many triggers that could contribute to worsen the disease (46, 47).

Atopy (production of specific Ig E antibodies) is considered one of the most important risk factors for asthma (21). According to The European Community Respiratory Health Survey

(ECRHS), the overall attributable fraction (AF) of asthma symptoms caused by atopy in adults was 30%, with variations between countries (49, 50). Atopic people may have symptoms of other allergic diseases, such as rhinitis or eczema, which suggests a genetic predisposition (21, 26). Allergens are common triggers of this syndrome and involved in allergic sensitization. Principally dust mites, domestic pets, cockroaches and some foods are among the most known allergens, with some evidence debating their actual role (51-54).

Infections are another important risk factor for the development of asthma (21), as shown by several cohort studies (47). Rhinovirus and Respiratory syncytial virus (RSV) infection during the first year of age has strong association with asthma later in childhood (55). Enteroviral infections have been described to be correlated with asthma later in life, as published in large a population-based study in Taiwan (56). Atypical bacterial infections were studied by Yeh and colleagues and found that incident cases of asthma where closely related to *M pneumoniae* infections (57). A registry-based study found that tuberculosis in parents was associated with higher risk of asthma in their offspring, suggesting a long-lasting immune influence transferred across generations (58). Further, a study found higher asthma risk and lower lung function among persons who were seropositive to the helminths *Toxocara Canis* and *Ascaris*, respectively (59, 60). On the other hand, negative associations have been found between some infections and asthma. However, this is believed to be explained by immune training from microbial diversity rather than benefit of clinical infections and has generally not been confirmed in LMIC settings (61-63).

Occupational exposure is considered to be a common cause of asthma, with attributable fraction that suggested to be around 15-20% of asthma (21, 64-66). Approximately 300 agents have been identified as sensitizers, including substances found in agricultural work, animal facilities and laboratories (67, 68). Also, painting, dyes and cleaning products are associated with an increased risk of asthma (19, 69). The mechanisms through which they act are thought to be immunologically mediated or direct irritants (70).

Other risk factors and triggers have been proposed to influence asthma, such as perinatal and early-life factors (prematurity, tobacco use) (71, 72), outdoor air pollution (73), tobacco (20, 74, 75) and obesity (76). In addition to such risk factors, genetic influence has been shown to play a role (39). Current data show that diverse genes might take part in this process, principally genes involved in the production of specific Ig E, airway hyperresponsiveness, production of inflammatory mediators and T helper 2 cell activation (44, 77, 78).

Finally, recent work exploring different mechanisms for association between genetic factors and environmental influences suggests that epigenetic inheritance may play a role in the development of asthma (48, 79, 80). Studies that have looked at multigenerational associations, have found that parents and grandparents' exposures may have an effect on offspring (12, 45, 81-85). In particular, parental occupational exposures, long before conception of the offspring, is suggested to influence offspring health (86-88). Others have studied cohorts with twin patients and described differences in incidence and characteristics of asthma (78). Lastly, genome-wide association studies have been conducted and found specific changes in DNA in associations with certain exposures and allergic diseases (89, 90).

1.4.9 Asthma, respiratory symptoms and lung function in Guatemala

Guatemala has very limited information about respiratory health and diseases (29, 30, 91). The ISAAC study found a prevalence of asthma of 2.6% in children 13-14 years old in Guatemala (29). A randomized intervention trial, the Randomized Exposure Study of Pollution Indoors and Respiratory Effects (RESPIRE), studied Guatemalan adults and children, and characterized their respiratory health, with further interventions and follow-up (92). In this study, respiratory symptoms and lung function were assessed in Mayan women using biomass fuel for cooking (93, 94). It was found that among these women, 22.6% had cough, 15.1% had phlegm, 25.1% had wheezing and 31.4% had tightness in the chest (93). In addition, questionnaires about their offspring were used to estimate prevalence of asthma symptoms and respiratory infections, where 2.6% of children 4-6 years old were reported to have a diagnosis of asthma, consistent with the results from ISAAC, although for a slightly different age range (91, 95). According to the IHME, asthma represented about 0.65% of the total DALYs and 0.31% of total deaths for the general population in Guatemala in 2017. According to age groups, children between 5 and 14 years old had the higher burden with

2.83% of DALYS and 0.58% of total deaths attributable to asthma. Among people 15-49 years old, the corresponding percentages were 0.55% of DALYs and 0.18% of total deaths (33).

1.5 The textile industry

1.5.1 The industry of textiles and dyes

The textile industry has been part of the human life for thousands of years. Ancient civilizations were admired for their innovative use of textiles and coloring, representing a trademark for some of them, with records found as early as 3500 B.C. (96). Today, the textile industry represents a major source of employment and economy, with approximately 35 million workers around the world, and a contribution of 1 trillion American dollars annually (97).

This industry comprises the development, production, and distribution of textiles, in which yarn and diverse dyes are used to create fabrics (98). There are several hazards related to the textile industry, principally related to the yarns and the treatment of the these, including bleaching, dyeing, impregnating, coating, and weaving, among others (99-101).

The *yarn* itself is a well-studied material that is considered to affect the personnel that manipulates it, with dust and endotoxins being the principal actors (102). Both, natural and synthetic fibers (e.g., cotton, silk, etc.), have been associated with allergic and non-allergic pulmonary diseases in different studies (100). In addition, chemical compounds added to the yarn and the finished fabric, such as formaldehyde and softeners, are associated with different acute and chronic diseases, including cancer (100, 101).

Dyes are an important part of the textile industry, with vast available knowledge about their history, composition and usefulness (98). These can be renewable and biodegradable, which are obtained from natural resources and are named according to their source of extraction (plant, roots, flowers, animal, mineral and microbial) (103-105). On the other hand, dyes can also be synthetic or man-made dyes, defined as artificial colored substances that give textiles permanent colors and are more resistant to light, washing and other processes (106).

Among the different types of synthetic dyes used in the textile industry, azo dyes have been used increasingly due to their rapid production and reduced costs. These account for about 3000 varieties of dyestuff and 70% of the dyes used worldwide (107). As its use is widespread in different industries, they are among the most studied compounds when it comes to their impact on environmental and health problems (99, 107, 108). Finally, some dyes are required to be combined with other chemicals (i.e., mordants) to keep the color in the fabrics for longer time. In fact, there are several studies that support these chemicals are responsible for the health-related effects secondary to the manipulation of dyes (99, 100, 104, 105, 109).

1.5.2 Respiratory health impact of textiles and dyes

There is evidence of health challenges related to manipulation and contact with specific fabrics like cotton, wool and silk, , exemplifying the impact of exposures in the textile factories on the skin and the respiratory system (110). Several studies have described bronchopulmonary symptoms, changes in lung function and irritation of mucous membranes in textile workers who were in contact with synthetic fibers (111, 112). Fishwick et al. described, as well, an important association of exposure to cotton and man-made fibers, with decline in lung function (113).

Zuskin and colleagues found strong evidence that dust exposure in wool mills may cause chronic respiratory symptoms and impaired lung function, based on a study of 216 wool textile workers (114). In addition, in 1998, a study of 400 textile workers in a factory producing synthetic fiber hosiery, found that the exposure to synthetic fiber was associated with low lung function, proved by abnormalities in spirometry values (115).

There is a myriad of symptoms and signs reported in the literature secondary to the contact with textile dyes**.** Studies have shown that many reactive dyes and their metabolites have mutagenic, carcinogenic or cytotoxic properties (107, 108, 116-118). Clark comments that the toxicity of some of the dyes might be caused by oral ingestion and inhalation (98). In fact, several studies have confirmed associations between exposure to dyes and a range of diseases, such as cancer and other chronic conditions (118). Coughing, mucosal irritation, chest tightness, phlegm and dermatitis are all reported to be elicited by dyes, with different mechanisms proposed to explain these harmful effects (108, 115, 119). Evidence supports that direct irritation and formation of antigen-like compounds (serum albumin and reactive dyes) producing immunoglobulin E (Ig E), could be involved, yet other biological effects can be suspected but are not well understood (119-124).

Alanko et al., in 1978, described a relationship between reactive dyes and occupational allergy in patients. He reported four cases of immediate-type asthma and allergic rhinitis in people working with dyes for at least two years. Specific Ig E was demonstrated (120). Early in 1987, a study based on a questionnaire of 400 workers handling reactive dyes, revealed that 15% of the study participants had work-related respiratory and nasal symptoms, while clinical and laboratory investigations suggested an allergic disease mechanism in 21 of the workers with respiratory symptoms (121).

Several small case-series describes allergic reactions to dyes. Park and colleagues found nine patients sensitized to four reactive dyes at one dye industry in Korea (123). Topping et al., visited dye-houses in United Kingdom and found six patients with a clinical history of work-related respiratory symptoms; of which five had positive Ig E for reactive dyes, specifically Lanasol dyes (125). Similarly, in Sweden, a study found that ten workers out of 162 that were exposed to reactive dyes, were symptomatic and among these, five had an allergic confirmation to these dyes (124).

Finally, a study in 135 textile dyeing workers in Croatia found that the prevalence of chronic respiratory symptoms was higher in exposed people, with 6% of them having asthma. Measurements of lung capacity through spirometry were also lower in this cohort, and related to the duration of exposure (69). Recently, a cross-sectional study in Iran, with 101 dyeing workers and 90 workers in a control group were investigated. Questionnaire data revealed that nearly 12% of the exposed workers had asthma. Besides, across-shift spirometry showed lower values in the case cohort (126).

1.5.3 The textile industry among indigenous communities in Guatemala

According to the Association of the Apparel and Textile Industry of Guatemala and the Bank of Guatemala, textiles were the most exported product of the country in 2019. Exports reached 1,644 million American dollars and represented 8.9% of the country's GDP. It is estimated that around 20% of the exports came from traditional textiles (127).

This industry represents an important economic source in the general population. Given that around 45% of the population in Guatemala is indigenous, and that textiles are inherently linked to the Mayan culture, this economic activity is expected to be particularly important in this community (128). Unfortunately, reliable information about the percentage of indigenous people working specifically in this industry is not available in the national census (129).

