A SUPPLEMENT TO CHEST PHYSICIAN

PULMONOLOGY DATA TRENDS 2022

CHEST Physician®

Produced in collaboration with **CHEST**

Nucala
(mepolizumab)
Injection 100 mg/mL

The targeted therapy for 4 eosinophil-driven diseases

Severe eosinophilic asthma (SEA)

Chronic rhinosinusitis with nasal polyps (CRSwNP)

Eosinophilic granulomatosis with polyangiitis (EGPA)

Hypereosinophilic syndrome (HES)

NUCALA is for the:

- add-on maintenance treatment of patients 6+ with SEA. Not for acute bronchospasm or status asthmaticus.
- add-on maintenance treatment of CRSwNP in patients 18+ with inadequate response to nasal corticosteroids.
- treatment of adult patients with EGPA.
- treatment of patients aged 12+ with HES for ≥6 months without an identifiable non-hematologic secondary cause.

Important Safety Information

CONTRAINDICATIONS

NUCALA should not be administered to patients with a history of hypersensitivity to mepolizumab or excipients in the formulation.

Please see Brief Summary of Prescribing Information for NUCALA on the following pages.

Visit Nucala4EOS.com to learn more →

Important Safety Information (cont'd)

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Hypersensitivity reactions (eg, anaphylaxis, angioedema, bronchospasm, hypotension, urticaria, rash) have occurred with NUCALA. These reactions generally occur within hours of administration but can have a delayed onset (ie, days). If a hypersensitivity reaction occurs, discontinue NUCALA.

Acute Asthma Symptoms or Deteriorating Disease

NUCALA should not be used to treat acute asthma symptoms, acute exacerbations, or acute bronchospasm.

Opportunistic Infections: Herpes Zoster

Herpes zoster infections have occurred in patients receiving NUCALA. Consider vaccination if medically appropriate.

Reduction of Corticosteroid Dosage

Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of therapy with NUCALA. Decreases in corticosteroid doses, if appropriate, should be gradual and under the direct supervision of a physician. Reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.

Parasitic (Helminth) Infection

Treat patients with pre-existing helminth infections before initiating therapy with NUCALA. If patients become infected while receiving NUCALA and do not respond to anti-helminth treatment, discontinue NUCALA until infection resolves.

ADVERSE REACTIONS

Most common adverse reactions (≥5%) in patients receiving NUCALA:

- Severe asthma trials: headache, injection site reaction, back pain, fatigue
- CRSwNP trial: oropharyngeal pain, arthralgia
- EGPA and HES trials (300 mg of NUCALA): no additional adverse reactions were identified to those reported in severe asthma clinical trials

Systemic reactions, including hypersensitivity, occurred in clinical trials in patients receiving NUCALA. Manifestations included rash, pruritus, headache, myalgia, flushing, urticaria, erythema, fatigue, hypertension, warm sensation in trunk and neck, cold extremities, dyspnea, stridor, angioedema, and multifocal skin reaction. A majority of systemic reactions were experienced the day of dosing.

USE IN SPECIFIC POPULATIONS

A pregnancy exposure registry monitors pregnancy outcomes in women with asthma exposed to NUCALA during pregnancy. To enroll call 1-877-311-8972 or visit www.mothertobaby.org/asthma.

The data on pregnancy exposures are insufficient to inform on drug-associated risk. Monoclonal antibodies, such as mepolizumab, are transported across the placenta in a linear fashion as the pregnancy progresses; therefore, potential effects on a fetus are likely to be greater during the second and third trimesters.

BRIEF SUMMARY

NUCALA (mepolizumab) for injection, for subcutaneous use
NUCALA (mepolizumab) injection, for subcutaneous use
The following is a brief summary only; see full prescribing information for complete product information.

1 INDICATIONS AND USAGE

1.1 Maintenance Treatment of Severe Asthma

NUCALA is indicated for the add-on maintenance treatment of adult and pediatric patients aged 6 years and older with severe asthma and with an eosinophilic phenotype *[see Use in Specific Populations (8.4) and Clinical Studies (14.1) of full prescribing information]*.

Limitations of Use

NUCALA is not indicated for the relief of acute bronchospasm or status asthmaticus.

1.2 Maintenance Treatment of Chronic Rhinosinusitis with Nasal Polyps

NUCALA is indicated for the add-on maintenance treatment of chronic rhinosinusitis with nasal polyps (CRSwNP) in adult patients 18 years of age and older with inadequate response to nasal corticosteroids.

1.3 Eosinophilic Granulomatosis with Polyangiitis

NUCALA is indicated for the treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).

1.4 Hypereosinophilic Syndrome

NUCALA is indicated for the treatment of adult and pediatric patients aged 12 years and older with hypereosinophilic syndrome (HES) for ≥6 months without an identifiable non-hematologic secondary cause.

4 CONTRAINDICATIONS

NUCALA is contraindicated in patients with a history of hypersensitivity to mepolizumab or excipients in the formulation *[see Warnings and Precautions (5.1) and Description (11) of full prescribing information]*.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Hypersensitivity reactions (e.g., anaphylaxis, angioedema, bronchospasm, hypotension, urticaria, rash) have occurred following administration of NUCALA. These reactions generally occur within hours of administration, but in some instances can have a delayed onset (i.e., days). In the event of a hypersensitivity reaction, NUCALA should be discontinued *[see Contraindications (4)]*.

5.2 Acute Asthma Symptoms or Deteriorating Disease

NUCALA should not be used to treat acute asthma symptoms or acute exacerbations. Do not use NUCALA to treat acute bronchospasm or status asthmaticus. Patients should seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment with NUCALA.

5.3 Opportunistic Infections: Herpes Zoster

Herpes zoster has occurred in subjects receiving NUCALA 100 mg in controlled clinical trials *[see Adverse Reactions (6.1)]*. Consider vaccination if medically appropriate.

5.4 Reduction of Corticosteroid Dosage

Do not discontinue systemic or inhaled corticosteroids (ICS) abruptly upon initiation of therapy with NUCALA. Reductions in corticosteroid dosage, if appropriate, should be gradual and performed under the direct supervision of a physician. Reduction in corticosteroid dosage may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.

5.5 Parasitic (Helminth) Infection

Eosinophils may be involved in the immunological response to some helminth infections. Patients with known parasitic infections were excluded from participation in clinical trials. It is unknown if NUCALA will influence a patient's response against parasitic infections. Treat patients with pre-existing helminth infections before initiating therapy with NUCALA. If patients become infected while receiving treatment with NUCALA and do not respond to anti-helminth treatment, discontinue treatment with NUCALA until infection resolves.

6 ADVERSE REACTIONS

The following adverse reactions are described in greater detail in other sections:

- Hypersensitivity reactions *[see Warnings and Precautions (5.1)]*
- Opportunistic infections: herpes zoster *[see Warnings and Precautions (5.3)]*

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

6.1 Clinical Trials Experience in Severe Asthma

Adult and Adolescent Patients Aged 12 Years and Older

A total of 1,327 patients with severe asthma were evaluated in 3 randomized, placebo-controlled, multicenter trials of 24 to 52 weeks' duration (Trial 1, NCT01000506; Trial 2, NCT01691521; and Trial 3, NCT01691508). Of these, 1,192 had a history of 2 or more exacerbations in the year prior to enrollment despite regular use of high-dose ICS plus additional controller(s) (Trials 1 and 2), and 135 patients required daily oral corticosteroids (OCS) in addition to regular use of high-dose ICS plus additional controller(s) to maintain asthma control (Trial 3). All patients had markers of eosinophilic airway inflammation *[see Clinical Studies (14.1) of full prescribing information]*. Of the patients enrolled, 59% were female, 85% were White, and ages ranged from 12 to 82 years. Mepolizumab was administered subcutaneously or intravenously once every 4 weeks; 263 patients received NUCALA (mepolizumab 100 mg subcutaneous) for at least 24 weeks. Serious adverse events that occurred in more than 1 patient and in a greater percentage of patients receiving NUCALA 100 mg (n = 263) than placebo (n = 257) included 1 event, herpes zoster (2 patients vs. 0 patients, respectively). Approximately 2% of patients receiving NUCALA 100 mg withdrew from clinical trials due to adverse events compared with 3% of patients receiving placebo.

The incidence of adverse reactions in the first 24 weeks of treatment in the 2 confirmatory efficacy and safety trials (Trials 2 and 3) with NUCALA 100 mg is shown in Table 1.

Table 1. Adverse Reactions with NUCALA with ≥3% Incidence and More Common than Placebo in Patients with Severe Asthma (Trials 2 and 3)

Adverse Reaction	NUCALA (Mepolizumab 100 mg Subcutaneous) (n = 263) %	Placebo (n = 257) %
Headache	19	18
Injection site reaction	8	3
Back pain	5	4
Fatigue	5	4
Influenza	3	2
Urinary tract infection	3	2
Abdominal pain upper	3	2
Pruritus	3	2
Eczema	3	<1
Muscle spasms	3	<1

52-Week Trial: Adverse reactions from Trial 1 with 52 weeks of treatment with mepolizumab 75 mg intravenous (IV) (n = 153) or placebo (n = 155) and with ≥3% incidence and more common than placebo and not shown in Table 1 were: abdominal pain, allergic rhinitis, asthenia, bronchitis, cystitis, dizziness, dyspnea, ear infection, gastroenteritis, lower respiratory tract infection, musculoskeletal pain, nasal congestion, nasopharyngitis, nausea, pharyngitis, pyrexia, rash, toothache, viral infection, viral respiratory tract infection, and vomiting. In addition, 3 cases of herpes zoster occurred in patients receiving mepolizumab 75 mg IV compared with 2 patients in the placebo group.

Systemic Reactions, including Hypersensitivity Reactions: In Trials 1, 2, and 3 described above, the percentage of patients who experienced systemic (allergic and non-allergic) reactions was 3% in the group receiving NUCALA 100 mg and 5% in the placebo group. Systemic allergic/hypersensitivity reactions were reported by 1% of patients in the group receiving NUCALA 100 mg and 2% of patients in the placebo group. The most commonly reported manifestations of systemic allergic/hypersensitivity reactions reported in the group receiving NUCALA 100 mg included rash, pruritus, headache, and myalgia. Systemic non-allergic reactions were reported by 2% of patients in the group receiving NUCALA 100 mg and 3% of patients in the placebo group. The most commonly reported manifestations of systemic non-allergic reactions reported in the group receiving NUCALA 100 mg included rash, flushing, and myalgia. A majority of the systemic reactions in patients receiving NUCALA 100 mg (5/7) were experienced on the day of dosing.

Injection Site Reactions: Injection site reactions (e.g., pain, erythema, swelling, itching, burning sensation) occurred at a rate of 8% in patients receiving NUCALA 100 mg compared with 3% in patients receiving placebo.

Long-term Safety: Nine hundred ninety-eight patients received NUCALA 100 mg in ongoing open-label extension studies, during which additional cases of herpes zoster were reported. The overall adverse event profile has been similar to the asthma trials described above.

Pediatric Patients Aged 6 to 11 Years

The safety data for NUCALA is based upon 1 open-label clinical trial that enrolled 36 patients with severe asthma aged 6 to 11 years. Patients received 40 mg (for those weighing <40 kg) or 100 mg (for those weighing ≥40 kg) of NUCALA administered subcutaneously once every 4 weeks. Patients received NUCALA for 12 weeks (initial short phase). After a treatment interruption of 8 weeks, 30 patients received NUCALA for a further 52 weeks (long phase). The adverse reaction profile for patients aged 6 to 11 years was similar to that observed in patients aged 12 years and older.

6.2 Clinical Trials Experience in Chronic Rhinosinusitis with Nasal Polyps

A total of 407 patients with CRSwNP were evaluated in 1 randomized, placebo-controlled, multicenter, 52-week treatment trial. Patients received NUCALA 100 mg or placebo subcutaneously once every 4 weeks. Patients had recurrent CRSwNP with a history of prior surgery and were on nasal corticosteroids for at least 8 weeks prior to screening *[see Clinical Studies (14.2) of full prescribing information]*. Of the patients enrolled, 35% were female, 93% were White, and ages ranged from 18 to 82 years. Approximately 2% of patients receiving NUCALA

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6 ADVERSE REACTIONS *(cont'd)*

100 mg withdrew from study treatment due to adverse events compared with 2% of patients receiving placebo.
Table 2 summarizes adverse reactions that occurred in ≥3% of NUCALA-treated patients and more frequently than in patients treated with placebo in the CRSwNP trial.

Table 2. Adverse Reactions with NUCALA with ≥3% Incidence and More Common than Placebo in Patients with CRSwNP

Adverse Reaction	NUCALA (Mepolizumab 100 mg Subcutaneous) (n = 206) %	Placebo (n = 201) %
Oropharyngeal pain	8	5
Arthralgia	6	2
Abdominal Pain Upper	3	2
Diarrhea	3	2
Pyrexia	3	2
Nasal dryness	3	<1
Rash	3	<1

CRSwNP = Chronic Rhinosinusitis with Nasal Polyps.

Systemic Reactions, including Hypersensitivity Reactions
In the 52-week trial, the percentage of patients who experienced systemic (allergic [type I hypersensitivity] and other) reactions was <1% in the group receiving NUCALA 100 mg and <1% in the placebo group. Systemic allergic (type I hypersensitivity) reactions were reported by <1% of patients in the group receiving NUCALA 100 mg and no patients in the placebo group. The manifestations of systemic allergic (type I hypersensitivity) reactions included urticaria, erythema, and rash and 1 of the 3 reactions occurred on the day of dosing. Other systemic reactions were reported by no patients in the group receiving NUCALA 100 mg and <1% of patients in the placebo group.
Injection Site Reactions
Injection site reactions (e.g., erythema, pruritus) occurred at a rate of 2% in patients receiving NUCALA 100 mg compared with <1% in patients receiving placebo.

