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Improving Differential Diagnosis of Vocal Cord Dysfunction

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Improving Differential Diagnosis of Vocal Cord Dysfunction

by

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Thesis

Presented to the Faculty of the Graduate School of

The University of Texas at Austin

in Partial Fulfillment

of the Requirements

for the Degree of

Master of Arts

The University of Texas at Austin

May 2014

Acknowledgements

I would like to thank Dr. Courtney Byrd, my advisor and mentor, for her unparalleled guidance and support throughout every step of the research and writing process. Working with her has been truly a privilege. I would also like to thank Elizabeth Hampton for taking time out of her incredibly busy schedule to serve as my second reader. Finally, I would like to thank my research assistants, Deidra Tafolla and Robyn Croft for their assistance with coding data and troubleshooting figures in excel.

Abstract

Improving Differential Diagnosis of Vocal Cord Dysfunction

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Purpose: The purpose of this study was to assess whether the factors historically presented in the literature to differentiate vocal cord dysfunction (VCD) from breathing difficulties of other etiologies accurately predict and identify patients who have VCD. The researchers were also interested in whether patients with VCD have a higher risk of misdiagnosis than patients with breathing difficulties of other etiologies. Finally, the present study investigated whether patients with VCD were more likely to have their symptoms attributed to psychological factors than patients with breathing difficulties of other etiologies.

Method: A survey comprised of 23 questions regarding the participants' previous and current diagnoses, triggers that precede breathing difficulty, and whether or not the participants have ever been misdiagnosed was posted to internet support groups, websites, blogs, and forums. The final participant pool included 20 participants with VCD and 25 participants with asthma.

Results: None of the factors investigated accurately differentiated participants with asthma from participants with VCD one hundred percent of the time. However, participants with VCD were more likely to report throat tightness during an attack, association of an attack with symptoms of acid reflux, and rapid resolution of symptoms without treatment. Conversely, participants with asthma were more likely to report expiratory stridor and chest tightness, full resolution of symptoms with use of asthma medications, nocturnal symptoms or symptoms just after waking, and symptoms that seemed to be triggered by environmental agents or allergens. Preliminary findings from the present study suggest that patients with VCD are both more likely to receive a misdiagnosis and have their symptoms attributed to psychological factors than participants with asthma.

Conclusion: A diagnosis of VCD must be made very carefully, ideally with instrumental evaluation of the vocal mechanism during an acute "attack" of breathing difficulty. The factors identified in the literature to differentially diagnose patients with asthma from patients with VCD do not accurately differentiate these populations. These findings suggest that continued education about the nature of VCD and differential diagnosis should be paramount to medical professionals.

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INTRODUCTION

Acute Presentation

Vocal Cord Dysfunction (VCD) [also known as Paradoxical Vocal Fold Movement Disorder, Paradoxical Vocal Cord Movement Disorder, Paradoxical Vocal Cord Dysfunction] is a disorder often misdiagnosed as asthma because of its acute presentation (Nascimento & Tenenbaum, 2013). In VCD the vocal folds are adducted during inspiration, narrowing the airway. During normal inspiration, the vocal folds are in the abducted position, allowing for dilation of the airway. Adduction of the vocal folds upon inhalation does not, however, manifest in all VCD patients in exactly the same way.

In fact, the symptoms of VCD are not universally agreed upon in the medical literature. Gimenez and Zafra (2011) describe an acute attack of VCD as being characterized by shortness of breath, wheezing, throat or chest tightness, and cough. Alternatively, Gallena and Kerins (2013) consider chest tightness to be more indicative of asthma but identify noise on inhalation, reported feeling of throat tightness, distinct difficulty inhaling as compared to exhaling, voice change or loss during an episode, and rapid onset and resolution of symptoms as markers of VCD. Yelken, Yilmaz, Guven, Eyibilen, and Aladag (2009) state this unique group of symptoms that are frequently associated with VCD can together be described as extrathoracic airway obstruction. Others report that patients with VCD may describe this disorder as a "choking" sensation upon inspiration (Koufman & Block, 2008). Differences in definitions aside, the presentation of VCD varies significantly from patient to patient.

VCD may also manifest concurrently with voice changes. Dysphonia or aphonia has been described as frequently co-occurring between acute "attacks" of respiratory distress. Yelken, Gultekin, Guven, Eyibilen, and Aladag (2010) found that in a group of 12 patients with asymptomatic VCD, voice quality was significantly impaired compared to a control group, including false vocal cord adduction, anteroposterior constriction of the supraglottic larynx, decreased amplitude, decreased mucosal wave, and significantly high mean jitter and shimmer rates. Functional voice disorders do not arise in all VCD patients but it is important to note that these differences do present for some.

VCD is associated with various psychological constructs but it is *not* a factitious disorder. That is, the related symptoms are not contrived and cannot be voluntarily controlled by the patients (Gimenez & Zafra, 2011). During an attack, many patients experience a sense of panic and anxiety, and may have a history of emergency intubation and/or tracheostomy (Noyes & Kemp, 2007). Patients with VCD may be erroneously categorized as "malingerers" because they are reported to have elevated levels of stress, anxiety, and depression compared to the general public and even patients with other voice disorders (Nascimento & Tenenbaum, 2013). In a case study of five elite athletes, Nascimento and Tenenbaum (2013) found that the athletes were likely to experience psychological factors related to burnout or the perception of inadequate personal accomplishment. Additionally, they found that the athletes were at risk for the following: physical exhaustion, emotional exhaustion, questioning whether the benefit of the sport was worth the cost, feelings of isolation, reduced sense of accomplishment and confidence, questioning athletic identity, worsening mood, decreased determination, denial of fear, and

feelings of unfairness. However, the lack of a control group is a crucial flaw in this study. It is impossible to know whether the elevated levels of stress, anxiety, and other psychological correlates that these elite athletes present with are a byproduct of the intensive nature of their career, or whether they are related to VCD. Many have interpreted this increased stress and anxiety as indicators that VCD is psychogenic. However, causal studies have yet to establish a direct link between the etiology of VCD and psychological correlates. The present study intends to investigate whether participants with VCD are more likely to have their symptoms attributed to these psychological correlates than participants with asthma. Patients with VCD may be at higher risk for this attribution of symptoms to psychological correlates, because Asthma is a more commonly understood disorder within the medical field than VCD.

The potential impact that undiagnosed and uncontrolled VCD can have on a person's overall quality of life further increase the need for differential diagnosis and best practice of management of VCD. Unfortunately, patients who present with the disorder are typically either misdiagnosed and/or have a protracted period between onset of symptoms and arrival at a final diagnosis.

Etiology

The etiology of VCD is unknown. Part of the difficulty that medical professionals encounter in diagnosing VCD is that the triggers of VCD can vary significantly among patients. Additionally, VCD can occur as the primary disorder or secondary to another disorder. Yelken et al. (2009) suggest that some patients who have asthma are at a higher

risk for developing VCD than the general population, though the presence of VCD was not explained by asthma severity. Additionally, Yelken et al. (2009) found that the presence of laryngopharyngeal reflux (LPR) and allergy were more prevalent in the group with VCD than the general population. Other possible triggers reported include inhaled irritants such as strong perfume, changes in temperature (frequently cold weather), allergens, chemicals, laryngeal dystonia and brainstem abnormality (Koufman & Block, 2008). Gaafar and Fasyh (2011) described an extreme and rare cause of VCD as secondary to multiple-system organ failure and myasthenia gravis. Gimenez and Zafra (2010) state that there is probably no singular cause, but rather a "constellation" of triggers.

Incidence and Prevalence

Compared to other disorders that impact breathing, VCD has an extremely high rate of misdiagnosis (Gimenez & Zafra, 2011; Nascimento & Tenenbaum, 2013; Thurston & Fiedorowicz, 2009). Given the apparent discrepancies in the diagnosis of VCD, it is not surprising that the incidence and prevalence of this complex disorder is unknown. Estimates of VCD prevalence and incidence is complicated by the fact that each study uses different parameters for diagnosing VCD. Gimenez and Zafra (2011) assert that VCD is a fairly uncommon disorder in the general population, but may be higher in specific subsets of the population such as elite athletes, patients with asthma, gastroesophageal reflux, laryngopharyngeal reflux, laryngeal dystonia, or brainstem abnormality. The prevalence of VCD is reported to be as high as 3% in intercollegiate athletes, however this report may be compromised by the high rate of misdiagnosis of exercise-induced asthma in this

population (Gurevich-Uvena et al., 2010). Most reported cases occur in adult women. In fact, VCD has been reported to be three times more likely in females than males. Cases in children have been documented (Gaafar & Fasyh, 2011).

The Role of the Speech-Language Pathologist

As more and more speech-language pathologists encounter patients with VCD, clinical competence in the areas of diagnosis and management of the disorder is paramount. Traditionally, the role of speech-language pathologists has focused on training the patient strategies to terminate acute attacks of VCD. However, speech-language pathologists are becoming increasingly involved in the assessment of VCD as a part of an interdisciplinary diagnostic team. Mathers-Schmidt (2001) states the role of the speech-language pathologist "extends to assessment, diagnostic input, patient education, supportive counseling, [VCD] symptom management, and possible voice therapy". Mathers-Schmidt (2001) further specified that the speech-language pathologist's protocol for assessment of a patient with VCD should include a comprehensive case history including pertinent medical history, a comprehensive history of the onset and description of their VCD symptoms, social history, evaluation of respiratory support and control, respiratory driving pressure control, laryngeal musculoskeletal tension, and structural/functional integrity of the oral mechanism for speech.

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Similar to Mathers-Schmidt (2001), Gallena et al. (2013) asserts that speech-language pathologists play a special role in the screening and diagnosis of pediatric VCD/PVFM. They should educate school personnel about the characteristics of VCD so that possible cases can be identified and referred to the speech-language pathologist for screening. After a speech-language pathologist completes a screening, observes the child, consults with the nurse, and confirms a case of possible VCD, the speech-language pathologist should recommend further medical evaluation to rule out other conditions. After physician confirmation of VCD, the speech-language pathologist should perform a full evaluation and plan a treatment program. Upon consideration of all the factors that the speech-language pathologist must consider coupled with the challenges with differential diagnosis that are unique to VCD, there is a need for more data regarding

whether or not the factors that are thought to be unique to this disorder are accurate. Understanding of the factors that could reliably differentiate patients with VCD from patients with breathing impairments of other etiologies would be of significant benefit to speech-language pathologists. This information could be used for identification of VCD in both pediatric and adult populations as part of a broader speech and oral mechanism evaluation.

