The Use of Biologics in Treatment of Patients With Severe Asthma

Clinical Perspectives™

Introduction

Patients with severe asthma are among the most challenging cases to manage. Biologics are an emerging avenue of therapy holding significant promise for impacting the course of disease and quality of life for these patients. In this premier *Clinical Perspectives™* issue, the American College of Chest Physicians (CHEST) is investigating how pulmonologists are adopting biologics for the treatment of severe asthma. There is a lack of consensus in the field on the current use of these therapies, and not all existing guidelines are evidence-based, leaving clinicians in limbo when choosing a biologic therapy for their patients with severe asthma. With more biologics in the pipeline, this is a timely and important topic for our field.

Read on to learn more about:

- The rate at which biologics are being used relative to traditional treatment approaches for patients with severe asthma.
- Key barriers affecting the development of optimal treatment plans.
- The extent to which biomarkers are being used to plan and manage biologic therapy.
- Variations in adoption among different segments of pulmonologists.

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METHODOLOGY

The findings presented in this report are based on an online survey conducted by CHEST with a random sample (n=103) of pulmonologists actively involved in the treatment of asthma. Respondents were randomly sampled from the CHEST membership database and practice in the United States. The survey was fielded during January 31 to February 20, 2017.

The questionnaire utilized in this survey was designed by the *Clinical Perspectives* Expert Advisory Panel and CHEST Analytics. A literature review was also conducted to profile key issues related to the use of biologics and biomarkers for the treatment of severe asthma. The survey comprised 59 questions ranging across behavioral, descriptive, and attitudinal measures and, on average, took 9 minutes 30 seconds to complete. Content was organized into the following domains:
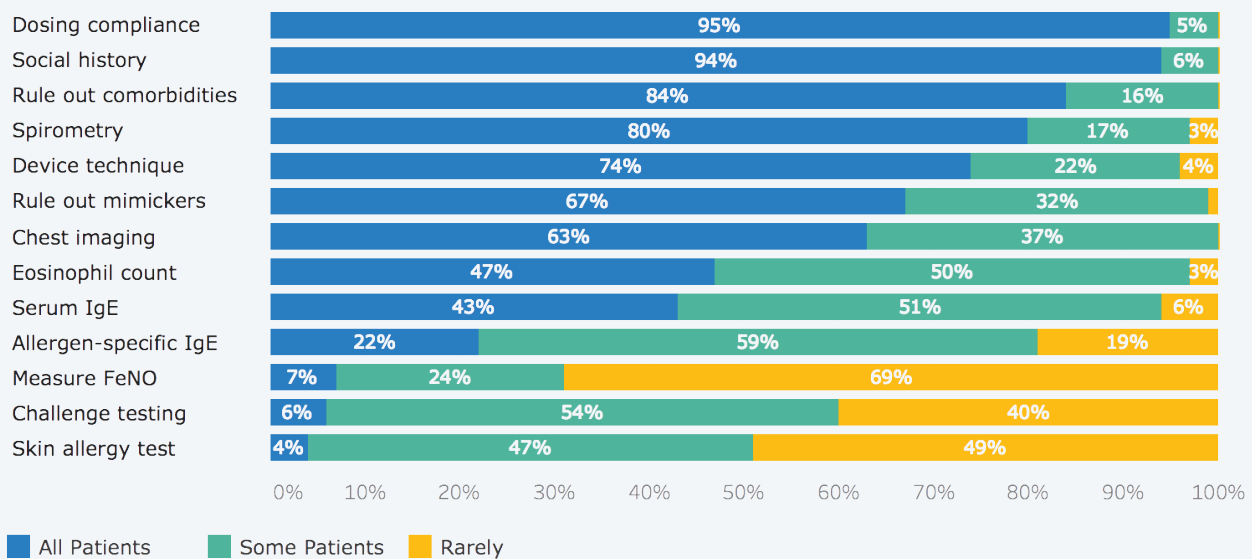
- Screening and profiling (clinical role of respondent, asthma caseload, severity of asthma, assessment of degree of control)

- Overview of asthma care (prevalence of diagnostics, treatment goals)

- Role and choice of pharmacologic approaches (use of different treatments, barriers to determining optimal therapy)

- Use of biomarkers (frequency of use in patients with severe asthma, type, purpose)

- Choice of biologics (effectiveness, frequency, safety, use by phenotype, administration)

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TRADITIONAL DIAGNOSTICS AND THERAPIES STILL DOMINATE TREATMENT PLANS FOR SEVERE ASTHMA.