6.3 Clinical Trials Experience in Eosinophilic Granulomatosis with Polyangiitis
A total of 136 patients with EGPA were evaluated in 1 randomized, placebo-controlled, multicenter, 52-week treatment trial. Patients received 300 mg of NUCALA or placebo subcutaneously once every 4 weeks. Patients enrolled had a diagnosis of EGPA for at least 6 months prior to enrollment with a history of relapsing or refractory disease and were on a stable dosage of oral prednisolone or prednisone of greater than or equal to 7.5 mg/day (but not greater than 50 mg/day) for at least 4 weeks prior to enrollment *[see Clinical Studies (14.3) of full prescribing information]*. Of the patients enrolled, 59% were female, 92% were White, and ages ranged from 20 to 71 years. No additional adverse reactions were identified to those reported in the severe asthma trials.
Systemic Reactions, including Hypersensitivity Reactions
In the 52-week trial, the percentage of patients who experienced systemic (allergic and non-allergic) reactions was 6% in the group receiving 300 mg of NUCALA and 1% in the placebo group. Systemic allergic/hypersensitivity reactions were reported by 4% of patients in the group receiving 300 mg of NUCALA and 1% of patients in the placebo group. The manifestations of systemic allergic/hypersensitivity reactions reported in the group receiving 300 mg of NUCALA included rash, pruritus, flushing, fatigue, hypertension, warm sensation in trunk and neck, cold extremities, dyspnea, and stridor. Systemic non-allergic reactions were reported by 1 (1%) patient in the group receiving 300 mg of NUCALA and no patients in the placebo group. The reported manifestation of systemic non-allergic reactions reported in the group receiving 300 mg of NUCALA was angioedema. Half of the systemic reactions in patients receiving 300 mg of NUCALA (2/4) were experienced on the day of dosing.
Injection Site Reactions
Injection site reactions (e.g., pain, erythema, swelling) occurred at a rate of 15% in patients receiving 300 mg of NUCALA compared with 13% in patients receiving placebo.

6.4 Clinical Trials Experience in Hypereosinophilic Syndrome
A total of 108 adult and adolescent patients aged 12 years and older with HES were evaluated in a randomized, placebo-controlled, multicenter, 32-week treatment trial. Patients with non-hematologic secondary HES or FIP1L1-PDGFRα kinase-positive HES were excluded from the trial. Patients received 300 mg of NUCALA or placebo subcutaneously once every 4 weeks. Patients must have been on a stable dose of background HES therapy for the 4 weeks prior to randomization [*see Clinical Studies (14.4) of full prescribing information*]. Of the patients enrolled, 53% were female, 93% were White, and ages ranged from 12 to 82 years. No additional adverse reactions were identified to those reported in the severe asthma trials.
Systemic Reactions, including Hypersensitivity Reactions
In the trial, no systemic allergic (type I hypersensitivity) reactions were reported. Other systemic reactions were reported by 1 (2%) patient in the group receiving 300 mg of NUCALA and no patients in the placebo group. The reported manifestation of other systemic reaction was multifocal skin reaction experienced on the day of dosing.
Injection Site Reactions
Injection site reactions (e.g., burning, itching) occurred at a rate of 7% in patients receiving 300 mg of NUCALA compared with 4% in patients receiving placebo.

6.5 Immunogenicity
In adult and adolescent patients with severe asthma receiving NUCALA 100 mg, 15/260 (6%) had detectable anti-mepolizumab antibodies. Neutralizing antibodies were detected in 1 patient with asthma receiving NUCALA 100 mg. Anti-mepolizumab antibodies slightly increased (approximately 20%) the clearance of mepolizumab. There was no evidence of a correlation between anti-mepolizumab antibody titers and change in eosinophil level. The clinical relevance of the presence of anti-mepolizumab antibodies is not known. In the clinical trial of children aged 6 to 11 years with severe asthma receiving NUCALA 40 or 100 mg, 2/35 (6%) had detectable anti-mepolizumab antibodies during the initial short phase of the trial. No children had detectable anti-mepolizumab antibodies during the long phase of the trial.
In patients with CRSwNP receiving NUCALA 100 mg, 6/196 (3%) had detectable anti-mepolizumab antibodies. No neutralizing antibodies were detected in any patients with CRSwNP.
In patients with EGPA receiving 300 mg of NUCALA, 1/68 (<2%) had detectable anti-mepolizumab antibodies. No neutralizing antibodies were detected in any patients with EGPA.
In adult and adolescent patients with HES receiving 300 mg of NUCALA, 1/53 (2%) had detectable anti-mepolizumab antibodies. No neutralizing antibodies were detected in any patients with HES.
The reported frequency of anti-mepolizumab antibodies may underestimate the actual frequency due to lower assay sensitivity in the presence of high drug concentration. The data reflect the percentage of patients whose test results were positive for antibodies to mepolizumab in specific assays. The observed incidence of antibody positivity in an assay is highly dependent on several factors, including assay sensitivity and specificity, assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease.

6.6 Postmarketing Experience
In addition to adverse reactions reported from clinical trials, the following adverse reactions have been identified during postapproval use of NUCALA. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. These events have been chosen for inclusion due to either their seriousness, frequency of reporting, or causal connection to NUCALA or a combination of these factors.
Immune System Disorders
Hypersensitivity reactions, including anaphylaxis.

7 DRUG INTERACTIONS
Formal drug interaction trials have not been performed with NUCALA.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Pregnancy Exposure Registry
There is a pregnancy exposure registry that monitors pregnancy outcomes in women with asthma exposed to NUCALA during pregnancy. Healthcare providers can enroll patients or encourage patients to enroll themselves by calling 1-877-311-8972 or visiting www.mothertobaby.org/asthma.
Risk Summary
The data on pregnancy exposure are insufficient to inform on drug-associated risk. Monoclonal antibodies, such as mepolizumab, are transported across the placenta in a linear fashion as pregnancy progresses; therefore, potential effects on a fetus are likely to be greater during the second and third trimester of pregnancy. In a prenatal and postnatal development study conducted in cynomolgus monkeys, there was no evidence of fetal harm with IV administration of mepolizumab throughout pregnancy at doses that produced exposures up to approximately 9 times the exposure at the maximum recommended human dose (MRHD) of 300 mg subcutaneous (*see Data*). In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.
Clinical Considerations
Disease-Associated Maternal and/or Embryofetal Risk: In women with poorly or moderately controlled asthma, evidence demonstrates that there is an increased risk of preeclampsia in the mother and prematurity, low birth weight, and small for gestational age in the neonate. The level of asthma control should be closely monitored in pregnant women and treatment adjusted as necessary to maintain optimal control.
Data
Animal Data: In a prenatal and postnatal development study, pregnant cynomolgus monkeys received mepolizumab from gestation Days 20 to 140 at doses that produced exposures up to approximately 9 times that achieved with the MRHD (on an AUC basis with maternal IV doses up to 100 mg/kg once every 4 weeks). Mepolizumab did not elicit adverse effects on fetal or neonatal growth (including immune function) up to 9 months after birth. Examinations for internal or skeletal malformations were not performed. Mepolizumab crossed the placenta in cynomolgus monkeys. Concentrations of mepolizumab were approximately 2.4 times higher in infants than in mothers up to Day 178 postpartum. Levels of mepolizumab in milk were ≤0.5% of maternal serum concentration.
In a fertility, early embryonic, and embryofetal development study, pregnant CD-1 mice received an analogous antibody, which inhibits the activity of murine interleukin-5 (IL-5), at an IV dose of 50 mg/kg once per week throughout gestation.

(continued on next page)

8 USE IN SPECIFIC POPULATIONS *(cont'd)*

The analogous antibody was not teratogenic in mice. Embryofetal development of IL-5–deficient mice has been reported to be generally unaffected relative to wild-type mice.

8.2 Lactation

Risk Summary

There is no information regarding the presence of mepolizumab in human milk, the effects on the breastfed infant, or the effects on milk production. However, mepolizumab is a humanized monoclonal antibody (IgG1 kappa), and immunoglobulin G (IgG) is present in human milk in small amounts. Mepolizumab was present in the milk of cynomolgus monkeys postpartum following dosing during pregnancy *[see Use in Specific Populations (8.1)]*. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for NUCALA and any potential adverse effects on the breastfed infant from mepolizumab or from the underlying maternal condition.

8.4 Pediatric Use

Severe Asthma

The safety and efficacy of NUCALA for severe asthma, and with an eosinophilic phenotype, have been established in pediatric patients aged 6 years and older. Use of NUCALA in adolescents aged 12 to 17 years is supported by evidence from adequate and well-controlled trials in adults and adolescents. A total of 28 adolescents aged 12 to 17 years with severe asthma were enrolled in the Phase 3 asthma trials. Of these, 25 were enrolled in the 32-week exacerbation trial (Trial 2, NCT01691521) and had a mean age of 14.8 years. Patients had a history of 2 or more exacerbations in the previous year despite regular use of medium- or high-dose ICS plus additional controller(s) with or without OCS and had blood eosinophils of ≥150 cells/mcL at screening or ≥300 cells/mcL within 12 months prior to enrollment. *[See Clinical Studies (14.1) of full prescribing information.]* Patients had a reduction in the rate of exacerbations that trended in favor of NUCALA. Of the 19 adolescents who received NUCALA, 9 received 100 mg and the mean apparent clearance in these patients was 35% less than that of adults. The safety profile observed in adolescents was generally similar to that of the overall population in the Phase 3 studies *[see Adverse Reactions (6.1)]*.

Use of NUCALA in pediatric patients aged 6 to 11 years with severe asthma, and with an eosinophilic phenotype, is supported by evidence from adequate and well-controlled trials in adults and adolescents with additional pharmacokinetic, pharmacodynamic, and safety data in children aged 6 to 11 years. A single, open-label clinical trial (NCT02377427) was conducted in 36 children aged 6 to 11 years (mean age: 8.6 years, 31% female) with severe asthma. Enrollment criteria were the same as for adolescents in the 32-week exacerbation trial (Trial 2). Based upon the pharmacokinetic data from this trial, a dose of 40 mg subcutaneous every 4 weeks was determined to have similar exposure to adults and adolescents administered a dose of 100 mg SC *[see Clinical Pharmacology (12.3) of full prescribing information]*.

The effectiveness of NUCALA in pediatric patients aged 6 to 11 years is extrapolated from efficacy in adults and adolescents with support from pharmacokinetic analyses showing similar drug exposure levels for 40 mg administered subcutaneously every 4 weeks in children aged 6 to 11 years compared with adults and adolescents *[see Clinical Pharmacology (12.3) of full prescribing information]*. The safety profile and pharmacodynamic response observed in this trial for children aged 6 to 11 years were similar to that seen in adults and adolescents *[see Adverse Reactions (6.1), Clinical Pharmacology (12.2) of full prescribing information]*.

The safety and effectiveness in pediatric patients aged younger than 6 years with severe asthma have not been established.

Chronic Rhinosinusitis with Nasal Polyps

The safety and effectiveness in patients aged younger than 18 years with CRSwNP have not been established.

Eosinophilic Granulomatosis with Polyangiitis

The safety and effectiveness in patients aged younger than 18 years with EGPA have not been established.

Hypereosinophilic Syndrome

The safety and effectiveness of NUCALA for HES have been established in adolescent patients aged 12 years and older. The safety and effectiveness in pediatric patients aged younger than 12 years with HES have not been established. Use of NUCALA for this indication is supported by evidence from an adequate and well-controlled study (NCT02836496) in adults and adolescents and an open-label extension study (NCT03306043). One adolescent received NUCALA during the controlled study and this patient and an additional 3 adolescents received NUCALA during the open-label extension study *[see Clinical Studies (14.4) of full prescribing information]*. The 1 adolescent treated with NUCALA in the 32-week trial did not have a HES flare or an adverse event reported. All adolescents received 300 mg of NUCALA for 20 weeks in the open-label extension.

8.5 Geriatric Use

Clinical trials of NUCALA did not include sufficient numbers of patients aged 65 years and older that received NUCALA (n = 79) to determine whether they respond differently from younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other drug therapy. Based on available data, no adjustment of the dosage of NUCALA in geriatric patients is necessary, but greater sensitivity in some older individuals cannot be ruled out.

10 OVERDOSAGE

There is no specific treatment for an overdose with mepolizumab. If overdose occurs, the patient should be treated supportively with appropriate monitoring as necessary.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Hypersensitivity Reactions

Inform patients that hypersensitivity reactions (e.g., anaphylaxis, angioedema, bronchospasm, hypotension, urticaria, rash) have occurred after administration of NUCALA. Instruct patients to contact their physicians if such reactions occur.

Not for Acute Symptoms or Deteriorating Disease

Inform patients that NUCALA does not treat acute asthma symptoms or acute exacerbations. Inform patients to seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment with NUCALA.

Opportunistic Infections: Herpes Zoster

Inform patients that herpes zoster infections have occurred in patients receiving NUCALA and where medically appropriate, inform patients that vaccination should be considered.

Reduction of Corticosteroid Dosage

Inform patients to not discontinue systemic or inhaled corticosteroids except under the direct supervision of a physician. Inform patients that reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.

Pregnancy Exposure Registry

Inform women there is a pregnancy exposure registry that monitors pregnancy outcomes in women with asthma exposed to NUCALA during pregnancy and that they can enroll in the Pregnancy Exposure Registry by calling 1-877-311-8972 or by visiting www.mothertobaby.org/asthma *[see Use in Specific Populations (8.1)]*.