The indigenous communities around the country, including at least 24 ethnic groups, have been internationally known during several decades for their handcraft textile works (128). These fabrics and their patterns has traditions dating back to ancient Mayans; there was even a Mayan goddess of weaving, Ixchel (130-132) (Chase et al., 2008; Foster, 2002; Halperin, 2008). Nowadays, Guatemalan female weavers (or "tejedoras", in Spanish) continue to create traditional textiles and pass on their skills and knowledge across generations (132-135).

1.6 Socioeconomic status and health situation of indigenous weavers in Guatemala

According to the 2016 report from the Pan American Health Organization (PAHO) on the health of the indigenous groups in Guatemala, poverty and lack of opportunities are the common denominator among these communities. The report explains that the regions with a predominant indigenous population are allocated the least economic resources, and poverty levels reach more than 70% in average. In terms of economic activities, informal jobs are the most common, with agriculture day workers as the most important. Regarding accessibility to health services, the authorities state that rural communities are only partially covered by the health system, mainly due to the centralization of human resources and equipment. This is importantly reflected in the high mortality rates and the extensive use of traditional medicine as an alternative (136).

Mayan weavers represent such a group with limited access to health facilities, and they encounter social exclusion, racism and discrimination when they try to make use of the public health system (137). Furthermore, enrolment of these weavers in taking health decisions at a community level is an important issue that has been focused on in local and national agendas for several decades, with active efforts from different organizations to understand and improve the Mayan weavers' situation as active representatives in the policy making process (137-139).

To the extent of our knowledge, and based on the evidence that supports this project, there are no studies about the lung function, asthma and other respiratory symptoms of the Mayan weavers and their household members in Guatemala, nor on the potential health effects of exposures in the traditional textile industry. There is thus a need to study, through high-quality tools, the respiratory health of these indigenous communities, and investigate the possible association with the several exposures linked to the traditional textile industry.

2 Research questions

1) What is the prevalence of asthma and respiratory symptoms among Mayan communities in Guatemala?
2) What are the characteristics of lung function in these communities?
3) Are there any association between exposures in the textile industry with asthma, respiratory symptoms and low lung function in these communities?

3 Problem statement and rationale

In general, there is scarce knowledge about the characterization of respiratory health of inhabitants in Guatemala, markedly among the numerous indigenous communities settled around the country. Specifically, traditional textile workers in Guatemala, commonly known as weavers, are directly exposed to dusts from the textile fibers they manipulate, as well as to the artificial and natural dyes they use for coloring the fabrics. Members of their households, including husband, offspring, and other relatives (e.g., grandmothers and grandchildren) might be indirectly or directly exposed as well. Moreover, due to the rural location of the villages where they live, other chemical and environmental exposures might be present (e.g., pesticides). Previous studies in countries outside Latin America, suggest that exposures to dusts and dyes in the textile industry may be associated with respiratory symptoms related to asthma and COPD, and may lead to low lung function through irritative or specific immunological mechanisms. Furthermore, limited literature supports that this work environment may have exposures with mutagenic, carcinogenic, or cytotoxic properties.

To the best of our knowledge, there are no available data on the characterization of the lung function, prevalence of asthma and respiratory symptoms of Mayan weavers and their household members in Guatemala. Moreover, there are no published studies that investigate the relationship between the exposure to textile fibers and dyes, and respiratory health outcomes in these populations. This study represents an ambitious project that aims to describe the respiratory health of the inhabitants of indigenous communities in Guatemala dedicated to the traditional textile industry, and their household members. Furthermore, it aims to study possible respiratory health effects associated with occupational exposures in the textile industry, mainly to promote the recognition of potential hazards among traditional weavers and their relatives, and finally help prevent health risks.

4 Objectives

The main aim is to assess the lung function, asthma and respiratory symptoms in indigenous families living in communities in the Sololá region located in Guatemala, and the possible association with exposures in the traditional textile industry.

4.1 Primary

1) To characterize respiratory health in terms of asthma, respiratory symptoms and lung function among inhabitants of the Sololá region in Guatemala working in the traditional textile industry and their household members.
2) To study whether working in the traditional textile industry in this Guatemalan region is associated with asthma, respiratory symptoms and low lung function among these inhabitants.

4.2 Secondary

1) To determine the demographic characteristics of the women involved in the traditional textile industry in these communities and their household members.
2) To characterize the exposures in the weavers' occupational environment and record other potential chemical and environmental risk factors for the development of asthma symptoms and changes in lung function in this population.

5 Hypotheses

We hypothesize the exposures in the textile industry in traditional weavers in Guatemala, may be associated with low lung function, asthma and respiratory symptoms in this population.

6 Methodology

In the following paragraphs, we include a description of the planning and execution of our study as well as the ethical procedures. It is important to mention that this project was planned as a pilot study, with a limited number of participants given its exploratory purpose, and with the vision to expand the study once this pilot study has been completed and more funds are obtained.

As part of the measures taken after the Covid-19 pandemic started, the research team in Norway decided to hire a project coordinator located in Guatemala, Fernando Jerez (FG), who had experience first, on working with the communities in rural Guatemala, mainly with the weavers, and second, in performing fieldwork in the area. Moreover, this project coordinator built a team conformed by a local social worker, Paulina Collum (PC), and other health workers (HWs), to implement the project according to the protocol developed by the research team. In the following paragraphs, I give a detailed description of these processes and the tools that were used.

To be noted, this study was designed to collect information providing data for two master theses with partially interrelated topics. The present thesis is focused on the lung health (mainly lung function and asthma) of the participants and the relation to occupational exposures in the textile industry, and specific details are given for the methods that are relevant for this purpose.

6.1 Study design

This project was designed as a both descriptive and analytical cross-sectional study. By using a detailed interviewer-led questionnaire and several clinical investigations (i.e., anthropometry and spirometry) and obtention of bio samples of a cohort of participants living in rural Guatemala, we assessed exposures and outcomes at the same time, recording potential confounding factors and other relevant information as well. Associations between exposure to the traditional textile industry and respiratory symptomatology were estimated with the information collected.

6.2 Location and setting

Guatemala is a country located in Central America. It is divided in 22 regions or departments, with Solola being one of them. In this region, the Lake Atitlan is surrounded by several villages where indigenous Mayan people known for their traditional textile products live (140). This study was based in San Pablo la Laguna, a village close to the lake and where the study site was set up. Participants who lived in this and other close villages were invited to travel to San Pablo la Laguna to complete the interviews and the clinical assessments. The maps in **(Figure 3)** shows the region and an approximate location of the village where the study site was set.

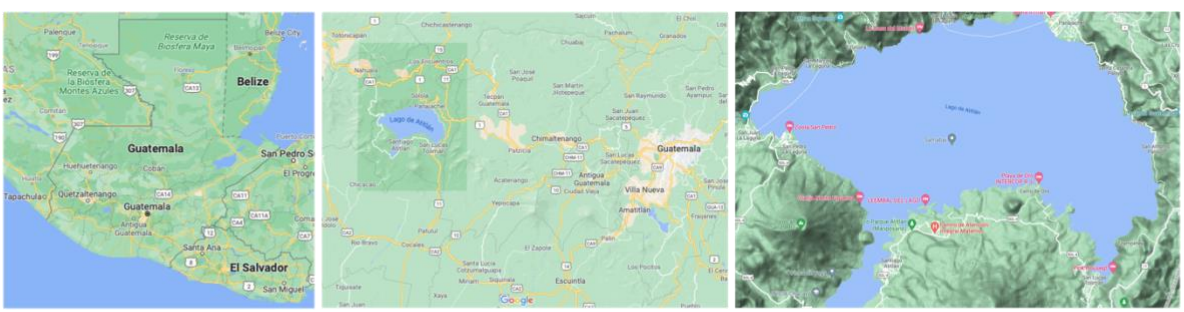


Figure 3. Map of Guatemala, the Solola region, Lake Atitlan and approximate location of San Pablo La Laguna (study site). From: Google Maps, 2022. Google Maps (online). Available through: <https://www.google.com/maps/> (Accessed 3 January 2022).

6.3 Target and study population

The Solola region has an estimated population of 430,000 inhabitants, of which around 90% belong to an indigenous ethnicity (141). The target population for our study was the indigenous women (weavers) working in traditional textile industries and their household members, living in communities around the Lake Atitlan.

6.3.1 Approaching the weavers

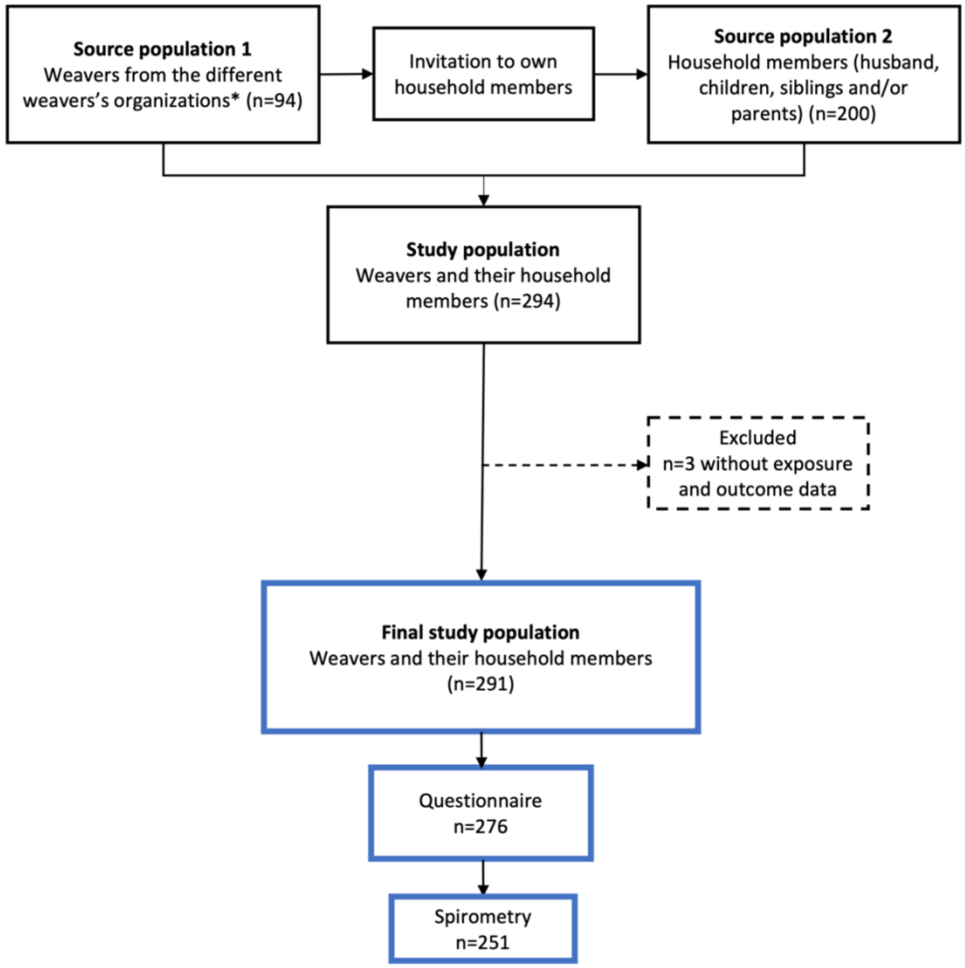
Our first approach to the target population was performed by our co-investigator Ana Lorena Ruano (ALR) in conjunction with the Center for Equity and Governance for Healthcare in Guatemala (CEGSS) (<https://cegss.org.gt/en/>). An exploratory informal survey was done among some of the weavers' organizations, where great interest in participating in this research was shown and commentaries were received that a study on lung health and asthma/allergies, as well as the investigation of these in relation to their occupation, would be useful.