According to our survey, the most frequently utilized diagnostic tools in assessing uncontrolled severe asthma in patients include spirometry, dosing compliance assessment, social history assessment, comorbidities/asthma mimickers elimination, and chest imaging. Similarly, short-acting beta-agonists (SABAs), long-acting beta-adrenoceptor agonists (LABAs), and inhaled corticosteroids (ICS) are the most frequent treatments deployed to treat these patients.
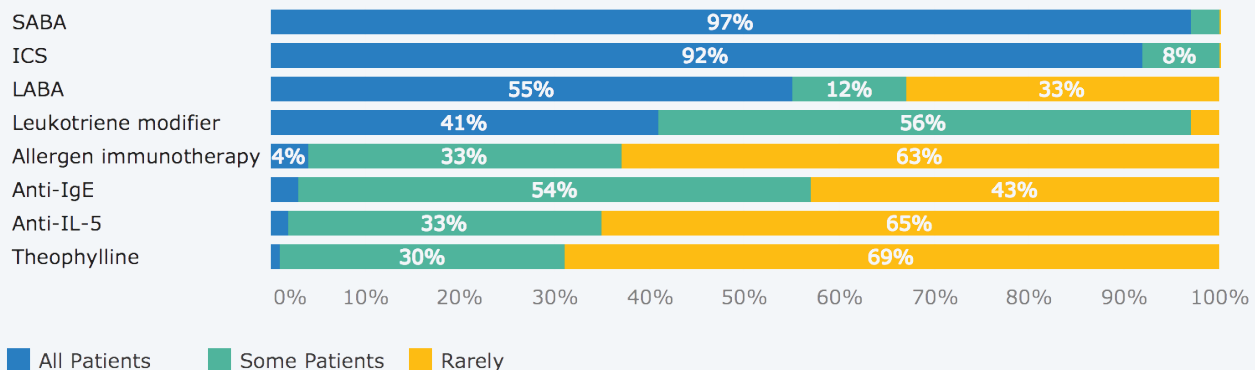
The use of biomarkers, including blood eosinophil count, exhaled NO, and serum IgE, are employed less frequently, and biologics are much less likely to be used.

Frequency of Diagnostics on Patients With Uncontrolled Severe Asthma

Diagnostic	All Patients	Some Patients	Rarely
Dosing compliance	95%	5%	
Social history	94%	6%	
Rule out comorbidities	84%	16%	
Spirometry	80%	17%	3%
Device technique	74%	22%	4%
Rule out mimickers	67%	32%	
Chest imaging	63%	37%	
Eosinophil count	47%	50%	3%
Serum IgE	43%	51%	6%
Allergen-specific IgE	22%	59%	19%
Measure FeNO	7%	24%	69%
Challenge testing	6%	54%	40%
Skin allergy test	4%	47%	49%

Legend: ■ All Patients ■ Some Patients ■ Rarely

Q: How frequently do you or do members of your support staff take the actions above when diagnosing patients who may have severe, uncontrolled asthma?
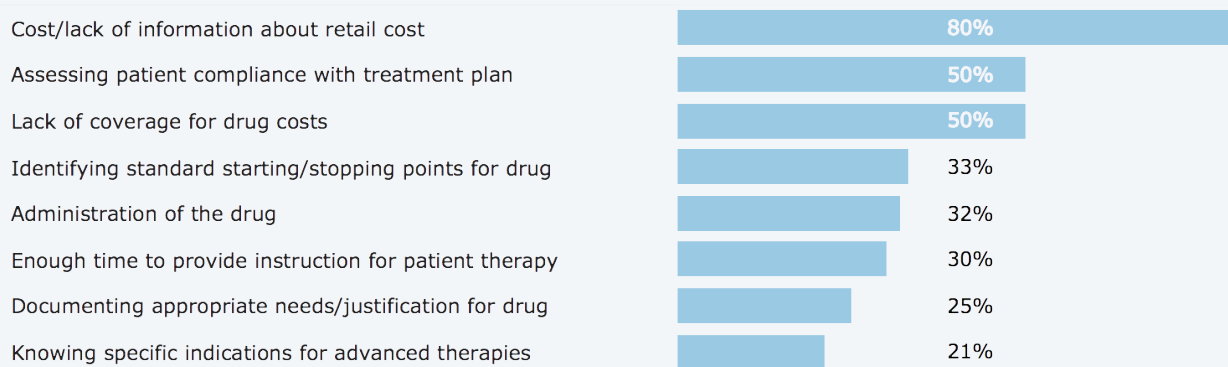
Frequency of Treatments

