Acid Reflux Screening in Idiopathic Pulmonary Fibrosis:

An Assessment of Provider's Belief and Readiness in Evidence-Based Practice

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Author Note

I have no known conflict of interest to disclose.

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Abstract

Importance: Idiopathic Pulmonary Fibrosis (IPF) is a worldwide deadly disease with a mortality rate of nearly 100% without lung transplantation (IPF Foundation, 2020). The exact cause of this disease is unclear. Evidence has shown that IPF patients have a high risk of having abnormal acid reflux. Chronic acid reflux can worsen IPF prognosis.

Objective: To assess the effectiveness of an online educational intervention in enhancing clinician's belief, confidence and readiness in implementing an acid reflux screening protocol in IPF patients.

Methods: Physicians and nurse practitioners in primary care and pulmonary specialties within the United States were asked to complete online pre- and post-surveys after reviewing a webpage presenting up-to-date research evidence showing the relationship between IPF and gastroesophageal reflux disease (GERD).

Main Outcomes and Measures: Questionnaires adapted from the Evidence-Based Practice Beliefs and Implementation Scales by Melnyk were utilized to evaluate changes in belief, confidence and readiness to implement evidence-based practice recommendations.

Results: Percentage of participants who strongly believed in acid reflux screening in IPF increased from 60% pre-survey to 80% post survey (M=4.75, SD=0.58). The percentage of participants who thought they were ready to implement this screening protocol decreased from 60% pre-survey to 50% post survey (M=4.44, SD=0.63). More participants felt strongly confident during the post-survey. The pre-survey had 130 views with a completion rate of 12.3%.

Conclusion and Relevance: An online educational tool such as a webpage was an effective way to enhance clinician's belief and confidence in acid reflux screening in IPF.

Keywords: idiopathic pulmonary fibrosis, gastroesophageal reflux disease, abnormal acid reflux screening, evidence-based practice

Acid Reflux Screening in Idiopathic Pulmonary Fibrosis:

An Assessment of Provider's Belief and Readiness in Evidence-Based Practice

Idiopathic Pulmonary Fibrosis (IPF) is a worldwide deadly disease that has a mortality rate of nearly 100% without lung transplants (IPF Foundation, 2020). IPF is a specific form of chronic, progressively fibrosing interstitial pneumonia. It belongs to a family of interstitial lung diseases that are characterized by cellular proliferation, interstitial inflammation, fibrosis, or a combination of such characteristics within the alveolar wall that is not associated with infection or malignancy (Selman & Pardo, 2020). IPF is associated with high morbidity and mortality. It is also the most common type of interstitial pneumonia without known cause in older adults.

Problem Statement

Little is known about the exact cause of this disease and many aspects of clinical management of the disease is largely driven by individual clinician's judgement. With more evidence showing that IPF patients have a higher risk of having gastroesophageal reflux disease (GERD) compared to patients without this disease, researchers believe that a standard approach should be established to address this finding (Ghisa, Marinelli, V. Savarino & E. Savarino, 2019).

Acid reflux not only can cause a range of physical symptoms, it may also worsen the prognosis of pulmonary treatment in IPF patients. Many researchers believe chronic micro-aspiration of gastric content may play a role in the pathogenesis in the pulmonary fibrosis in IPF (Ghisa, Marinelli, V. Savarino & E. Savarino, 2019). Even though there are arguments about whether universal pharmacological approach should be standardized such as using a proton pump inhibitor in all IPF patients, it is commonly agreed that early detection and intervention of acid reflux should be established as part of the management of IPF.

Purpose and Rationale

IPF is often misdiagnosed and traditionally managed with immunosuppressive therapy, which is associated with a high mortality rate. Therapies that slow disease progression are now available but lack treatment standards and consistency. In 2015, an official updated clinical practice guideline from the American Thoracic Society, European Respiratory Society, Japanese Respiratory Society, and Latin American Thoracic Association, has included the recommendation of regular anti-acid treatment for patients with IPF. This recommendation has been controversial since more evidence has emerged in recent years that suggest little benefit of this practice recommendation. There have been studies presenting evidence of the benefit of long-term anti-acid therapy in improving lung function and survival rate in IPF patients. However, in more recent studies, researchers increasingly found data supporting the opposite. Whether using anti-acid therapy regularly to treat patients with IPF regardless the presence of GERD is an optimal approach remains an ongoing learning project for now.

This lack of practice guideline and knowledge gap of high risk of GERD in IPF patients leads to many unmet needs in patient care. This project was developed to promote an evidence-based approach to managing GERD in IPF patients using an educational intervention and assessing its effectiveness in enhancing providers in primary and pulmonary care's belief, confidence and readiness in implementing an evidence-based acid screening protocol in IPF patients.

Background and Significance

Population Description

IPF occurs worldwide. The national IPF registry finds the most affected population to be persons over the age of 65 (Puglisi et al., 2016). The incidence and prevalence have been

estimated in different regions by different researchers. It appears to be more prevalent in North America and Europe than South America and East Asia. Raghu and colleagues (2015) reported the prevalence of IPF in the United States was 495 cases per 100,000 adults over the age of 65 in 2011, which was twice as high as the number of reported cases 10 years prior. This disease is often fatal with a 5-year survival rate of 20% after diagnosis. It has a 100% mortality rate without a lung transplant.

More recent studies have identified contributary factors to IPF including GERD as the source of chronic tissue injury (Puglisi et al., 2016). Similarly, another review published in 2018 also identified GERD as a comorbidity risk factor along with other intrinsic and extrinsic risk factors (Zaman & Lee, 2018). In a study examining common comorbidities in IPF patients, the authors discussed that both IPF and GERD co-exist in over 80% of individuals with IPF (Cano-Jiménez et al., 2018). Published in 2019, the first European IPF epidemiological study conducted in primary care, systemically analyzed candidates' determinants of risk. The researchers of this study stated that patients aged 61 years or older who suffer GERD were statistically significantly at greater risk of incurring IPF (Harari et al., 2019).

The American Thoracic Society (ATS) and European Respiratory Society (ERS) updated its guidelines and recommendations of IPF treatment and management in 2015 and it suggests that clinicians should use regular anti-acid treatment for IPF patients (Raghu et al., 2015).

An analysis of data from three randomized controlled trials concluded that anti-acid treatment could be beneficial in patients with IPF, and GERD seems to contribute to disease progression (Lee et al., 2013). In 2016, a retrospective review of 786 adult patients with IPF at Seoul National University Bundang Hospital discovered proton pump inhibitor (PPI) use for at least 4 months may have a protective effect against IPF-related mortality (Lee et al., 2016). A

more recent systemic review and meta-analysis concluded that pharmacological treatment of GERD is associated with a reduction in IPF-related mortality (Fidler et al., 2018).

Current management of IPF in older adults shows great inconsistency in real practice due to gap in knowledge and lack of practice guidelines. Many unmet needs remain to be addressed including diagnosis, timing of initiating treatment, assessment of treatment response and disease progression, and management of comorbidity such as GERD, and long-term effect of anti-fibrosis medication (Valenzuela et al., 2020). In 2016, a survey conducted in Poland aimed to assess common practice in terms of diagnosis and treatment of IPF in older adults revealed that great inconsistence is a common issue in both diagnosis and treatment. Specifically, regarding anti-acid treatment, the survey stated only 43% of respondents would use anti-acid therapy in case of symptomatic GERD, and only 11% would prescribe these drugs regardless of GERD diagnosis (Piotrowski et al., 2017).

