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Chart Review Observing Depression And Anxiety In A Cohort Of Nontuberculous Mycobacteria Patients

by

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Abstract:

Previous work has shown that elderly women with chronic or infectious disease are at an especially high risk for mental health disorders such as depression and anxiety [1]. Although, Nontuberculous mycobacterium (NTM) is a common lung disease in Oregon, little research has been published on fundamental epidemiological measures such as prevalence, or incidence, populations risks, and disease comorbidities [2] [3] [4]. The objective of the study is to build a rationale for screening for anxiety and depression in NTM patients through a review of current literature of other lung diseases. Additionally, this project includes a chart review that shows the proportion of patients with NTM who lack history of mental health diagnosis or medication prescription, but have high scores on the Patient Health Questionnaire (PHQ-8) and/or Generalized Anxiety Disorder (GAD-7), reflecting potentially significant symptomology of either depression, anxiety, or both. A cutoff score for "positive" vs. "negative" presence of each disorder was established, based on prior studies using these scales. Questionnaire data have been accumulated on patients in the study. These data were gathered, originally, for a larger biobank study by OHSU's Center for Infectious Disease team. In addition to the screening results, data regarding the patients' anxiety and/or depression diagnosis history and psychotherapeutic medication prescription history has been included in analysis. This has been done through a chart review of the patients' electronic medical records using the Epic system. Statistical analysis using a chi-square has helped ascertain if the prevalence of patients who show symptoms, but no intervention is significantly higher than in those who do not. For both depression and anxiety there is a statistically significant relationship ($p<0.05$ and $p<0.001$ respectively) between

screening score and the presence of a diagnosis/medication. Most participants who screened

positive had both a diagnosis and took medications or they had neither. With these data I provide

a recommendation that once patients are found positive for NTM, providers should screen for

both depression and anxiety regardless of mental health history.

Acknowledgements:

Background/Literature Review

What is Nontuberculous mycobacterium:

Nontuberculous mycobacterium (NTM) is a non-contagious, chronic, pulmonary lung condition. NTM is most commonly caused by the pathogenic complex *Mycobacterium avium-intracellulare*. However, dozens of bacteria that result in NTM have been documented. The mechanism of disease onset is currently unknown, although research has linked infection to vaporized water and airborne soil [5].

Similar to tuberculosis (TB), chronic obstructive pulmonary disease (COPD), and cystic fibrosis (CF), the symptoms of NTM include shortness of breath (SOB), excessive coughing, fever and/or fatigue [5]. Although this disease affects mostly older people, for years patients are often misdiagnosed with other lung conditions such as asthma. In order to correctly diagnose this disease, two positive sputum samples or one bronchoscopy and a chest CT is needed. The disease displays itself differently among patients, which is part of the reason why it is often misdiagnosed. Some patients are asymptomatic and others, due to severe comorbidities and other clinical issues, may require oxygen. Another interesting differentiation between patients is that some patients may clear or contain the infection without further disease progression. For other patients, the disease will progress typically for several years causing chronic airway infection, destruction of lung tissue, shortness of breath, fatigue, decreased quality of life, and in some cases death. Treatment of this disease requires an antibiotic regime of 3-5 drugs for typically 18-24 months [5]. Multiple drugs are required to control the symptoms and prevent disease spread, but the treatments are rarely curative. Additionally, the antibiotics often have irreversible negative side effects like the risk of hearing and vision loss. Finally, another major barrier to treating

NTM is the high rate of comorbidities with other diseases such as COPD, bronchiectasis, and CF [5].

Due to minimal availability of epidemiological data and literature on NTM, few sources have obtained reports of the average age of NTM diagnosis, which is estimated to be around 69 years [2][6]. Women have been found to be affected disproportionately more often than men; they comprise approximately 56 % of patients with NTM [2]. The prevalence of NTM in 2006 was twenty per one-hundred thousand [7]. Although, the prevalence was low, the incidence has been steadily increasing over the last decade [2].