Using reference information obtained from PC, we were provided with names of the specific weavers' organizations in the area that have previously worked and collaborated with ALR, FJ and PC. The weavers' organizations that participated in our project were the "Red de Defensores Comunitarios por el Derecho a la Salud (REDC Salud)", "Red de Mujeres Estrella Tzutujil", "Asociación de Mujeres Ixoq Ajqne" and "Fundación Tradiciones Mayas". FJ and PC carried out a recognition trip at the beginning of March 2021 and visited different villages where the weavers and their families live and work. Meetings were held with part of the organizations' members and an introduction to the study was given, with an invitation to participate. FJ and PC kept constant communication with the weavers' organizations until the fieldwork took place.

6.3.2 Number of participants and sampling of the study population

The number of participants invited to the pilot study was determined by available funding. (Observations from the pilot study will be used for power calculations when planning a subsequent extended study). Sampling of the cohort was done through the leaders of the weavers' organizations ("Red de Defensores Comunitarios por el Derecho a la Salud (REDC

Salud)", "Red de Mujeres Estrella Tzutujil", "Asociación de Mujeres Ixoq Ajqne" and "Fundación Tradiciones Mayas"), who extended the invitation to weavers in each organization, as well as soliciting them to invite three family members living in their same household, including offspring, husband, siblings, and/or the weavers' parents. A representative final sample was built by including inhabitants of several small villages surrounding the study site, which allowed us to characterize the respiratory health of more areas around the lake. Originally, we planned to include participants older than 4 years of age. However, after communicating with the leaders of the weavers' organizations and collaborators, a lower age cutoff of 14 years was set, given the concerns that possible problems might have arisen if any of the younger participants should have experienced any disagreeable effect (even if explained in the informed consent). In total, 94 weavers (each representing a household) were invited to participate in the pilot study and 291 participants were included in the final sample. The sample selection is depicted in Figure 4.



***Weavers' organizations:** Red de Defensores Comunitarios por el Derecho a la Salud (REDC Salud), Red de Mujeres Estrella Tzutujil, Asociación de Mujeres Ixoq Ajqne and Fundación Tradiciones Mayas

Figure 4. Study population. Flowchart that shows sample selection, and numbers who completed a questionnaire and spirometry.

6.3.3 Inclusion and exclusion criteria

Concerning the index participants, we included Guatemalan female weavers, members of one of the weavers' organizations, living in any village in the Solola region, and who were 18 years old or above. Moreover, we included family members living in the same household as the index person: offspring of age 14 years or older (any gender); husband (father of the offspring); and the weavers' parents or siblings (any gender). Persons with a serious health condition were not invited.

6.4 Materials and Methods

Different research tools were used during the execution of this project, which was planned and developed based on the protocol used in the Respiratory Health In Northern Europe, Spain and Australia (RHINESSA) studies in several countries (see <www.rhinessa.net> for more information). The study protocol included a detailed standardized interviewer-led questionnaire, anthropometric measurements including height, weight and abdominal circumference, measurement of blood pressure, spirometry to measure lung function, skin prick tests for common local allergens, and collection of blood and urine samples. The data collection was supervised by FJ and performed by a team of local HWs trained for the study. See Figure 5 for an overview of the protocol.

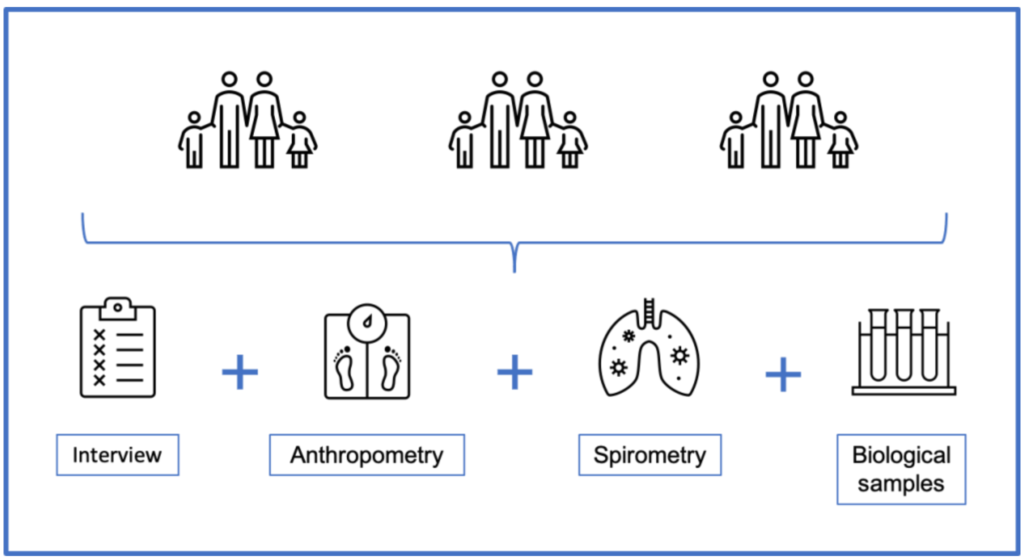


Figure 5. Overview of the study protocol. Index participants and household members were invited to answer an interviewer-led questionnaire, provide anthropometric measurements, perform a spirometry and give biological samples.

6.4.1 Health personnel and training

A group of Guatemalan health workers were recruited by the project coordinator to perform the field work. These were inhabitants of the same region where the study site was set, with a nursing background or similar, and sufficient knowledge of Spanish and of the local indigenous languages (Tzutujil or Kaqchikel). The training was undertaken prior to the initiation of the study, with didactic videos and an informative presentation which included important aspects of the different steps included in the protocol.

6.4.2 Standardized interview (Appendix A)

Standardized questionnaires previously used on the multinational studies ECRHS, ISAAC and RHINESSA were used as basis, and adapted according to the necessities of the project. Different age-specific versions of these questionnaires were created, which included, among other aspects:

(a) Personal details are, *i.e.*, age, gender, occupational tenure and its duration, and number of hours daily, number of children, smoker/non-smoker status, and family history of diseases.
(b) Asthma and respiratory symptoms – type, onset, duration, and frequency. Questions concerning other respiratory diseases, physical disorder, and other conditions.
(c) Chemical and biological exposures of the participants at their work and home environments.
(d) Access and use of traditional and non-traditional medicines and health facilities.
(e) For the index participants, questions about their job as weavers were included.

A basic set of questions about respiratory symptoms was included in all versions of the questionnaires, while there were differences according to age regarding the information sought about occupations, relatives, etc. Questions related to allergic conditions were also included, however, these questions are not under the scope of this specific project.

Paper-based questionnaires were filled in as a face-to-face standardized interview by the HWs, who translated the questionnaires to one of the two important local languages (Tzutujil or Kaqchikel). A parent or a legal representative was present when interviews were performed with participants under age 18 years.

6.4.3 Clinical assessments

Standard operation procedures (SOP) (Appendix C) were based on procedures previously used in the RHINESSA studies and using similar equipment. Following the attached SOPs, we performed measurement of the blood pressure, height, weight, waist and hip circumference, and spirometry of the participants.

6.4.3.1 Blood pressure and anthropometry

Initially, the systolic and diastolic blood pressure in a seated position were measured in each of the participants. A maximum of two measurements was performed using a digital upper arm blood pressure monitor (Model Omron 705-IT®). In addition, participants were weighed with a digital flat scale (Model Seca 813®), and height was recorded using a portable stadiometer. The measurements were recorded to the nearest 1kg or 1cm, respectively. Finally, hip and waist circumferences were measured with a tape calibrated in millimeters, with all measurements taken to the nearest millimeter.

6.4.3.2 Spirometry

Spirometric measurements were done following specific SOP based on the ATS/ERS recommendations for standardization of lung function testing (6). Participants answered a short questionnaire (Appendix B) before the clinical assessments were done, with the purpose of excluding them from performing spirometry if they had a respiratory infection in the last three weeks and/or had a major surgery in the last month.

After the anthropometric measurements were recorded, eligible participants were invited to perform a lung function test using an ATS/ERS authorized portable spirometer (ndd EasyOne® Air). Disposable single-use Flow Tubes (EasyOne®) were used. No periodic calibrations were needed, according to the manufacturer's manual. Participants received a demonstration by the HWs on how to complete the procedure, and doubts were clarified before it took place. All the measurements were led by the same nurse. Each participant had a maximum of five attempts to achieve at least three acceptable and reproducible spirograms. Data was immediately secured and stored in a portable computer at the study site, further collected by the project coordinator at the end of each day of fieldwork. Only simple spirometry was performed, bronchodilator spirometry was not included as this would have reduced the feasibility of the study.