Differential Diagnosis

VCD can be a complicated disorder to identify due to overlapping symptomology and comorbidity with other disorders that impact breathing. VCD is most frequently misdiagnosed as asthma, though the two disorders can be comorbid within the same patient. Both asthma and VCD present with dyspnea (shortness of breath) and wheezing (Tilles & Inglis, 2009). However, positive response to asthma medications, reported feeling of chest tightness, wheezing on exhalation, excessive mucus and nocturnal symptoms are more typically associated with asthma. By comparison, noise on inhalation, reported feeling of throat tightness, harder to inhale versus exhale, and rapid resolution of symptoms are most commonly associated with VCD (Gallena et al., 2013). Nascimento and Tenenbaum (2013) reported that an acute attack can be differentiated from asthma by listening for stridor and identifying whether or not there is tightness in the chest or throat. They also note that symptoms tend to resolve spontaneously within five minutes. The purpose of the present study is to investigate whether or not these factors accurately discriminate between patients

who have asthma and those who have VCD. If in fact they do discriminate accurately, the resultant outcomes can be used to enhance differential diagnosis of this complex disorder.

Best practices for diagnosis of exercise-induced asthma include ruling out VCD (Carlsen et al., 2008). Carlsen et al. 2008 reports that most athletes referred for respiratory problems do not have asthma or exercise-induced asthma. That said, many patients referred for respiratory problems are still not screened for VCD. The reason for this is unclear, but it may be due to the fact that some patients present with both asthma *and* VCD and experience at least some relief of symptoms from bronchodilator use.

Misdiagnosis of VCD has several implications for both medical professionals and patients. Acute asthma-like symptoms may lead medical professionals to make inappropriate specialist referrals and prescribe unsuitable medications. Mikita and Mikita (2006) recognize that patients with VCD may undergo numerous subspecialty evaluations and treatments before receiving a final diagnosis. This unnecessary medical treatment prior to a final diagnosis of VCD was confirmed by Cohen (2010) who found that patients with VCD have a high rate of both office and emergency room visits. Mikita and Parker (2006) compared 25 patients with VCD and 25 age and sex-matched patients with asthma. The VCD cohort used significantly more medical provider resources and similar amounts of pharmaceutical services compared to those patients with moderate persistent asthma. Thus, improvement of differential diagnosis of asthma and VCD is imperative to decrease inappropriate treatment practices.

The current "gold standard" for differential diagnosis of VCD is direct visualization of the vocal folds through rhinolaryngoscopy during an acute attack with positive

identification of adduction of the vocal folds upon inspiration. Koufman and Block (2008) generated a checklist to aid in differential diagnosis of the specific etiologies/triggers of VCD (laryngopharyngeal reflux, respiratory type laryngeal dystonia, asthma associated and hyper-immune laryngeal dysfunction, brainstem abnormalities, and drug-induced laryngeal dystonic reactions), but their checklist necessitates the direct visualization of the vocal folds, an expensive procedure that requires specialized equipment and training to complete. Many general practitioners who misdiagnose VCD patients with asthma may not have access to this type of equipment. Additionally, because VCD is episodic, it may be difficult to visualize the vocal folds during an attack. Also, even if the clinician is able to induce an attack (which may be contraindicated in some settings wherein there is no immediate access to emergency services), it may be difficult to visualize the vocal folds during the attack due to the nature of respiratory distress. Furthermore, it may be difficult to get the patient calm enough to pass the scope while still symptomatic (Rhodes, 2008). Within the school setting, the onus of identification of possible VCD in pediatric populations may rely heavily on observation, case history, and evaluation by a speech-language pathologist (Gallena et al., 2013) as schools typically do not have access to rhinolaryngoscopy equipment. Thus, it is necessary to establish other diagnostic methods that do not require the patient to be symptomatic at the time of the evaluation and do not require direct visualization of the vocal folds.

Other methods that are used to differentiate VCD from asthma are spirometry, chest radiography, and arterial blood gas measurement. However, these methods have limitations as well. Mikita and Mikita (2006) identify that spirometric readings can be transient and

may lack sensitivity and specificity for VCD. In addition, some patients may not be able to be identified at all through traditional diagnostic methods. Davis, Brugman, and Larsen (2007) identified a patient through videography of the patient exercising who could not be diagnosed using any of the classic diagnostic procedures for both exercise-induced asthma and VCD. The patient was only identified upon examination of a video of an attack. The researchers were unable to replicate her symptoms in a clinical setting. The identification of the key factors that differentiate VCD from other disorders that impact breathing (most often asthma) without the need for direct visualization of the vocal folds would lead to increased diagnostic accuracy or at the very least an appropriate referral.

Increased accuracy in the identification of patients with concomitant VCD and asthma is critical as well. This population may have non-classical symptoms of VCD. Undiagnosed VCD in patients with asthma can give medical professionals the impression that the asthma is not well-controlled and lead to unnecessary medication adjustments and pharmacological intervention (Parsons et al., 2010). Evidently, better diagnostic methods across the board for both patients that present with asthma and VCD and VCD as the primary disorder are necessary.

Present Study

In summary, the purpose of the present study was to obtain more information about persons who have been previously diagnosed and or misdiagnosed with VCD, asthma, exercised-induced asthma and/or reflux. We hope to use the report of their past and final diagnoses coupled with their description of triggers to better determine what factors are

critical to differential diagnosis. The purpose of gathering information about each group's triggers is to identify if the factors that are historically used to differentiate VCD from other disorders indeed differentiate the various groups. Assessing these features will allow for improved differential diagnosis of Vocal Cord Dysfunction (VCD) within the medical community, as patients with VCD are often treated for disorders for years based on a misdiagnosis, with little resolution of symptoms.

Research Questions

The main research questions to be addressed are:

1. Do the factors historically presented in the literature to differentiate VCD from breathing difficulties of other etiologies accurately predict and identify patients who have VCD?

2. Do patients with Vocal Cord Dysfunction (VCD) have a higher risk of misdiagnosis than patients with breathing difficulties of other etiologies?

3. Are patients with VCD more likely to have their symptoms attributed to psychological factors than patients with breathing difficulties of other etiologies?

Hypotheses

The main hypotheses proposed for this study were:

1. The factors presented in the literature and reflected in this survey will accurately identify patients who have VCD and differentiate them from patients with breathing difficulties of other etiologies.

2. Participants with VCD will be more likely to experience misdiagnosis/ misdiagnoses prior to arrival at their final diagnosis than patients with asthma.

3. Patients with VCD will be more likely to experience attribution of symptoms of breathing difficulty to psychological factors than patients with breathing difficulties of other etiologies.

METHOD

Survey Development

Participants completed a three-part survey addressing previous and current diagnoses, triggers that precede breathing difficulty, and whether or not the participants have ever been misdiagnosed. Questions on this survey were developed based on published data regarding differential diagnosis. The role of the SLP in the evaluation of VCD was of particular interest to the present study. Thus, the factors presented in the Gallena et.al (2013) study as differentiating VCD from asthma were adapted for use in this survey instrument. Each factor was converted from a statement to a yes or no question (e.g. "Reported feeling of chest tightness" → "When you have difficulty breathing, do you feel tightness in the upper or lower chest?").

However, there were a few factors identified in the Gallena et al. (2013) study that were not included on the current survey instrument. One factor was voice changes during an episode of breathing difficulty, as this tends to occur in only some patients who have VCD and therefore would not be critical in differential diagnosis of the disorder in all patients. Another factor was the presence of excessive mucus. Gallena et al. (2013) identifies that this is typically a symptom of asthma and not VCD, but there are conflicting studies that report frequent comorbidity of both asthma and VCD with seasonal allergies, sinusitis and rhinitis (Cohen & Bellucci, 2011; Gimenez & Zafra, 2011; Gurevich-Uvena et al., 2010; Tilles & Inglis, 2009). Therefore, this factor was also excluded from the present survey as it would not reliably differentiate the two groups.

Questions unique to the present study that were not in Gallena et al. (2013) study included questions about the onset of symptoms and whether or not the participants had ever been told that their symptoms are psychological. The onset of symptoms is historically established in the literature to be more gradual in asthma, and in exercise-induced asthma symptoms typically occur after exercise ceases (Carlsen et al., 2008). If bronchodilators are used, exercise-induced asthma is usually well controlled and symptoms do not return. By comparison, if exercise is a trigger for the patient, VCD generally comes on rapidly and ends quickly after exercise ceases, and bronchodilators do not resolve symptoms (Mathers-Schmidt, 2001; McFadden & Zawadski, 1996).

Survey participants were contacted via internet support groups, websites, blogs, and forums for professionals and individuals affected by VCD, gastroesophageal reflux, asthma, exercise-induced asthma and related disorders. Participants completed the survey online via qualtrics. The survey took approximately 5-10 minutes to complete. Upon completion of the survey, the participants were thanked for their participation via an on-screen dialogue box.

In an effort to balance the number or responses from the two primary groups of interest (VCD and asthma), the survey was posted to twice as many groups for asthma than for VCD. This method was used because it was assumed that participants with VCD would be more likely to respond to a survey that would help facilitate accurate diagnosis of the disorder, due to high-rates of misdiagnosis in this population. In total, the link was posted to three social media groups for VCD, six social media groups for asthma, one social media group for people with laryngopharyngeal reflux, one social media group for people with

gastroesophageal reflux, and two forums for professionals in the field of speech-language pathology.

Informed Consent

An invitation to complete the survey was posted on internet support groups, websites, blogs, and forums for professionals and people affected by VCD, acid reflux, asthma and related disorders. This invitation described the general purpose of the research and also served as a document of informed consent. If the participant chose to complete the survey, this agreement would represent their intent and a link in the invitation would take them directly to the qualtrics page on which they could complete the survey anonymously.