Internal Evidence

One of the nations leading medical centers for the diagnosis and treatment of lung, esophageal, and chest diseases in the southwestern United States observed that over 90% of their patients with IPF have a comorbidity of GERD. This institute is one of the Pulmonary Fibrosis Foundation (PFF) Registry network care centers within the United States. Its internal evidence is consistent with the other PFF centers within the country (R. Edwards, personal communication, November 18th, 2019). PFF is a national organization that actively engages in pulmonary fibrosis communities and has developed essential programs available to those living and working with pulmonary fibrosis. The PFF patient registry is a nationwide database that provides great resources for researchers in taking steps toward a cure.

PICOT Question

In older adult patients with IPF, how does standard anti-acid therapy compared to no standard anti-acid therapy affect the patient's lung function in 6 months?

Evidence Synthesis

Search Strategy

An exhaustive review of the most current evidence took place to answer the PICOT question. Three databases were searched – PubMed, Cumulative Index of Nursing and Allied Health Literature (CINAHL), and the Cochrane Database. These databases were selected for their relevancy to the topics of anti-acid therapy and patients with IPF. Additionally, these databases are known for their rigor and contributions to the medical field.

The databases were searched using combinations of the index terms and free text words that addressed all aspects of the PICOT question and included: *IPF*, *GERD*, *anti-acid therapy*, *IPF-related mortality*, *IPF lung function*, and *IPF disease progression*. Key terms for the intervention included the terms: *proton pump inhibitors, histamine-2 receptor antagonists,* and *anti-acid therapy*. The outcome was specified using the terms: *IPF-related mortality, lung function, six-minute walk distance, forced vital capacity.* Filters applied included date of publication (2015 to 2020), English language, and peer-review journal articles. Mesh terms were to broaden the search. The titles and abstracts of all articles were assessed for searches yielding under 150 results. Inclusion criteria included interventions focusing on treating GERD or non-GERD comorbidities using standard anti-acid therapy, either a PPI or H2 blocker, targeting measurable outcomes include improved lung function (FVC, 6-minute walk distance, dyspnea score) and decreased IPF-related mortality. Since limited randomized controlled trial studies (RCT) and systematic reviews (SR) were very limited in the past 5 years, the eligible studies were expanded to be those directly related to the research question of interest and the date of

publication was expanded as needed to include studies within last 10 years for more higher level of evidence.

An initial search of PubMed using key terms *idiopathic pulmonary fibrosis and GERD* yielded 188 results. So, filters were added as "published in the last 5 years, which shrunk the result counts to 94. Further, term *GERD treatment* was used instead of *GERD,* with the same filter and this resulted in 28 articles. Additionally, the outcome term *improved lung function* was added as an explorative approach with the same filter and terms resulting in only 3 articles. It was decided that these particular search terms were too specific and narrow.

The initial CINAHL search included the key terms *idiopathic pulmonary fibrosis, GERD,* and *pulmonary function.* Initial results produced 0 article. Eliminating the term *pulmonary function* significantly increased the search results to 189. Filters were applied to this search to lower the article count to 21 results.

One of the initial Cochrane Library searches included the terms *idiopathic pulmonary fibrosis* and *GERD* produced a limited three results. Changing the search term *GERD* to *anti-acid therapy* increased these article results to 7. Given the rigor of systematic reviews included on Cochrane Library, it is not surprising that these searches yielded fewer results than those completed on other databases.

Reviewing the titles and abstracts of the articles identified in these database searches yielded 21 relevant studies for review. Rapid critical appraisal checklists as well as outlined inclusion and exclusion criteria were used to narrow the article pool down to the 10 most relevant and highest quality studies.

Critical Appraisal and Synthesis

Of the ten carefully selected studies, six concluded that routine anti-acid therapy without a definite time frame is beneficial in decreasing IPF-related mortality or improving lung function (see Appendix A, Table 1). These six studies include one randomized, double-blind, and placebo-controlled pilot trial with a level II evidence strength. The major limitation is its small sample size (45 patients). One systemic review and meta-analysis with a level I evidence included 13 observational studies. The rest of them include one prospective observational study with a level III evidence, one non-randomized single-center, retrospective cohort study with level IV evidence, one retrospective, single-center cohort study with level IV evidence, and one study which included cohort patients from the placebo arms from a three parent randomized clinical trials, with a level IV evidence.

It is noted that, some studies' conclusion of routine anti-acid therapy benefit is conditional. Kulkarni et al., (2016) reported the recommendation of continuous anti-acid therapy is beneficial to patients when used in combination of other four interventions including yearly echocardiogram, yearly hypoxemia screening, yearly pulmonary rehabilitation visit and management by a specialist in interstitials lung disease. Kilduff et al., (2014) concluded that strategies for treating GERD in patients with IPF should target both acid and non-acid reflux by using combine therapy rather than anti-acid alone. One study remained neutral in the benefit of routine anti-acid therapy but recognized the increasing prevalence of GERD symptoms in IPF patients compared to non-IPF patients.

There are three studies in more recent years that showed evidence non-supportive of routine anti-acid therapy in treating IPF patients. One of them is a post-hoc analysis using pooled data from two randomized placebo-controlled trials. It concluded that anti-acid therapy was not associated with a more favorable course of disease and did not impact the treatment effect of

nintedanib (an anti-fibrosis medication), in patients with IPF. This study has a level II evidence. One cohort study using prospectively collected data from the Australian IPF Registry also concluded that antacid therapy may not be beneficial in IPF patients and GERD directed therapy should be considered on an individual basis to treat the symptoms of reflux. The last study was a post hoc analysis that included patients from three trials in which they received Pirfenidone as an anti-fibrosis medication. It showed that routine anti-acid therapy might not be beneficial as a treatment for IPF in combination with pirfenidone which is an anti-fibrotic medicine that is frequently used in treating IPF patients.

Conclusion

The research literature discusses that there are numerous gaps in knowledge and awareness from clinicians on treating abnormal acid reflux in IPF patients. Even though 10 studies do not agree all together on the benefit of routine anti-acid therapy in all IPF patients, they commonly acknowledge the need for early detection and intervention treating GERD to prevent complications. Another important commonality amongst these studies is the increase of prevalence of GERD comorbidity in IPF patients. Having IPF diagnosis can increase one's risk of having GERD. The evidence supports an intervention developed to screen for GERD in IPF patients, such as a questionnaire screening protocol. With successful implementation of a standard approach in acid reflux screening for all IPF patients, early detection of acid reflux can be achieved promoting prompt treatment with anti-acid therapy. However, the delay in the identification and treatment of abnormal acid reflux especially silent acid reflux is an ongoing clinical problem. The gap between the evidence and practice warrants further investigation. Effort should be established to assess clinician's belief and readiness of implementing an evidence-based acid reflux screening protocol in IPF patients and the effectiveness of an

interventional presentation of high-quality evidence in enhancing clinician's readiness. The outcome of such study can provide insight to better prepare a future successful project of implementing a standard screening protocol.