6.4.4 Biomaterials and biobank

Biological samples were collected and stored in a biobank for future analyses. The samples collected were:

- Whole blood (1-2 EDTA tubes, 10 ml each);
- Whole blood for nucleic acid preserving medium (One Paxgene tube®, 2.5 ml);
- Urine (One BD Vacutainer® urinalysis preservative tube, 7-9 ml).

The samples were obtained at the study site by our group of HWs, following specific SOP for secure handling of biomaterial (See Appendix C). The material was kept at room temperature (according to the manufacturers' indications) and stored in a freezer at approximately -20 degrees after three hours from the extraction/obtention. The biomaterial will be shipped to Norway where they will be frozen to -80 degrees in facilities belonging to the RHINESSA team. Once funds are available, metabolites, immunological and omics assessments will be done on the samples, aiming to link this information to the already assessed exposures and outcomes (from questionnaire and clinical investigations).

6.4.5 Fieldwork and data collection

In the study site, a multipurpose room belonging to the municipality was used for one week. In coordination with FJ, PC and the HWs, different stations, each with a specific task, were set up for the execution of the project. Participants were received in family groups and informed consents (see Appendix D) were delivered and verbally explained in detail in the local languages. Once the consents were signed and doubts were clarified, the participants were conducted, one by one, through each of the stations to complete the four parts of the protocol for this project (questionnaire, anthropometry/blood pressure, spirometry, and bio sampling). Once the protocol was completed, an economic compensation was given to each of the participants in accordance with the information previously given and included in the informed consent (for ethical concerns, see "Ethical and security considerations"). Restrictions and recommendations announced by the local government concerning Covid-19 were taken into consideration to avoid risks for the participants and the HWs/collaborators.

6.4.6 Outcomes

6.4.6.1 Respiratory symptoms and conditions

The following outcomes were analyzed in this project: asthma, wheeze, chest tightness, shortness of breath, and other respiratory symptoms and conditions. These were obtained from a set of questions included in the interviewer-led questionnaire responded to by all the participants. Table 1 shows the outcomes and the questions used to define these symptoms and illnesses.

Table 1. Respiratory symptoms/diseases and their definition.

Respiratory symptoms or conditions	**Definition[1]**
Ever wheezing	Have you had wheezing or whistling in your chest at any time in the last **12 months**?
Wheezing with breathlessness	Have you been at all breathless when the wheezing noise was present?
Wheezing without cold	Have you had this wheezing or whistling when you did ***not*** have a cold?
Tightness in chest	Have you woken up with a feeling of tightness in your chest at any time in the last **12 months**?
Shortness of breath at rest in the day	Have you had an attack of shortness of breath that came on during the day when you were at rest at any time in the last ***12 months***?
Shortness of breath when active	Have you had an attack of shortness of breath that came on ***following*** strenuous activity at any time in the last ***12 months***?
Ever woken by shortness of breath	Have you been woken by an attack of shortness of breath at any time in the last **12 months**?
Morning cough	Do you ***usually*** cough first thing in the morning?
Chronic cough	Do you usually cough like this on most days for as much as three months each year?
Morning phlegm	Do you ***usually*** bring up any phlegm from your chest first thing in the morning?
Chronic phlegm	Do you bring up phlegm like this on most days for as much as three months each year?
Ever difficulty breathing	Do you ever have trouble with your breathing?
Difficulty breathing when walking on ground level	Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill?
Ever asthma	Have you ever had asthma? / Have you used traditional medicine during the last 12 months for breathing problems, asthma or wheezing/wheezing in the chest?
Ever chronic bronchitis	Has a doctor ever told you that you have chronic bronchitis?
Ever tuberculosis	Have you ever been treated for tuberculosis?

[1]Taken from questionnaires. See Appendix A.

6.4.6.2 Criteria for use of lung function measurements and reference equations

Acceptable quality measurements were defined as those obtained after three acceptable maneuvers, with an exhalation of at least six seconds, and explosive start with a back-extrapolation volume <100mL or ≤5% of FVC, with no glottis closure, cessation of airflow or evidence of a leak, no coughs and that met the end-of-test criteria (exhaling for ≥6 s with <50mL being exhaled in the last 2 s). Repeatability criteria, meaning that the difference between the two largest FVC values must be ≤0.150 L, and the difference between the two largest FEV1 values must be ≤0.150 L, was also taken into consideration (6).

6.4.7 Exposure assessment

Specific occupation and environmental exposures were assessed using the interviewer-led questionnaires (Appendix A). In weavers, we included textile industry-related questions investigating hours and days of exposure to different processes: manipulation of yarn or fabric before it is dyed, dying process of the yarn/fabric (including type of dye-synthetic/natural/both), and weaving-finishing the product. In **household members** older than 10 years we recorded occupations/professions and the duration of each of their jobs. Finally, for both the **weavers and the household members**, we assessed frequency of exposure to pesticides, insecticides, and disinfectants at home and at work; type of animals kept close to their houses; use of solid-fuel stoves or other appliances to cook and heat water; current and previous exposure to tobacco smoking and quantity (second-hand tobacco smoking included); and use and frequency of different medications, both, traditional and Western medicine.

In **children under 10 years**, an age-specific questionnaire was used, investigating: household-related factors for them and their parents (location, relatives living or sharing rooms and livestock near home); own and parental previous medical history (diverse infections, other health-related conditions and use of medicines); and exposure to second-hand tobacco smoke.

6.4.8 Statistical analyses

Descriptive analyses were performed to present the general characteristics of the population, the prevalence of asthma, respiratory symptoms and lung function measurements obtained from the spirometry, and the reported environmental hazards. Directed acyclic graph (DAG) was used as a tool to help identify confounders and other covariates in the statistical model. Regression models were included to analyze the association between occupations and the presence of asthma, respiratory symptoms, and low lung function. Logistic regressions with adjustment for age were used for analysis of asthma and respiratory symptoms; linear regressions were used for analyses of FVC with adjustment for sex, age and height. The analyses were done using STATA 17.0 (StataCorp, College Station, TX) and Microsoft Excel.

7 Ethical and security considerations (Appendix D and E)

Approvals from the Regional Committees for Medical and Health Research Ethics (REK nord with reference 203917) in Norway and from the Ministry of Ethics in Health in Guatemala (Reference 29-2020) have been granted. Local authorities and the weavers' organizations were informed about the project, with general agreement before the development of the protocol and before conduction of the field work. Written informed consents (explained thoroughly in local languages-Tzutujil or Kaqchikel) were signed by all the participants, or by a parent or guardian for study participants aged 16 years or less before starting the investigation, and a copy of this was given to each study participant.

Included in the informed consent, a detailed description of the protocol was given, as well as the process of bio sampling and further securement of the data. An economic compensation (170 NOK or equivalent in local currency) was given to the participants older than 15 years, aiming to partially cover the expenses for transportation to the study site, meals and possible loss of working hours during the visit. The compensation was given to all who fully or partially participated in the project.

To keep collected information secure, the paper-based questionnaires, consents, bio samples and the results from the spirometry were coded with a unique ID and later secured by the project coordinator on the study site. The questionnaires and consent forms were scanned and sent, together with the spirometry results, to the team in Norway through a safe file server. The electronic files are kept in a secure server of HelseVest, and the key between IDs and personal identification details is kept in a separate location on the secure server and is only available to the Bergen RHINESSA lead data manager (Ane Johannessen -AJ). The hard copy of the documents was shipped to Norway and further secured in facilities of the RHINESSA team, with key available to the lead data manager. The bio samples collected were kept by the project coordinator in a freezer at -20 degrees, in Guatemala, and will be shipped to the Bergen RHINESSA biobank in Norway to be stored at -80 degrees until further investigation.

Important to note, before the investigation of the participants started, we included a "Getting ready questionnaire" (Appendix B), principally to make sure that the participants had no recent respiratory infections or other conditions that could possibly pose a risk to the participants and the health personnel/collaborators. In addition, we maintained a safe distance and asked everyone to wear facemask, measures that were in line with the local authorities' advice for the pandemic.

8 Results

8.1 General characteristics of the study sample

We included a total of 291 participants who answered to an interviewer-led questionnaire. A core questionnaire was used in all study participants, while some questionnaire parts differed with regard to whether the participant was a weaver or not or according to their age. In **Table 2** we present the general characteristics of the study sample, and we include three subgroups of the sample according to the participant's occupation and sex: weavers, female non-weavers, and male non-weavers. The general mean age of the participants was 34.2 years, ranging from 14 to 77 years old. The mean age was somewhat lower in the male non-weavers' group (31.9), 82% of all the study participants were female, and the majority (95%) of those asked about their ethnicity, responded that they belonged to a Mayan group.

Table 2. Characteristics of the study population.