Voluntary enrollment was ensured by using an Informed Consent letter that was provided in the first question of the survey. The letter was approved by the University of Texas at Austin Institutional Review Board, and informed the participants that participation was completely optional. Additionally, the letter assured participants that their confidentiality and privacy would be protected and no identifying characteristics would be recorded with the survey responses.

Length of Time for Response

The survey was accessible for completion for a period of 10 weeks following the initial posting of the invitation to complete the survey on November 13, 2013, and was

officially closed on January 23, 2014. At the five week mark, an additional invitation was posted to each group to remind members of the opportunity to participate in the survey. At the close of the survey, 143 participants had responded.

Participant Characteristics

Between November 13,' 2013 and January 23, 2014, 143 people answered the online survey. Of the 143 respondents, 40 were excluded as they did not complete the survey. 46 participants were excluded because they reported that they had current diagnoses of both asthma and VCD, making any interpretations about differential diagnosis impossible. An additional 6 participants were excluded because they reported both current and previous misdiagnoses of the same disorder (e.g. the participant reported that they had a current diagnosis of VCD and a previous misdiagnosis of VCD). 1 participant was excluded because he/she did not report any current diagnoses or past misdiagnoses of asthma, exercise-induced asthma, or VCD. Finally, 1 participant was excluded from the final participant pool because he or she only reported symptoms of acid reflux but no other disorders that affect breathing.

Final Participant Pool

The final participant pool included 48 respondents. 20 participants had a primary diagnosis of vocal cord dysfunction (VCD), 3 participants had a current diagnosis of exercise-induced asthma, and 25 participants had a current diagnosis of asthma (not

exercise- induced). Because the exercise-induced asthma group was small, the main comparisons in this analysis are drawn between the asthma (non-exercise induced) and the VCD groups.

Response Rate per Question

Although there was a total of 48 completed surveys, not every question was answered for each survey as two questions regarding triggers of breathing difficulty included a 'not applicable' option, as not all participants were expected to have breathing difficulty that was triggered by exercise or use inhaled corticosteroids or bronchodilators. Additionally, if a participant reported that they had never been diagnosed or misdiagnosed with a particular disorder, then they were not required to answer a subsequent question about who made the diagnosis/misdiagnosis. Thus, the number of respondents reported per question varies.

RESULTS

Demographics

Demographic data were obtained to ensure that there were no confounding variables and to enable comparison of the obtained results to previously published studies. These data were not used in the statistical analysis and comparison of the groups. Charts of the demographic data may be found in Appendix B.

Age

Because a wide variability in ages of participants was expected, participants reported their age in a census-style age brackets (e.g. 20-24, 25-29). Therefore, a mean age was not calculated for each group. The median bracket for both the VCD group and the asthma group was 40-44years. The range for the VCD group was 15-19 years old to 55-59 years old. The range for the asthma group was 5-9 years old to 55-59 years old.

Gender

Of the 20 participants with VCD, 85% (n=17) identified as female and 15% (n=3) identified as male. Of the 25 participants with asthma, 84% (n=21) identified as female and 16% (n=4) identified as male.

Identification of Current and Past Diagnoses

It was critical to the design of the present study to identify potential confounding diagnoses of the participants. Therefore, the first section of the current survey instrument

focused on identification of potentially confounding diagnoses of the participants. All participants were asked if they had current diagnoses of asthma (not exercise-induced), exercise-induced asthma, acid reflux (gastroesophageal reflux or laryngopharyngeal reflux), and/or vocal cord dysfunction (VCD). Participants in the final participant pool reported a primary diagnosis of VCD (n=20) or asthma (not exercise-induced) (n=25) with no confounding diagnosis of asthma, VCD, or exercise-induced asthma. Results are not reported for the group that reported exercise-induced asthma with no confounding diagnoses of VCD or asthma (not exercise-induced), as only three participants met the criteria for inclusion in this group. Participants with a primary diagnosis of VCD or asthma (not exercise-induced) that reported a concurrent diagnosis of acid reflux were not excluded from either final participant pool, as acid reflux is a known trigger of VCD (Gurevich-Uvena et al., 2010; Parsons et al., 2010; Yelken, Yilmaz, Guven, Eyibilen, & Aladag, 2009).

Of the 47 participants total that reported a current diagnosis of VCD, 27 of those participants reported some combination of VCD and asthma (not-exercise induced), VCD and exercise-induced asthma, or VCD and both exercise-induced asthma and asthma (not-exercise induced). Additionally, of the 45 participants that reported a current diagnosis of asthma (not-exercise induced) that did not report a current diagnosis of VCD, twenty participants reported concurrent diagnoses of both exercise-induced asthma and asthma (not-exercise induced). Participants with multiple current diagnoses of breathing-related disorders were excluded from the final participant pool, as differential diagnosis of triggers of breathing difficulty would be difficult (if not impossible) to determine in this population.

Triggers of Acute Attacks

The second section of the current survey instrument focused on triggers of acute attacks. Results for each question are reported descriptively here.

Throat Tightness or Sensation of the "Throat Closing Up"

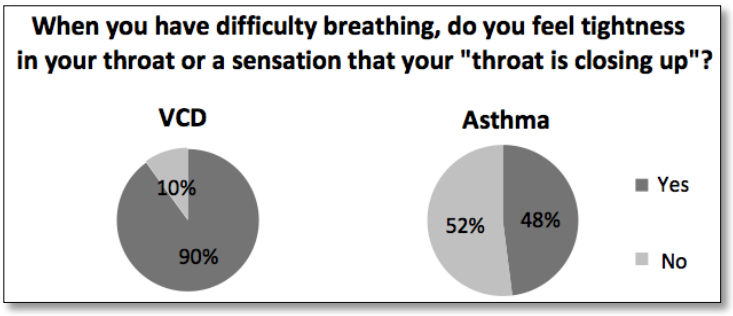


Figure 1. Participants with VCD and asthma were asked if during episodes of breathing difficulty they experience tightness in the throat or the sensation that their throat is "closing up".

90% of VCD participants (n=18) reported that during an acute attack of breathing difficulty they felt as if their throat was "closing up" or tightness in the throat, while 10% (n=2) reported that they did not have this symptom during an acute attack of VCD. 48% of participants with asthma (n=12) also felt tightness in the throat or the sensation that their throat was "closing up." In contrast, 52% of participants with asthma (n=13) did not report this symptom during an acute attack.

Exercise or Physical Activity

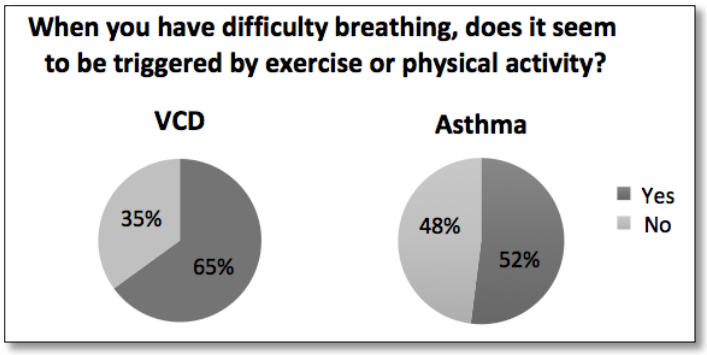


Figure 2. Participants with VCD and asthma were asked if episodes of breathing difficulty seemed to be triggered by exercise or physical activity.

65% of VCD participants (n=13) reported that exercise was a trigger of an acute attack of breathing difficulty, but 35% of VCD participants (n=7) did not have acute attacks triggered by exercise. 52% of asthma participants (n=13) reported that difficulty breathing was triggered by exercise or physical activity, while 48% of asthma participants (n=12) did not have breathing difficulty triggered by exercise or physical activity.

Rapid Onset with Exercise

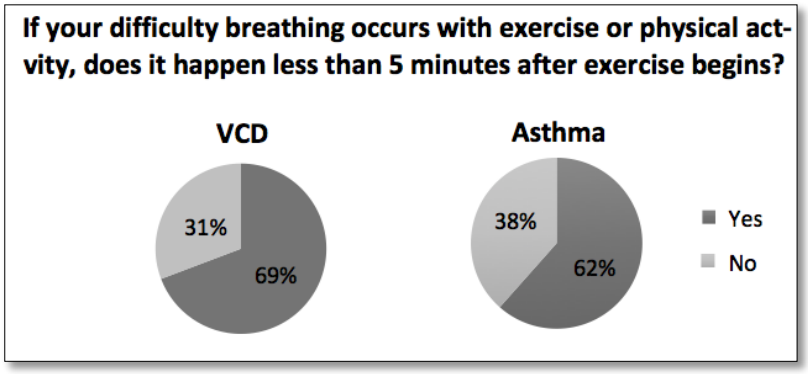


Figure 3. Participants with VCD and asthma were asked if breathing difficulty began within five minutes of beginning exercise or physical activity, if exercise and physical activity was a trigger for breathing difficulty for that participant.

Of the participants who indicated that exercise was a trigger of breathing difficulty, 61.5% of asthma participants (n=8) reported that difficulty breathing occurred within 5 minutes of beginning the activity, while 38.5% (n=5) did not experience onset of breathing difficulty within this time frame. A similar proportion of participants with VCD (69%, n=9) also reported that difficulty breathing during exercise occurred less than 5 minutes after beginning the activity, while 31% (n=4) of participants with VCD reported that they did not experience this rapid onset of breathing difficulty.

Return to Exercise

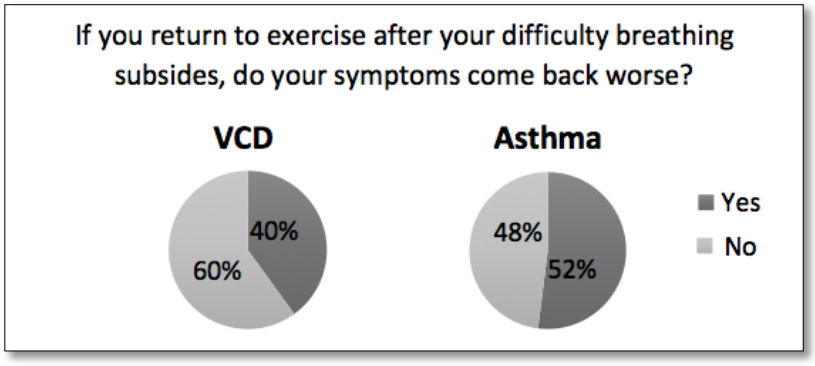


Figure 4. Participants with VCD and Asthma were asked if they returned to exercise after breathing difficulty subsided if they experienced a second, more severe onset of symptoms.