Conceptual Framework and EBP Model

Theoretical frameworks and conceptual models are useful tools to promote an in-depth understanding of complex and seemingly abstract ideas, events, behaviors and situations. Theoretical domains framework (TDF) provides an integrative model for assessing barriers to behavioral changes in order to suggest interventions for improvement in behavior and ultimately outcomes in healthcare professionals (Michie et al., 2005) (Appendix B, Figure 1). The EBP model, implementation framework, selected to guide this project is the Promoting Action on Research Implementation in Health Services (PARIHS) (Appendix B, Figure 2). This framework provides a way to implement research into practice and promotes examination of the interactions between three key elements for knowledge translation: evidence, context and facilitation. The framework emphasizes the need for appropriate facilitation to improve the likelihood of success. The needs of the organization determine the type of facilitation and the role and skill of the facilitator. Facilitators work with individuals and teams to enhance the implementation process (Rycroft-Malone & Bucknall, 2011).

Application of TDF comes down to intervention design and development. TDF can aid intervention development by systematically identifying key determinants of provider practice change. Under guidance of the framework, identify determinants (barriers, facilitators) of implementation of evidence-based practice from providers perspectives; (ii) identify key domains to target for provider behavior change; and (iii) map key domains to intervention

components of behavior change techniques that could be delivered in an intervention within a practice setting (Michie et al., 2005).

EBP model, PARIHS, is applied through the identification of its three key conceptual elements in participants and their work settings: their knowledge, belief, confidence, environment, years of practice and perceived barriers. These elements are translated into the concept of evidence, context and facilitation in the application this EBP model.

Methods

Design

The study was approved under social behavioral protocol by the institutional review board from Arizona State University.

The target population for the project consisted of clinicians who provide care to IPF patients including physicians, nurse practitioners and physician assistants in pulmonary specialty or general practice. Recruitment consisted of personally emailing and inviting participants to take part in the survey and educational intervention. All participants were emailed an introductory video explaining the purpose of the project and how to participate. Pre- and post-surveys were self-administered to assess participants' belief and readiness towards an evidence-based acid screening protocol in IPF patients. Participants were informed that all data gathered would be anonymous with survey IDs randomly generated by the survey platform QuestionPro.com. The entire project was delivered online within the United States through email containing a private link to the content. Enrollment occurred between December 23rd, 2020 and January 1st, 2021. Survey collection took place until March 1st, 2021.

The educational intervention consisted of a video introducing topic background and significance and a webpage presenting current high-quality evidence showing the relationship between IPF and GERD.

The survey questions used to assess the participants' belief and readiness were adapted from the validated measurement tool the Evidence-Based Practice Beliefs and Implementation Scales by Melnyk. Melnyk's scale is based on the belief that implementation of evidence-based practice (EBP) by health professionals is a key strategy for improving health care quality and patient outcomes as well as increasing professional role satisfaction (Melnyk & Fineout-Overholt, 2008). The Pre and post surveys (Appendix C) consisted of the same questions asked in regards of belief and readiness towards implementing an evidence-based acid screening protocol in IPF patients. Only pre-survey collected demographic data including age and gender.

Funding

The author received no financial support for the study or authorship. The project incurred minimal cost including the onboarding fee to shadow a provider at the site institute. The webpage and survey platform were at no cost.

Results

Fifteen participants (n=15), completed both the pre-survey and post-survey. The sample consisted of physicians and nurse practitioners from general practice (80%). The rest of the participants were from pulmonary specialty and other non-identified settings. Female participants consist 53% of the total sample. 60% of the participants have less than 3 years practice experience. 13% of them have more than 9 years of practice experience. 80% of the participants age between 25 and 44.

Primary outcomes included an increase in the number of participants who strongly believe in evidence-based intervention screening for acid reflux in IPF patients from 60% pre-survey to 80% post survey (Mean=.75, SD=0.58), and a decreased in the number of participants who think they are ready to implement this evidence-based intervention (Mean=4.44, SD=0.63). Secondary outcomes included clinician's perceived barriers and confidence level of evidence-based intervention acid reflux screening implementation. In both surveys, the majority of participants believe that critical appraisal of evidence is an important step in evidence-based practice such as implementing an acid reflux screening in IPF patients. 20% of participants strongly feel confident in implementing acid reflux screening in IPF patients in the pre-survey (Mean=3.87, SD=0.74) and that number increased to 56.25% post-survey (Mean=4.38, SD=0.81).

Discussion

The results of this project illustrate that there is a need for an educational program to fill the gap between the evidence and practice in screening for abnormal acid reflux in IPF patients. A traditional face-to-face based intervention was not possible due to demand for social distancing because of the pandemic. This project tested the feasibility for an online intervention in providing education and high-quality evidence to clinicians to make informed practice change decision. According to QuestionPro, the pre-surveys were viewed 130 times and the post-survey were viewed 100 times. This is a larger number than anticipated. This could imply the efficiency of an online educational program in reaching its target audience in the times social distancing is encouraged.

The increase in self-rated belief rating of evidence-based acid reflux screening proves the effectiveness of an online educational tool such as the webpage in enhancing clinician's belief in

evidence-based practice implementation. The increase in self rated confidence level after the intervention further support this finding. The decrease in the self-rated readiness scale could be due to clinicians perceived existing barriers such as time, resource of evidence, and difficult in evidence appraisal. This finding provides insights for a more comprehensive educational tool that incorporates these identified facilitators and barriers in the future to be more successfully prepare clinicians for implementing an evidence-based acid reflux screening protocol.

Limitations

The sample size n=15 is small. This small sample size cannot be generalized for a larger population. To protect participants privacy, the survey platform QuestionPro did not allow linking pre-surveys and post-surveys. This limits further investigation on which demographic variable such as gender, practice setting and age, is linked to certain outcomes. However, by comparing the two survey results as a whole, a percentage and frequency change was able to be identified for analysis and discussion. It is not certain how many individuals were reached by the recruitment email. The total number of invitation emails were not able to be tracked because some invitations were forwarded by certain recipients of the original invitation emails. The completion rate based on total views was 12.3%. Whether this number was calculated by IP address from which the link of surveys was accessed is not known.

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Appendix A

Evaluation and Synthesis Tables

Table A1

Evaluation Table Quantitative Studies

Table 1

Evaluation Table

Citation	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting	Major Variables & Definitions	Measurement/ Instrumentation	Data Analysis	Findings/ Results	Level/Quality of Evidence; Decision for practice/ application to practice
Costabel, U. et al., (2018) Anti-acid therapy in idiopathic pulmonary fibrosis: insights from the INPULSIS trials. *Respiratory Research 19*(167). doi: 10.1186/s12931-018-0866-0 Funding: Boehringer Ingelheim Bias: Not discussed Country: Germany	Health Belief Model Analytic framework	**Design:** Post-hoc analysis of outcomes in patients receving or not receving anti-acid medication at baseline using pooled data from the two Phase III randomized placebo controlled	**N1:** 406 taking anti-acid n 1: 244 nintedanib n 2: 162 placebo **N2:** 655 not taking anti-acid n 1: 394 nintedanib n 2: 261 placebo Setting: in 24 countries across the Americas, Europe, Asia and Australia Inclusion criteria:	**IV1:** anti-acid therapy **IV2:** nintedanib **DV1:** annual rate of decline in FVC **DV2:** disease progression **DV3:** acute exacerbation **DV4:** quality of life **DV5:** adverse events	Disease progression measured by the time to absolute decline in FVC ≥10% predicted or death over 52 weeks Acute exacerbation is investigator reported and by chart review	A Cox regression model and Statistical Analysis System (SAS) version 9.4 was used for all the analyses.	1. Adjusted annual rate of decline in FVC in placebo arm, pts on anti-acid meds: − 252.9 mL/yr pts not on meds: − 205.4 mL/yr (difference of − 47.5 mL/yr [95% CI: –105.1,	**LOE:** II **Strength:** Data obtained from a well-designed large multi-site RCT. Large sample size. **Weakness:** No disclosure or discussion of study limitations or bias.