Treatment	All Patients	Some Patients	Rarely
SABA	97%		
ICS	92%	8%	
LABA	55%	12%	33%
Leukotriene modifier	41%	56%	
Allergen immunotherapy	4%	33%	63%
Anti-IgE		54%	43%
Anti-IL-5		33%	65%
Theophylline		30%	69%

Legend: ■ All Patients ■ Some Patients ■ Rarely

Q: How often do you prescribe the treatments above to patients with severe asthma?

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COST ISSUES PREDOMINATE, BUT KNOWLEDGE ABOUT INDICATIONS AND PROTOCOLS CAN ALSO BE CHALLENGES IN DEVELOPING OPTIMAL TREATMENT PLANS FOR SEVERE ASTHMA.

Cost-related issues are mentioned most frequently as a barrier to developing the best therapy for patients with severe asthma. However, pulmonologists also acknowledge the need for greater information about treatment options, including identification of standards about starting and stopping points for drug therapy and knowing specific indications for advanced therapies, such as biologics.

Challenges to Choosing Best Therapy for Patients With Severe Asthma
Percentage of respondents identifying each factor as a challenge

Factor	Percentage
Cost/lack of information about retail cost	80%
Assessing patient compliance with treatment plan	50%
Lack of coverage for drug costs	50%
Identifying standard starting/stopping points for drug	33%
Administration of the drug	32%
Enough time to provide instruction for patient therapy	30%
Documenting appropriate needs/justification for drug	25%
Knowing specific indications for advanced therapies	21%

Q: What are some of the most significant obstacles or challenges you face in determining the best therapy for your patients with severe asthma?

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TRIAL OF BIOLOGICS IS WIDESPREAD, ESPECIALLY AMONG PULMONOLOGISTS WITH HEAVIER ASTHMA CASELOADS.

Initial trial of biologics is relatively high, with nearly 8 out of 10 pulmonologists (78%) reporting that they prescribed the therapy as part of a severe asthma treatment plan. Pulmonologists with higher asthma caseloads (10+ per week) are more likely to prescribe biologics (87%) compared with those who have lighter asthma caseloads (63%). Use of biomarkers, however, is infrequent, with only 36% saying they use them some or all of the time.

Use of Biomarkers to Phenotype/Endotype

	Fewer than 10 patients	10 or more patients
Frequently	15%	20%
Infrequently	23%	42%

Q: To what extent do you use biomarkers with your patients with severe asthma to phenotype or endotype their condition?

Use of Biologics in Treatment of Severe Asthma

	Fewer than 10 patients	10 or more patients
Yes	24%	54%
No	14%	8%
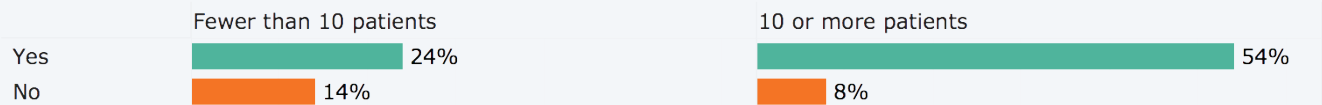
Q: Do you currently use anti-IgE (omalizumab) or anti-IL-5 (mepolizumab and reslizumab) when treating your patients with severe asthma?

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PULMONOLOGISTS NOT COMPLETELY SOLD ON BIOLOGIC TREATMENT OPTIONS.