52% of asthma participants reported that if they returned to exercise after their difficulty breathing subsided, symptoms re-occurred worse than the initial acute attack of breathing difficulty (n=13), while 48% of asthma participants (n=12) did not experience a second more severe onset of symptoms after returning to exercise. 40% of VCD participants reported that symptoms came back worse if exercise was resumed (n=8), while 60% (n=12) did not experience this.

Expiratory Stridor

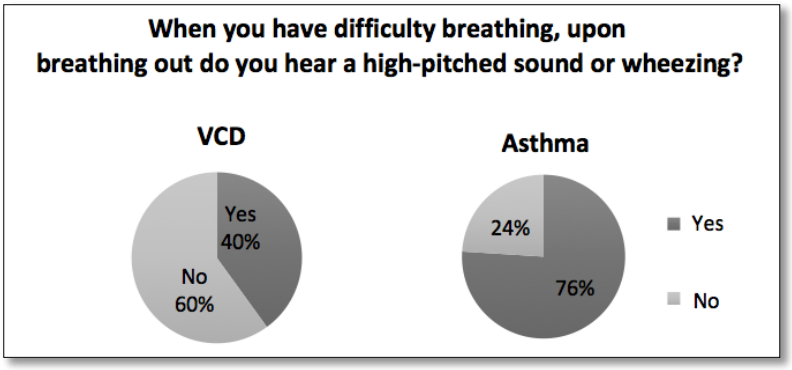


Figure 5. Participants with VCD and asthma were asked if they experienced wheezing or a high-pitched sound (stridor) upon expiration.

76% of participants with asthma (n=19) reported that during an acute attack of breathing difficulty, they experienced stridor (wheezing or a high-pitched sound) upon expiration while 24% of participants (n=6) did not report stridor upon expiration. 40% of participants with VCD (n=8) reported stridor upon expiration. By comparison, 60% of participants with VCD (n=12) did not experience stridor upon expiration.

Inspiratory Stridor

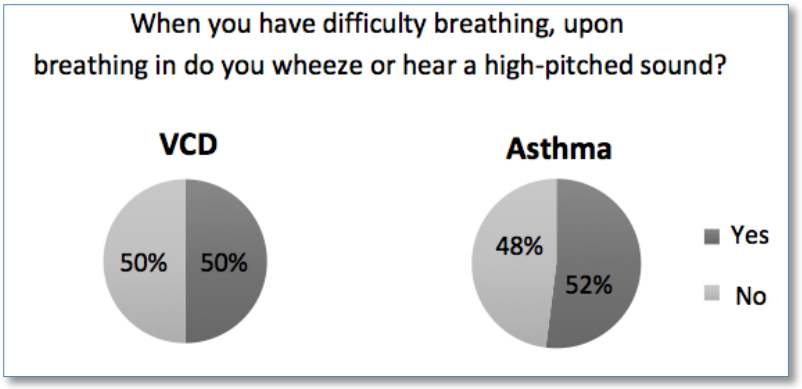


Figure 6. Participants with VCD and asthma were asked if they experienced wheezing or a high-pitched sound upon inspiration.

52% of participants with asthma (n=13) reported that during an acute attack of breathing difficulty, they experienced stridor upon inspiration, whereas 48% of participants with asthma did not report inspiratory stridor (n=12). 50% of participants with VCD (n=10) reported inspiratory stridor, but 50% of participants with VCD denied inspiratory stridor (n=10).

Rapid Resolution of Symptoms without Treatment

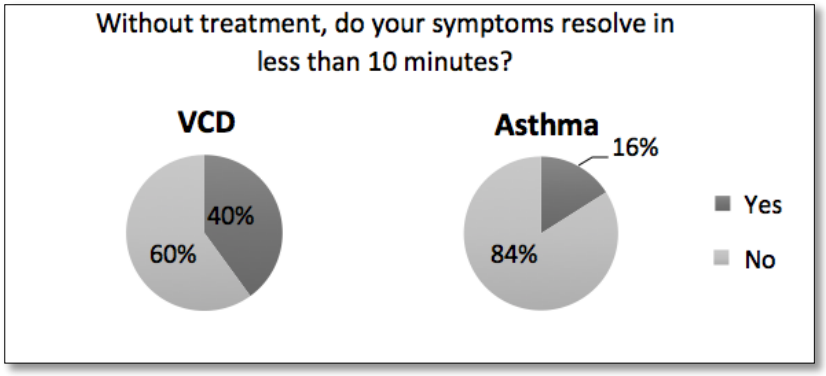


Figure 7. Participants were asked if they experienced resolution of symptoms of breathing difficulty within ten minutes of onset.

16% of participants with asthma (n=4) reported that their breathing difficulty fully resolved within ten minutes without treatment, while 84% (n=21) did not experience rapid resolution of symptoms without treatment. 40% of participants with VCD (n=8) reported that their symptoms of breathing difficulty fully resolved within ten minutes, while 60% (n=12) of participants with VCD did not experience resolution of symptoms within ten minutes of onset.

Extended Duration of Symptoms without Treatment

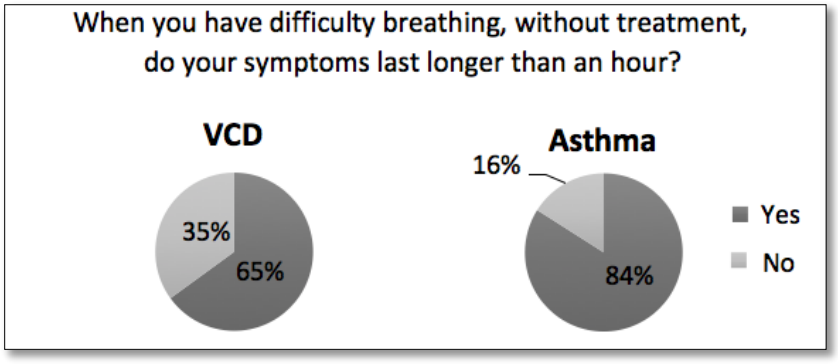


Figure 8. Participants with VCD and asthma were asked if their symptoms of breathing difficulty lasted longer than an hour without treatment.

84% of participants with asthma (n=21) reported that their symptoms lasted longer than an hour without treatment, whereas only 16% of participants with asthma (n=4) experienced resolution of symptoms within an hour without treatment. 65% of VCD participants (n=13) reported that their symptoms lasted for longer than one hour without treatment, while 35% of VCD participants (n=7) reported that their symptoms resolved within an hour without treatment.

Environmental Agents such as Allergens or Irritants

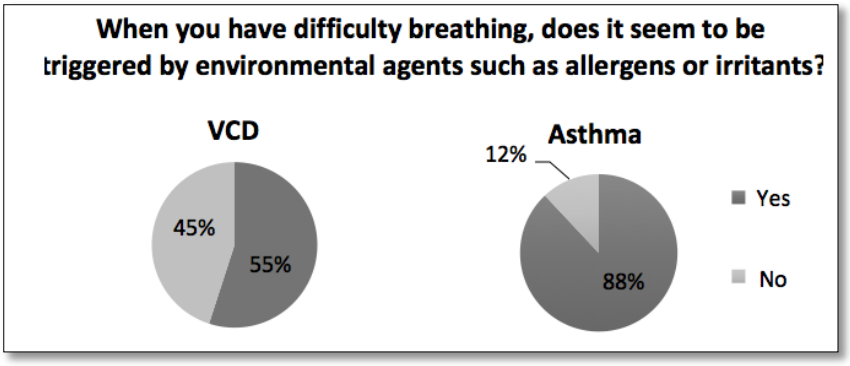


Figure 9. Participants with VCD and Asthma were asked whether their breathing difficulty seemed to be triggered by environmental agents or allergens.

88% of participants with asthma reported that acute attacks were triggered by environmental agents (n=22). By comparison, 12% (n=3) reported that acute attacks of breathing difficulty were not triggered by these agents or allergens. 55% of VCD participants (n=11) reported acute attacks of difficulty breathing were triggered by environmental agents or allergens, while 45% (n=9) of participants with VCD reported that their breathing difficulty did not seem to be triggered by environmental agents, irritants, or allergens.

Acid Reflux

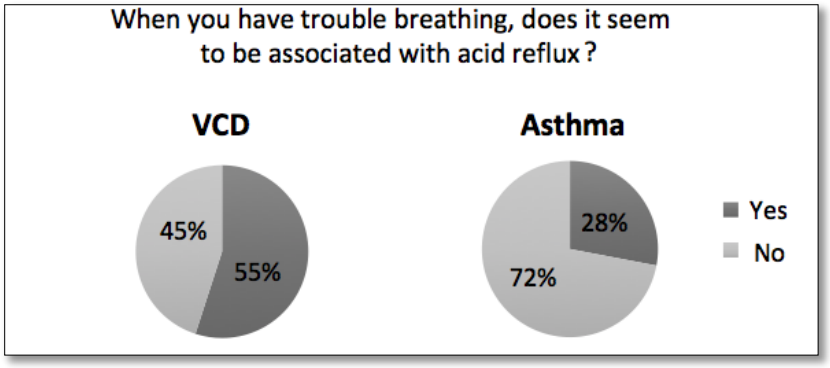


Figure 10. Participants with VCD and asthma were asked if their symptoms seemed to be associated with acid reflux or any of the following signs and symptoms of reflux: heartburn, bad taste in the mouth in the morning, hoarse voice in the morning that improves throughout the day, throat clearing/coughing or a lump-in-the-throat sensation.