Anxiety and Depression in the General Population:

The CDC defines depressive disorder as a prolonged feeling of sadness that interferes with normal functioning of life [8]. The NIH defines anxiety disorder as prolonged feeling of uneasiness or worry that, like depression disorder, interferes with normal functioning of life [9]. According to the Anxiety and Depression Association of America, the prevalence of Major Depressive Disorder and Generalized Anxiety Disorder are 6.7% and 3.1% respectively [10]. Healthy geriatric patients have been shown to have a prevalence of depression 1-4%. Women in the elderly population are found to have depression twice as often compared to elderly men [11]. One study also found that healthy geriatric patients have also shown a prevalence anxiety of 4.6%, with only 36% being treated for it [11]. Anxiety, in elderly populations, have a prevalence of comorbidity with depression to be 38.6 %, which means it is not uncommon for patients to experience both [12].Overall, with regards to risk, elderly patients who are single, younger, female, and low income are more likely to experience anxiety and depression symptoms [12][13].One of the

reasons why mental health is studied in this population is that affective disorders like depression

and anxiety have been shown to be major drivers of patient's health and quality of life [14].

Treatment for depression, as well as anxiety, is mainly pharmacotherapy and psychotherapy.

Other forms of therapy like exercise, yoga, and music can also reduce anxiety and depression

symptoms [15] [16].

What started the conversation of mental health in NTM patients:

In 2015, the Center of Infectious Disease team (CIDS) at OHSU gathered together

clinicians, patients, and providers from all around the state. They spent an entire day discussing

the lack of research in NTM research and clinical care. One of the topics that was brought up

was the need for assistance in lessening the impact of mental health for patients with NTM [17].

This had kickstarted the conversation surrounding mental health for this patient population and

exemplified the need for research. Currently, there appears to be little or no research being done

to determine the prevalence and impact of mental health disturbances in patients with NTM. This

is the case, although depression and/or anxiety in bronchiectasis, TB, COPD, and CF are widely

studied. To show the importance of studying mental health in this population, other lung disease

research will be used as a baseline of information. The three lung diseases most like NTM are

chronic obstructive pulmonary disease (COPD), cystic fibrosis (CF), and tuberculosis (TB).

COPD is a chronic lung condition that causes obstructed airflow. CF is a chronic genetic disorder

that allows thick mucus to get clogged in the patient's airways. TB, on the other hand, is the

most similar lung condition to NTM, because it is a chronic infectious disease. TB and NTM are

also similar with regards to patient clinical symptoms and signs, and chest radiograph results [18].

Depression and Anxiety in Lung Disease Populations:

Chronic disease, as well as lung disease populations have high rates of anxiety and depression. Depression in TB patients have been shown to be present in up to 70 % of ambulatory populations and 80 % in hospitalized populations [14]. It's also been found that depression and anxiety in TB patients has a prevalence of 43 % and 41 % respectively, with a comorbidity of both to be 40 % [19]. One study found that one in four COPD patients experience significant depression symptoms [20]. COPD patients are ten times more likely to experience anxiety symptoms or panic attacks compared to the general population [20]. Anxiety has shown to have a prevalence of about 40% in COPD patients [20]. For patients with interstitial lung disease, the prevalence of depression is 21 % [21]. Anxiety, on the other hand has been observed in 31% of patients with interstitial lung disease [22]. Looking at CF patients, in one study 19 % have shown depressive symptoms and 32 % have shown anxiety symptoms. Overall, the symptom elevations were 2–3 times those of community samples [23]. With increasing symptom severity, the number of symptoms, and the amount of medications, comes an increasing rate of depression and anxiety [20] [21]. It is unclear what happens first, the lung disease symptoms severity or the depression, but with interstitial lung it is argued that it is actually health related quality of life, dyspnea, and lack of physical activity that leads to the mental disorder symptoms [20].

Knowing that lung disease populations have high rates of anxiety and depression, there are several reasons why this is detrimental to the lives of these patients. Anxiety and depression have been shown to have a significant association with disease symptoms like pain and dyspnea severity [21]. When controlling for physical ailments, the presence of anxiety and depression were

found to increase the cost of care by 45% in COPD patients [20]. COPD patients with these diagnoses are also more likely to have increased utilization rates and costs associated with their care during their visit at the hospital [20]. Along with an increased cost of care, the presence of depression in a COPD population is associated with an 12% increase in COPD-related physician visits, 2% higher number of annual hospitalizations, and 48% more COPD-related ER visits [24]. This same population is also more likely to have an increased length of stay at hospitals. Mental health has also been shown to affect patients' ability to self-manage disease [25] [26]. Although all of these are important factors that pulmonologists need to keep in mind when treating their lung disease patients, none of this matters if the patient isn't being adequately treated for their mental health. One study found that in COPD patients with depression, only 27-33% were being treated for it [25]. Anxiety also has been shown to affect a large portion of patients not being treated for it [27].