Key: **AAT**-anti-acid treatment; **IPF**-Idiopathic Pulmonary Fibrosis; **ILD**-interstitials lung disease; **GERD**-Gastroesophageal Reflux Disease; **COPD-**chronic obstructive pulmonary disease; **PPI**-Proton Pump Inhibitor; **H2B**-histamine-2 blocker; **FVC-**forced vital capacity; **EGD-**esophagealgastroduodenoscopy; **HTN**-hypertension; **DM**-diabetes mellitus; **DV**-dependent variable; **IV**- independent variable; **N**-number of studies; **n**- number of participants; **HR**-hazard ratio; **LOE**-level of evidence; **RCT**-Randomized controlled trial; **IPFnet**-Idiopathic Pulmonary Fibrosis Clinical Research Network; **HR**-Hazard Ratio; **CI**-Confidence Interval; **6MWD**-6-minute walk distance; **DLco-**hemoglobin-corrected predicted diffusing capacity of the lung for carbon monoxide; **USCD-SOBQ-**University of California at San Diego Shortness of Breath Questionnaire; **SGRQ-** St George's Respiratory Questionnaire

Table 1

Evaluation Table

Citation	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting	Major Variables & Definitions	Measurement/ Instrumentation	Data Analysis	Findings/ Results	Level/Quality of Evidence; Decision for practice/ application to practice
		INPULSIS trials of nintedanib in patients with IPF. **Purpose:** investigate whether use of anti-acid medication at baseline was associated with differences in the natural course of disease or influenced the treatment effect of nintedanib in patients with IPF.	patients aged ≥40 years with a diagnosis of IPF established within five years before randomization. Patients also had to have an FVC of ≥50% predicted and a diffusing capacity of the lungs for DLco of 30–79% predicted. **Patients demographic:** Baseline characteristics were generally similar between the subgroups by use of anti-acid medication use at baseline. **Attrition rate**: NA		Quality of life measured by SGRQ score		10.1]; $p = 0.10$ 57). 2. Difference in time to absolute decline in FVC ≥10% predicted or death in placebo arm, Between pts on anti-acid meds vs no anti-acid meds: no significant difference. (HR 1.33 [95% CI: 0.98, 1.80]; $p = 0.06$ 61). 3. Time to first acute exacerbation	**Conclusion:** anti-acid medication use at baseline was not associated with a more favorable course of disease, and did not impact the treatment effect of nintedanib, in patients with IPF.

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							in nintedanib vs placebo groups, 0.40 (95% CI: 0.19, 0.83) in pts on anti-acid and 0.99 (95% CI: 0.49, 2.00) in pts who were not, ($p = 0.0949$). 4. SGRQ total scores, in placebo group, pts on anti-acids vs no anti-acids were 6.54 vs 4.04; in nintedanib group, it was 4.83 vs 2.80. There was no significant difference ($p = 0.8536$).	

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Dutta, P. et al., (2019). Randomized. Double-blind, placebo-controlled pilot trial of omeprazole in idiopathic pulmonary fibrosis. *Thorax 2019*(74): 346-353. Doi:10.1136/thoraxjnl-2018-212102 **Funding:** by a grant from the British Lung Foundation. **Bias:** None recognized	Health Belief Model	**Design:** single-center, randomized, double-blind placebo-controlled pilot trial. (Treatment group received omeprazole 20mg twice daily for 3 months).	**N:** 45 **n:** 23(omeprazole) **n:** 22(placebo) **Setting:** Newcastle upon Tyne Hospital NHS Foundation Trust. **Sample demographics:** No significant differences in 2 groups **Attrition rate:**	**IV:** omeprazole 20mg twice daily for 3 months **DV1:** cough frequency **DV2:** 6-min walk distance **DV3:** pulmonary function tests	De Meester reflux-related symptoms questionnaire; the Reflux Symptoms Index; the Gastrointestinal Quality of Life Index; the Leicester Cough Questionnaire; Ambulatory cough recorder	ANCOVA (analysis of covariance) models were used	Geometric mean cough frequency at the end of treatment, adjusted for baseline, was 39.1% lower (95% CI, 66% lower to 9.3% higher) in the omeprazole group compared with placebo.	**LOE:** II **Strength:** Strong design of a randomized, double-blind placebo-controlled pilot trial **Weakness:** Single-center, small sample size with low generalizability. **Conclusion:**

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Country: United Kingdom		**Purpose:** Primarily to assess feasibility and acceptability of trial procedures.	Low 11% **Inclusion criteria:** IPF diagnosis; history of cough; radiological feature of honeycombing on high resolution CT; bibasal inspiratory crackles and features of a restrictive ventilatory defect. Patients taking warfarin, diazepam, phenytoin or ketoconazole are excluded due to potential drug-drug interaction with omeprazole.				No clinically meaningful differences in PFTs and 6MWD at baseline and end of treatment for the two groups.	A large randomized controlled trial of PPIs for cough in IPF patients appears feasible and justified.

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Fahim, A. et al. (2011). Gastroesophageal reflux and idiopathic pulmonary fibrosis: A prospective study. *Medicina (Kaunas), 47*(4). https://www-ncbi-nlm-nih-gov.ezproxy1.lib.asu.edu/pubmed/21829051 **Funding:** Not disclosed. **Bias:** not discussed **Country:** United Kingdom	Health Belief Model	**Design and purpose:** prospective cross-sectional study of subjective evaluation of GERD symptoms and objective evaluation of Helicobacter pylori prevalence and extraesophageal reflux by measurement of pepsin concentration in EBC.	**N:** 170 **n 1:** 90 in reflux cough questionnaire group (40 with IPF vs 50 control) **n 2:** 23 for measurement of pepsin (17 with IPF vs 6 controls) **n 3:** 57 for H.pylori detection (34 with IPF vs 23 controls) **Setting:** Interstitial Lung Disease Clinic at the University Hospital. **Demographic:** IPF diagnosis according to the ATS/ ERS criteria attending the Interstitial Lung Disease Clinic at the University Hospital.	**IV:** IPF dx **DV1:** HARQ **DV2:** EBC pepsin positivity **DV3:** H. pylori serology positivity	Hull airway reflux questionnaire (HARQ) Exhaled breath condensate (EBC) for measurement of pepsin by the lateral flow technique. Prevalence of stomach bacterium by H. pylori antibody detection ELISA	SPSS (version 13, Chicago IL). unpaired t test, Mann-Whitney U test, Pearson chi-square test. An α value of 5% was considered statistically significant.	Significantly higher HARQ scores in patients with IPF compared with controls (19.6 [SD, 12.4] vs. 3 [SD, 2.9], P<0.001). There was no significant difference in EBC pepsin positivity between patients with IPF and controls (2 of the 17 patients vs. none of the 6 controls, P=0.38). There was no significant	**LOE:** IV **Weakness:** The measurement of IgG antibody for H. pylori infection has limitations as it may persist for years after eradication of H. pylori **Conclusion:** Patients with IPF had significantly increased scores of airway reflux symptoms. However, no objective evidence of extraesophageal reflux or H. pylori infection