28% of participants with asthma (n=7) associated signs and symptoms of acid reflux (either gastroesophageal or laryngopharyngeal type) with acute attacks of difficulty breathing. 72% of participants with asthma did not report an association of acid reflux with acute episodes of breathing difficulty. 55% of participants with VCD (n=11) reported signs and symptoms of acid reflux were associated with acute attacks of VCD. In contrast, 45% (n=9) of participants reported that attacks of VCD did not seem to be associated with signs and symptoms of acid reflux.

Resolution of Symptoms with Use of Asthma Medications/ Inhalers

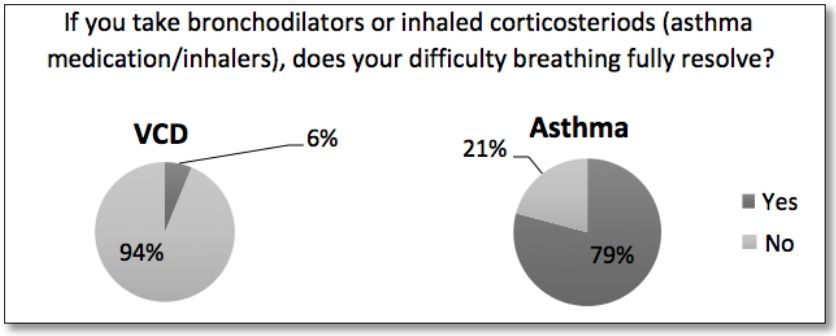


Figure 11. Participants with VCD and asthma were asked if their symptoms fully resolved with use of asthma medication/ inhalers.

79% of participants with asthma (n=19) reported that their symptoms fully resolved with use of asthma medication/inhalers, while 21% of participants with asthma did not experience resolution of symptoms with (n=6). Conversely, 6% of the participants in the VCD group (n=1) reported that their symptoms fully resolved with use of these medications, while 94% (n=19) of participants with VCD reported that their symptoms did not fully resolve with use of asthma medication or inhalers.

Chest Tightness

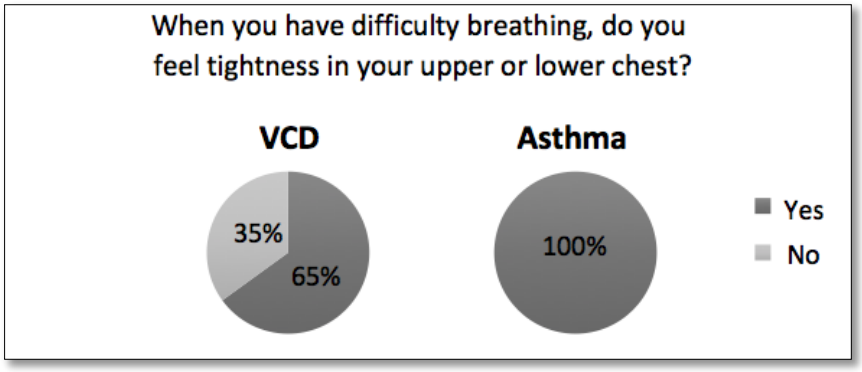


Figure 12. Participants with VCD and asthma were asked if they experienced chest tightness during an acute attack of breathing difficulty.

100% of participants with asthma (n=25) reported that during an acute attack of breathing difficulty, they felt tightness in the upper or lower chest. 65% of participants with VCD (n=13) reported that during an acute attack, they experienced tightness in the upper or lower chest, while 35% of participants with asthma (n=7) did not report chest tightness during an acute attack of breathing difficulty.

Nocturnal Symptoms or Symptoms that Occur in the Morning After Waking

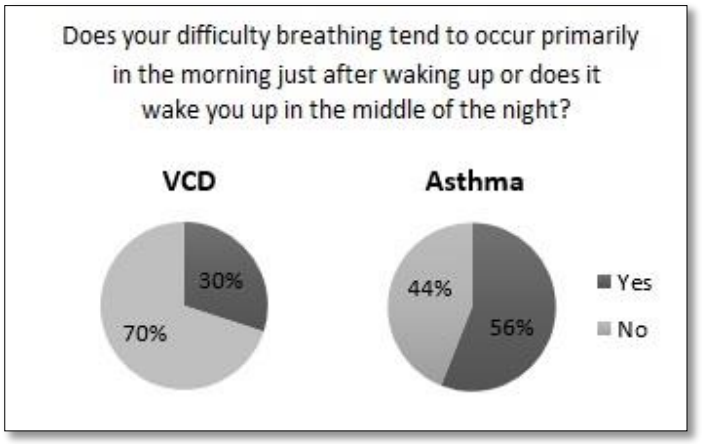


Figure 13. Participants with asthma and VCD were asked if they experienced nocturnal symptoms or symptoms in the morning just after waking.

56% percent of participants with asthma (n=14) reported nocturnal symptoms or symptoms just after waking up. 44% did not experience these symptoms (n=11). 30% of participants with VCD (n=6) reported that they experienced nocturnal symptoms or symptoms that occurred primarily in the morning just after waking up, while 70% of participants with VCD (n=12) did not experience these symptoms.

Misdiagnosis

In addition to specific triggers of breathing difficulty, we were also interested in whether or not the two groups (asthma and VCD) would report different rates of misdiagnosis prior to the diagnosis of their primary disorder of asthma or VCD.

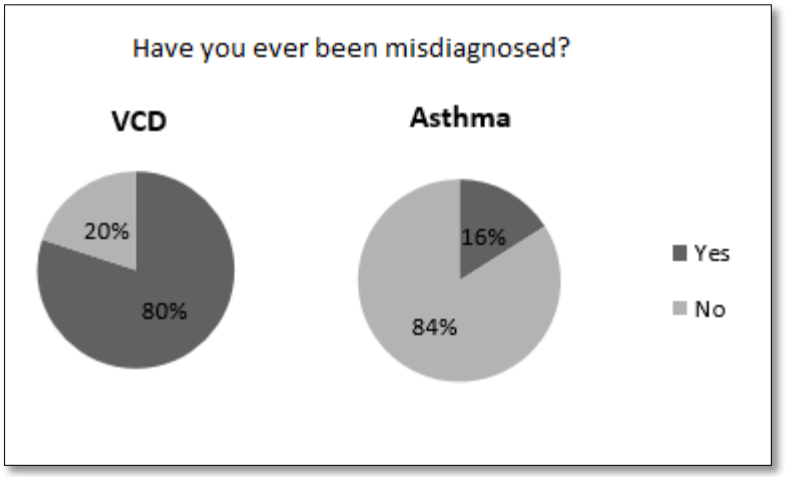


Figure 14. Participant responses to whether or not they have been misdiagnosed with any of the following: VCD, asthma (not exercise-induced), exercise-induced asthma, or acid reflux.

80% of participants with VCD (n=16) reported that they experienced at least one misdiagnosis, while 20% (n=2) reported no misdiagnosis. Conversely, only 16% of participants with asthma (not exercise-induced) (n=4) were misdiagnosed prior to receiving a final diagnosis of asthma (not-exercise induced), while 84% (n=21) of these patients experienced no misdiagnosis. Additionally, participants with VCD who reported misdiagnoses prior to diagnosis of VCD reported on average a greater number of misdiagnoses (n=16, average of 1.75 misdiagnoses) than participants with asthma (n=4, average of 1 misdiagnosis).

Attribution of Symptoms to Psychological Factors

In addition to the triggers and the past/present diagnoses, we also were interested in whether or not participants had ever been informed that their breathing difficulties were psychological in nature.

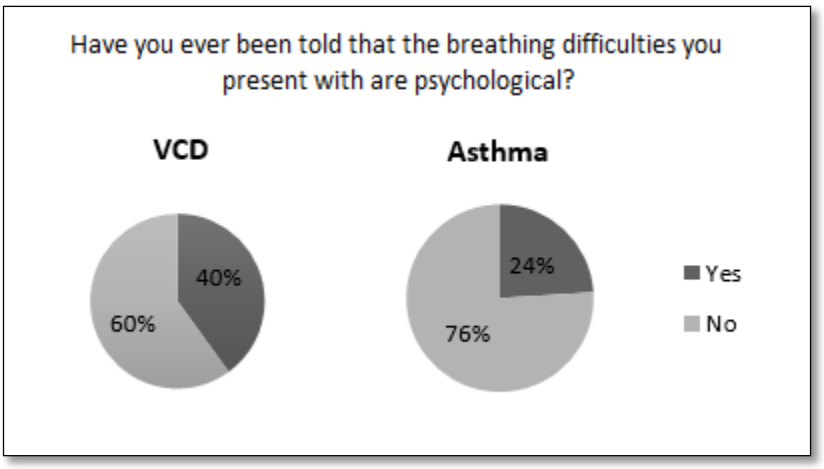


Figure 15. Participants with VCD and asthma were asked if they had ever been told their breathing difficulties were psychological in nature.

40% of participants with VCD (n=8) reported that they had been told that their symptoms were psychological, while 60% (n=12) of participants with VCD did not have this experience. 24% of participants in the asthma group (n=6) also reported that they had been told their symptoms were psychological, while 76% (n=19) of participants with asthma did not report having this experience. Participants who reported that they had had been told their symptoms were psychological were required to provide a text response to identify who had identified their symptoms as psychological. Participants with VCD were

informed their symptoms were psychological by a greater variety of medical professionals (pulmonologist [n=1], respiratory therapist [n=1], primary care physician [n=2], therapist [n=1], allergist [n=1], emergency room physician [n=1], and otolaryngologist [n=1]). By comparison, participants with asthma were informed their symptoms were psychological by a more limited variety of different types of medical professionals (primary care physician [n=1], psychologist [n=2], allergist [1], pulmonologist [n=1], and emergency room physician [n=2]).

DISCUSSION

To review, the primary purpose of the present study was to investigate whether or not factors historically presented in the literature to differentiate patients with VCD from patients with breathing difficulties of other etiologies accurately predict and identify patients with VCD. The secondary purpose was to determine whether or not patients with VCD are at higher risk of misdiagnosis than patients with asthma. The third and final interest was to determine whether patients with VCD were more likely to have their symptoms attributed to psychological factors than patients with breathing difficulties related to other etiologies.

Triggers of Breathing Difficulty

The first hypothesis that we tested was whether the factors historically presented in the literature to differentiate patients with VCD from patients with asthma accurately differentiated the two groups.