Roughly two in three pulmonologists judge biologic therapy to be only somewhat effective in treating severe asthma (65%); a similar share express at least some concern about the safety of biologic therapy.
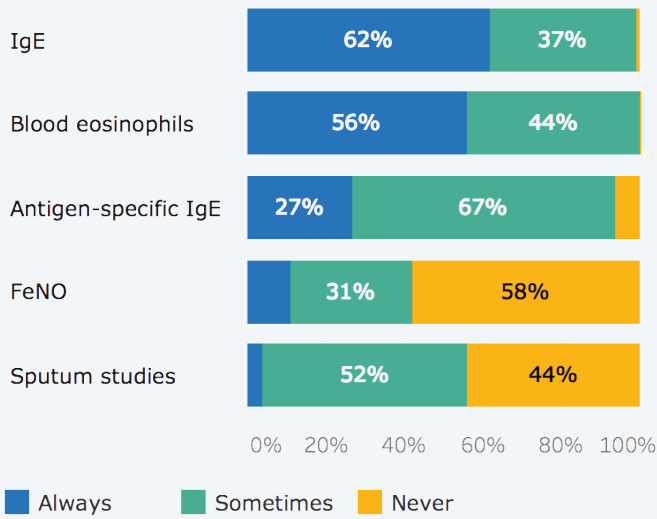
Perceived Effectiveness of Biologic Therapy

Inconclusive
10%

Highly Effective
25%

Somewhat Effective
65%
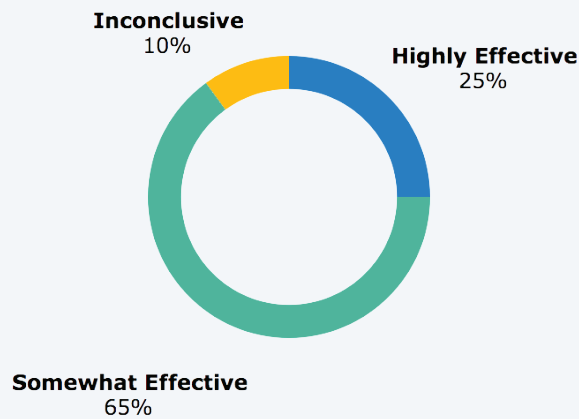
Concerns About Biologic Safety

Some concern	Anti-IgE	60%
	Anti-IL-5	69%
Little to no concern	Anti-IgE	34%
	Anti-IL-5	25%
Significant concern	Anti-IgE	6%
	Anti-IL-5	6%

Anti-IgE
Anti-IL-5
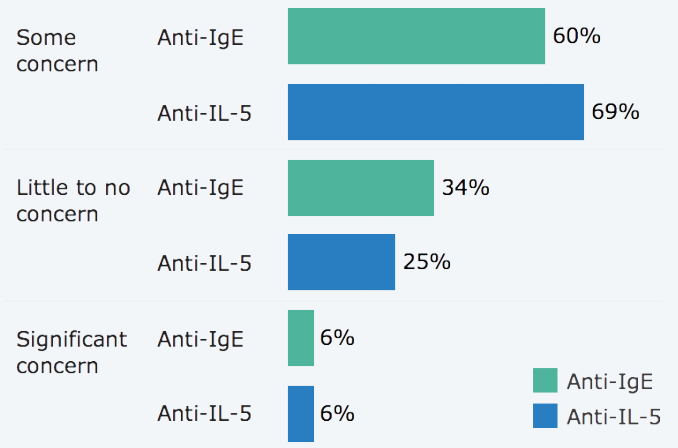
Q: How effective do you feel these biologics are in providing better control for patients with severe asthma?

To what extent do you have concerns about the safety of the biologics above?

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BENEFITS OF BIOMARKERS MAY NOT BE FULLY LEVERAGED AT THIS TIME.

Pulmonologists indicate that IgE and blood eosinophils are the biomarkers they use most frequently in assessing their patients with severe asthma. Biomarkers are being used primarily to identify patients who are most likely to respond positively to biologic therapy; they are less likely to be used to assess the impact of biologic therapy, setting/adjusting dosing, and typing the stage/progression of the patient's asthma.