Overall, although no studies have determined it to be so, based on the risks for depression and anxiety for patients with similar lung diseases, NTM patients may have high risk of anxiety and depression. NTM patients are mostly elderly, female, with many medications and symptoms, all of which are risk factors for depression and anxiety. The importance of researching depression and anxiety in this patient population goes beyond helping patients feel better. Research suggests that depression and anxiety may impact treatment adherence, as suspected with coronary artery disease patients [28]. This is especially important since both CF and bronchiectasis patients have shown low treatment adherence over the course of several months [29]. CF patients tend to report high treatment burden due to the intensive measures required to take the medication, much like how involved NTM medication regimens are [26].

To help determine if patients experience affective disorder symptoms, providers and researchers use screening tools. The most common screening tools for anxiety are the Anxiety Inventory for Respiratory Disease (AIR) and the Generalized Anxiety Disorder Scale (GAD-7). The most common screening tools for depression are the Hospital Anxiety and Depression Scale (HADS) and Patient Health Questionnaire Scale (PHQ-9). Although there are two scales that were specifically made for the elderly population; Geriatric Depression Scale (GDS-15) and Geriatric Anxiety Scale (GAS-10), since some NTM patients are not elderly, using the geriatric scales are not justified [30] [31]. This study will use the PHQ-8, a depression screening tool, and the GAD-7, an anxiety screening tool. Both screening tools, similar to other tools of the same purpose, have been shown to have high validity and reliability in screening for these two mental health diseases [32] [33]. The PHQ-8 gives a maximum value of 24 and the GAD-7 gives a maximum value of 21. A score greater than or equal to 10 is deemed diagnostic as seen from literature for the PHQ-8 and GAD-7 [34] [32].

This thesis will determine if there is inadequate surveillance of mental health care from Primary care physicians (PCP's). Additionally, as explained in the abstract, this thesis will determine if there is a need for Pulmonologists to screen for depression/anxiety in NTM patients. The authors of one article, deemed the largest anxiety and depression screening to date for CF patients, recommends yearly screenings for both disorders [35]. Additionally, the US Preventative Task Force recommends that anyone over the age of 60 years old should have regular screening for depression. But this screening should be paired with an environment that can treat, diagnose, and follow up with the patient [36] [37]. The process of deciding who will screen the patients may be problematic since PCPs bear the greatest burden of diagnosing and treating mental health disorders in their patients, but the nature of primary care practice (high patient loads, short office

visits, multiple diagnoses, etc.) may sometimes cause problems to fall through the cracks. Since mental health has been shown to affect disease outcomes like treatment adherence and success, all providers must make it a priority to discover what obstacles the patient may face that will prevent clinical success.

Methods/Project Design:

Main study methods:

The study took place at the Oregon Health and Science University (OHSU) Hospital's Pulmonology Medicine clinic. The two attending physicians were Dr. Kevin Winthrop and Dr. Luke Strnad. The consent and survey process took place at the clinic. Following consent, the research coordinator (myself and other IDS staff) gave the patients two surveys; The PHQ-8, and the GAD-7 scale. The original study was made to create a repository of NTM-positive patient information for multiple studies. The biobank repository allows the Infectious Disease staff to analyze and observe disease activity, quality of life, NTM module validity, and human specimen immune response for our NTM population. Although this thesis is primarily a chart review of cohort NTM patients, patient recruitment and screening will continue indefinitely, by both myself and OHSU IDS staff.

Thesis project:

The data taken at enrollment was date of birth, ethnicity, gender, marital status, highest education level, GAD-7 score, and PHQ-8 score. The screening scores were stored in OHSU's HIPAA approved research database, REDcap. Patient information in REDcap was paired with a study ID. In order to connect the study ID with the patient's name and MRN, a separate password protected database was accessed.