Based on a review of the literature, the researchers expected to find that patients with VCD only would report that during an acute exacerbation of breathing difficulty they experienced throat tightness, inspiratory stridor, and rapid resolution of symptoms without treatment. It was also expected that these participants would not experience a complete resolution of symptoms with use of bronchodilators or inhaled corticosteroids (asthma medication), an extended duration of symptoms without treatment, would not have expiratory stridor, and would be less likely to report association of breathing difficulty with allergens or irritants. Additionally, if exercise was a trigger of VCD for the participant, the

researchers expected to find that patients with VCD would experience a rapid onset of symptoms and breathing difficulty that comes back worse if exercise is resumed. It was further hypothesized that these participants would be more likely to have breathing difficulties associated with signs and symptoms of acid reflux (gastroesophageal or laryngopharyngeal type).

Conversely, patients with asthma only were hypothesized to present with expiratory stridor, extended duration of symptoms without treatment, association of breathing difficulty with allergens and irritants, complete resolution of symptoms with use of inhaled corticosteroids or bronchodilators (asthma medications), and chest tightness. It was expected that participants with asthma only would not be likely to report throat tightness, inspiratory stridor, rapid resolution of symptoms without treatment, and association of breathing difficulties with signs and symptoms of acid reflux. If exercise was a trigger of asthma, it was expected that these participants would not experience a rapid onset of symptoms with exercise and breathing difficulty that comes back more severely after exercise is resumed.

Interestingly, none of the factors presented in the literature accurately differentiated the two groups one hundred percent of the time. However, some factors were more likely to be associated with one group or the other.

Throat Tightness or Sensation that the Throat Is "Closing Up"

Throat tightness or the sensation that the "throat is closing up" during an acute exacerbation of breathing difficulty is considered to be a hallmark symptom of VCD.

Gallena et al. (2013) identifies that throat tightness is associated with VCD and not typically associated with asthma. The current survey results diverge from this historical assumption. Though participants with VCD were more likely to report throat tightness than participants with asthma (90% of participants with VCD reported throat tightness), a large portion of participants with asthma (48% of participants with asthma) reported throat tightness when they had an acute exacerbation of breathing difficulty. It remains unclear whether these participants were actually experiencing extra-thoracic laryngeal constriction (a comorbid VCD component), upper chest constriction but felt referred constriction at the level of the larynx, or another unidentified disorder such as anaphylaxis that contributed to a sense of laryngeal constriction upon acute exacerbation of asthma. Regardless, patient report of laryngeal tightness or a sense of the "throat closing up" should alert medical professionals to investigate a diagnosis of VCD further, as an overwhelming majority of participants with VCD report laryngeal tightness. That said, the absence of laryngeal constriction is not sufficient to rule out a diagnosis of VCD, as 10% of participants with VCD as a primary diagnosis did not report this symptom.

Exercise or Physical Activity

It is well established in the literature that both asthma and VCD can be triggered by exercise (Ahrens, Seibt, & Kitz, 2001; Carlsen et al., 2008). This was confirmed in the current study (65% of participants with VCD and 52% of participants with asthma reported that they experienced breathing difficulty with exercise). Though participants in the asthma

group did not have specific diagnoses of exercise-induced asthma, a substantial proportion of participants reported association of exercise or physical activity with exacerbation of symptoms. Although difficulty breathing occurs in both populations with exercise, it was the researchers' hypothesis that the two groups would vary in their presentation of exercise-induced breathing difficulty. Factors related to exercise that were measured specifically in the current survey instrument were time of onset of breathing difficulty and return of symptoms after resolution of symptoms and return to exercise.

Rapid Onset with Exercise

Davis, Brugman, and Larsen (2007) identify that exercise-induced VCD is usually characterized by rapid onset of symptoms with exercise, whereas exercise-induced asthma is typically associated with a more gradual onset of symptoms. However, participants with asthma (62% reported onset of symptoms within five minutes of beginning exercise or physical activity) and participants with VCD (69% reported onset of symptoms within five minutes of beginning exercise or physical activity) reported similar rates of rapid onset of symptoms with exercise. Worth noting is that participants in the asthma group of the current study did not specifically have a diagnosis of exercise-induced asthma. Further research is needed in this area to identify whether patients with a confirmed diagnosis of exercise-induced asthma experience rapid onset of symptoms with exercise similar to the findings of the present study.

Return to Exercise

The current study hypothesized that patients with exercise-induced VCD would experience a more severe exacerbation of symptoms upon return to exercise than the preliminary onset of symptoms, with the reasoning that participants with asthma would use a rescue inhaler that would preclude them from further exacerbation of symptoms upon return to exercise. However, this hypothesis was not supported by the current study. 40% of participants with VCD reported a more severe exacerbation of symptoms upon return to exercise, while 52% of participants with asthma reported a more severe exacerbation of symptoms upon return to exercise. The design of the present study restricts the interpretation of this finding. Possible explanations include: participants who experienced a return of symptoms may have had an unidentified VCD component to their breathing difficulty or they did not use a rescue inhaler. Ambiguity in the wording of the survey question was also present; it is unclear whether participants who answered that they did not experience a more severe return of symptoms upon return to exercise did not experience a return of symptoms at all, or if they experienced a return of symptoms that was less severe or equally severe as the first exacerbation of breathing difficulty. Further research is needed to identify if patients with a confirmed diagnosis of exercise-induced asthma experience rates of secondary exacerbations upon return to exercise similar to patients with VCD, as was found in the current study.

Stridor

Inspiratory stridor is a very common finding in patients with VCD (Cohen, 2010; Gaafar & Fasyh, 2011; Rhodes, 2008). However, an unexpected finding in the present study was that patients with VCD were about as likely to report inspiratory stridor as participants with asthma (52% of participants with asthma and 50% of participants with VCD reported inspiratory stridor). Koufman and Block (2008) identify that asthma patients who have inspiratory stridor should be evaluated for VCD, as they may have a VCD component that exacerbates and/or complicates their asthma diagnosis. VCD may confound asthma as it occurs across the spectrum of asthma severity (Parsons et al., 2010). Within the confines of the present study, it is impossible to know whether the participants with asthma had inspiratory stridor due to unidentified comorbid VCD.

Another possible explanation could include a lack of awareness of when stridor occurs (participants may actually be experiencing generalized dyspnea with expiratory stridor). Kaufman and Block (2009) also identify that inspiratory stridor can be present in patients with bilateral vocal fold paralysis, swelling/edema due to fungal, bacterial, viral infection or inflammation, obstructing benign growths or laryngeal cancer, glottis stenosis. More research in this area is needed to explore and identify why participants with asthma report similar rates of inspiratory stridor as patients with VCD.

Perhaps, more importantly, was the finding that half of the patients with VCD in the present study reported no inspiratory stridor. Koufman and Block (2008) report that some patients with VCD do not have stridor but rather have mild airway obstruction. They identify that patients with VCD triggered by exercise may or may not have symptoms of

stridor. Though inspiratory stridor should cause medical professionals to suspect VCD, absence of inspiratory stridor should not preclude patients from a diagnosis of VCD.

Asthma is associated with expiratory stridor (Davis et al., 2007; Gimenez & Zafra, 2011). 76% of participants with asthma in this present study reported expiratory stridor, while 40% of participants with VCD also reported expiratory stridor. Though participants with asthma were more likely to report expiratory stridor than participants with VCD, a significant proportion of participants with VCD presented with expiratory stridor as well. Some sources identify that patients with VCD can present with both inspiratory and expiratory stridor (Koufman & Block, 2008) and VCD can manifest as biphasic adduction of the vocal folds (Ahrens et al., 2001; Yelken et al., 2009). Thus, the presence of expiratory stridor should not preclude the patient from a diagnosis of VCD.

Duration of Symptoms

Historically, VCD has been associated with sudden onset and rapid resolution of symptoms (Gallena et al., 2013; Mathers-Schmidt, 2001), and asthma has been associated with extended duration of attacks (30-60 minutes or longer) when no treatment is administered with a more gradual onset (Cohen, 2010; Davis et al., 2007). The present study confirms the idea that without treatment, patients with asthma typically experience extended duration of symptoms (only 16% of participants with asthma reported resolution of symptoms in less than 10 minutes without treatment, and 84% of participants with asthma report that without treatment their symptoms last longer than an hour). However, results from the present study also challenge the idea that patients with VCD experience a

rapid resolution of symptoms (only 40% of participants with VCD reported a resolution of symptoms within 10 minutes of onset). Thus, extended attacks of VCD symptoms that endure for longer than 10 minutes should not preclude patients from a diagnosis of VCD, as 60% of patients with VCD in the present study reported that their attacks did not resolve within 10 minutes and 65% of participants with VCD reported that their symptoms last longer than an hour without treatment. Further research is needed to identify whether or not there are specific subsets or subtypes of patients with VCD that experience protracted resolution of symptoms.

Additionally, a limitation of the current research design is that some patients with VCD reported that their symptoms resolved within 10 minutes without treatment, but also that their attacks last longer than an hour without treatment (n=5). Further investigation outside of the scope of the current study is needed to understand these contradictory findings, but they may point to a variability in the presentation of attacks within the same patient. Regardless, it is clear that extended duration of symptoms should not preclude medical professionals from further investigation of a diagnosis of VCD.

Environmental Triggers (Allergens/Irritants)

The literature reports that both VCD and asthma can be triggered by environmental agents such as allergens and irritants, though asthma usually presents with a diverse set of triggers and VCD usually presents with a singular trigger (Mathers-Schmidt, 2001). The current study sought to confirm the idea that both asthma and VCD could be triggered by environmental agents. 88% of participants with asthma reported that their symptoms of

breathing difficulty were triggered by allergens or irritants, while 55% of participants with VCD reported that they experienced an exacerbation of symptoms when exposed to these triggers. Though patients with asthma were more likely to identify allergens or irritants with their symptoms, a significant proportion of patients with VCD also reported this association. The present study confirmed the historical hypothesis that both VCD and asthma can be triggered by allergens and irritants. Therefore, though identification of these triggers is important to treatment of VCD, presence of these triggers is not useful for differential diagnosis.