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			Attrition: 0%.				difference in H. pylori serology between patients with IPF and controls (17 of the 34 patients vs. 14 of the 23 controls, P=0.42).	in patients with IPF was obtained in this study. The role of gastroesophageal and extraesophageal reflux in pathogenesis of IPF should be evaluated in a larger prospective study.
Fidler, L. et al., (2018). Treatment of gastroesophageal reflux in patients with idiopathic pulmonary fibrosis: A systemic review and meta-analysis. *Chest: The cardiopulmonary and critical care journal,*	Analytic framework	**Design:** Systemic review and meta-analysis, using MEDLINE, Embase, Central, and ClinicalTrials	**N:** 13 observational studies. **Inclusion:** observational, randomized, quasi-randomized, pre-post, and historical control studies that are directly related to the	**IV1**-PPI **IV2**- PPI and H2B **IV3**-PPI or H2B **IV4**-PPI and/or H2B, fundoplication **IV5**-fundoplication **DV1**-IPF-related mortality rate	Cochran Collaboration tool to assess risk of bias, and the Newcastle-Ottawa Scale	Review Manager version 5.3 from the Cochrane Collaboration; statistical heterogeneity assessed by	**DV1**: IPF-related mortality reduced in three studies (95% CI): HR 0.6 (0.38-0.97); and in another three studies	**LOE:** I **Strength:** Systemic search strategy, and meta-analysis of study results. **Weakness:** Low quality evidence. The resulting

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153(6): 1405-1415. DOI: https://doi.org/10.1016/j.chest.2018.03.008 **Funding:** No funding was received for this study. **Bias:** Resulting treatment effects from nonrandomized studies are at increased risk of bias and confounding. The risk of immortal time bias in several studies warrants highlighting; where subjects may have had to survive a certain length of time (duration of antacid therapy required for inclusion to the experimental group) before the effect of treatment on survival could be analyzed.		.gov. These databases were searched until Sep 2017 without language restrictions for randomized and observational studies. **Purpose:** To review the efficacy of the pharmacological and non-pharmacological treatments of GERD in IPF patients.	search question of interest. **Exclusion:** case reports, case series, letters to the editor, editorials, and commentaries.	**DV2**-All-casue mortality rate		calculating I^2 values;	(95% CI), HR 0.45 (0.24-0.84); **DV2**: all-cause mortality with no reduction, in three studies (95% CI) HR 0.73 (0.45-1.2); and four studies (95% CI) HR 0.76 (0.31-1.84).	articles being restricted to observational study designs and the heterogeneity between individual studies. **Conclusion**: Pharmacologic treatment of GERD is associated with a reduction in IPF-related mortality but not overall mortality. Randomized trials of antacid therapy in IPF are needed.

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Country: Canada								
Jo, H. E. et al., (2019). Gastroesophagral reflux and antiacid therapy in IPF: analysis from the Australia IPF registry. *BMC Pulmonary Medicine, 19*(1). doi: 10.1186/s12890-019-0846-2 **Funding:** National Health and Medical Research Council and the Centre of Research Excellence in Pulmonary Fibrosis (funded by the NHMRC and supported by Foundation Partner Boehringer Ingelheim and Program Partners Roche and Galapagos). **Bias:** Self-reported GERD dx may under or overestimate prevalence;	Health Belief Model	**Design:** Cohort study using prospectively collected data from the Australian IPF Registry. **Purpose:** Explore the use of antacid therapy in Australia IPF registry population; and the presence of GERD symptoms, on disease progression and survival.	**N:** 587 **n 1:** 384 taking anti-acid (193 with significant symptoms vs 191 with less significant symptoms). **n 2:** 203 not taking **Setting:** Australia national IPF registry data base **Inclusion criteria:** All participants from the Australian IPF Registry who had completed questionnaires regarding co-morbidities, treatment and reflux symptoms **Demographic and baseline characteristics:** Age	**IV1:** anti-acid therapy at baseline **IV2:** GERD symptoms severity **DV1:** survival **DV2**: disease progression	Survival measured by mortality and transplant rate during a medial follow up period of 2.2 years. Disease progression measured by annual decline in FVC% predicted Frequency scale for the symptoms of GERD (FSSG) **Definition:** A symptom score of > 8/48 was used to define	t test or chi squared; unstructured and linear mixed model with random intercepts and slopes; Cox proportional hazards and Kaplan Meier methodology.	No difference in survival between antacid therapy groups (HR = 1.02; 95% CI 0.72–1.43; p = 0.928) No difference in survival in antacid group (HR = 0.88, 95% CI = 0.64,1.20; p = 0.415) between those with significant GERD symptoms (FSSG> 8), vs without.	**LOE:** IV **Strength:** one of the largest retrospective cohort studies of antacid therapy in IPF. It is also the first study to use the FSSG score, collected prospectively, in patients with IPF and shows that GERD symptom severity does not predict decline. **Weakness:** not a randomized trial, it may be

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self-reported anti-acid therapy did not include duration or dosage which is clinically significant. **Country:** Australia			71.0 ± 8.5 years, mostly male (*n* = 406; 69%) and ex/current smokers (*n* = 424; 72%). Mean FSSG score was 8.39/48 (SD 7.45), with 43% (n = 251) patients having a FSSG score > 8		significant symptoms in categorical analysis.		No difference in the annual fall in FVC %predicted, regardless of whether patients were receiving antacid therapy (compared to those not on therapy), or had significant GERD symptoms (FSSG> 8) (compared to those without significant GERD symptoms.	possible that pts who had the worst reflux were already on long-term treatment, mitigating their risk for disease progression **Conclusion:** Neither the use of antacid therapy nor the presence of GERD symptoms affects longer term outcomes in IPF patients. Antacid therapy may not be beneficial in IPF patients and that GERD directed therapy