During this chart review I looked into the patient's electronic medical records using Epic. Two things were searched for in Epic about depression and anxiety; history of diagnosis and psychotherapeutic medications. Since most of the patients do not maintain their primary care at OHSU, their medical records were shared to the OHSU Epic system, Care Everywhere. Diagnosis information was found in the "problems list", "resolved problems list", or "medical history" list. Anything posted in these categories on Epic require a diagnosis, prior to display. The presence of psychotherapeutic medications was found by going into the "Chart Review" section of Epic and finding the day of enrollment. By opening the provider's "Encounter summary", I was able to cross reference the list of medications they were taking with a list of the most common depression and anxiety medications. This list included both generic and brand name medications as shown from Table 1 and Table 2. The sources for this list include the FDA, the Mayo clinic, WebMD, Healthyplace, and Healthline, with every medication on the list being sourced from at least two places. For those with a diagnosis and a medication that was dual-purpose for anxiety or depression, I paired the medication intent with the diagnosis. For those with a dual-purpose medication, but no diagnosis, both anxiety and depression were labeled as the intent for the medication.

Table 1. List of Depression Medications Used in Analysis		
Class type	**Brand Name**	**Generic Name**
Selective Serotonin Reuptake Inhibitors (SSRIs)	Celexa *	Citalopram *
	Lexapro *	Escitalopram *
	Paxil, Pexeva *	Paroxetine *
	Prozac	Fluoxetine *
	Luvox*	Fluvoxamine*
	Zoloft *	Sertraline *
Monoamine Oxidase Inhibitors (MAOIs)	Emsam *	Selegiline *
	Marplan *	Isocarboxzaid *
	Nardil *	Parnate *
	Phenelzine *	Tranylcypromine *
Tricyclic Antidepressants	Elavil, Endep, Levate	Amitriptyline
	Asendin	Amoxapine
	Norpramin, Pertofrane *	Desipramine *
	Adapin, Silenor, Sinequan *	Doxepin *
	Tofranil *	Imipramine *
	Anafranil *	Clomipramine *
	Aventyl, Pamelor	Nortriptyline
	Vivactil	Protriptyline
	Surmontil, Trimip, Tripramine	Trimipramine
Atypical Antidepressants	Ludimol	Maprotiline
	Desyrel*	Trazodone *
		Nefazodone
	Remeron	Mirtazapine
	Viibryd	Vilazodone
	Trintellix, Brintellix	Vortioxetine
	Wellbutrin, Wellbutrin, Aplenzin, Forfivo XL, Budeprion SR, Budeprion XL, Buproban, Wellbutrin SR, Wellbutrin XR, Zyban	Bupropion
Selective Serotonin and Norepinephrine Reuptake Inhibitors (SNRI)	Cymbalta *	Duloxetine *
	Effexor, Effexor XR *	Venlafaxine *
	Pristiq, Khedezla	Desvenlafaxine
	Fetzima	Levomilnacipran
Medications with astrisk (*) can be used on both anxiety and depression		

Table 2. List of Anxiety Medications Used in Analysis		
Class type	**Brand Name**	**Generic Name**
Benzodiazepines	Xanax	Alprazolam
	Librium	Chlordiazepoxide
	Klonopin	Clonazepam
	Valium	Diazepam
	Ativan	Lorazepam
	Serax	Oxazepam
Anticonvulsants	Depakote, Depakote ER	Divalproex
	Neurontin	Gabapentin
	Lyrica	Pregabalin
Beta-Blockers	Tenormin	Atenolol
	Corgard	Nadolol
	Inderal, Betachron E-R, InnoPran XL	Propranolol
Antipsychotic	Moban	Molindone
	Zyprexa	Olanzapine
	Seroquel	Quetiapine
	Risperdal	Risperidone

Once medication use and diagnosis data were extracted, the access dataset was converted to a delimited comma-separated file and imported to Stata. Once in Stata the categorical marital status was recorded to become a dichotomous variable. Ethnicity, a once categorical variable, was also recorded to become dichotomous variable. For statistical analysis, a chi-square was taken for both anxiety and depression, between positive screening scores and the presence of a diagnosis or medication.

Results:

As shown in Table 3, the participants are mostly white (89%), with a partner (67%), and have a variety of education levels. Although about fifty percent of the patient population don't have a college degree, the proportions between education levels listed are nearly the same proportion between categories. The percentage of those with a high school diploma, college degree, some college, and professional degrees are 29%, 25%, 26%, and 20% respectively. The average age is 70 years old, which classifies the patient population as "old or elderly" [38]. Another important factor is that the participants were disproportionately female, with 78% being female and 22% being male. The ethnicity, average age, and gender proportions in this study were consistent with previous research done in Oregon, as listed in the Literature review section. Finally, the average score for the GAD-7 and the PHQ-8 are 4.5 and 5 respectively.