Use of Biomarkers With Patients With Severe Asthma

Biomarker	Always	Sometimes	Never
IgE	62%	37%	
Blood eosinophils	56%	44%	
Antigen-specific IgE	27%	67%	
FeNO		31%	58%
Sputum studies		52%	44%

Legend: Always, Sometimes, Never

Purpose of Using Biomarkers

Purpose	Always	Sometimes	Never
Identify patients likely to respond	57%	39%	
Assess impact of therapy	22%	60%	18%
Set/adjust dose	20%	57%	23%
Identify stage of asthma	18%	53%	29%

Legend: Always, Sometimes, Never
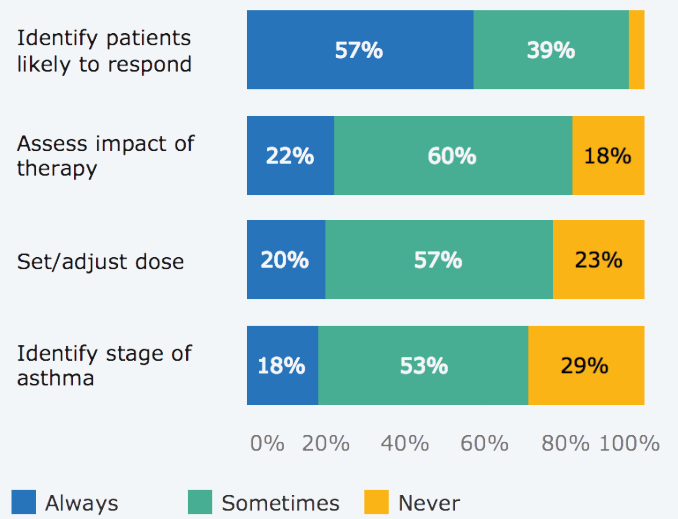
Q: Which of these biomarkers do you use with your patients with severe asthma?

For which of these purposes do you use biomarkers?

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ADOPTION CURVE IS EMERGING AMONG DIFFERENT SEGMENTS OF PULMONOLOGISTS.

Using cluster analysis to group pulmonologists according to their use of biologics and biomarkers, different segments of pulmonologists emerge based on their rate of adoption of biologics and the use of biomarkers to guide that therapy.

- "High Volume Adopters" (52% of survey respondents) are characterized by their widespread use of biologics and higher use of biomarkers compared with other segments. They tend to report that their patients' asthma is likely to be well controlled.

- "Trial Users" (21%) have lower asthma caseloads but are using both biologics and biomarkers. They have a positive attitude toward the therapy but are not achieving the best outcomes based on self-reported perceptions about control of their patients' asthma.

- "Samplers" (27%) have tried biologics but report lower overall knowledge about the therapy and express the most skepticism about its impact on patients with uncontrolled severe asthma.

SAMPLERS (27%)

- High severe asthma caseload
- Mix of primary disease managers and consultant
- Low use of biologics/biomarkers
- Patients' asthma tends to be less severe and better controlled
- Low overall knowledge about this therapy
- Skepticism about therapy

TRIAL USERS (21%)

- Low severe asthma caseload
- Tend to be primary disease manager
- Higher use of biologics/biomarkers
- Patients' asthma tends to be more severe and less well-controlled
- Positive attitudes toward biologics but not fully bought in
- Primarily using anti-IgE

HIGH VOLUME ADOPTERS (52%)