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Common Abbreviations

ACO, asthma and COPD overlap; **BMI,** body mass index; **CF,** cystic fibrosis; **COPD,** chronic obstructive pulmonary disease; **CT,** computed tomography; **FDA,** US Food and Drug Administration; **FEV_1,** forced expiratory volume in the first second; **FVC,** forced vital capacity; **GERD,** gastroesophogeal reflux disease; **HIV,** human immunodeficiency virus; **ILD,** interstitial lung diseases; **OS,** overall survival; **PAH,** pulmonary arterial hypertension; **PFS,** progression-free survival; **TB,** tuberculosis; **VHA,** Veterans Health Administration

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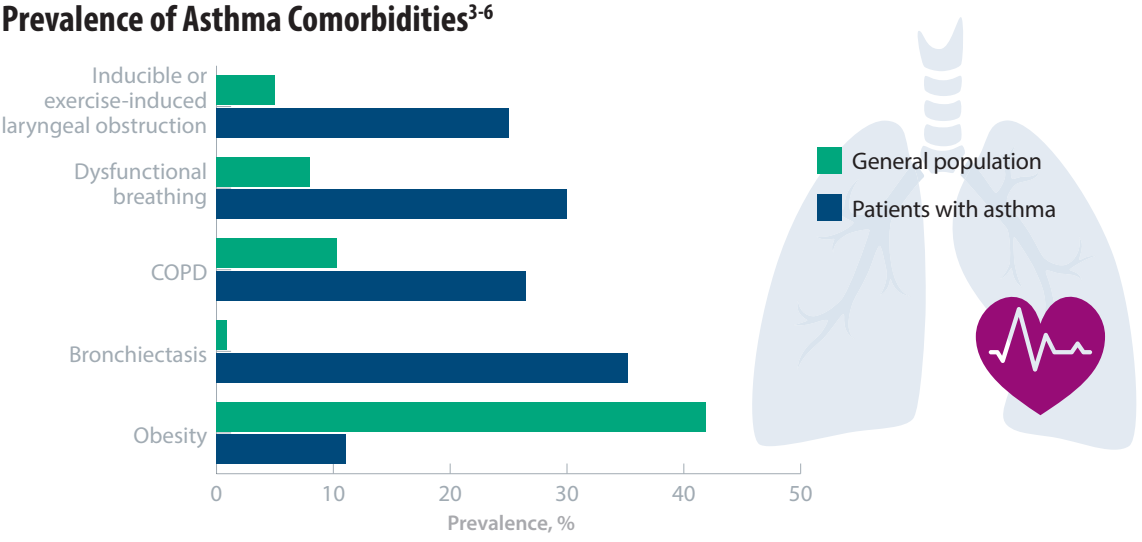
Comorbidities, Racial Disparities, and Geographic Differences in Asthma

Navitha Ramesh, MD, FCCP

Asthma management is becoming increasingly personalized, making it crucial to evaluate the various comorbidities and socioeconomic factors affecting patient care. Asthma is no longer simply understood as the typical allergic asthma requiring treatment with corticosteroids. There is an evolving distinction between allergen-specific T helper 2 (Th2) and non-Th2 asthma.[1] In Th2 asthma, eosinophilic inflammation plays a key role, whereas in non-Th2 asthma, neutrophils are the primary inflammatory cells involved.[1] Asthma masqueraders, such as vocal cord dysfunction, chronic obstructive pulmonary disease, eosinophilic granulomatosis with polyangiitis, etc, must be considered in the differential diagnosis, and asthma comorbidities, such as upper airway cough syndrome, gastroesophageal reflux, depression, and anxiety, have to be actively sought out and managed appropriately.[2]

Racial, socioeconomic, and geographic characteristics are also key patient factors that affect asthma symptoms and control, quality of life, and asthma-related morbidity and mortality. Assessing and understanding the multiple factors that affect each patient is crucial in the optimal management of asthma symptoms, and also preventing exacerbations, which in turn lead to accelerated loss of lung function.

Prevalence of Asthma Comorbidities[3-6]



Ways Obesity Affects Asthma Symptoms[6]

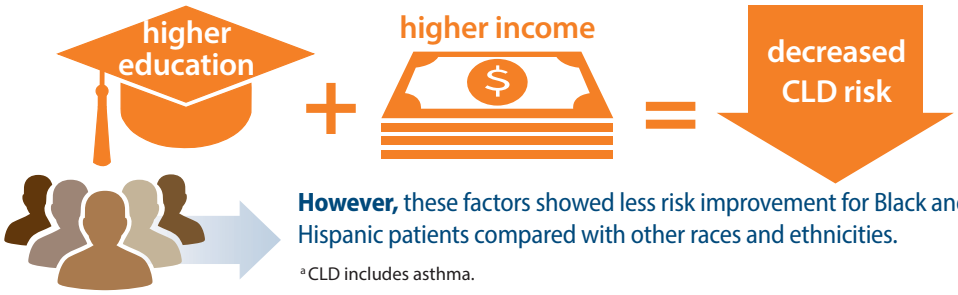
- Alters chest wall dynamics, affecting ventilation
- Increases airflow limitation
- Worsens airway closure
- Increases airway inflammation from dietary changes

Ways Obesity Affects Asthma Treatment[6]

- Affects biomarkers normally used to identity asthma
- Affects selection of biologics used for treatment
- Pivots focus to treating obesity first

Race, ethnicity, socioeconomic, and geographic factors significantly affect the quality of life and asthma control in most patients. These considerations should be actively reviewed and managed as part of holistic asthma care. A study of 25,659 American adults found that level of education and income had varying impact on the risk of chronic lung disease (CLD), including asthma, in different racial and ethnic groups.

The Impact of Education, Income, and Race and Ethnicity on Risk of CLD[7,a]

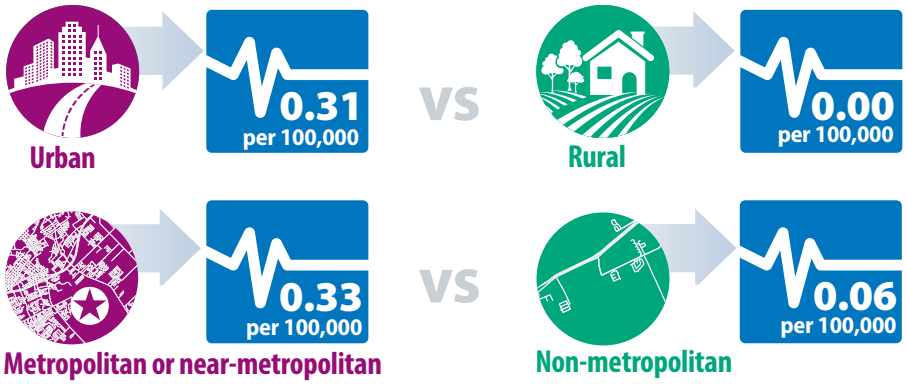


However, these factors showed less risk improvement for Black and Hispanic patients compared with other races and ethnicities.

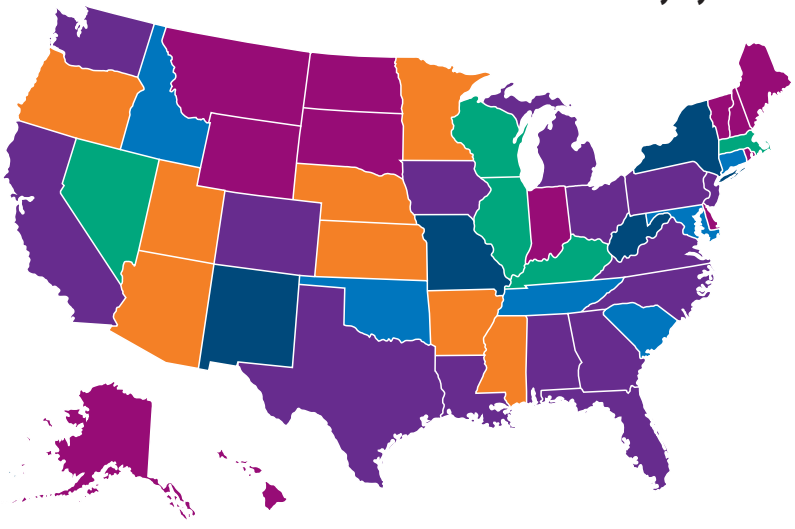
[a] CLD includes asthma.

Geographic location has also been shown to affect the incidence of asthma.[8] Different states and types of communities have varying degrees of asthma prevalence and mortality.

Asthma Age-Adjusted Mortality Rates in Rural vs Urban Areas[8]



Percentile Rank of Asthma Mortality by State[8]



85th-100th percentile
Average mortality rate: **1.38** per 100,000

75th-84th percentile
Average mortality rate: **1.12** per 100,000

65th-74th percentile
Average mortality rate: **1.02** per 100,000

55th-64th percentile
Average mortality rate: **0.94** per 100,000

25th-54th percentile
Average mortality rate: **0.70-0.86** per 100,000

0-24th percentile
Average mortality rate: **≤0.11** per 100,000

Adapted from *Annals of Allergy, Asthma & Immunology,* 128(1):11, Bleecker ER et al, Mapping geographic variability of severe uncontrolled asthma in the United States: Management implications, ©2022, with permission from Elsevier.

Post-COVID-19 Effects

Viren Kaul, MD, FCCP, FACP

Millions of Americans have been affected by the COVID-19 pandemic, with 93.2 million cases as of August 19, 2022.[1] Many of these individuals are experiencing long-term effects after infection with the COVID-19 virus, and various disparities are affecting access to care. Post-acute COVID-19 syndrome is defined as symptoms that persist 4 weeks after the onset of symptoms from COVID-19 infection. Although COVID-19 is primarily a respiratory infection, the long-term effects have been seen in various organ systems. The effects of this condition reach beyond physical health, taking a toll on a patient's economic and psychological well-being. Different racial/ethnic and economic factors also influence likelihood of illness and disease outcomes. Physicians must remain aware of the long-term role these factors will continue to play in patient outcomes.

Long-term Effects of COVID-19[2-5,a]

Musculoskeletal
Fatigue, muscular weakness and post exertional malaise, joint pain

Cardiac
Palpitations, chest pain, cardiomyopathy

Gastrointestinal
Abdominal pain, altered bowel patterns

Pulmonary
Dyspnea, cough, persistent supplemental oxygen requirement

Hematologic
Thromboembolism

Integumentary
Hair loss, rash

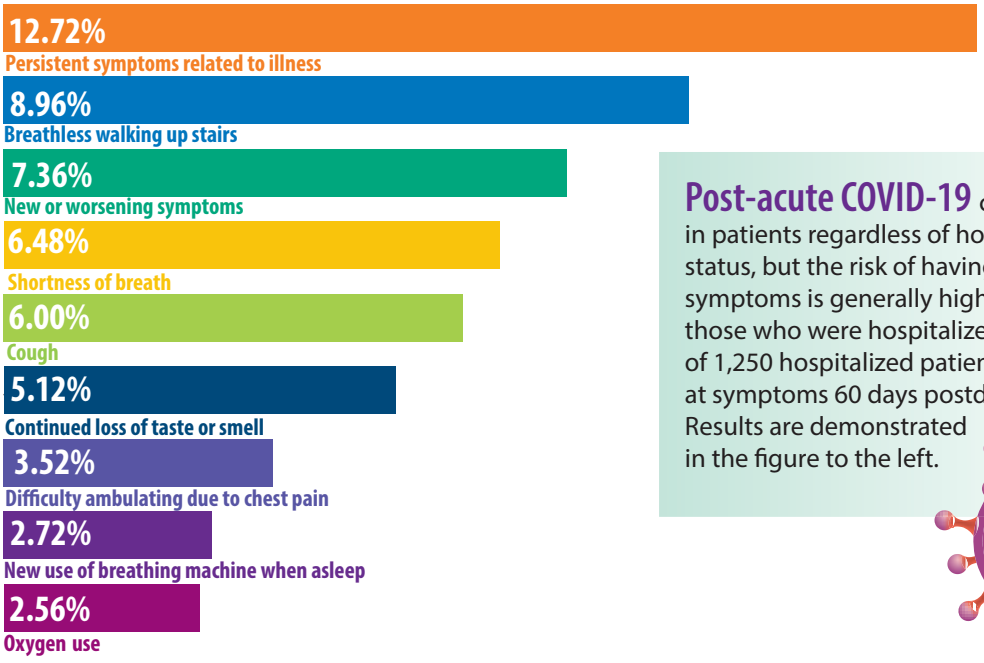
Neurologic
Anxiety, depression, sleep disturbances, PTSD, cognitive disturbances (also known as brain fog), headaches, dizziness, sensory disturbances, altered smell and taste

Nephrological
Chronic kidney disease

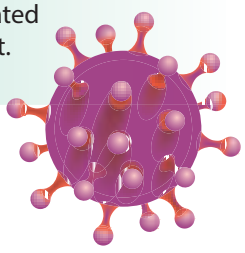
Gynecologic
Changes in menstrual cycles

[a] This includes effects that persist 4 weeks after symptom onset in both hospitalized and nonhospitalized individuals.