	All participants (n=291)	**Weavers (n=130)**	**Female non-weavers (n=95)**	**Male non-weavers (n=47)**
Mean age, years (SD)	34.2 (13.4)	34.3 (12.2)	34.5 (13.9)	31.9 (13.2)
Age groups, n (%)				
14-24 years	79 (27.1)	33 (25.3)	26 (27.4)	14 (29.8)
25-34 years	85 (29.2)	38 (29.2)	23 (24.2)	20 (42.6)
35-44 years	71 (24.4)	37 (28.5)	27 (28.4)	5 (10.6)
45-54 years	25 (8.6)	9 (6.9)	10 (10.5)	4 (8.5)
≥55 years	31 (10.7)	13 (10)	9 (9.5)	4 (8.6)
Sex, n (%)				
Female	239 (82.1)	126 (96.9)	95 (100)	0
Males	52 (17.9)	4 (3.1)	0 (0.0)	47 (100)
Height, cm (SD) [1]	147.9 (6.8)	146.4 (5.1)	145.3 (4.8)	158.5 (5.8)
Weight, kg (SD)	63.7 (12.3)	64.6 (12.1)	62.8 (12.9) [2]	64.8 (12.1) [2]
BMI, mean (SD)	29.1 (5.7)	30.1 (5.6)	29.7 (5.9) [3]	25.6 (4.3) [3]
Ethnic group, n (%) [a]	**n=134**	**n=79**	**n=45**	**n=8**
Mayan	127 (94.8)	75 (94.9)	43 (95.6)	8 (100)
Ever smoking, n (%) [a]	**n=276**	**n=130**	**n=95**	**n=47**
Yes	6 (2.2)	0 (0.0)	0 (0.0)	6 (12.8)
No	261 (94.6)	126 (96.9)	90 (94.8)	41 (87.2)
Occupation, n (%)				
Weaver	130 (44.7)	130 (100)	0 (0.0)	0 (0.0)
Farmer	20 (6.9)	0 (0.0)	0 (0.0)	20 (42.5)
Handcraftman	28 (9.6)	0 (0.0)	21 (22.1)	7 (14.8)
Unemployed	6 (2.2)	0 (0.0)	3 (3.2)	3 (6.4)
Housewife	61 (22.1)	0 (0.0)	61 (64.2)	0 (0.0)
Student	3 (1.1)	0 (0.0)	2 (2.1)	1 (2.1)
Poor health	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	24 (8.2)	0 (0.0)	8 (8.4)	16 (34.0)
Education level, n (%) [a]	**n=68**	**n=51**	**n=15**	**n=2**
None	17 (25)	11 (21.6)	5 (33.3)	1 (50)
Primary incomplete	25 (36.7)	19 (37.3)	5 (33.3)	1 (50)
Primary complete	3 (4.4)	2 (4.0)	1 (6.7)	0 (0.0)
Secondary incomplete	17 (25)	14 (27.5)	3 (20)	0 (0.0)
Secondary complete	1 (1.5)	1 (2.0)	0 (0.0)	0 (0.0)

Healthcare services, n (%) [a]	**n=208**	**n=98**	**n=65**	**n=42**
Traditional healer	21 (10.1)	15 (15.3)	4 (6.2)	2 (4.8)
Nurse	48 (23.1)	34 (34.7)	8 (12.3)	7 (16.7)
Medical doctor	9 (4.3)	5 (5.1)	2 (3.1)	2 (4.8)
Hospital	3 (1.4)	2 (2.0)	1 (1.5)	0 (0.0)
Other	4 (1.9)	0 (0.0)	4 (6.1)	0 (0.0)
Use of medicine, n (%)[a]				
Traditional	80 (38.1)	33 (33.3)	28 (42.6)	18 (42.9)
Western	41 (19.5)	22 (22.2)	12 (19.1)	6 (14.3)
None	24 (11.9)	16 (17.2)	2 (2.9)	6 (14.3)
Covid-19 infection, n (%)[a]				
Yes	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
No	196 (94.8)	91 (92.9)	62 (95.6)	40 (95.2)

[1]Height measurements shown for participants equal and older than 18 years (all participants – n=271/weavers – n=123/female non-weavers – n=88/male non-weavers – n=42)
[2]Weight measurements shown for participants equal and older than 18 years (female non-weavers – n=88/ male non-weavers – n=42)
[3]BMI calculations shown for participants equal and older than 18 years (female non-weavers – n=88/ male non-weavers – n=42)
[a]Not part of the core questionnaire. Only asked to the shown subsample (n).

The mean height was about 145 cm in women and 159 cm in the men, this was calculated in participants older than 18 years who are likely to have attained their adult height. The mean weight was measured to 63.7 kg and mean BMI calculated to 29.1. The mean weight in women was 62.8 and mean BMI was 29.7, while for men, the mean weight was measured to 64.8 kg and the mean BMI calculated to 25.7.

Considering other characteristics of the study population (**Table 2**), only 2.2% of the participants smoked tobacco. Regarding their occupation, 45% answered that they were weavers and 22% housewives, the rest responded that they were farmers, performed handcraft work, and few were unemployed or students. With regard to their education level, most had incomplete primary school (37%) and 25% had incomplete secondary school, while 25% reported no education. When reporting use of healthcare services in the last 12 months, 23% of the participants answered that they visited a nurse to seek for help, 10% used a traditional healer, and low percentages responded that they visited a medical doctor, attended a hospital or visited other healthcare services. Furthermore, use of medicine in the last 12 months was reported: 38% answered that they used traditional medicine and 19% used Western medicine. Finally, no participants reported having had Covid-19.

8.2 Other exposures

The participants reported, as part of the standardized interview, about other chemical exposures not strictly related to their occupation (**Table 3**). A subsample was asked about the use of heating appliances at home (mainly to heat water), and practically all reported using solid fuel while only 3 persons reported using gas. This subsample was also asked about the type of stove the participants had at home, with solid fuel stove being the most prevalent (82%). None of the participants reported using electric stove or microwave.

Table 3. Chemical exposures at home and at work.

	All participants (n=276)	**Weavers (n=130)**	**Female non-weavers (n=95)**	**Male non-weavers (n=47)**
Pesticides at home, n (%)[1]				
Never	47 (17)	34 (26.19)	7 (7.4)	6 (12.8)
Sporadically	161 (58.3)	58 (44.6)	72 (75.8)	31 (65.9)
Depending on season	19 (6.9)	12 (9.2)	4 (4.2)	3 (6.4)
Whole year	15 (5.4)	6 (4.6)	7 (7.4)	2 (4.3)
Pesticides at work, n (%)[1]				
Never	62 (22.5)	46 (35.4)	7 (7.4)	8 (17)
Sporadically	153 (55.4)	48 (36.9)	75 (78.9)	31 (65.9)
Depending on season	15 (5.4)	11 (8.5)	2 (2.1)	3 (6.4)
Whole year	10 (3.6)	5 (3.8)	4 (4.2)	1 (2.1)
Heating appliances, n (%)[a]	**n=138**	**n=84**	**n=45**	**n=8**
Solid fuel	120 (86.8)	80 (95.2)	33 (73.3)	7 (87.5)
Gas	3 (2.2)	2 (2.4)	1 (2.2)	0 (0.0)
Type of stove, n (%)[a]				
Solid fuel	113 (81.9)	66 (78.6)	42 (93.3)	5 (62.5)
Gas	5 (3.6)	4 (4.7)	1 (2.2)	0 (0.0)
Electric	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Microwave	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Other	2 (1.4)	1 (1.2)	0 (0.0)	1 (12.5)
Cleaning at home, n (%)[1 a]	**n=203**	**n=127**	**n=65**	**n=42**
Never	2 (0.98)	2 (1.5)	0 (0.0)	0 (0.0)
<1 day/week	74 (36.5)	50 (39.3)	8 (12.3)	16 (38.1)
1-3 days/week	30 (14.8)	13 (10.2)	9 (13.8)	8 (19.0)
4-7 days/week	94 (46.3)	30 (23.6)	47 (72.3)	17 (40.5)

[1]In the last 12 months
[a]Not part of the core questionnaire. Only asked to the shown subsample (n).

Finally, another important aspect related to hazardous chemical exposures was the use of pesticides in these communities. We asked about the frequency of use of pesticides at home and at work, and 58% of the participants reported using pesticides sporadically at home and 55% at work. Important to note, 5% responded they used pesticides at home all year around, while 4% answered the same with regard to their workplace.

8.3 Respiratory symptomatology and conditions

The participants described several respiratory symptoms and lung-related conditions (**Table 4**). Overall, wheezing was reported by 9.4% of the participants, wheezing with breathlessness by 4% and wheezing without a cold by 2.5% of them. Tightness in the chest was reported by almost 5% of the respondents. Furthermore, shortness of breath at different situations was also asked: only 3% responded having shortness of breath at rest during the day, 4.3% answered that they have had the same symptom when they were active, and 4% that were woken up by shortness of breath. The presence of breathing difficulty was reported by 7% while breathing difficulty while walking on ground level was reported by 5.4%.

Regarding specific respiratory conditions, asthma was considered as present if the participant responded "yes" to either one or both of the following questions: "Have you ever had asthma?" and "Have you used traditional medicine during the last 12 months for breathing problems, asthma or wheezing / wheezing in the chest?". Only 3 persons responded "yes" to ever having had asthma (around 1%), while the use of traditional medicine for asthma was a more common answer, reported by almost 5% of the weavers. Moreover, diagnosis of chronic bronchitis was reported only by 1% of weavers and of female non-weavers, while none of the participants reported ever having received treatment for tuberculosis.

Table 4. Description of respiratory symptoms and respiratory diagnoses, classified according to occupation related to weaving.

	All participants (n=276)	**Weavers (n=130)**	**Female non-weavers (n=95)**	**Male non-weavers (n=47)**	**p[1]**
N (%)					
Ever wheezing	26 (9.4)	17 (13.1)	5 (5.3)	3 (6.4)	0.103
Wheezing with breathlessness	11 (3.9)	6 (4.6)	2 (2.1)	2 (4.3)	0.589
Wheezing without cold	7 (2.5)	3 (2.3)	1 (1.1)	2 (4.3)	0.465
Tightness in chest	13 (4.7)	7 (5.4)	2 (2.1)	3 (6.4)	0.379
Shortness of breath at rest in the day	8 (2.9)	3 (2.3)	2 (2.1)	3 (6.4)	0.291
Shortness of breath when active	12 (4.3)	4 (3.1)	5 (5.3)	2 (4.3)	0.053
Ever woken by shortness of breath	11 (3.9)	4 (3.1)	4 (4.2)	2 (4.3)	**0.032**
Morning cough	12 (4.3)	7 (5.4)	3 (3.2)	2 (4.3)	0.672
Chronic cough	9 (3.3)	6 (4.6)	2 (2.1)	1 (2.1)	0.469
Morning phlegm	8 (2.9)	6 (4.6)	2 (2.1)	0 (0.0)	0.214
Chronic phlegm	6 (2.2)	5 (3.8)	1 (1.1)	0 (0.0)	0.178
Ever difficulty breathing	20 (7.2)	12 (9.2)	4 (4.2)	3 (6.4)	0.325
Difficulty breathing when walking on ground level	15 (5.4)	7 (5.4)	5 (5.3)	2 (4.3)	0.481
Asthma					
Ever asthma	3 (1.1)	1 (0.8)	1 (1.1)	1 (2.1)	
Traditional medicine for asthma	7 (2.5)	6 (4.6)	1 (1.1)	0 (0.0)	0.113
Ever chronic bronchitis	2 (0.7)	1 (0.8)	1 (1.1)	0 (0.0)	
Ever tuberculosis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	

[1]All p-values <0.05 = significant and are marked bold. P-values are estimated from chi-squared test for categorical values weavers, female non-weavers and male non-weavers.