Table 3. Demographics

	N (%)	Mean (SD)	Range
Anxiety Screening Score		4.00 (4.00)	(0-21)
Depression Screening Score		4.50 (5.09)	(0-23)
Highest Education Level			
High school or less	61 (28.65)		(0, 1)
Some college	55 (25.82)		(0, 1)
Bachelor's degree	70 (25.35)		(0,1)
Professional or graduate degree	43 (20.19)		(0, 1)
Race			
White	189 (88.73)		(0, 1)
Marital Status			
In a relationship	142 (66.66)		(0, 1)
Gender			
Female	166 (77.93)		(0, 1)
Age		70.02 (12.34)	(27-95)
Participants (n)	213		

As demonstrated in Table 4, the proportion of patients who screened positive on the depression screening tool or anxiety screening tool were 20% and 14% respectively. Out of all the patients, 32% had a depression diagnosis and 28% were taking medication for depression. On the other hand, 34% had a diagnosis and 34% were taking medication for anxiety.

Table 4. Descriptive statistics of Anxiety and Depression

	N (%)
Screened Positive:	
Anxiety	30 (14.00)
Depression	42 (19.70)
Had diagnosis:	
Anxiety	72 (33.80)
Depression	68 (31.92)
Took medication:	
Took Anxiety Medication at enrollment	72 (33.80)
Took Depression Medication at enrollment	60 (28.17)

Table 5 demonstrates the difference in diagnosis and medication status between those who screened positive and those who screened negative for anxiety and depression. Within those who screened positive using the GAD-7, 43% had both a diagnosis and were taking medication, 17% had just a diagnosis. 20% had neither, and 20% were just taking medications. On the other hand, of those who screened positive for the PHQ-8; 38% had both a diagnosis and were taking medications, 14% had just a diagnosis, 2% were just taking medications, and 45% had neither.

Table 5: Comparing Those Who Screened Positive For Depression v.s. Anxiety

	N (%)	Mean Score
PHQ-8 >=10		
Diagnosis and Medications	16 (38.10)	12.81
Just Diagnosis	6 (14.29)	15.17
Just Medications	1 (2.38)	10.00
Neither	19 (45.24)	14.00
GAD-7 >=10		
Diagnosis and Medications	13 (43.33)	13.46
Just Diagnosis	5 (16.67)	13.20
Just Medications	6 (20.00)	15.67
Neither	6 (20.00)	15.17

Table 6 shows the Chi-square of screening results and prescription/diagnosis status. The mean GAD-7 score for those who had a diagnosis and were prescribed medication were 5.71 and 6.06 respectively. On the other hand, the mean PHQ-8 score for those who had a diagnosis and were prescribed medication were 7.05 and 6.3 respectively. The number of those who screened positive on the PHQ-8 and had a diagnosis or had a depression medication prescription was 68 and 60 respectively. On the other hand, the number of those who screened positive on the GAD-7 and had a diagnosis or had a depression medication prescription was 72 and 72 respectively. The chi-square showed that there is a significant relationship between PHQ-8 results and the presence of a diagnosis ($p<0.05$). Additionally, there was a significant relationship between the PHQ-8 results and the presence of a prescribed depression medication ($p<0.001$). The chi-square also showed that there is a significant relationship between GAD-7 results and the presence of a diagnosis ($p<0.001$). Finally, there is a significant relationship GAD-7 results and the presence of prescribed medication ($p<0.001$).

Table 6: Chi-square of Sreening Results versus Diagnosed & Perscribed Medication

	N	N (%) Screened Positive	Mean (SD)	Chi-Square P-value
PHQ-8				
Perscribed Medication	60	17 (40.00)	6.30 (4.93)	0.000
Diagnosed	68	22 (52.38)	7.05 (5.53)	0.048
GAD-7				
Perscribed Medication	72	19 (63.33)	6.06 (5.52)	0.000
Diagnosed	72	18 (60.00)	5.71 (5.17)	0.000

Discussion:

As seen from Table 4, a higher percentage of patients had a diagnosis or took medications for anxiety, compared to depression. But a greater proportion screened positive for depression, as opposed to anxiety. This suggests that patients were more likely to be depressed at enrollment. The screening tool is useful for determining whether or not someone has depressive symptoms, but is not absolutely diagnostic. There are several reasons why a greater portion have a diagnosis and medications for anxiety. Firstly, feelings of anxiousness are a common overarching symptom in chronic disease patients. Additionally, anxiety symptoms are objectively easier to identify compared to depressive symptoms. Also, symptoms for depression are often more subtle. Finally, because of the immediate connection to depression disorder and the stigma that inherently goes with saying someone is "sad" or feeling depressed", patients may feel less inclined to voluntarily offer up information surrounding this topic. Whereas with anxiety, expressing feelings of anxiousness or stress are more normalized, therefore a patient might offer information relating to this more freely.

Additionally, a number of patients were given medications without a diagnosis for both anxiety and depression. There are three possible reasons for this. Firstly, there could be fewer depression medications that have dual purposes with other disorders compared to anxiety medications. Secondly, anxiety symptoms are more generalizable to many other disorders, such as Post-traumatic stress disorder, panic disorder, phobias, social anxiety disorder, and insomnia. Someone might take the medication for a different anxiety disorder, other than general anxiety disorder. Third, it's possible that the after initial evaluation, the symptoms presented differently for a different diagnosis than before [39]. Someone could be diagnosed for anxiety, then years later develop depression, but since the medication is often dual-purpose, they could use it for both. Fourth, maybe providers are prescribing psychotherapeutic medications without a diagnosis. Finally, patients may request that depression or anxiety not be listed as a diagnosis in their medical file, for fear of stigma.

To break down Table 5 further, when looking into those who scored positive in the GAD-7, 80% had either a diagnosis or took medications, while 20% had neither. For those who screened positive on the PHQ-8, 56% had either a diagnosis or took medications, while 45% had neither. A greater proportion of patients who scored positive for anxiety compared to depression, already had a diagnosis or prescription compared to those within the same group who didn't have an either of those things. Whereas, a greater proportion of those who scored positive for depression, compared to anxiety, have unrecognized depression with no intervention.

For those with seemingly unrecognized symptomology, there are several possible reasons for this. First, their PCP might not be regularly screening them. Second, the patient could have requested the information be removed from their medical record. Third, there might be records missing from the Care Everywhere and EPIC system from other institutions.

Besides those with no clinical history, the other group who screened positive are those with medications or a diagnosis. It's important to note that EPIC does not provide information on other forms of therapy like talk therapy, Yoga, exercise, art therapy, or music therapy. It's possible that those with just a diagnosis declined taking medication, were using alternative therapy styles, or did nothing at all. For those who were taking medications without a diagnosis, since the medical records available during chart review were incomplete, the diagnosis may be missing in other medical record files. Additionally, the medication that the patient used at time of diagnosis needed modifications or supplemental therapies to do alongside the pharmaceutical. Finally, it's possible the patient wasn't taking the medication as intended so the desired effects were not presenting. Overall, those who screened positive and had a diagnosis or prescription psychotherapeutic need follow up for re-evaluation of treatment.

Table 6 demonstrated that the screening results for both anxiety and depression were dependent on the presence of a diagnosis or medication prescription. This shows that follow up with patients who have pre-existing symptoms is important for future mental health management.

Limitations:

There are several limitations to this study. First, when looking into the medications prescribed to patients, it was found that most of the time neither Care-everywhere, OHSU Epic system, or the Encounter summary from the provider would describe what the medication was used for. This is a limit because the data may overestimate those who took one type of

psychotherapeutic medication over the other. While several charts showed indications attached to medications, it was a common trend for the indications to be absent. This also could have been done via the patients request for privacy. Ultimately it is better practice to always provide indications for medications to facilitate continuity of care and viability of these data for future research.

Second, the time of diagnosis was not listed in the patient's problem list, resolved problem list, or medical history list. Marking when the diagnosis or start of symptoms appeared for the patient not only can be helpful for providers, but also researchers who want to look into treatment success for mental health interventions. This is a limit to the study because the chart review process sometimes happened years after the enrollment date. Essentially, some patients could have been diagnosed after the screening date.

Third, it's possible that patients weren't taking their medications due to adverse side effects, complications with other medications, or polypharmacy from multiple illnesses that make keeping track difficult. Although there is no for sure way to determine if patients are taking their medications, this needs to be considered when discussing limitations.