Patient Symptoms and Impairments Remaining 60 Days After Hospitalization[6]



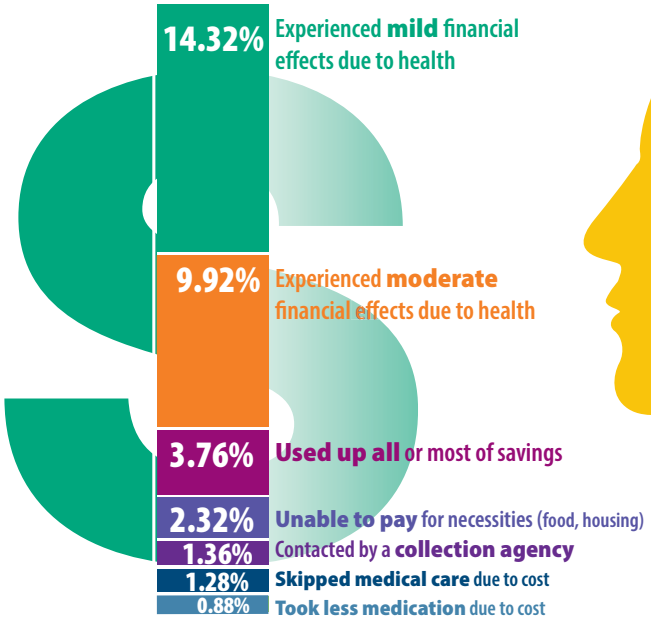
Post-acute COVID-19 can develop in patients regardless of hospitalization status, but the risk of having long-term symptoms is generally higher among those who were hospitalized.[3] A study of 1,250 hospitalized patients looked at symptoms 60 days postdischarge.[6] Results are demonstrated in the figure to the left.



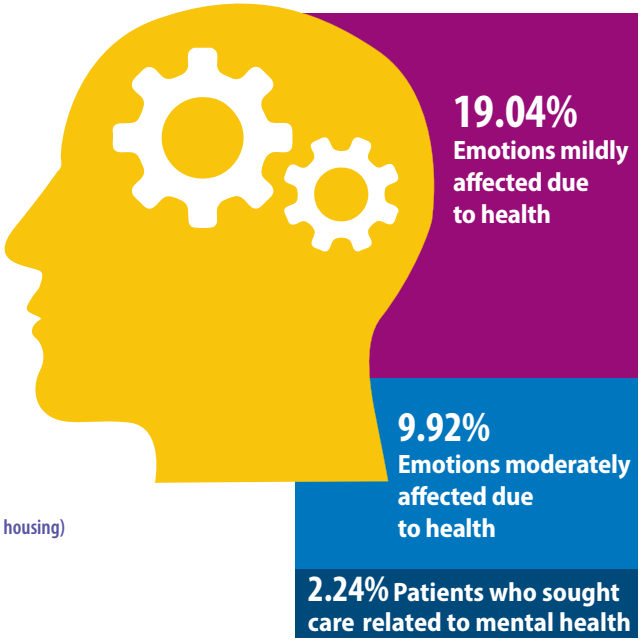
Post-COVID-19 Burdens and Disparities

Apart from the physical effects of post-acute COVID-19 syndrome,
economic and psychological consequences are profound.[6]

Economic Burden 60 Days After Hospitalization for COVID-19[6]

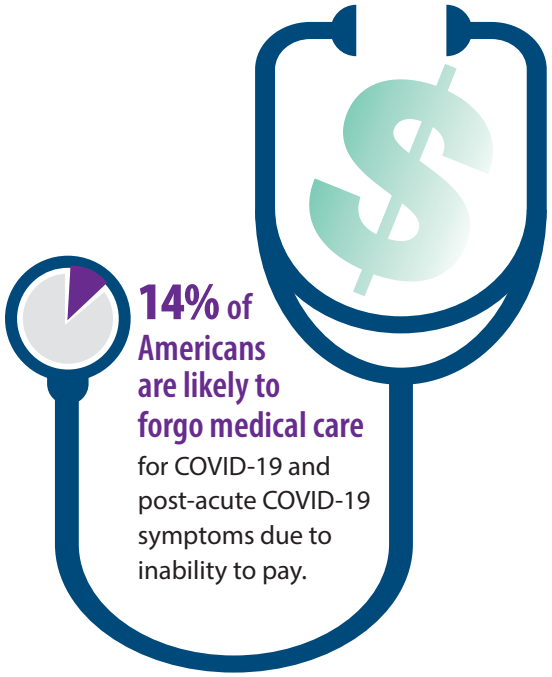


Psychological Burden 60 Days After Hospitalization for COVID-19[6]



Effects of Income, Race/Ethnicity, and Underlying Conditions on Post-COVID-19 Outcomes[7]

Social and economic disparities further affect access to care for those suffering from post-acute COVID-19.[7]



People most affected by COVID-19 and post-acute COVID-19 include:

- Individuals with low income
- People of color

Racially/ethnically diverse patients and individuals with low income have:

- Higher rates of underlying health conditions
- Higher rates of obesity

New Pathogens, COVID-19, and Antibiotic Resistance in the Field of Pneumonia

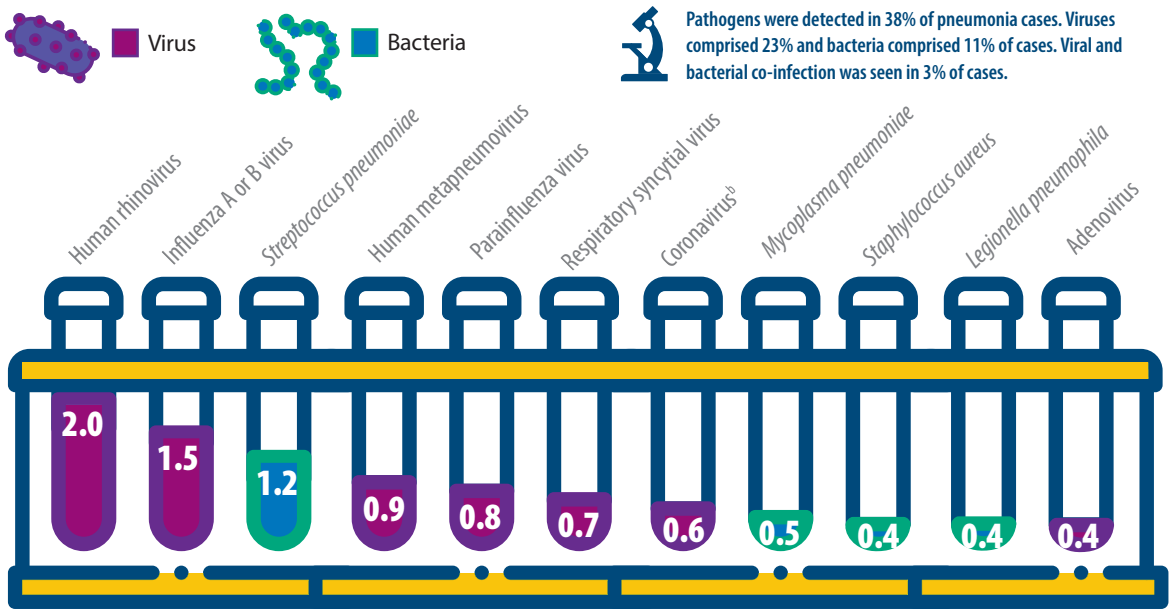
Marcos I. Restrepo, MD, MSc, PhD, FCCP

Before the onset of the COVID-19 pandemic, researchers in the field of pneumonia were grappling with the increase in the number of pathogens, antimicrobial-resistant strains causing pneumonia, and high mortality in short-term and long-term cases in those with comorbidites and with severe pneumonia.[1,2] In 2015, a landmark study identified that the most common pathogens causing community-acquired pneumonia (CAP) were viruses such as rhinovirus and influenza virus, and that the most common bacterial pathogen remained *Streptococcus pneumoniae*.[1] Just as the rest of world was forced to shift their focus in 2020 because of the pandemic, those of us in the pulmonary space were challenged to understand the impact that COVID-19 would have on treating our patients, particularly those with pneumonia. SARS-CoV-2, the virus that causes COVID-19, in a short time became the leading pathogen causing pneumonia. In addition, severely ill patients with COVID-19 were found to have a higher risk of developing hospital-acquired pneumonia and ventilator-associated pneumonia (VAP). The rate of VAP increased during the pandemic due to several factors, one of them being the time patients with COVID-19 spent on ventilators.[3,4]

Now that the pandemic has passed its peak, the field of pneumonia is revisiting earlier concerns—assessment of new pathogens and antibiotic resistance—as well as addressing issues brought to light by the COVID-19 pandemic.

A pre-COVID 19 study of 2,488 patients hospitalized with CAP in the United States investigated the causes of pneumonia and assessed burden of disease by collecting blood and respiratory specimens for pathogens.[1]

Pathogens Detected in Patients With CAP Pre-COVID-19 Pandemic[1,a]



[a] Participants all >18 years of age.
[b] Refers to coronaviruses identified prior to COVID-19.

After the onset of the COVID-19 pandemic, the treatment of viral pneumonia had to be reassessed. COVID-19 had to be taken into consideration when differentiating causes, risk factors, potential therapeutic and preventive interventions, and clinically relevant patient outcomes.

Viral Pneumonia vs COVID-19 Pneumonia[3]

	Viral Pneumonia	COVID-19 Pneumonia
Epidemiology	» Viral more common than bacterial » Predominant in children <5 years and adults >50 years	» Spreads rapidly when CAP viruses peak, having a competitive effect on circulation of other respiratory illnesses » High mortality in elderly and immunocompromised patients
Presentation	Varies, but commonly includes: » Mild: Fever, cough, shortness of breath, chills, fatigue » Severe: Sepsis, respiratory distress	» Fever, cough, dyspnea » Loss of olfactory and gustatory function » GI issues » Headache » Severe: sepsis, respiratory distress

» **50% of patients with COVID-19 and pneumonia have relevant comorbidities, and 20% have bacterial coinfections at time of ICU admission.**

A study of 225 patients looked at the incidence of VAP and COVID-19 compared with control patients.[4]

VAP vs COVID-19 Pneumonia

Higher incidence

» **COVID-19** patients are **2× more likely** to **develop VAP** than patients **without COVID-19**

More ventilator days

» **COVID-19 VAP patients:** 28/1,000 ventilator days

» **Without COVID-19:** 13/1,000 ventilator days

Different lung microbiota

» **COVID-19 patients:** Invasive **aspergillosis** + ***Herpesviridae*** activation

Along with changes associated with the COVID-19 pandemic, providers will have to deal with issues that were present in the pre-pandemic era and new issues that arose in the post-pandemic era, including newly discovered pathogens, known pathogens, and resistant pathogens.

Prevalence of Antibiotic-Resistant CAP Deaths Worldwide[5]

Global deaths associated with antibiotic-resistant pneumonia: 4.95 million

Regions most affected: Western sub-Saharan Africa, with 27.3 deaths per 100,000

Region least affected: Australia, with 6.5 deaths per 100,000

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COPD Characteristics and Health Disparities

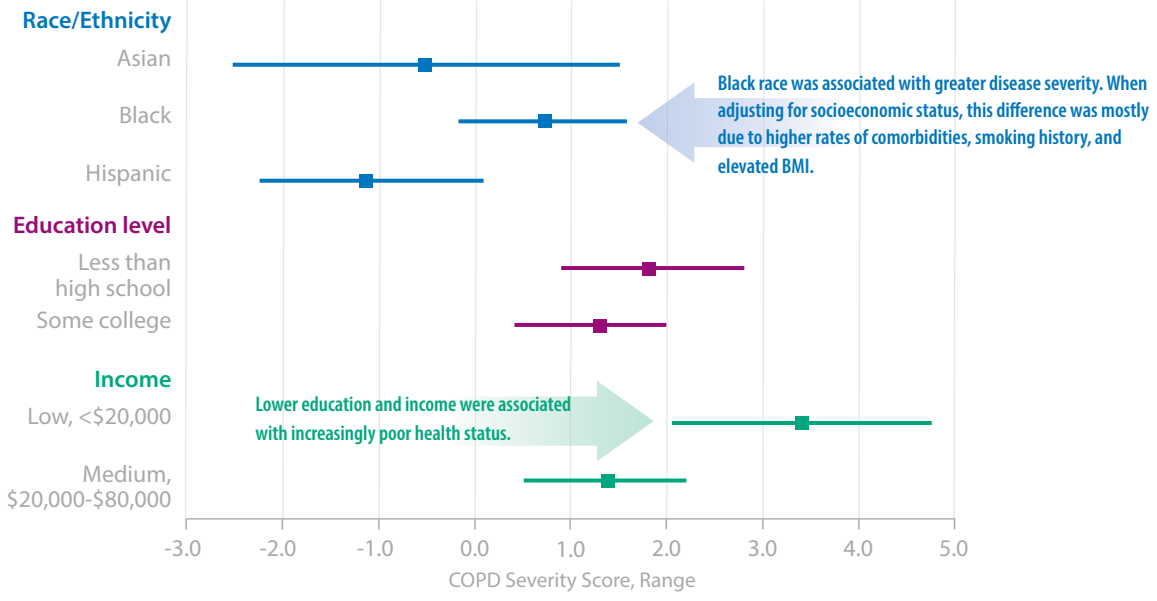
Muhammad Adrish, MD, MBA, FCCP

An estimated 16 million Americans have been diagnosed with chronic obstructive pulmonary disease (COPD), which is the fourth leading cause of death in the United States.[1] Many of the health disparities in COPD diagnosis and care stem from the usual suspects: racial and ethnic barriers, lack of access, and socioeconomic burdens. Overall, COPD affects about 6.1% of Black Americans and 6.3% of non-Hispanic White Americans.[2]

However, while lower education and income are generally associated with poorer outcomes, Black and Hispanic patients with COPD who are highly educated and who have high incomes still show worse health status than their White counterparts.[3] Incidence of COPD also varies by region, with rural states such as Alabama, Arkansas, and Kentucky having some of the highest rates.[2,4] These inequalities support the need for continued research to address the varying health behaviors, comorbidities, and systemic barriers causing disparities for Black and Hispanic patients with COPD.