Weavers reported higher prevalence of wheezing (13%) and of ever having breathing difficulty (9.2%), and slightly more symptoms like morning and chronic cough and phlegm (table 4). On the other side, non-weavers, especially male, responded “yes” more often to the presence of tightness in the chest and breathlessness at rest and when being active.

In addition to the prevalence of the respiratory symptoms/conditions, we estimated the associations of selected symptoms (those reported by at least 5 persons) with the occupation-related subgroups the participants belonged to. **Table 5** shows the results from logistic regressions of three models, with the reference category defined as the non-weavers group. Overall, the results indicated a consistent, though mostly non-significant, higher risk of presenting several of the symptoms among participants working with weaving. This was more convincing for symptoms such as ever wheezing, wheezing with breathlessness and the presence of tightness in the chest, related to the spectrum of symptoms in asthma, and statistically significant only for ever wheeze. Some symptoms such as those related to shortness of breath, appeared to be less common among weavers. Higher risks among weavers were suggested for presenting cough and phlegm, but there were very low numbers reporting these symptoms.

The results were quite similar with no adjustment (Model 1), with adjustment for age (Model 2), and when only women were included (Model 3). Considering only the women, the weavers presented a higher risk of having wheezing (OR 2.91; 95%CI 0.99-7.92) and indicated higher risk of wheezing without cold (2.43; 0.25-23.9), wheezing with breathlessness (2.35; 0.46-11.9) and tightness in the chest (3.05; 0.60-15.4).

Weavers showed a borderline significant higher risk of asthma treated with traditional medicine (6.99; 0.83-59.2, p 0.075), quite consistent when adjusting for age and when excluding males from the model.

Table 5. Logistic regression analyses of respiratory symptoms and conditions as related to weaving (reference category non-weavers).

	All (Model 1) [1]		**All (Model 2) [2]**		**Women only (Model 3) [3]**	
	Crude OR (95% CI) [4]	**p[5]**	**Adj OR (95% CI)**	**p**	**Adj OR (95% CI)**	**p**
Ever wheezing	2.52 (1.05-6.06)	**0.039**	2.53 (1.05-6.08)	**0.038**	2.91 (0.99-7.92)	**0.050**
Wheezing with breathlessness	1.67 (0.46-6.06)	0.435	1.68 (0.46-6.11)	0.429	2.35 (0.46-11.9)	0.302
Wheezing without cold	1.10 (0.22-5.58)	0.904	1.25 (0.24-6.42)	0.793	2.43 (0.25-23.9)	0.448
Tightness in chest	1.55 (0.48-5.01)	0.465	1.55 (0.48-5.03)	0.464	3.05 (0.60-15.4)	0.179
Shortness of breath at rest in the day	0.64 (0.15-2.74)	0.550	0.65 (0.15-2.79)	0.559	1.25 (0.20-7.90)	0.812
Shortness of breath when active	0.85 (0.50-1.44)	0.541	0.83 (0.49-1.42)	0.503	0.55 (0.31-0.99)	**0.047**
Ever woken by shortness of breath	0.92 (0.54-1.56)	0.752	0.91 (0.53-1.56)	0.729	0.59 (0.33-1.05)	0.074
Morning cough	1.64 (0.51-5.31)	0.407	1.69 (0.52-5.55)	0.386	2.00 (0.50-8.07)	0.327
Chronic cough	2.36 (0.58-9.65)	0.231	2.38 (0.58-9.74)	0.228	2.46 (0.48-12.4)	0.278
Morning phlegm	3.50 (0.69-17.7)	0.129	3.53 (0.70-17.9)	0.127	2.46 (0.48-12.5)	0.279
Chronic phlegm	5.88 (0.68-51.1)	0.108	6.01 (0.69-52.3)	0.104	4.07 (0.47-35.5)	0.204
Ever difficulty breathing	2.00 (0.76-5.25)	0.159	1.99 (0.76-5.24)	0.161	2.3 (0.76-7.79)	0.136
Difficulty breathing when walking on ground level	1.34 (0.56-3.21)	0.516	1.34 (0.56-3.23)	0.509	1.86 (0.63-5.49)	0.261
Asthma						
Traditional medicine for asthma	6.93 (0.82-58.4)	0.075	6.99 (0.83-59.2)	0.074	4.95 (0.58-42.2)	0.143
Ever chronic bronchitis	1.09 (0.7-17.7)	0.950	1.09 (0.7-17.8)	0.949	0.77 (0.05-12.6)	0.855

[1]Model 1: crude values.
[2]Model 2: adjusted for age.
[3]Model 3: stratified by sex, adjusted for age; shown values from women participants.
[4]OR (95% CI): Odds Ratio (95% Confidence Interval).
[5]All p-values <0.05 are marked bold.

8.4 Lung function

Lung function measurements of the participants were obtained with an EasyOne Air spirometer. Participants were instructed by a HW (only one HW oversaw the test during the entire study) on how to perform a FVC maneuver; the training of this HW included instruction by a video. However, the results/curves showed that many participants performed a slow vital capacity (SVC) maneuver (i.e., complete expiration after a maximal inspiration without forced or rapid face), rather than a true forced maneuver. These results, though useful to a certain degree, should be used with caution to describe lung health.

From a total of 251 spirograms, only 143 were considered acceptable according to the ATS/ERS specifications previously mentioned in Section Methodology. Furthermore, we restricted the upper limit of the values to discard outliers, using as reference the maximum FVC values (7.0 L) suggested by the equation described by Hankinson et al., for Mexican American populations (9), leaving only 111 measurements for further analysis. **Table 6** shows the measured FVC, FEV_1 and FEV_6 values in terms of median values with 25 and 75 percentiles, in all and stratified by occupation. A box plot (**Figure 6**) is further included to depict the distribution of values and the remaining expected outliers.

Table 6. Description of spirograms classified according to occupation related to weaving.

	All (n=111)	**Weavers (n=57)**	**Non-weavers (n=54)**
Median (p25-p75)			
FVC	2.76 (2.03-3.84)	2.57 (2.13-3.20)	3.04 (2.02-4.06)
FEV_1	1.52 (1.09-2.07)	1.49 (1.12-1.88)	1.63 (1.10-2.22)
FEV_6	2.74 (2.11-3.61)	2.68 (2.12-3.38)	2.95 (2.04-3.99)

FEV_1, FEV_6, FVC-values in liters (L)

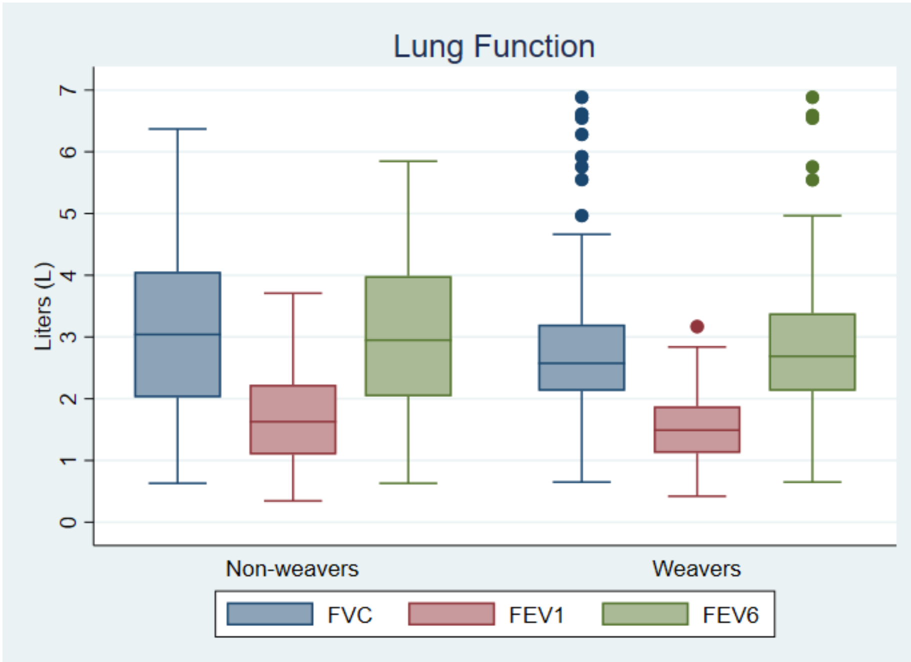


Figure 6. Box plot of the lung function measurements (FVC, FEV_1 and FEV_6) in weavers and non-weavers.

Overall, the median values for FVC in weavers were lower than for non-weavers with a difference of approximately 0.5L. The box plot shows the distribution of the values around the median, in which weavers' group presented a higher dispersion of data.

Finally, a linear regression model was performed to analyze the association of the occupation as weaver in relation to the FVC, while adjusting for age, sex and height. The model showed that weavers, compared to non-weavers, had indicated lower FVC of -0.13 L (95%CI -0.72-0.46; p 0.659). This is in line with the general impression of lower lung function measurements among weavers seen in **Table 6**.

9 Discussion

This thesis presents a pilot study with focus on the general and respiratory health, and potential relation to occupational exposures, in Mayan indigenous communities in Guatemala dedicated to the traditional textile industry or "weaving". The study was undertaken after communication with weavers' organizations in the Lake Atitlan area and will report back to the study population through these same organizations. Due to the COVID-19 pandemic the study protocol was subject to major modifications, and the field work was led by a local project coordinator under long-distance supervision. Approximately 300 persons with mean age 34 years were included in the study, 80% of these were women and about half reported to be weavers. This study population was characterized by low education, and by health services provided by a traditional healer and nurses rather than doctors. The study population was generally short in stature with a mean height of 148cm; overweight was common with a mean BMI of 29 kg/m^2. While sporadic use of pesticides was common, very few study participants smoked tobacco. In standardized interviews with the study participants in their own languages, diagnoses like asthma or chronic bronchitis were reported very rarely, while respiratory symptoms were reported more often; wheeze, reported in almost 10%, was the most commonly reported respiratory symptom. Wheeze was statistically significantly more common in weavers than in non-weavers, and several other asthma-like symptoms appeared to be more common among the weavers. Lung function measurements were technically problematic in over half of the study population; in those with acceptable maneuvers with FVC within a "normal" range lower values were indicated among weavers than in the group with non-weavers. With regard to the proposed objectives and hypotheses of my thesis, the obtained data allowed characterization of important aspects of respiratory health in the study population in terms of respiratory symptoms, asthma and lung function, thus responding to objective 1. Only to a limited extent, could this pilot data elucidate the possible association of lung health with the exposures in the traditional textile industry; concerning objective 2, the study mainly serves as a basis to develop a feasible protocol for better assessment of the work environment. In addition, a biobank including urine samples will allow characterization of a range of toxic exposures when appropriate funding is obtained.