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								should be considered on an individual basis to treat the symptoms of reflux.
Kilduff, C. E. et al., (2014). Effect of acid suppression therapy on gastroesophageal reflux and cough in idiopathic pulmonary fibrosis: an intervention study. *Cough, 10*(4). https://link.springer.com/article/10.1186/1745-9974-10-4 **Funding:** not discussed **Bias:** not discussed **Country:** not stated	Health Belief Model	**Design:** Prospective observational study **Purpose:** investigate the impact of high-dose acid suppressant therapy on GERD and cough in this condition.	**N:** 18 **Setting:** not described **Inclusion:** consecutive non-smoking subjects meeting the American Thoracic Society/European Respiratory Society criteria for the diagnosis of IPF **Exclusion:** Has other causes of cough **Demographic and baseline data:** mean age 65; 5 females and 13 males; FVC predicted mean 83.1%;	**IV1**: 8-week high-dose anti-acid therapy **DV1**: acid reflux events **DV2**: non-acid reflux events **DV3**: cough frequency	24-hour total reflux; 24-hour acid reflux; 24-hour weakly acid reflux and; 24-hour non-acid reflux. 24-hour cough count	Wilcoxon signed-rank test; Kruskal-Wallis test; Fishers Exact Test; Spearman's rank order correlation; SPSS version 18.	Following high dose acid suppression therapy there was a significant decrease in the number of acid reflux events ($p = 0.02$), but an increase in the number of non-acid reflux events ($p = 0.01$). There was no change in cough	**LOE:** III **Strength:** direct and relevant observations of the empirical intervention in target population. **Weakness:** Very small sample size, nonrandomized selection. **Conclusion:**

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			Attrition: 22%. (14 out of 18 followed through)				frequency ($p = 0.70$).	strategies for treating GERD in patients with IPF should target both acid and non-acid reflux, perhaps by including prokinetic therapies, rather than acid suppression therapy alone.
Kreuter, M. et al., (2017). Anti-acid therapy and disease progression in patients with idiopathic pulmonary fibrosis who received Pirfenidone. *Respiration, 93*(6): 415-423. https://doi-org.ezproxy1.lib.asu.edu/10.1159/000468546	Health Belief Model	**Design:** Post hoc analysis included patients from three trials in which they received Pirfenidone as an anti-fibrosis medication	**N:** 623 n: 273 received AAT (PPI and/or H2B) n: 330 received no AAT. **Setting:** Original 3 trials took place at 127 sites in 9 countries (11 sites in Australia, 6 in Brazil, 2 in Croatia, 5 in Israel, 5 in Mexico,	**IV:** AAT **DV1:** All-cause death HR 95% CI 0.8(0.3-2.5) *p*=0.716 **DV2:** IPF-related death HR 95% CI 0.4(0.1-2.4) *p*=0.348 **DV3:** 6MWD decrease HR 95% CI 0.9(0.6-1.4) *p*=0.699	Pulmonary function measured by FVC and DLco, 6MWD. Dyspnea measured by UCSD-SOBQ score.	Independent sample *t* test for continuous variables χ^2 test for categorical variables Shared frailty model	Risk of all-cause or IPF-related death was not significantly reduced in the AAT group compared with the non-AAT group (all-cause mortality: HR,	**LOE:** IV **Weakness:** relatively small sample size, analyses were probably underpowered; non-randomized population and non-stratified comorbidities making it a

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Funding: Boehringer Ingelheim, InterMune, Roche, Chiesi Farmaceutici, Genentech, Santhera Pharmaceuticals, Bayer, Takada, and etc. **Bias:** Although the analyses were adjusted - based on observed factors - to address potential confounders, the results may be biased due to differences in unobserved factors. **Country:** Germany		**Purpose:** To evaluate the effect of AAT on IPF progression in pirfenidone-treated patients.	2 in New Zealand, 8 in Peru, 1 in Singapore, and 87 in the United States) **Demographics at baseline:** similar between groups except group with AAT having higher rate of GERD, hiatal hernia, Barret esophagus and hypercholesterolemia. **Attrition:** N/A.	**DV4:** FVC decrease >10%, HR 95% CI 0.6(0.3-1.1) *p*=0.102		Corresponding multivariate models Mean of covariates method Likelihood ratio test	0.8; 95% CI, 0.3-2.5; *p* = 0.716; IPF-related mortality: HR, 0.4; 95% CI, 0.1-2.4; *p* = 0.348)	confounding issue. **Conclusion:** AAT might not be beneficial as a treatment for IPF in combination with pirfenidone. The inconsistencies in findings underscore the need for prospective randomized, double-blind, placebo-controlled studies assessing the role of AAT in IPF.

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Citation	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting	Major Variables & Definitions	Measurement/ Instrumentation	Data Analysis	Findings/ Results	Level/Quality of Evidence; Decision for practice/ application to practice
Kulkarni, T. et al., (2016). A bundled care approach to patients with idiopathic pulmonary fibrosis improves transplant-free survival. *Respiratory Medicine, 115*:33-38. https://doi.org/10.1016/j.rmed.2016.04.010 **Bias:** selection bias and other potential unmeasured confounders, as patients were not randomly assigned a level of adherence to the BOC. **Funding:** funded by the UAB Interstitial Lung Disease Program and the NIH grant PO1HL114470. **Country:** America	Health Belief Model	**Design:** non-randomized single center, retrospective cohort study **Purpose:** to determine if "bundling" some recommendations by the 2011 American Thoracic Society/European Respiratory Society/Japanese Respiratory Society/Latin American Thoracic	**N: 284** **Setting:** University of Alabama at Birmingham (UAB) **Demographic:** Age, gender, smoking status, BMI, %FVC, %DLCO did not differ between levels **Attrition:** N/A **Inclusion criteria:** patients at the clinic data base that fulfilled IPF diagnosis criteria according to the 2011 guidelines. **Exclusion:** pts that did not follow up and pts with emphysema	**IV1:** BOC (bundle of care score) at 5 levels: ≤1, >1-2, >2-3, >3-4 and >4. **DV1:** transplant-free survival time **DV2:** absolute change in %FVC **Definition:** BOC included: visits to a specialized ILD center at least q6mon; referral to pulmonary rehabilitation at least once a year; timed walk test to screen for hypoxemia at least once a year; echocardiogram at least once a year; continuous	Chart audit method	ANOVA, Chi-square test or Fisher's exact test, Kaplan-Meier survival analysis and log-rank test, Cox proportional-hazards regression analysis	A lower year 1 BOC score was associated with a higher risk for transplant or death independent of age at diagnosis and initial %FVC (≤1 vs. >4, HR 2.23 (1.18–4.24), p = 0.014; >1–2 vs. >4, HR 1.87 (1.15–3.04), p = 0.011; >2–3 vs. >4, HR 1.72 (1.09–2.72), p = 0.019).	**LOE:** IV **Strength:** support a "bundled" approach to the recommendations **Weakness:** single center cohort study; the recommendations for patient management contained in the 2011 guidelines have not been informed by randomized controlled trials **Conclusion:**