Acid Reflux

Acid reflux (gastroesophageal or laryngopharyngeal type) is often associated with VCD (Gurevich-Uvena et al., 2010; Koufman & Block, 2008). The current study confirmed this association. Participants with VCD were more likely to report that their acute attacks of breathing difficulty were associated with acid reflux or the signs and symptoms of acid reflux (heartburn, bad taste in the mouth in the morning, hoarse voice in the morning that improves throughout the day, throat clearing/coughing and/or a lump-in-the-throat sensation) than participants with asthma (55% of participants with VCD and 28% of participants with asthma reported that their acute attacks of breathing difficulty were associated with reflux). These preliminary findings suggest that patients with breathing difficulty should be screened for reflux, as presence of reflux may be more indicative of VCD than asthma.

Resolution of Symptoms with Use of Asthma Medication/Inhalers

One of the hallmark symptoms of VCD is dyspnea with a lack of response to asthma medication or inhalers (Gallena et al., 2013; Gimenez & Zafra, 2011; Noyes & Kemp, 2007). The current study supports this historical assertion- 79% of participants with asthma reported that their symptoms fully resolved with the use of these medications, while only 6% (n=1) of participants with VCD reported that their symptoms fully resolved with use of asthma medication. These results suggest that if a patient presents with persistent, uncontrolled symptoms that do not respond to asthma medication, a screening to rule out VCD as a possible cause or comorbid condition is recommended.

Chest Tightness

One symptom that is inconsistently associated with VCD is chest tightness. Some research asserts that this symptom is more commonly associated with asthma whereas in VCD constriction is usually felt at the level of the throat (Koufman & Block, 2008; Nascimento & Tenenbaum, 2013; Rhodes, 2008). Others assert that both VCD and asthma can present with chest tightness (Gimenez & Zafra, 2011; Mikita & Mikita, 2006; Noyes & Kemp, 2007). The current survey was administered to determine if both patients with VCD and asthma experienced chest tightness during an acute attack of breathing difficulty. 100% of participants with asthma in the current study reported chest tightness during an acute attack of asthma, while only 65% of participants with VCD reported chest tightness during an acute exacerbation. These findings support the idea that some patients with VCD

experience the sensation of chest tightness or constriction. Therefore, chest tightness should not preclude patients with VCD from a diagnosis of VCD. These results also suggest that medical professionals should be highly suspicious of VCD if a patient presents with difficulty breathing that is *not* associated with chest tightness, as 100% of participants with asthma in the current study report this symptom.

Nocturnal Symptoms

Nocturnal symptoms are a well-established symptom of asthma and found very rarely in VCD (Gimenez & Zafra, 2011; Mathers-Schmidt, 2001; McFadden & Zawadski, 1996). The current survey instrument sought to investigate whether participants in both groups experienced symptoms in the morning just after waking or symptoms that woke them up at night. 56% of participants with asthma reported symptoms just after waking or nocturnal symptoms, while only 30% of participants with VCD reported these symptoms. Participants with asthma were more likely to report these symptoms, but a substantial portion of participants with VCD also reported these symptoms. Due to ambiguity in the wording of the survey question, it is impossible to identify whether the VCD participants were more likely to experience nocturnal symptoms or morning symptoms (which could be associated more with reflux). Further research is needed to fully understand the nature of nocturnal symptoms and symptoms just after waking in patients with VCD.

Misdiagnosis

A secondary hypothesis of the present study was that participants with VCD would be more likely to have been misdiagnosed prior to their final diagnosis of VCD than participants with asthma. The literature states that participants with VCD, especially those with exercise-induced VCD have a high rate of misdiagnosis (Ahrens et al., 2001; Gallena et al., 2013; Gurevich-Uvena et al., 2010). The present study confirmed this assertion. Participants with VCD (80% of participants in the present study) were overwhelmingly more likely to be misdiagnosed (with asthma, acid reflux, or exercise-induced asthma), and on average had a greater number of misdiagnoses than participants with asthma (1.75 misdiagnoses per person). Participants with asthma had a drastically lower rate of misdiagnosis (only 16% of participants in the sample reported experienced a misdiagnosis of VCD, exercise-induced asthma, or acid reflux) and of the participants with asthma that experienced a misdiagnosis, they had fewer misdiagnoses on average (1.0 misdiagnoses per person).

Attribution of Symptoms to Psychological Factors

VCD symptoms have consistently been mistakenly associated with psychological correlates and malingering. For this reason, the researchers were interested in whether or not this inaccurate association still exists in the medical field. Interestingly, 40% of participants with VCD identified that a medical professional had attributed their symptoms to psychological factors. However, 24% of participants who had asthma also reported that

their symptoms had been attributed to psychological factors by a medical professional. Though participants with VCD were more likely to have their symptoms attributed to psychological factors, a significant percentage of participants with asthma also reported this. Therefore, from these data, it is unclear whether or not the association between VCD symptoms and psychological disorders or correlates still exists. Further investigation into the attitudes and practice of professionals that encounter patients with VCD is needed.

Limitations

The primary limitation of this current research design was that the researchers were unable to confirm the diagnoses and/or review the medical records of the participants in the final participant pool due to the limitations of survey research. Therefore it is possible that some participants did not accurately report all of their current diagnoses or past misdiagnoses. It is also possible that participants had confounding and unidentified diagnoses that were not reported, due to the difficulty that differential diagnosis of vocal cord dysfunction poses for medical professionals.

Worth noting is that a large portion of participants that responded to the survey reported multiple diagnoses that impact breathing, and therefore were not included in the final participant pool. This could be due to the high rates of misdiagnosis of patients with VCD (patients reported multiple diagnoses, but their symptoms are actually explained by the primary diagnosis of VCD) that is noted in the literature (Gimenez & Zafra, 2011; Nascimento & Tenenbaum, 2013; Zelcer, Henri, Tewfik, & Mazer, 2002). The comorbidity

of VCD with other breathing disorders (namely asthma) is also reported in the literature (Gurevich-Uvena et al., 2010; Koufman & Block, 2008; Yelken et al., 2009). Because of the nature of the present survey, it was impossible to determine whether the participants that reported multiple current diagnoses that affect breathing actually had multiple diagnoses or whether or not they had been misdiagnosed. Thus, these participants were excluded from the final participant pool. Future research designs should investigate the nature of the diagnoses of all participants and use instrumental analysis to confirm diagnoses of participants. Unique profiles or participants with multiple diagnoses that impact breathing may emerge with this type of analysis.

CONCLUSION

The present study sought primarily to investigate whether factors historically presented in the literature to differentiate vocal cord dysfunction (VCD) from breathing difficulties of other etiologies accurately predict and identify patients who have VCD. None of the factors investigated accurately differentiated participants with asthma from participants with VCD one hundred percent of the time. However, the factors that were more likely to be reported by participants with VCD were throat tightness during an attack, association of an attack with symptoms of acid reflux, and rapid resolution of symptoms without treatment. Participants with asthma were conversely more likely to report that during an acute exacerbation of breathing difficulty they experienced expiratory stridor and chest tightness, full resolution of symptoms with use of asthma medications, nocturnal symptoms or symptoms just after waking, and symptoms that seemed to be triggered by environmental agents or allergens. That said, for each of the previously mentioned factors, some participants from each group experienced each factor. Therefore, a diagnosis of VCD must be made very carefully, ideally with instrumental evaluation of the vocal mechanism, as the factors identified in the literature do not accurately differentiate patients with VCD from patients with asthma.

The present study was also interested in whether patients with VCD have a higher risk of misdiagnosis than patients with breathing difficulties of other etiologies and if patients with VCD are more likely to have their symptoms attributed to psychological factors than patients with breathing difficulties of other etiologies. Preliminary findings from the present study suggest that patients with VCD are both more likely to receive a

misdiagnosis and have their symptoms attributed to psychological factors than participants with asthma. These findings suggest that continued education about the nature of VCD and differential diagnosis should be paramount to medical professionals, including but not limited to: speech-language pathologists, otolaryngologists, allergists, emergency room and urgent care physicians, and primary care physicians.

Appendix A- Survey Questions

Demographic Questions:

1. What is your age? Note: This survey may only be completed by persons 18 years or older. Parents and Guardians over the age of 18 may complete the survey for their dependent. [under 5, 5-9, 10-14, 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, 85-89, 90-94, 95-99]

2. What is your gender? [Male, Female, Prefer not to answer]

The following questions are about your current diagnosis/diagnoses. Please note that it is understood that you may have more than one diagnosis.

3. Do you have a current diagnosis of exercise-induced asthma? [yes, no]

   If so, at what age were you diagnosed?

   If so, who made the diagnosis? [ear nose and throat doctor (ENT), allergist, primary care physician (family doctor), pulmonologist, other]

4. Do you have a current diagnosis of asthma (not exercise-induced)? [yes, no]

   If so, at what age were you diagnosed?