Impact of Race and Socioeconomic Status on COPD Severity Scores[3]

White patients, college degree or higher, and high income (>$80,000) are reference points. Higher scores reflect poorer status.



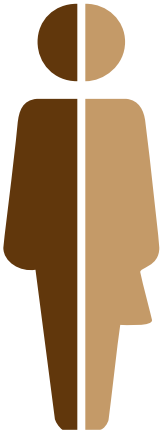
Factors Contributing to Worse Health Outcomes

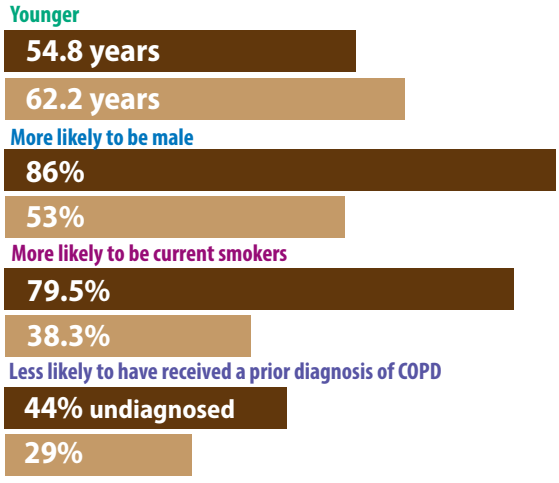
Among Black and Hispanic patients – even those with higher education and income levels – factors may include:[5]

- Increased cigarette and e-cigarette use
- Increased alcohol use
- Poorer diet
- Increased suicide attempts
- Increased obesity
- Residential segregation
- Extra costs of upward social mobility

A study of Black and Hispanic patients with airway obstruction looked at the effects of race and gender on the likelihood of COPD diagnosis.[6]

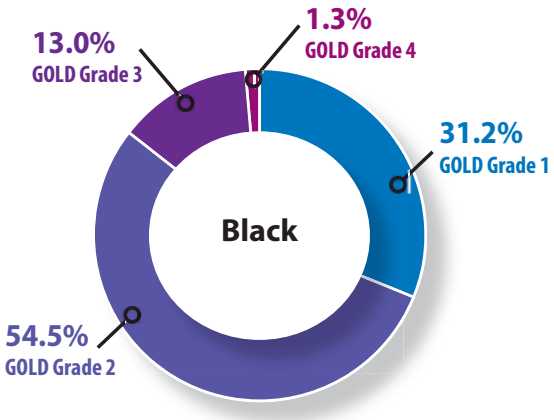
Black patients with airway obstruction were…[6]

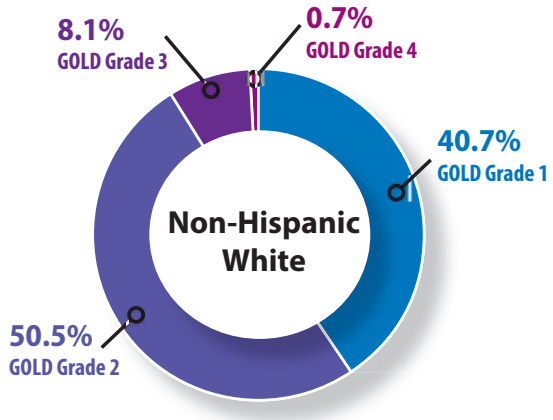


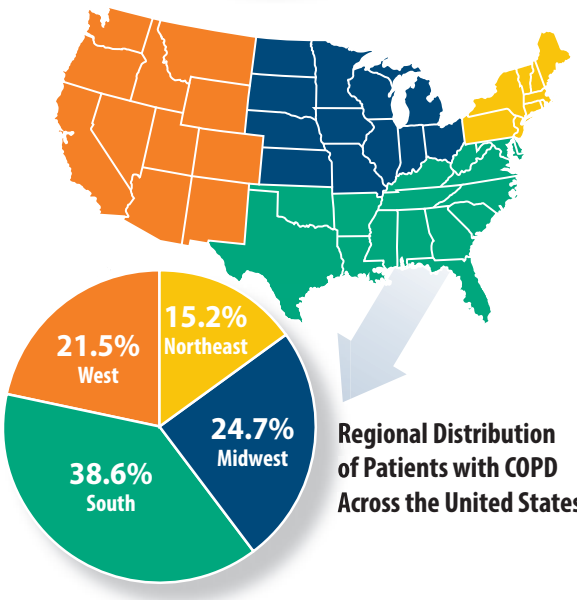


Severity of Undiagnosed COPD in Black and Non-Hispanic White Patients[6]

GOLD grades range from 1 (mild) to 4 (very severe). GOLD, Global Initiative for Chronic Obstructive Lung Disease.







Regional Distribution of Patients with COPD Across the United States[5]

Prevalence of COPD Based on Urban/Rural Status[7]

Urban – Poor: 9.0%
vs Non-poor: 6.1%

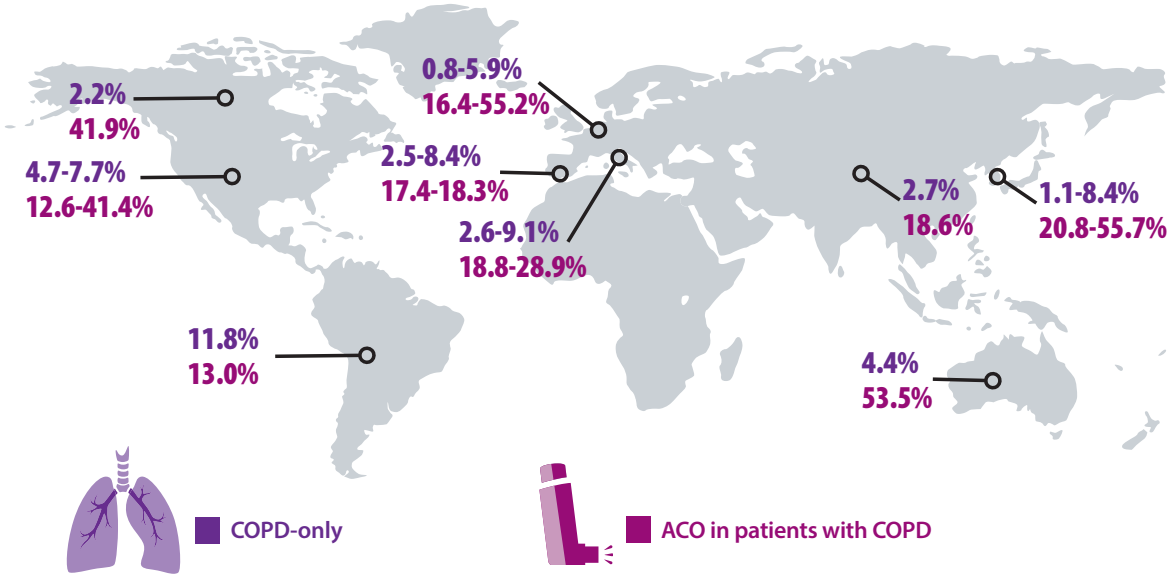
Suburban – Poor: 11.0%
vs Non-poor: 6.7%

Medium Metro – Poor: 11.1%
vs Non-poor: 8.0%

Small Metro – Poor: 10.9%
vs Non-poor: 9.5%

Rural – Poor: 15.7%
vs Non-poor: 12.0%

Estimated Worldwide Prevalence of Asthma-COPD Overlap in Patients With COPD[8]



Identifying At-Risk Patients[9]

Symptoms	Incidence of COPD or Related Outcomes
Chronic cough and phlegm	**4× higher incidence of COPD** vs those without symptoms
Chronic productive cough	**3× higher incidence of COPD in smokers** vs nonsmokers
Chronic bronchitis	» **Higher risk of airflow obstruction** » **Greater FEV_1 decline** » **Higher mortality among smokers**
Any respiratory symptoms	» **Decline in FEV_1** » **Decline in FVC** » **Airflow obstruction**

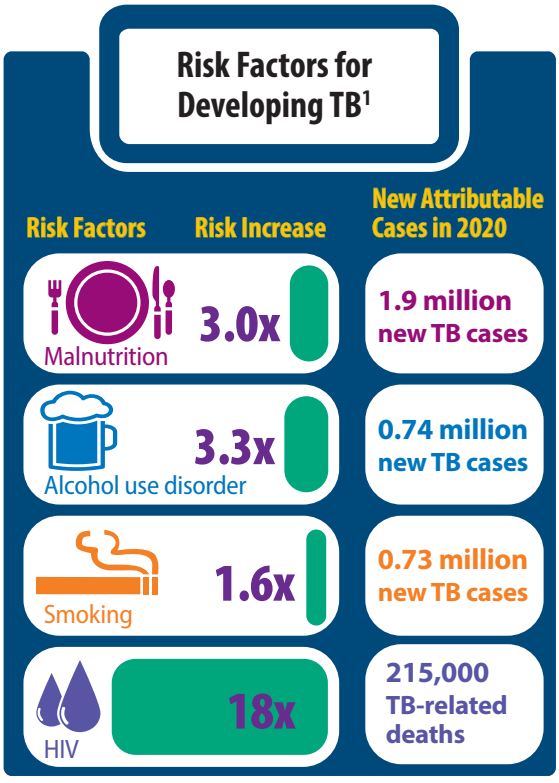
Reducing Tuberculosis Globally and the Impact of COVID-19

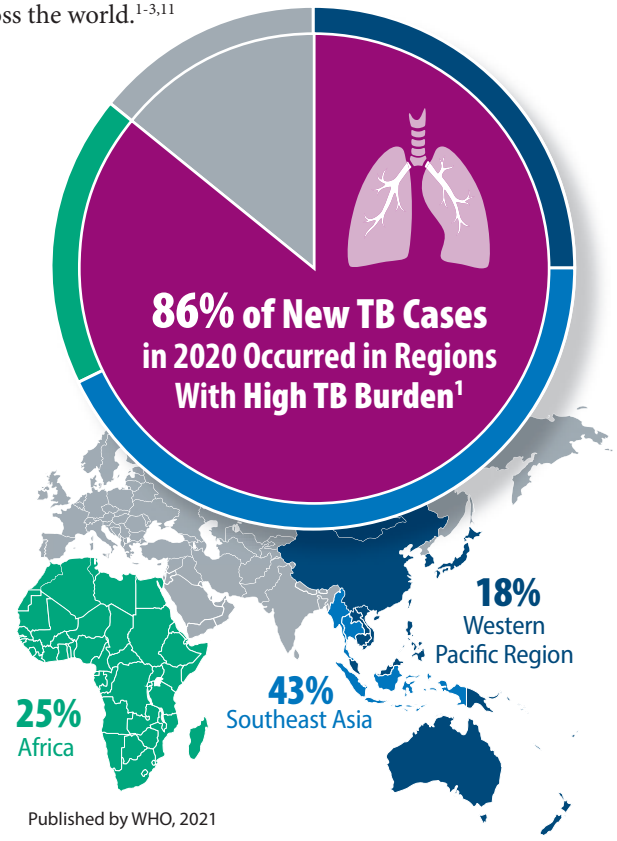
Patricio Escalante, MD, MSc, FCCP and Paige K. Marty, MD

In 2020, more than 1.5 million people died of tuberculosis (TB), and 10 million people contracted the illness globally.[1] The World Health Organization (WHO) End TB Strategy aimed to reduce the number of deaths by 35% between 2015 and 2020, yet reduction was just 9.2% (one-quarter of the goal) during this period.[2]

TB remains the 13th leading cause of death worldwide and is second only to COVID-19 in terms of pathogen-related mortality.[1] In fact, due to a significant shift in attention and resources to COVID-19, the death toll for TB has risen for the first time in over a decade.[2,3] This disruption has led experts to take a closer look at the characteristics and disparities surrounding those deaths. Areas of focus are the health and socioeconomic consequences of TB and COVID-19 as they relate to a TB-related deaths and biosocial inequities in access to essential care. These factors are predicted to lead to a 20% increase in TB death in high-burden countries.[4,5]

TB management needs to improve at the clinical and public health levels. Adults and children exposed to patients with TB or subclinical pulmonary TB, often with their own conditions that affect their immune response, are at a particularly high risk for acquiring latent tuberculosis infection (LTBI) and developing active TB. Thus, improved prevention, screening, and treatment strategies are urgently needed.[6-8] While efforts are ongoing to improve TB vaccines, recent discoveries and technical developments have shown the potential to substantially improve TB prevention efforts through rapid and accurate diagnostic management and innovation that can benefit people at risk of developing TB in resource-limited settings.[9-11] Despite this recent progress, multiple challenges remain, including suboptimal investment in global TB control efforts and innovation, increasing rates of drug-resistant TB, as well as lack of and unequal access to services to patients and individuals in need in many countries across the world.[1-3,11]

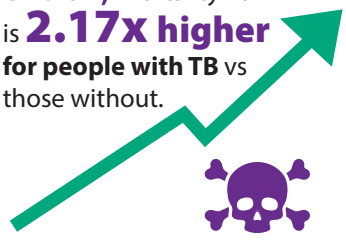




Comorbidities and Social Determinants of Health Leading to Increased Vulnerability in TB and COVID-19 Infection[12,13]

- Chronic lung diseases
- Immunocompromised state
- Cancer
- Type 2 diabetes mellitus
- Poverty
- Malnutrition
- Over age 60
- HIV co-infection

Overall, mortality risk is **2.17x higher for people with TB** vs those without.