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		Association (ATS/ERS/JRS/ALAT) consensus guidelines in the management of patients with IPF impacts clinical outcomes.		pharmacological anti GERD therapy. BOC score, 1 is given for each of the 5 care in the bundle that is met per yearly follow up. Transplant-free survival time is the time from the initial visit to the center to the first occurrence of either lung transplantation or death up to December 31, 2013.			The year 1 BOC did not correlate with absolute change in %FVC from the initial visit to either the last %FVC prior to death or lung transplantation, or up to December 31, 2013 (r = −0.11, p = 0.11).	adherence to a bundle of care that includes the management recommendations of the 2011 ATS/ERS/JRS/ALAT consensus statement may improve IPF survival.
Lee C. M. et al., (2016). Protective effect of proton pump inhibitor for survival in patients with gastroesophageal reflux disease and idiopathic pulmonary fibrosis. **Funding:**	Health Belief Model	**Design:** Retrospective, single-center cohort study **Purpose:** Investigate the prevalence of	**N:** 786 **n:** 107(with GERD) **n:** 679(without GERD) **Setting:** Seoul National University Bundang Hospital	**IV1**: initial FVC; **IV2**: age **IV3**: duration of PPI treatment **DV1**: IPF-related mortality **Definition:**	Measurement of mortality rate related to IPF using chart audit method.	Chi-square test or Fisher's exact test, Kaplan-Meier analysis, log-rank test, Cox	Patients using PPI for more than 4 months had a lower IPF-related mortality rate than those on PPI less than 4 months (log-	**LOE**: IV **Strengths**: Adequate sample size with a retrospective cohort study design with long duration of

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Citation	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting	Major Variables & Definitions	Measurement/ Instrumentation	Data Analysis	Findings/ Results	Level/Quality of Evidence; Decision for practice/ application to practice
Authors received no financial support for the research, authorship, &/or publication of this article. **Bias:** None recognized **Country:** South Korea		GERD in Korean patients with IPF, and to compare the differences in survival according to the duration of PPI treatment.	**Sample demographics:** No significant differences between 2 subgroups in mean age, BMI, and sex. However, the proportion undergoing EGD was significantly higher for those with GERD than in those without GERD (78.5% vs 16.8%, P<0.001). Initial FVC was significantly higher and duration of follow-up was also significantly longer in patients with GERD. In addition, comorbidity of HTN, DM, and angina were more likely in patients with GERD. **Inclusion criteria:**	IPF-related mortality: All IPF-related causes of death including pneumonia or respiratory failure		proportional hazard regression analysis	rank p-value =0.024 in Kaplan-Meier curve). In univariate and multivariable Cox regression hazard model, younger age(HR, 1.06; 95%Cl, 1.03-1.10; p=0.001), higher initial FVC (HR, 0.98; 95% Cl, 0.96-0.99; p=0.004), and longer duration of PPI use (HR, 0.97; 95% Cl, 0.95-1.00; p=0.022), were significantly	follow-up (mean duration 2.6+_2.8 years) **Weakness:** Sampling limited to patients of Seoul National University Bundang Hospital. Single-center retrospective study. **Conclusion**: In Korean patients with IPF, PPI use for at least 4 months may have a protective effect against IPF-related mortality.

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			Consecutive adult patients with IPF at Seoul National University Bundang Hospital between April 2003 and March 2015 excluding underlying asthma or COPD. **Attrition:** Non-applicable for retrospective study				associated with lower IPF-related mortality.	
Lee, J. S. et al., (2013). Anti-acid therapy and disease progression in idiopathic pulmonary fibrosis: An analysis of data front here randomized controlled trials. *The Lancet. Respiratory Medicine*, *1*(5), 369–376. https://doi.org/10.1016/S2213-2600(13)70105-X	Health Belief Model	**Design:** From three parent IPFnet randomized clinical trials, patients from the placebo arms were studied prospectively. **Purpose:** To determine the	**N:** 242 **n:** 124 (taking PPI or H2B) **n:** 118 (not taking) **Setting:** Amongst various IPFnet centers in the United states. **Sample demographics:** There were no significant differences	**IV:** standard anti-acid therapy **DV1:** FVC at 30 weeks **DV2:** acute exacerbation **DV3:** all-cause hospitalization, **DV4:** all-cause mortality.				**LOE:** IV (even though the 3 parent studies are RCT but this substudy is not a randomized controlled trial of PPI/H2Btherapy in IPF.

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Citation	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting	Major Variables & Definitions	Measurement/ Instrumentation	Data Analysis	Findings/ Results	Level/Quality of Evidence; Decision for practice/ application to practice
Funding: Parent IPFnet trials were funded by the National Heart, Lung, and Blood Institute, and The Cowlin Family Fund at the Chicago Community Trust. This subgroup study was supported by grants. **Bia:** None recognized. **Country:** America		relationship between the routine use of anti-acid therapy (PPI and/or H2B) and IPF disease progression using prospectively collected data.	in demographics and pulmonary physiology between patients taking and not taking anti-acid therapy. **Inclusion criteria:** Not discussed.	**Definition:** Standard anti-acid therapy identified as "taking PPI or H2B" if patients report either of these medication at the baseline visit prior to randomization and during each follow-up visits.				**Strength:** Good power and generalizability **Weakness:** No specification on the duration of the anti-acid therapy **Conclusion:** The use of anti-acid therapy was associated with a slower decline in FVC over time and fewer acute exacerbation in patients with IPF.

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Table A2

Synthesis Table

Author	Costabel, U. et al.	Dutta, P. et al.	Fahim, A. et al	Fidler, L. et al.	Jo, H. E. et al.	Kilduff, C. E. et al.	Kreuter, M. et al.	Kulkarni, T. et al.	Lee C. M. et al.,	Lee, J. S. et al.,
Study Characteristics										
Year	2018	2019	2011	2018	2019	2014	2017	2016	2016	2013
Design/ LOE	Post-hoc analysis/ II	RCT/ II	CCS/ IV	SR/ I	CS/ IV	Prospective observational study III	Post hoc analysis/ IV	Retrospective cohort study/ IV	Cohort study/ IV	Cohort study/ IV
Demographics										
Age (Mean y.o.)	67	71	70		71	65	67	65	75	68
Male (%)	73	83	78		69	72	71	69	71	75
IPF dx	X	X	X	X	X	X	X	X	X	X
Setting:	In 24 countries	One hospital	Clinic		Australia national IPF registry data base		127 sites in 9 countries	University of Alabama at Birmingham	Seoul National University Bundang Hospital	Amongst various IPFnet centers in the United states.
Sample Size/# of Studies Included	406	45	170	13	587	18	623	284	786	242

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Measurement Tools	FVC predicted, chart review, SGRQ score	RSI, GQLI, LCQ, ambulatory cough recorder	HARQ, EBC	Cochran Collaboration tool to assess risk of bias, and the Newcastle-Ottawa Scale	FVC% predicted, FSSG	24-hour total reflux; 24-hour acid reflux; 24-hour weakly acid reflux and; 24-hour non-acid reflux. 24-hour cough count	FVC % predicted, DLco, 6MWD. UCSD-SOBQ score.	Chart audit method	Chart audit method.	
Duration of Treatment	Continuous at baseline and through 52 weeks of follow up	3 months			Continuous at baseline	8 weeks			4 months	
IV-Intervention										
Anti-acid therapy	X	X		X	X	X	X	X	X	X
No anti-acid therapy										
DV										
IPF-mortality/exacerbation	≠			↓	≠		≠	↓	↓	↓
Lung function decline	≠	≠			≠		≠	↓		↓
Quality of life/Better in Cough	≠	↑				↑				
6MWD		≠								