To the extent of our knowledge, this pilot study is the first to generate data that describes the asthma, respiratory symptoms and lung function in difficult-to-reach and not previously studied indigenous communities in Guatemala. In a standardized questionnaire, the participants gave information about several respiratory symptoms (Table 3). Few participants reported having at least one symptom. **Ever wheezing** was the most prevalent symptom, both among all the participants (9.4%) and the subgroup of weavers (13%). **Ever difficulty breathing** was reported by 9.2% of the weavers, and 7.2% of the total study population. The presence of cough or phlegm was not notably high in any subgroup, similar to the rest of the symptoms. When we compared our results to the available evidence, we found a study that suggests a higher prevalence of respiratory symptoms in similar indigenous communities in Guatemala. In 2007, Diaz et al., using comparable standardized questionnaires with Guatemalan women of indigenous communities, found a notably higher prevalence of cough (22.6%), phlegm (15.1%), wheeze (25.1%) and tightness in the chest (31.4%) (93), percentages notably higher than in the weavers and non-weavers in our study.

In addition to asking about several respiratory symptoms, we included specific questions about the diagnosis of several lung-related conditions. With regard to **asthma**, we found a very low percentage (around 1%) of participants that reported having such a diagnosis, both in weavers and in females and males dedicated to non-weaving occupations. We also sought information on whether the participants had used **traditional medicines** to treat asthma; this question was answered positively by 4.6% of weavers. Finally, we asked about the diagnosis of other conditions such as **chronic bronchitis** and **tuberculosis** among the population, which were reported only by less than 1% and 0% of the participants, respectively. Our results differ from the existing evidence regarding asthma diagnosis in Guatemala or other LMIC in Latin America. The ISAAC project found that among Guatemalan children (age 13-14 years), the prevalence of asthma reached 2.6% (29), almost twice as much as we found in the present project. Furthermore, with regard to chronic bronchitis, which is considered part of the spectrum of the COPD, a multinational study in capital cities in Latin America (Proyecto Latinoamericano de Investigación en Obstrucción Pulmonar, in Spanish - PLATINO) found a COPD prevalence that ranged from 7.8 to 19.7%, distant from the 1% reported in our study population (142). Even though the ISAAC and PLATINO studies are not directly comparable to the population in our study, mainly given the ethnic and age range differences, we may have expected a higher prevalence of both asthma and chronic bronchitis in the studied communities.

The consistently low prevalence of reported symptoms and lung health-related conditions may be secondary to several to reasons related to the social, cultural and economic conditions. We strongly believe that language barriers played an important role in our study. Our questionnaires were provided in Spanish, using different colloquial words to describe most of the symptoms. The HWs had the difficult task to translate these questions to local languages for most of the participants in order for them to fully understand, possibly giving space to misunderstandings or not-so-accurate translations. These challenges were also found in previous studies performed in indigenous Guatemalan communities, where local terms for symptoms like “wheeze” were difficult to find, thus raising concerns whether the questionnaires, given the medical terms in them, were suitable for these communities (93, 143). Another possible explanation is the educational attainment of our sample. More than 50% of the weavers reported either no or only incomplete primary school. Furthermore, we suggest that another possible reason for the low prevalence of reported symptoms, in particular of respiratory conditions, may be the lack of knowledge of the actual diagnosis (or the “Westernized“ name). This could to some extent be secondary to the poor coverage of national healthcare system, and the cultural trend among these communities to seek medical attention at more traditional or informal healthcare services (e.g., healers and nurses) and to consume more traditional medicine. For instance, we found that around 50% of the weavers had visited traditional healers and/or nurses in the last 12 months, with a slightly lower percentage among non-weavers. A similar trend was found regarding the consumption of traditional medicine and Western medicine, with more than 40% of non-weavers and 30% of weavers consuming traditional medication in the last 12 months before the study. Similarly, other researchers have proposed education level, health literacy and the preference to seek for help in traditional healthcare services among indigenous populations and other minorities as possible explanations for their health status and the knowledge about their health (144, 145), strongly advocating to consider these important factors as determinants of health.

Spirometric measurements of lung function were performed in 251persons, but only 143 rendered acceptable spirograms and only 111 with FVC <7.0 L were analyzed, which provided us with data to partially characterize the respiratory health of the weavers and non-weavers in terms of pulmonary capacity. Based on inspection of the flow-volume curves of the participants, I found that many participants did not perform a truly forced maneuver but rather a slow maneuver, which generated back a different set of values. These results represent a good attempt to describe some aspects of lung function of these indigenous communities. Nonetheless, the implications of the different maneuver performed during the spirometry are poor comparability and generalizability of our results, because of the uncommon use of the slow maneuver to provide lung measurements in scientific research. From lung function values thus obtained, we found that weavers, in comparison with non-weavers, appeared to have markedly lower FVC, FEV_1 and FEV_6, findings that were not statistically significant. To our understanding, reference values for this particular population are not available. Hankinson et al, in 1999, proposed a reference equation that described the lung function of different populations within the Mexican American ethnic groups (9), and that have been previously used to describe lung function tests in Guatemalan indigenous communities (93). However, we consider the lung function tests from our pilot study unsuitable for analyses in relation to reference equations. For that matter, our pilot study clearly shows that improvement of the lung function assessments will be important in further studies. Different steps are to be taken, starting with an enhancement of the training period to the HWs leading the assessment, making emphasis on a face-to-face traineeship, and followed by a strict supervision during the development of the protocol.

Importantly, we found a major challenge describing the second objective of our study, which includes the possible associations of the participants' occupation with changes in lung function, the prevalence of asthma and other respiratory symptoms. Due to the sanitary conditions, the research team was not allowed to travel, visit and perform the fieldwork. This situation shaped the pilot study so the information that could be gathered at this stage would allow the team to describe the populations' respiratory health and start understanding their occupations and the details about their specific tasks, mainly when it concerned the index participants. As a result, only a crude occupational history was obtained from the participants, while very few data were gathered on the processes that weavers performed before, during and after weaving. In addition, the cultural perception of the different occupations as "normal daily" tasks, posed a challenge for the team to recognize and classify specific occupations. Similarly, classification of exposures among the household members was almost impossible at this stage, because many participants responded they had a specific occupation different than weaving, but they were still likely be in touch with textile products because many of the weavers worked from home. Having these challenges in mind, we were still able to indicate that participants performing weaving activities were more likely to have lower FVC, compared to non-weavers, almost three-times higher risk of having wheezing and tightness in the chest, as well as double risk of presenting wheezing without a cold and wheezing with breathlessness. Other symptoms that appeared to be related to weaving, were the presence of morning and chronic cough and phlegm. These obtained results, though not completely comparable, go in line with findings from studies done among eastern European participants whose main occupation was in the textile industry (69, 114, 115). The authors also reported higher prevalence of acute respiratory symptoms and lower lung function tests in participants exposed to dyeing of cotton and to wool fibers than in the non-exposed group, thus suggesting a strong occupation-related influence. After analyzing our results, we suggest that a new approach is needed to properly answer the second objective. Based on the experience of this pilot study and the changes required to carry our research during the pandemic, a revised plan would need a formative stage with a focus on qualitative or ethnographic methods. These can improve the communication with the weavers' organizations and their members and provide the support and insight to properly build a questionnaire that would clearly describe the occupation history and further identify the processes and exposures. Furthermore, this stage could algo gather data from key informants and experts that could provide insight and help into how to develop different tasks and obtain targeted information from the participants with regard to their occupation and the exposures at their workplace. For instance, it would be preferable that an occupational hygienist visits the study site and take samples of the material used in the weaving processes, as well as dust samples, to inform the next stages of the study. Lastly, we would need funding to perform measurements of specific metabolites in urine or blood, which will help describe some hazards in these communities.

Regarding the secondary objectives, to describe other possible environmental and chemical exposures that could pose a risk for the participants, we were able to obtain plausible information in these indigenous communities (Table 3). Sporadic use of pesticides at work and at home was common among all subgroups, with a clear predominancy in persons not working in the textile industry. Moreover, the percentage of participants that used solid fuel at home (for heating and for the stove) was high, showing consistency among subgroups and suggesting a general practice among all the inhabitants in this region, similar to what several authors described around the RESPIRE study in Guatemala (92, 93, 95) . It is worth noting that a very high rate of participants reported not smoking tobacco, suggesting also a common practice in the general population, representing one less risk factor for lung-related diseases. At this stage of the study, we are only able to conclude that these communities are highly exposed to dangerous chemicals that do not arise from smoking tobacco. However, no details about these exposures are available (i.e., specific names of pesticides, quantitative measurements, etc.). The urine and blood samples we have collected will allow proper quantitative assessment of the individual body burden for a range of such agents. Such characterization may be of great benefit to the weavers and their relatives, with the perspective of environmental improvement of this situation in the foreseeable future.

9.1 Strengths

We have detected several **strengths** in this project which make it unique in many aspects. As a general consideration that is important to have in mind, we had to change plans and develop a long-distance project due to the pandemic and the consequent impossibility to travel. This influenced the theoretical and practical aspects of the study enormously, with great efforts to build a team and individualize the study protocol according to the local sanitary and geographical situations, our budget, the available assessment tools, the project coordinator, the ability to reach participants and the partially unknown population that we wanted to study. Despite these challenges, we were able to study a large group of participants, with almost 300 indigenous people assessed through different means, following standardized and validated protocols, which represent a considerable number of participants and information for a pilot study. The information gathered from these participants is unique in the sense that no other studies, to our knowledge, have extensively assessed the general demographic and occupational characteristics, the respiratory/allergic-related conditions and performed diverse clinical assessments of the indigenous populations in these geographical regions. Importantly, with this pilot study we were able to identify how feasible is to perform a study in this remote area and with these particular communities. In addition, we were able to acknowledge which clinical assessments were realizable during the pandemic and how online supervision influenced the performance of the project.