For patients with TB, the chance of **recovery is 25% lower in patients who also have COVID-19.**[14]

Characteristics and Implications of TB and COVID-19[12]

Characteristics	TB[12]	COVID-19[12]
Availability of effective vaccine	Yes[a] ✓	Yes[b] ✓
Availability of rapid diagnostics	Yes ✓	Yes ✓
Availability of cure	Yes ✓	Yes[c] ✓
Limitations of current treatments	An increased prevalence of drug resistance to available antibiotics and prolonged treatment regimens require public health resources to administer and monitor.	New SARS-CoV-2 variants have challenged the effectiveness of various monoclonal antibodies, but antivirals and anti-inflammatory therapies remain effective.[c]
Policy development	Slow	Rapid
Potential for stigma	Yes ✓	Yes ✓
Economic impact	Large (slow)	Large (rapid)
Stress on health systems	Large (slow)	Large (rapid)

Impact of COVID-19 on TB[12,15,16]

- Global TB deaths predicted to increase by 20%.
- $100 billion invested in COVID-19 vaccines vs barely $100 million invested per year for TB.
- 15% reduction in the number of people treated for drug-resistant TB.
- 21% decrease in patients receiving preventive TB treatment.
- $500 million decrease in global TB spending from 2019 to 2020.

[a] BCG vaccination is effective in preventing meningeal and disseminated TB in children but mostly ineffective in preventing pulmonary TB in adults.
[b] Updated due to availability of effective COVID-19 vaccine, after this article was published.
[c] Available treatment can reduce disease progression, morbidity, and mortality.

New Treatment Pathways for Cystic Fibrosis

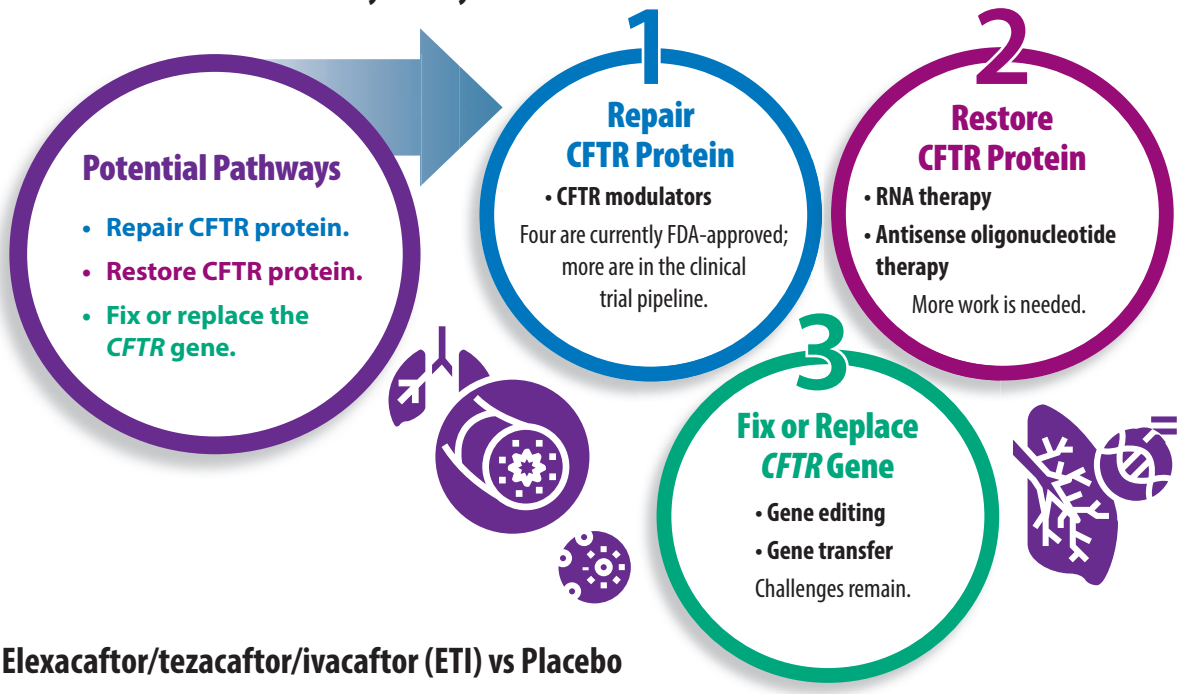
David Finklea, MD

Cystic fibrosis is a deadly genetic disorder, affecting 80,000 people worldwide.[1,2] The disorder is caused by mutations in the cystic fibrosis transmembrane conductance regulator *(CFTR)* gene.[2] This gene codes for a protein that creates epithelial channels in the respiratory track, along with other organs. Mutations in this gene can create improper ion balance, leading to thick and sticky mucus that blocks airways in the lungs and contributes to infections in people with CF (pwCF).[1]

Currently, there is no cure for cystic fibrosis, but newer research is looking into modulating the *CFTR* gene from multiple pathways by repairing, restoring, or replacing the CFTR protein.[1,2] At this point, CFTR modulators are the most promising new treatments for cystic fibrosis.

CFTR modulators involve repairing the CFTR protein made from this gene. To qualify for treatment with this class of drugs, people with cystic fibrosis need to have certain CFTR mutations. Fortunately, approximately 90% of pwCF qualify for CFTR modulators.[1,2] Due to this, the Cystic Fibrosis Foundation is working on finding alternative therapies that are listed below.[1]

Different Treatment Pathways for Cystic Fibrosis



Elexacaftor/tezacaftor/ivacaftor (ETI) vs Placebo

ETI is a CFTR modulator which, compared with placebo, has shown significant improvement in lung function and fewer pulmonary exacerbations.[2]

Estimated annualized pulmonary exacerbation rate:
>> **0.37 (ETI) vs 0.98** (placebo)
>> **63%** lower

Change in percentage of predicted FEV_1 at week 24:
>> **13.9 vs –0.4**
>> **14.3** mean treatment difference

Change in CFQ-R respiratory domain score at week 24:
>> **17.5 vs –2.7**
>> **20.2**-point difference (minimum clinically significant difference is 4)

Improvement in BMI at week 24:
>> **1.13 vs 0.09**
>> **1.04** mean treatment difference

Race and CFTR Modulators[3]

Unfortunately, not all pwCF can receive CFTR modulators. This is most pronounced based on racial and ethnic backgrounds.[3] Because of this, the Cystic Fibrosis Foundation is actively working to provide therapies to overcome this disparity.

Rate of Qualification for CFTR Modulators by Race/Ethnicity[3]

92.4% of non-Hispanic White patients

75.6% of Hispanic patients

69.7% of Black patients

Pregnancy and CFTR Modulators[4]

CFTR modulators are known to improve clinical symptoms. One way this is demonstrated is through increased pregnancy rates in women after taking CFTR modulators.[4] Alterations to cervical mucus viscosity and pH, secondary amenorrhea caused by stress, chronic illness, and/or inflammation, and low BMI are all speculated contributing factors to subfertility in patients with cystic fibrosis.

Infertility Rates[4]

Patients with cystic fibrosis, not taking CFTR modulators: 24% to 35%

Healthy controls 5% to 15%

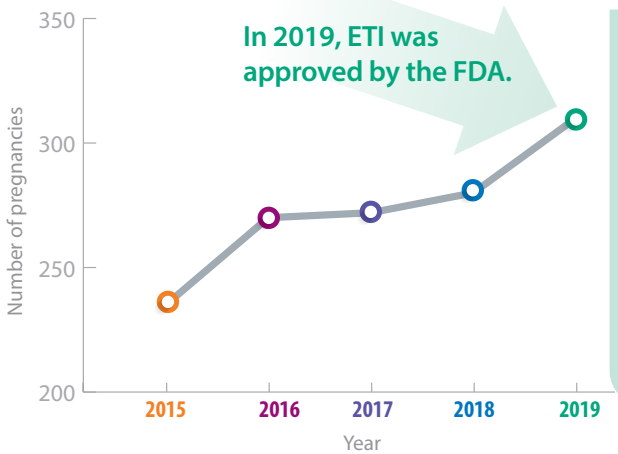
Women with cystic fibrosis taking **ETI** have experienced **increased fertility** and **increased unexpected pregnancies.**

In a small study of women with cystic fibrosis (n=201), 14 (6.9%) patients conceived after ETI initiation.

50% of these women were not trying to conceive (using contraceptive method).

Increased Number of Pregnancies Due to CFTR Modulators[5]

More women are becoming pregnant in the last decade as CFTR modulators are becoming widely available to all pwCF.



Effects of CFTR modulators on the fetus are currently unknown. More research is being done in this area. CFTR modulators are a step in the right direction in achieving the Cystic Fibrosis Foundation's goal to have CF stand for CURE FOUND for all, but there is more work to be done.[1]

Risk Assessment in Pulmonary Arterial Hypertension

Sandeep Sahay, MD, MSc, FCCP, ATSF

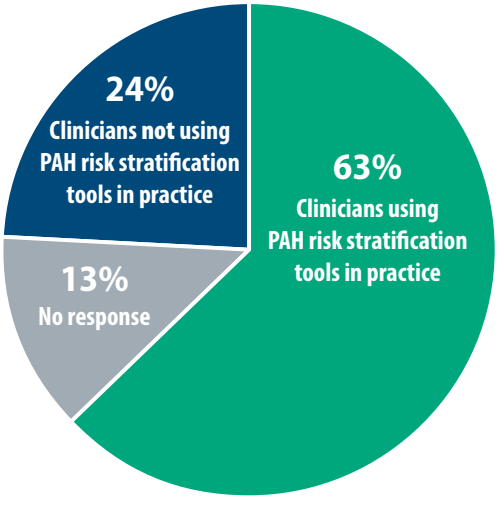
Properly assessing risk level at the time of diagnosis and follow up is crucial for understanding each patient's case, identifying modifiable barriers and the most appropriate treatment options, and, ultimately, optimizing survival outcomes for pulmonary arterial hypertension (PAH). Despite the variety of risk assessment tools and electronic medical records at clinicians' disposal, these resources remain underutilized.[1]

A survey, designed by CHEST's Pulmonary Vascular Disease section of the Pulmonary Vascular and Cardiovascular Network, asked members to share insight into their use and perceptions of PAH risk assessment tools in clinical practice. Although the ability of proper risk assessment to greatly improve patient care has been demonstrated in the literature and is recommended by most clinical guidelines, the results of this survey revealed that more than one-third of specialists were not using guideline-recommended risk tools to assess PAH, and only 7% reported that risk assessment tools impacted their treatment decision in new patient care and evaluation.[1-4]

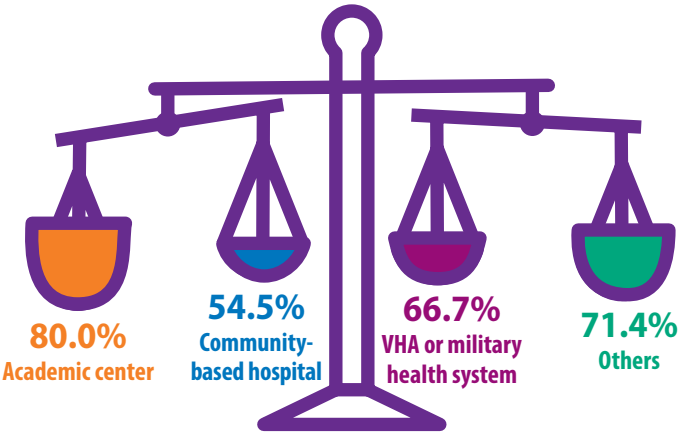
There is a lack of consensus in patterns of risk tool use among physicians, with 58% reporting that they use more than one tool. In addition to continued clinical research to support the use of available tools and the development of new ones, clinician education programs can help increase the positive impact that risk assessment has on patient survival and other outcomes.[1,5]

Who is using risk assessment tools for the stratification of PAH?

Users vs Non-users[1]



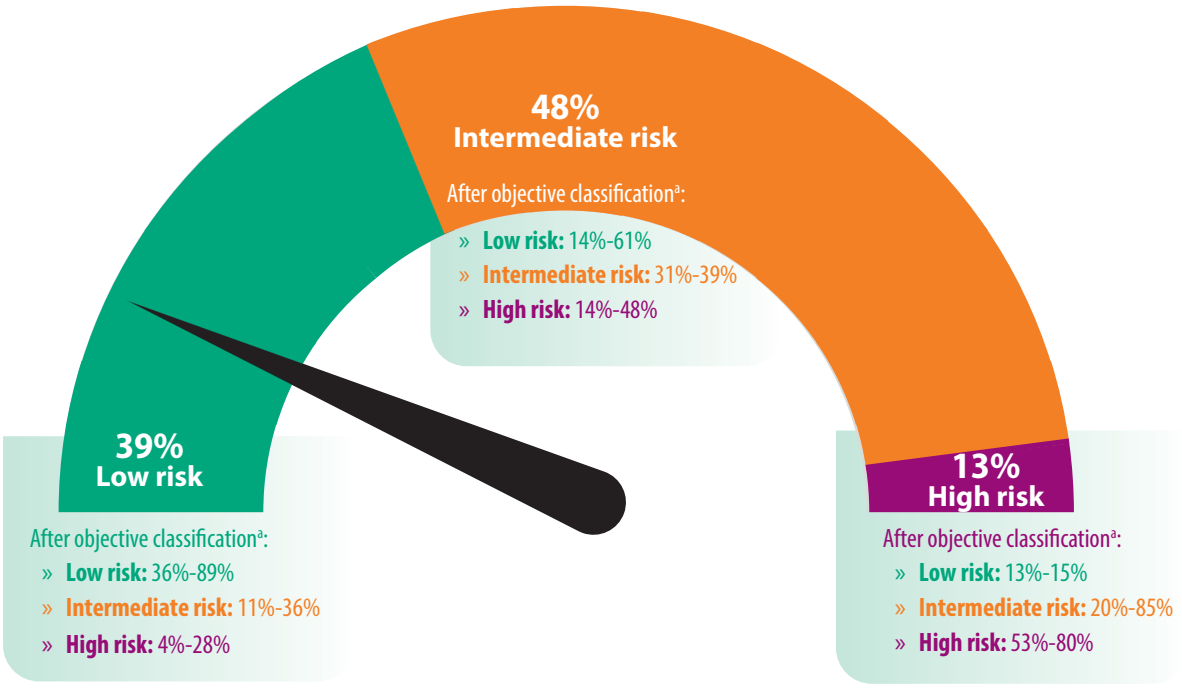
Use of PAH Risk Assessment Tools by Practice Setting[1]