Key: **AAT**-anti-acid treatment; **IPF**-Idiopathic Pulmonary Fibrosis; **ILD**-interstitials lung disease; **GERD**-Gastroesophageal Reflux Disease; **COPD-**chronic obstructive pulmonary disease; **PPI**-Proton Pump Inhibitor; **H2B**-histamine-2 blocker; **FVC-**forced vital capacity; **EGD-**esophagealgastroduodenoscopy; **HTN**-hypertension; **DM**-diabetes mellitus; **DV**-dependent variable; **IV**- independent variable; **N**-number of studies; **n**- number of participants; **HR**-hazard ratio; **LOE**-level of evidence; **RCT**-Randomized controlled trial; **IPFnet**-Idiopathic Pulmonary Fibrosis Clinical Research Network; **HR**-Hazard Ratio; **CI**-Confidence Interval; **6MWD**-6-minute walk distance; **DLco-** hemoglobin-corrected predicted diffusing capacity of the lung for carbon monoxide; **USCD-SOBQ-**University of California at San Diego Shortness of Breath Questionnaire; **SGRQ-** St George's Respiratory Questionnaire

Appendix B

Models and Frameworks

Figure 1

The Theoretical Domains Framework

Sources of behaviour

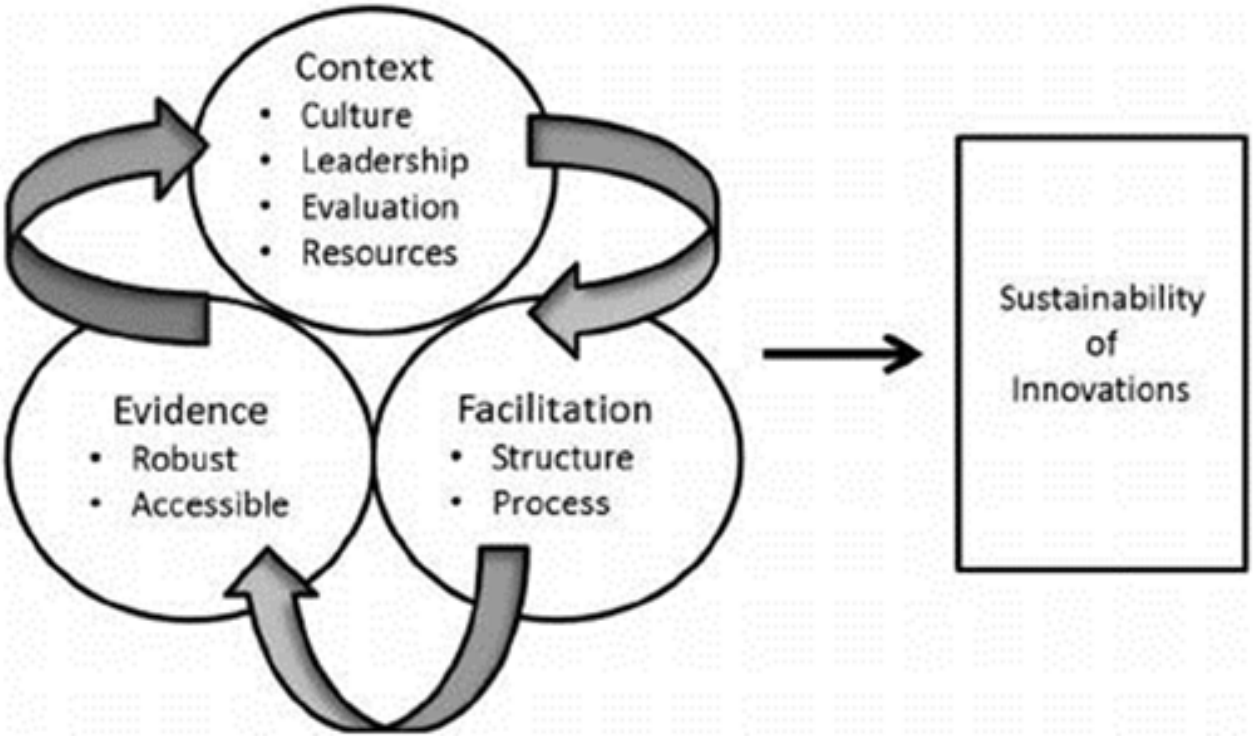
TDF Domains

Soc	- Social influences
Env	- Environmental context and resources
Id	- Professional role and identity
Bel Cap	- Beliefs about capabilities
Goals	-Goals, intentions and motivation
Bel Cons	- Beliefs about consequences
Em	- Emotion
Know	- Knowledge
Mem	- Memory, attention and decision process
Beh Reg	- Behavioural regulation
Skills	- Skills

Source: Michie, S., Johnston, M., Abraham, C., Lawton, R., Parker, D., Walker, A., & "Psychological Theory" Group (2005). Making psychological theory useful for implementing evidence-based practice: A consensus approach. *Quality & Safety in Health Care, 14*(1), 26–33.

Figure 2

PARIHS



University of Maryland (2019).

Appendix C

Pre-Survey

1.What is your age?

18-24

25-34

35-44

45-54

55-64

Above64

2.What is your gender?

Male

Female

Prefer not to answer

3.What is your practice setting?

General practice such as family medicine and internal medicine

Pulmonary medicine

Other thoracic disease

Other

4.How many years of practice experience do you have?

<3 years

3-5 years

5-7 years

7-9 years

>9 years

5.All remaining questions are scale-based, from 1-5, with 1 being "strongly disagree" and 5 being "strongly agree", how do you agree with the statement listed.

I believe that evidence-based practice (EBP) results in the best clinical care for patients.

1

2

3

4

5

6.I am sure that I am ready to implement EBP.

1

2

3

4

5

7.I believe that critically appraising evidence is an important step in the EBP process.

1

2

3

4

5

8.I believe that I can search for the best evidence to answer clinical questions in a time efficient way.

1

2

3

4

5

9.I believe that I can overcome barriers in implementing EBP.

1

2

3

4

5

10.I believe that EBP takes too much time.

1

2

3

4

5

11.I believe that EBP is difficult.

1

2

3

4

5

12.I am confident about my ability to implement EBP where I work.

1

2

3

4

5

13.I believe the care that I deliver is evidence-based.

1

2

3

4

5

Post-Survey

1.All remaining questions are scale-based, from 1-5, with 1 being "strongly disagree" and 5 being "strongly agree", how do you agree with the statement listed.

I believe that evidence-based practice (EBP) such as screening for GERD in IPF patients results in the best clinical care for patients.

1

2

3

4

5

2.I am sure that I am ready to implement EBP such as screening for GERD in IPF patients.

1

2

3

4

5

3.I believe that the presented evidence of GERD-IPF relationship needs more critical appraisal before implementing a screening protocol.

1

2

3

4

5

4.I believe that I can search for the best evidence to answer clinical questions in a time efficient way, such as searching for better evidence in the presented GERD-IPF relationship.

1

2

3

4

5

5.I believe that I can overcome barriers in implementing EBP such as screening for GERD in IPF patients.

1

2

3

4

5

6.I believe that EBP such as screening for GERD in IPF patients takes too much time.

1

2

3

4

5

7.I believe that EBP such as screening for GERD in IPF patients is difficult.

1

2

3

4

5

8.I am confident about my ability to implement EBP such as screening for GERD in IPF patients where I work.

1

2

3

4

5

9.I believe the care that I deliver is evidence-based and I do not need to implement additional EBP such as screening for GERD in IPF patients.

1

2

3

4

5