Another important strength includes the community-based steps that we followed to approach the study participants, steps that ensured local representation and visibility of several actors in these indigenous communities. We initiated the recruitment process with a local collaboration (FJ) that led us to closely work with a community leader or "gate keeper" (PC), who, through previous knowledge of the geographical area, close communication with representatives of weavers' organizations in the region and extensive work, was able to stablish a cohort interested in participating in our study. As previously commented, the organizations' interests were taken into consideration when planning the project, aiming to provide answers about their occupation exposures and health results. Importantly, these steps helped us reach specific populations and facilitated the identification of several study topics that were of great interest to communities and not only to the team. In addition, by actively including other local community actors (i.e., health workers) in the execution of the project at the study site (performing interviews and the clinical assessments directly in the local languages), we were able to positively influence the population to participate, given that important language and cultural barriers were not present, and which could, at a certain degree, have been detrimental for the participation rate and confidence in the team.

Finally, the utility of the chosen questionnaires and clinical assessment tools is based on their standardization and widespread use in many international studies (ECRHS, RHINE and RHINESSA). These tools are being used in a variety of settings, including LICs, and while there are challenges related to comparison across populations, these tools facilitated the obtention of large exposure data, extensive questions on several symptoms, conditions and comorbidities, and standardised measurements of important clinical parameters. Altogether, this has contributed to our generating a diverse and rich source of data, useful for many research purposes within this study and the planning of future studies in similar environments.

9.2 Limitations

By contrast, we were also able to identify several **limitations** or weaknesses in the process of conducting the study. At a large extent, limitations were secondary to the pandemic and to not being able to travel and perform the study ourselves, and consequently large challenges related to funding for services and equipment that we otherwise would have performed and brought ourselves. In the first place, we had to rely on the Guatemalan project coordinator to perform a large number of important activities for the preparation of the study and during fieldwork. This prevented us from getting to know firsthand the population's characteristics, its social environment, and special needs, and in the end, stopped us from experiencing the cultural encounter that was originally planned for our study fieldwork. Fortunately, we were able to partially know our study population through the eyes of our collaborators and detect the most important challenges when approaching it. On the other hand, the situation promoted education and experience for the local project collaborators and field workers, which can be considered an advantage of the project.

Another weakness detected on the previous stage to the conduction of the study was the inability to properly arrange sufficient training sessions with the field workers with regard to the use of the assessment tools (i.e., questionnaire, spirometer, etc.). Even though we provided interactive videos with detailed explanations of the procedures and all fieldworkers had a background working in health facilities, specific sensibilization to the questionnaires (including training in proper translation of medical words into local languages) and more intensive training based on the standard procedures for the use of medical equipment would have been needed. Furthermore, we found out that continuous quality control of these procedures was not optimal on the study site, and this could have been better if we could have been there ourselves. These flaws got reflected in missing data in the interviews, misunderstanding of questions and poor quality of some of the lung function tests we obtained. Regarding the use of a questionnaire, though it was individualized after a feedback session with our collaborators and was translated to the local languages, we were not able to fully grasp some of the exposures and symptoms, partially due to the difficulty of the questionnaire, to the attempt to translate complex medical words from Spanish, and possibly due to the low education level of the sample population, challenges that other researchers have previously found in similar settings in Guatemala and that were solved through specific training beforehand (93, 143).

After analyzing the data, we realized that misclassification may be a problem in different aspects during our study. First, we may have introduced selection bias as we were not able to do a clearly structured selection of our population, our collaborators invited several inhabitants of the smaller villages and/or the members of the weavers' organizations and we do not have good information on the source populations. Second, possibly secondary to i.e., use of medical words and low education level, some participants were not able to respond to important aspects of their own and their relatives' health status (e.g., diagnosis of asthma or other chronic conditions). This may have led us to underestimate the real prevalence of these diseases among the populations and not pay proper attention to important aspects of their wellbeing, reducing the possibility to give useful recommendations as feedback to them. Moreover, we most likely have misclassification regarding the weavers and their relatives' occupation, and limited information on their tasks related to textile work. Some persons considered exposed may have had neglectable contact with the products, leading us to overestimate the real exposures to yarn or dyes (e.g., relatives would only partially help in the family-owned textile business – selling or transporting, but not weaving). Similarly, in the particular case of the weavers, we were not able to categorize the different exposures and processes around weaving; we found difficulties asking uniform questions about these processes as the traditional industries vary from town to town and from one weaver's organization to the other. Misclassification in some other chemical exposures (e.g., pesticides, tobacco, detergents, among others) is likely to be of less importance, given the easiness in identifying these chemicals/products even in these communities and in their language.

Finally, after having analyzed our results, we found that another important limitation could be the generalizability. One may think that our results could be of importance for other Latin American populations, but the fact that the participants belong to indigenous ethnicities and have occupations that are strongly related to the traditional textile industry and to their rural geographical situation, could restrict the generalizability of the findings. However, our results could be applicable to Mayan populations living in southern Mexico or Central America countries, where costumes and origins are shared at a greater extent.

With all its limitations, we believe that our pilot study opens several possibilities for future research to complement the information obtained with more detailed assessments and individualized tools, with the purpose of disentangling the hazards and risks that the weavers and their relatives are exposed to in these communities. Further research is needed to enhance the responses we are obliged to provide to the weavers' communities in terms of health-related recommendations.

9.3 Challenges

We experienced great challenges before, during and after the execution of our project. The pandemic forced us to develop everything from Norway and maintain close communication with our local collaborators. We had to adapt the questionnaires and clinical assessments, modify the logistics of the field work, and the information and sample storage, and even develop a secondary plan for the safe transfer of data to the team in Norway. Fortunately, the team was flexible and experienced enough to solve these problems and yet conduct the project in the best possible way, with valuable information for both, the team, and the participants. Overall, we believe that the study has important characteristics that make it unique in many aspects. However, as any other pilot study and in these difficult times with the pandemic, expected limitations arose and restricted, at a certain degree, the use and interpretation of all the data collected. We believe that this pilot project gives important opportunities and provides an important basis for further development and complementation of the protocol, aiming to fill the identified knowledge gaps and explore deeper into the subject, but with a strong basis already built.

10 Plans

Several short-term and long-term plans are foreseen as a continuation of this project. As part of our ethical duty with the communities that participated in this study, and in accordance with the Ministry of Ethics in Health in Guatemala, we plan to present the results of this project with regard to general characteristics of their respiratory health, occupational/home exposures, and potential recommendations, to the involved communities. We believe these communities will be beneficiated with the description of the general respiratory health status, and specially with the description of the different exposures found. In meeting with the communities we will also aim to obtain feedback from the study participants. In conjunction with our collaborators in Guatemala, we have planned feedback sessions with the community leaders to reach the families included in our project, which will probably take place during the first semester of 2022. Furthermore, with the help of the RHINESSA group, we plan to apply for more funds to analyze the biological samples that were obtained, aiming to provide more valuable evidence to the results we have now. Finally, a publication of at least one original article in an international scientific journal (related with Occupational Health and/or Respiratory diseases) is foreseen in the upcoming months.

Moreover, medium-term plans comprise the extension of the project. We are in the process of establishing collaboration with local Guatemalan health authorities (e.g., Institute of Nutrition of Central America and Panama-INCAP) and the Rafael Landívar University; and of including other students from the Center for International Health (CIH) at the Global Health Master program, with the objective of conducting more fieldwork in the region. We will in collaboration with the user groups, attempt to get back to our study population in order to assess in more detail the exposures (mainly related to chemical agents), characterize other disease outcomes (such as nutrition status) and potentially include more participants. We also plan to include other experts in the field (e.g., occupational hygienist) who could investigate, through other precise means, chemical exposures specifically related to the weavers and their environment. This new approach would offer the possibility to adjust the assessment tools after the results of our pilot study, improve the planification and logistics, build stronger community collaborations, and thereby lay the foundation for a more extensive high-quality study. We firmly believe that these new efforts to continue and expand this project will multiply the benefits for these marginated populations in terms of health and social representation in the country.

11 Conclusions, implications and recommendations

The overall objective of this study was to assess asthma, respiratory symptoms and lung function in indigenous families located in the Sololá region of Guatemala, and the possible association with exposures in the traditional textile industry. This objective was addressed using several assessment tools (i.e., standardized questionnaires and lung function tests) and developed by a group of local health workers supervised by the team in Norway and on-site project coordinator. Despite challenging times during the pandemic, and after several changes in the study planification, we were able to obtain valuable, yet restricted information about the lung function of the population. Moreover, we gathered information to characterize, through the description of respiratory symptoms and lung conditions, several aspects of the respiratory health in these communities. Importantly, this study was not only beneficial for the participants, but opened several possibilities to other actors, including the local project coordinator, the health workers that performed the fieldwork, the facilitators of the study and the weavers' organizations in Guatemala. The results from this Master thesis show that weavers, in comparison to non-weavers, tended to have higher prevalence of asthma and other selected respiratory symptoms and lower levels of lung function. Further studies and reassessment of these communities are needed to corroborate the relationship between the lung function values, prevalence of asthma and other reported respiratory symptoms with the traditional weaving-related activities.

12 Funding and conflicts of interest

This project was funded and supported by the CIH through funds available for small studies for master students, and by two University of Bergen "småforsk" grants. Moreover, the project received co-financing and equipment from the RHINESSA research group.

The research team declares that it has **no conflicts of interest**.

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14 Appendix

-Appendix A – Standardized core and secondary questionnaires (English and Spanish)

-Appendix B – "Getting ready questionnaire/Results form" (English and Spanish)

-Appendix C – Standard Operation Procedure (English and Spanish)

-Appendix D – Informed consent (English and Spanish)

-Appendix E – Ethics committee approval (Norway and Guatemala)