Specialists Using PAH Risk Assessment Tools[1]

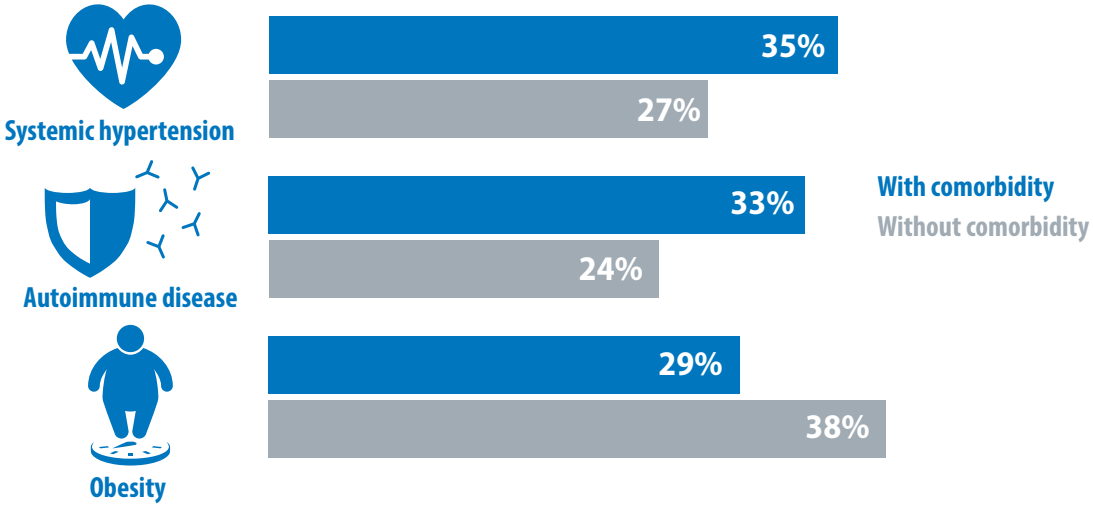
Another study evaluated the results of PAH risk assessment tools compared with physicians' risk assessment based on clinical judgment. Researchers found substantial incongruencies. Stratification based on clinical judgment resulted in both underestimation and overestimation of risk compared with assessments using objective methods.[2]

Initial Classification by Physician Assessment Compared With Objective Risk Assessment Tool[2,a]



[a]Risk was assessed objectively using the Comparative, Prospective Registry of Newly Initiated Therapies for Pulmonary Hypertension (COMPERA), French Pulmonary Hypertension Registry (FPHR), and the Registry to Evaluate Early and Long-Term PAH Disease Management (REVEAL 2.0) tools.

Comorbidities Associated With Risk Assessment Incongruencies[2]



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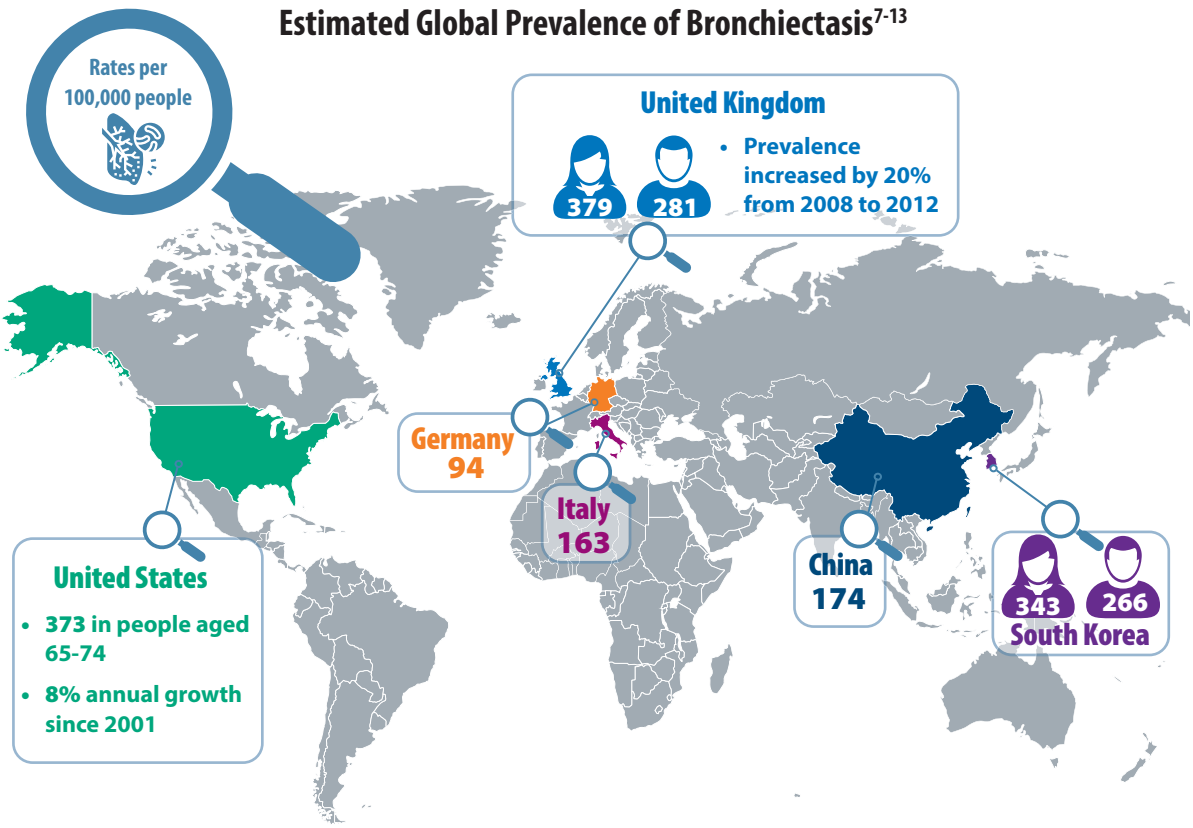
Rising Incidence of Bronchiectasis and Associated Burdens

Anne E. O'Donnell, MD, FCCP

Bronchiectasis has historically been considered an uncommon and often neglected disease in respiratory medicine.[1-3] Although bronchiectasis was previously thought to be an orphan disease, its incidence and prevalence have been on the rise since the early 2000s, and the disease is now estimated to affect between 0.25% and 0.5% of adults.[2] This observed increase can be attributed at least partially to two key factors: growing use of CT scanning has allowed for higher detection of abnormal airways, and the global population is aging.[2,4] Bronchiectasis is more common in elderly people, and the number of persons aged 65 and older is estimated to double by 2050.[2,4]

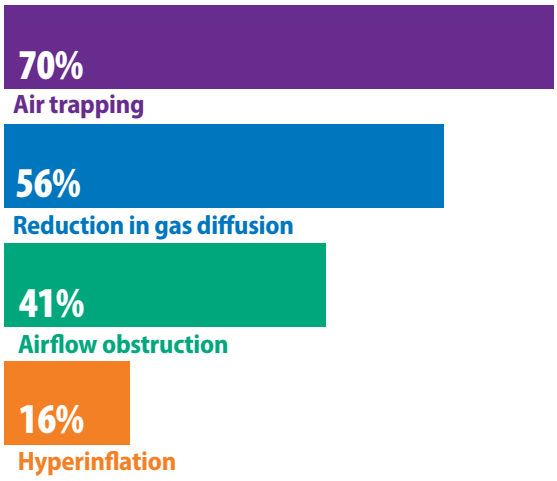
As bronchiectasis has become more widely recognized as a serious and prevalent condition, the need for clinical research and consensus in this area has also increased.[2,5,6] In 2017, the European Respiratory Society released the first international guidelines that provide recommendations for reducing exacerbations, symptoms, and risk for future complications, while improving quality of life.[6]

In 2022, clinicians are more equipped than ever to identify and treat bronchiectasis. However, the immense comorbidity and economic burdens that accompany this disease will continue to present challenges. Using a shared decision-making approach is important to understand and address each patient's unique goals and concerns and, thus, optimize their health outcomes.

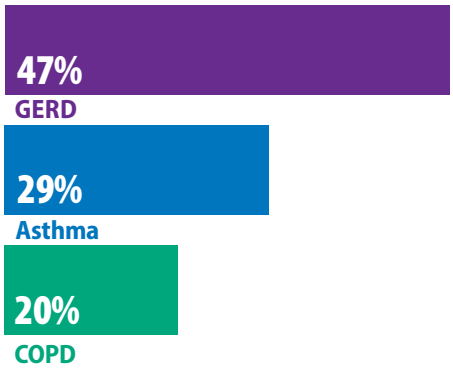


Health Concerns Associated With Bronchiectasis

Functional Abnormalities[2]



Common Comorbidities[14]

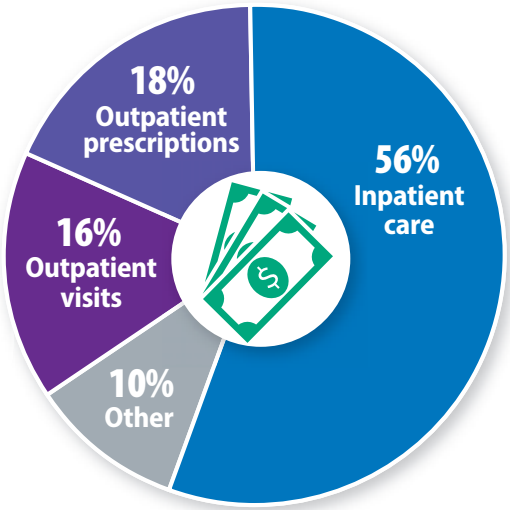


Utilization of Health Care Resources Over a 3-Year Period [1]

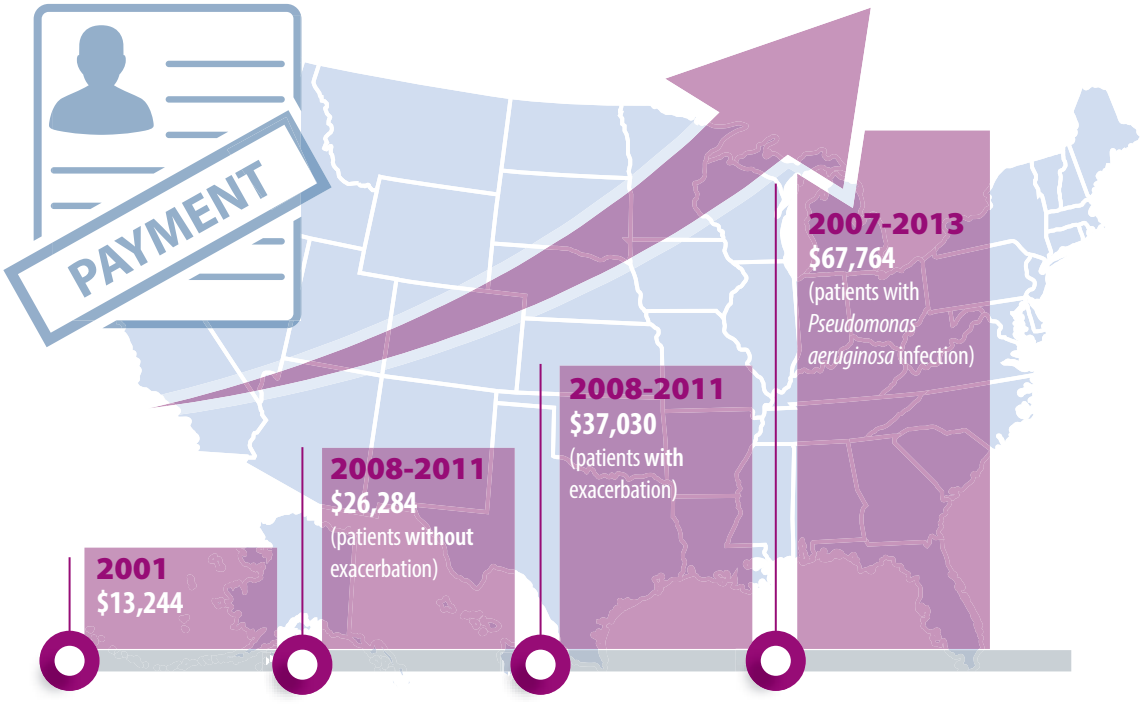
	Length of hospital stay, days	Hospital admissions, n	Outpatient encounters, n
Patients with bronchiectasis	4.5	0.6	20.1
Matched control subjects	2.5	0.4	14.0

Care-Associated Costs[1]

Increased resource use leads to **$5,681 more in costs** for patients with bronchiectasis compared with patients without bronchiectasis.