   If so, who made the diagnosis? [ear nose and throat doctor (ENT), allergist, primary care physician (family doctor), pulmonologist, other]

5. Do you have a current diagnosis of acid reflux (i.e. GERD, gastroesophageal reflux, laryngopharyngeal reflux) ? [yes, no]

   If so, at what age were you diagnosed? [text response]

   If so, who made the diagnosis? [ear nose and throat doctor (ENT), allergist, primary care physician (family doctor), pulmonologist, other]

6. Do you have a current diagnosis of vocal cord dysfunction (i.e. VCD, paradoxical vocal fold movement or vocal cord dysfunction)?
   If so, at what age were you diagnosed? [text response]
   If so, who made the diagnosis? [ear nose and throat doctor (ENT), allergist, primary care physician (family doctor), pulmonologist, other]

The following questions will ask about your triggers of breathing difficulty (i.e. "attacks")

7. When you have difficulty breathing, do you feel tightness in your throat or the sensation that your "throat is closing up?" [yes/no]
8. When you have difficulty breathing, does it seem to be triggered by exercise or physical activity? [yes/no]
9. If your difficulty breathing occurs with exercise or physical activity, does it happen less than 5 minutes after beginning the activity? [yes/no/not applicable]
10. When you have difficulty breathing, upon breathing out do you wheeze or hear a high-pitched sound? [yes/no]

11. When you have difficulty breathing, upon breathing in do you wheeze or hear a high-pitched sound? [yes/no]
12. Without treatment, do your symptoms resolve within 10 minutes? [yes/no]
13. If you return to exercise after your difficulty breathing fully subsides, do your symptoms come back worse? [yes/no]
14. When you have difficulty breathing, does it seem to be triggered by environmental agents such as allergens or irritants? [yes/no]
15. When you have trouble breathing, does it seem to be associated with acid reflux or any of the following symptoms: heartburn, bad taste in the mouth in the morning, hoarse voice in the morning that improves throughout the day, throat clearing/coughing or a lump-in-the-throat sensation? [yes/no]
16. When you have difficulty breathing, without treatment, do your symptoms last longer than an hour? [yes/no]
17. If you take bronchodilators or inhaled corticosteroids (asthma medication/inhalers), does your difficulty breathing fully resolve? [yes/no/ not applicable]
18. When you have difficulty breathing, do you feel tightness in your upper or lower chest? [yes/no]
19. Does your difficulty breathing tend to occur primarily in the morning just after waking up or does it wake you up in the middle of the night? [yes/no]

The following questions are about your previous misdiagnosis/misdiagnoses.

20. In your lifetime, have you been misdiagnosed with exercise-induced asthma? [yes/no]

    If you have been misdiagnosed with exercise-induced asthma, at what age were you misdiagnosed? [text response]

    Who made the misdiagnosis of exercise-induced asthma? [ear nose and throat doctor (ENT), allergist, primary care physician (family doctor), pulmonologist, other]

21. In your lifetime, have you been misdiagnosed with asthma (not exercise-induced)? [yes/no]

    If you have been misdiagnosed with asthma (not exercise-induced), at what age were you misdiagnosed? [text response]

    Who made the misdiagnosis of asthma (not exercise-induced)? [ear nose and throat doctor (ENT), allergist, primary care physician (family doctor), pulmonologist, other]

22. In your lifetime, have you been misdiagnosed with acid reflux (i.e. GERD, gastroesophageal reflux, laryngopharyngeal reflux)? [yes/no]

    If you have been misdiagnosed with acid reflux, at what age were you misdiagnosed? [text response]

    Who made the misdiagnosis of acid reflux? [ear nose and throat doctor (ENT), allergist, primary care physician (family doctor), pulmonologist, other]

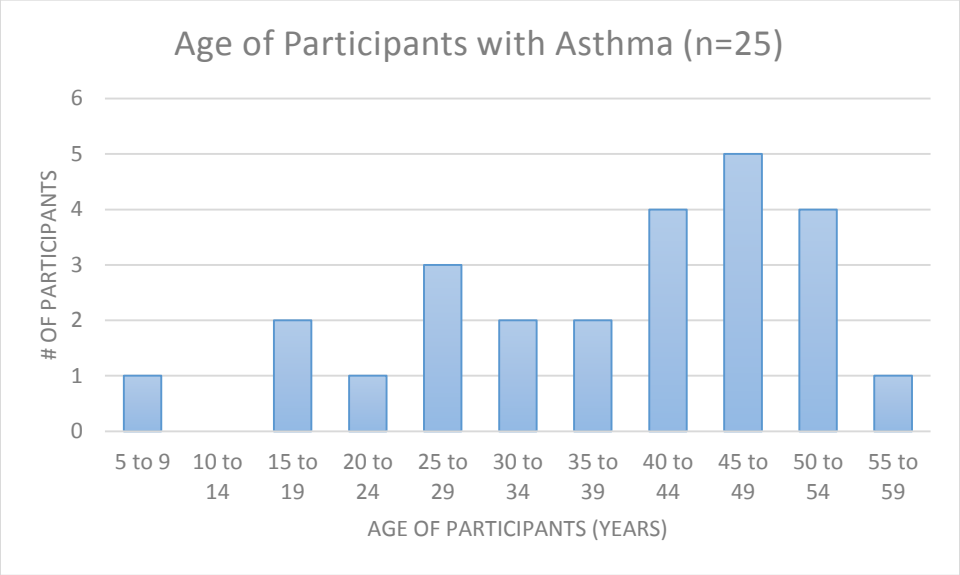
23. In your lifetime, have you been misdiagnosed with vocal cord dysfunction (VCD) (i.e. paradoxical vocal fold movement, vocal fold dysfunction)? [yes/no]

    If you have been misdiagnosed with vocal cord dysfunction (VCD), at what age were you misdiagnosed? [text response]

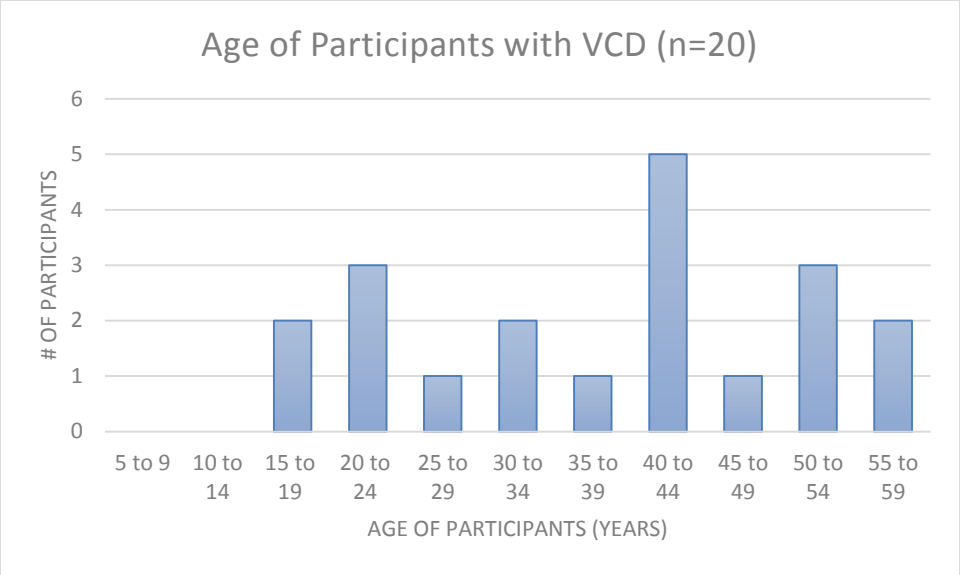
Who made the misdiagnosis of vocal cord dysfunction (VCD)? [ear nose and throat doctor (ENT), allergist, primary care physician (family doctor), pulmonologist, other]

Appendix B- Demographic tables

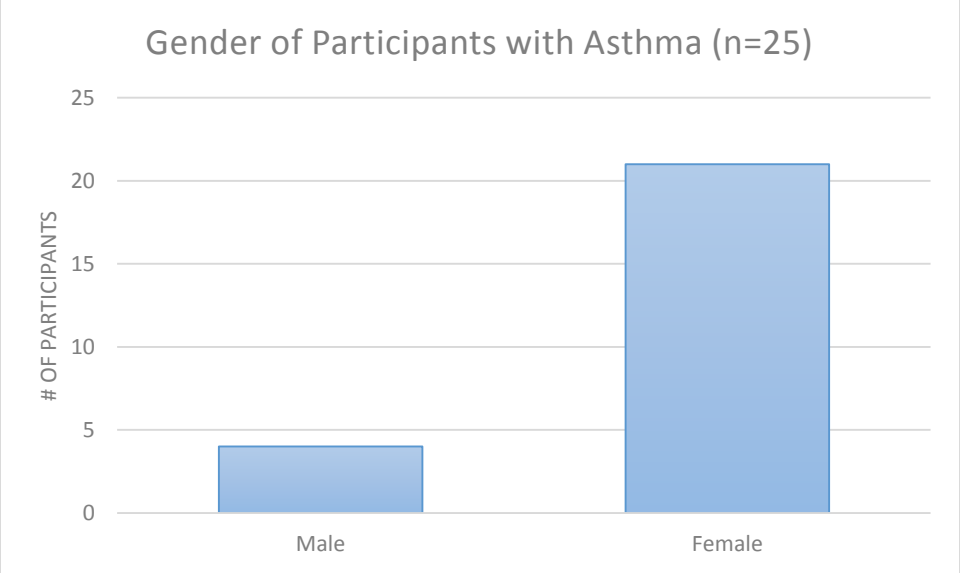
Age of Participants with Asthma



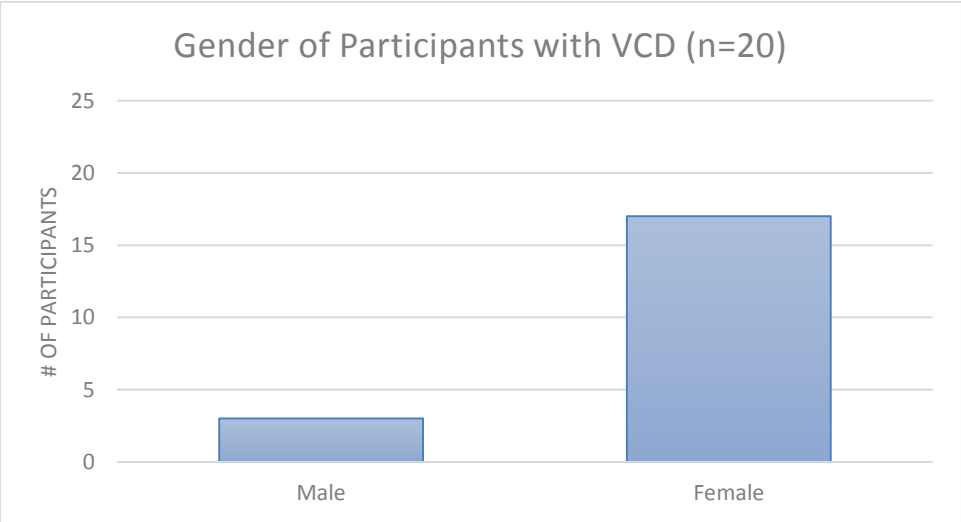
Age of Participants with VCD



Gender of Participants with Asthma



Gender of Participants with VCD



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