Fourth, the Epic system does not list other forms of treatment that the patient might access, like talk therapy, yoga, meditation, and exercise. All of these are valid forms of treatment for anxiety or depression but can only be accessed through the use of survey, not chart review. This is a limitation because the study maybe underestimating the proportion of patients receiving treatment.

Finally, the usage of the PHQ-8 instead of PHQ-9 is potentially problematic. Most studies looking at depression use the PHQ-9 over the PHQ-8, therefore there is more research on the cutoff for a positive screening score in the PHQ-9. The PHQ-9, compared to PHQ-8, includes

a question about suicidal ideations. The decision to use the PHQ-8 within the Infectious Disease lab was originally made because this lab doesn't have the ability to adequately follow up with patients if they indicate that they have suicidal ideations, as per state law.

Generalizability of results:

The demographic information gained from this study like average age and gender were similar to other studies in areas such as South Korea, Hawaii, the United States mainland, and Zambia. Overall, the average age of studied NTM populations seems to be between the ages of 60 and 70 years old. Additionally, in all of these locations women showed a higher prevalence, compared to men, for NTM diagnosis [40] [41] [42]. This study and other Oregon NTM studies have a higher proportion of patients that are white, compared to other races. When looking at an article that specifically studied the epidemiology of the NTM in the United States, excluding Hawaii, Puerto Rico, and Alaska, the proportion of white participants was 70% compared to the 88% found from this study [43]. Oregon, compared to the rest of the United States, is very white which explains the result differences in ethnicity. Overall, these results are most generalizable to the Oregon NTM population and less so for the rest of the United States due to the lack of racial diversity.

Possible Bias:

The most apparent bias from this study is convenience selection bias and extraction researcher bias. This researcher extraction bias was mitigated by creating clear extraction

procedures in regards where to find the data and by creating a set list of medications to cross reference. With regards to the selection bias, the patients needed to be recruited to OHSU from a different pulmonologist. There are several factors that could lead a patient to refuse the referral to OHSU such as difficulty reaching the location, cost, and availability.

Other possible biases that could have arose were procedural bias, measurement bias, and response bias. Procedural bias is possible because the questionnaire was filled out after the Pulmonology visit and right before the patient went in for a blood draw. Therefore, it is possible that they were rushing as they filled out the questionnaires. Measurement bias is possible because mental health is a personal topic that many Americans feel shame over. Since the questions are all about mental health, it's possible that patients underreported how often they felt those symptoms. Therefore, as said before, the current results could be underestimations of the true burden of mental health in the NTM populations. Although Response bias is always a possibility with surveys, this was mitigated by stating, during the consent process, the purpose of the experiment, rather than what we expect from the experiment.

Conclusion:

The prevalence, incidence, and impact of anxiety and depression in the NTM patient population has yet to be researched. Through this project, the prevalence of anxiety and depression, as well as the comorbidity of both was determined for one group of patients. With these data, I found that within this patient population, a higher proportion had a diagnosis or took a medication for anxiety, compared to depression. A higher proportion had a positive screening score for depression, compared to anxiety. The chi-square for both anxiety and depression showed a significant relationship between screening results and the presence of a diagnosis or

prescription of medication. Overall, this patient population has mostly unrecognized anxiety and unresolved symptomatology in both disorders. Therefore, patients who screen positive need follow up for either a first-time diagnosis and treatment plan, or re-evaluation and additional support.

My recommendation from these results would be to screen all NTM patients every six months, which is the time period between most visits in the Infectious Disease clinic at OHSU. I also recommend collaborative care for patients suffering with mental illness, between the pulmonologist and primary care provider, and in some cases, with a mental health professional. Direct follow-up with either the patient or PCP is important once a patient screens positive for either of these diseases. Without follow up, the patient may continue living with unresolved symptoms. These very same symptoms are known to affect health outcomes, treatment adherence, and symptom severity in other lung disease populations, as described in the literature review.

In conclusion, more research on mental illness within this population needs to be done. As more cases of NTM are discovered, the Infectious Disease research team will continue to monitor these aliments in NTM patients, and hopefully provide appropriate referrals for effective treatments. For future projects the IDS team will look at screening scores over the life course of treatment plans, treatment adherence, and NTM symptomatology, in order to better understand mental health burden in this population.

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