Increasing Economic Burden in the United States[1]



Mean total annual costs for bronchiectasis (per patient)

Bronchiectasis Symptoms, Untreated Outcomes, and Management Options[1]

Symptoms

- Chronic cough
- Sputum production
- Exacerbations

Untreated Outcomes

- Presented significant morbidity
- Reduced physical performance
- Impacted health-related quality of life

Management Options

- Airway clearance therapies
- Physiotherapy/exercise
- Antibiotic therapy
- Anti-inflammatory treatment
- Hospitalization with antibiotic treatment

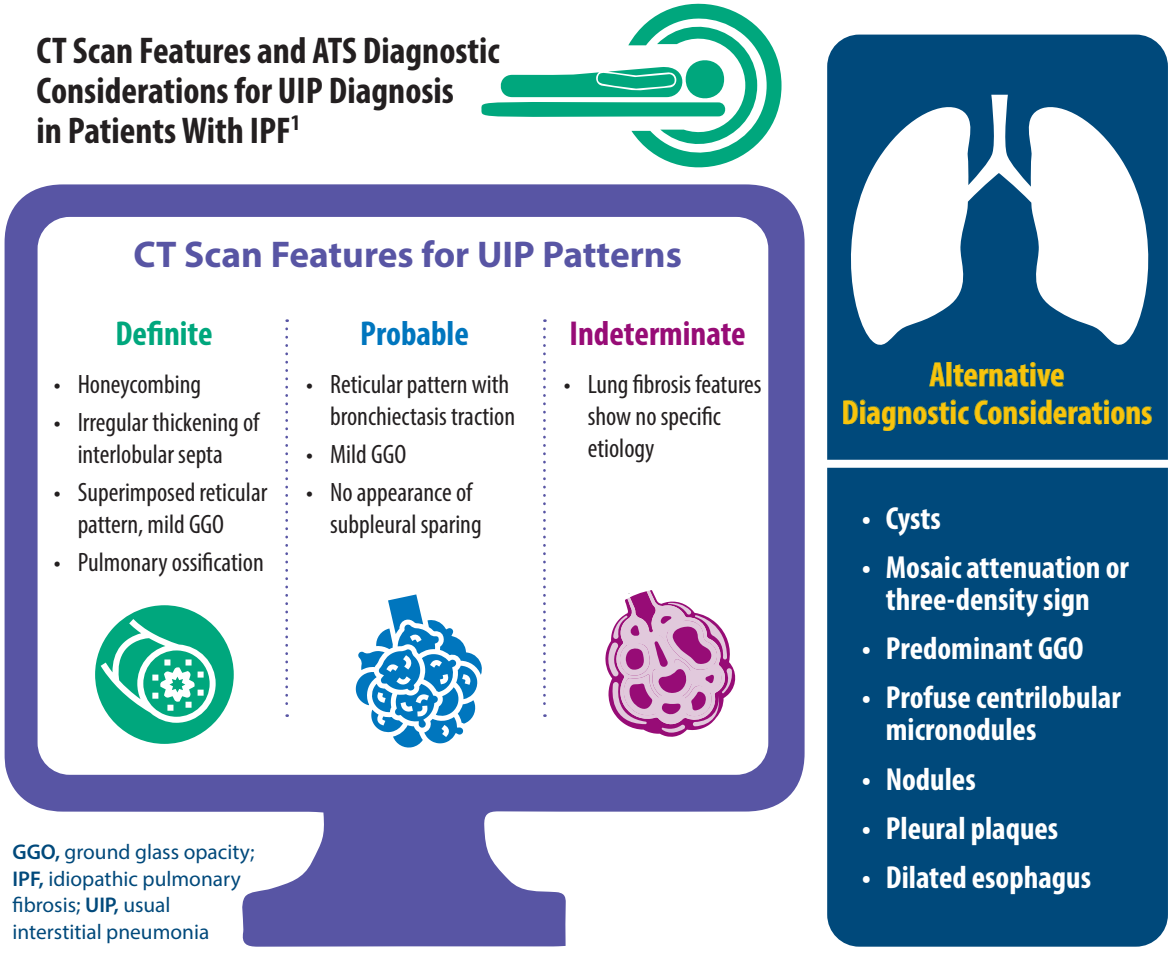
ILD: Diagnostic Considerations and Socioeconomic Barriers

Daniel Dilling, MD, FCCP, FACP, FAST

When navigating the multiple layers of interstitial lung disease (ILD), new American Thoracic Society (ATS) guidelines recommend a diagnostic approach through the lenses of radiologic progression, worsening symptoms, and physiologic progression. An interdisciplinary approach to diagnosis and treatment of patients with ILDs is key for informed decision-making and for optimizing outcomes.[1] Also, guidelines presented by CHEST on ILD dive deeper, addressing diagnostic decision-making, evaluation, gaps, challenges, and risk management failures, as they specifically pertain to hypersensitivity pneumonitis.[2]

Radiologists, pathologists, and pulmonologists look at newer methods of ILD diagnosis–such as transbronchial lung cryobiopsy and genomic classifiers–from a systemic point of view and utilize artificial intelligence to explore new techniques that may be beneficial to patients.[3] Additionally, characteristics associated with health disparities, inequities, social determinants, and neighborhood-level disadvantages all affect patients and show clear differences in access to care in the United States.[4]

Given the nature of ILD, patients may experience disease progression culminating in the need for lung transplantation or in death from their disease.[1,4] Ensuring proper care for patients with ILD is an urgent priority for pulmonologists. With further research and, hopefully, with changes to how we approach ILD care in society, our goal is to eradicate these socioeconomic disparities, so patients receive proper diagnosis and care.[5]

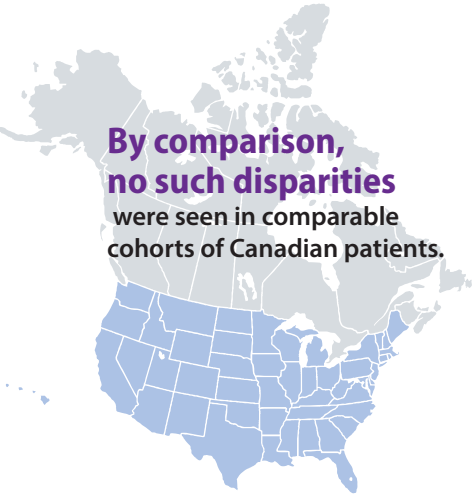


Disparities in Care and Outcomes in US Patients With Fibrosing ILD[4,5]

Among those living in the most deprived neighborhoods:

Death rates are **51% higher** compared with least deprived areas.

Patients are **64% less likely to have lung transplants.**



By comparison, no such disparities were seen in comparable cohorts of Canadian patients.

>40% of patients with idiopathic pulmonary fibrosis have not seen a pulmonologist.

Average out-of-pocket drug costs **>$4,700 per year.**

High costs can lead to a **~70% increase** in Medicare beneficiaries going **>30 days** without filling their prescriptions.

Cryobiopsy/Cryotransbronchial Biopsy vs Forceps Biopsy/Forceps Transbronchial Biopsy[6]

	CB/CTBB	FB/FTBB
Specimen area		
	Collects larger samples (standard mean difference 1.21)	
Diagnostic (IC) rate		
	91.67% (risk ratio 1.36)	**72.13%**
Bleeding severity		
	23.76% In this analysis, one of three studies that examined bleeding found significantly more bleeding with CB/CTBB.	**20.83%**

Advances in Lung Cancer Diagnostics and Treatment

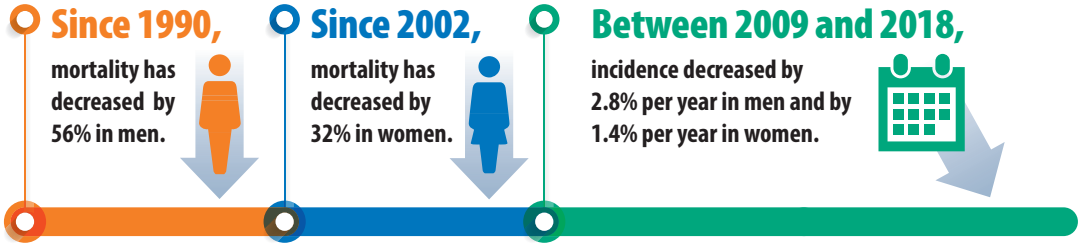
Eric S. Edell, MD, FCCP

Lung cancer remains the leading cause of cancer death worldwide, killing about three times as many men and women as prostate and breast cancer, respectively. The introduction of targeted therapy and immunotherapy has markedly increased survival rates over the last decade.[1] Robotic technologies at both the diagnostic and treatment stages have shown promise for the management of lung cancer in these patients.[2,3] Smoking rates have also been steadily declining in the United States—from 20.9% in 2005 to 12.5% in 2020.[4]

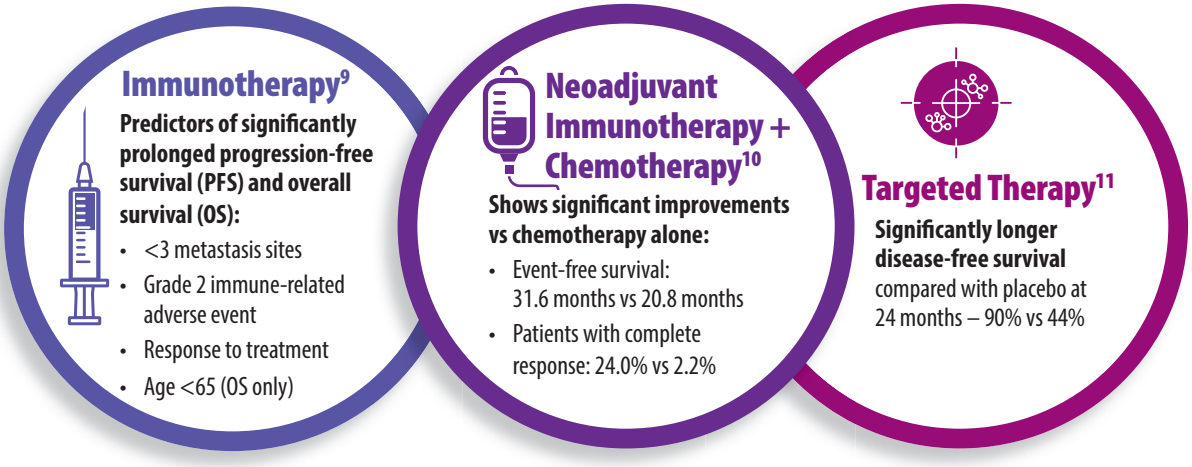
Based on these combined factors, the fact that lung cancer continues to outpace others in terms of cancer incidence and mortality may not be entirely due to a lack of innovation or improvement in health behaviors. A remaining piece of the puzzle might be sufficient uptake in screening among high-risk adults. Identifying lung cancer before it progresses beyond stage I significantly improves 5-year survival rates, but few patients are diagnosed that early.[5] The US Preventive Services Task Force, CHEST, and other organizations updated screening recommendations in 2021 to include earlier low-dose computed tomography (CT) scan screening (age 50 instead of 55) and to include people with even less smoking history (from 30 pack-years to 20).[6,7] Before these updates were made, it was estimated that about 4.5% of at-risk adults (aged 55-80 years) received a CT scan within the last year.[8]

We have yet to see what impact these guidelines will have in practice. Without physician awareness and patient education, it is likely that screening rates and the number of cases caught in early stages will stay low—despite the growing number of tools at our disposal.

Incidence and Mortality Steadily Decreasing[1]

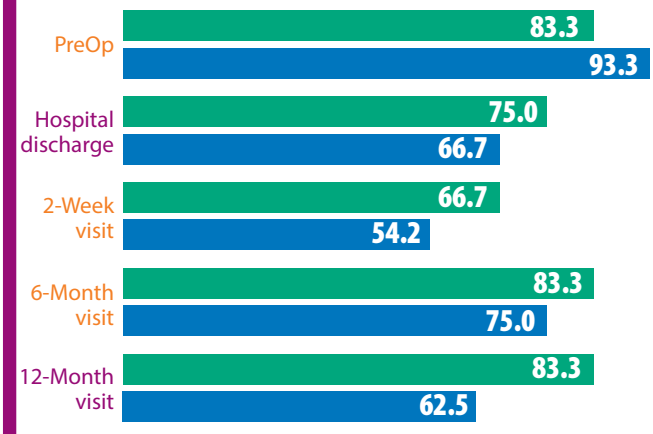


Immunotherapy and Targeted Therapy Survival Benefits[9-11]



Compared with muscle-sparing thoracotomy (OPEN), intervention with robotic surgery (RATS) has shown significant improvement in global health status scores and other quality of life measures at hospital discharge and 12-month follow-up.[2]

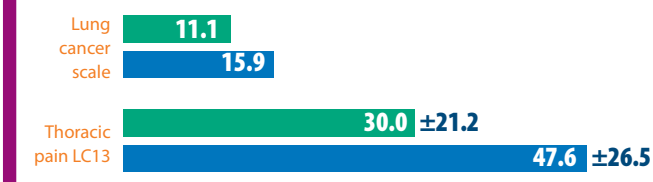
Global Health Status Scores



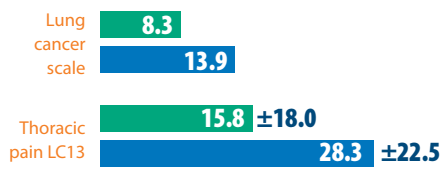
RATS
OPEN

Significant Differences in Disease Severity Scores

At hospital discharge



At 12-month visit



Robotic-assisted bronchoscopy has shown promising results in lesion localization, as well as safety, that is comparable to conventional bronchoscopy methods.[3]

- **Successful lesion localization: 96.2%**
  Time to median lesion confirmation: **13 minutes**
- **Pneumothorax occurred in 3.7%**
  No other significant adverse events noted
- **Diagnostic yield: 74% vs 40% to 60%** for alternative bronchoscopy approaches
  Diagnostic yield for eccentric lesions: **70% vs 30% to 40%** with alternative bronchoscopy approaches in this population

Timely Low-Dose CT Scan Screening Leads to Improved Outcomes[5]

Relative reduction in mortality at 10 years

Surgical resection is **3x more prevalent** in patients who were screened early vs those who were not.

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