- High severe asthma caseload
- Tend to be primary disease manager
- High use of biologics/biomarkers
- Patients' asthma tends to be more severe and better controlled
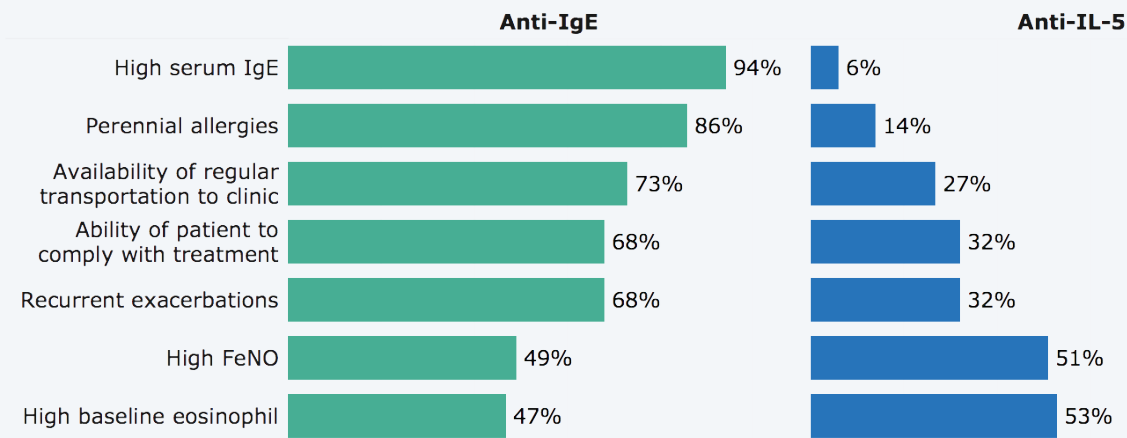- Generally positive attitudes toward the therapy

The clusters depicted above were derived from behavioral questions related to the use of biologics and biomarkers. The objective of the cluster analysis was to understand how different groups of pulmonologists behave relative to the use of biologics and biomarkers. Fifteen questions were included in the initial analysis. Initial clustering was conducted using hierarchical methods (Ward), which enabled the removal of dormant clustering variables and which helped to identify the optimal number of clusters. Subsequently, convergent K-means clustering using Ward centroids was employed to derive the final clusters.

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ANTI-IGE HAS ACHIEVED GREATER SHARE OF MIND AT THIS POINT.

Pulmonologists are more likely to prefer anti-IgE for most of the phenotypes and other patient considerations studied. Anti-IL-5 generates its strongest level of preference when considering patients who have high baseline blood eosinophils and FeNO scores. This preference for anti-IgE could be linked back to guidelines that emphasize anti-IgE but not anti-IL-5 or perhaps even the fact that anti-IgE pharmaceutical options have been on the market longer.

Choice of Biologic by Phenotype/Patient Consideration

Phenotype/Patient Consideration	Anti-IgE	Anti-IL-5
High serum IgE	94%	6%
Perennial allergies	86%	14%
Availability of regular transportation to clinic	73%	27%
Ability of patient to comply with treatment	68%	32%
Recurrent exacerbations	68%	32%
High FeNO	49%	51%
High baseline eosinophil	47%	53%

Q: For each of the phenotypes and other patient considerations above, are you more likely to use (or consider using) anti-IgE or anti-IL-5?

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VARIATIONS IN ADMINISTRATION OF BIOLOGICS SUGGEST OPPORTUNITY FOR PROTOCOL DEVELOPMENT.

Pulmonologists report variations in how they administer biologics to their patients with severe asthma. Method of administration (subcutaneous vs intravenous) is a consideration for 65% of respondents in determining which biologic will be prescribed. Further, more than half of respondents (60%) say they would take patient convenience into consideration when considering which biologic to prescribe, suggesting they would prescribe a biologic that patients could safely and effectively self-administer at home—even if it was not their preferred option.

Does the Method of Administration Determine Biologic?

Yes   65%
No   35%

Q: Does the method of administration for a biologic—subcutaneous versus intravenous—play a role in determining which biologic you will prescribe?

Self-Administration's Impact on Prescribing Choices

Would use preferred biologic even if it means that the patient needs to make 1-2 trips to the clinic each month for administration   40%

Would use the biologic that the patient could self-administer safely and effectively at home, even if it was not my preferred choice   60%

Q: If one of these biologics (anti-IgE or anti-IL-5) could be self-administered at home and the other would require an office visit for administration, how would that impact your choice of which biologic to prescribe?

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DISCUSSION

Biologic use is widespread among pulmonologists, even if they are only deploying the therapy for a minority of their patients with severe asthma. However, much work remains to be done to address perceptions of effectiveness and concerns about safety.

Despite the opportunity posed by the emergence of biologics for treatment of severe asthma, pulmonologists identify notable barriers to more widespread adoption. While cost and patient compliance are universal factors impacting any treatment, a variety of pulmonologists point to a greater need for understanding protocols for biologic therapy, including indications for use and standards for starting and stopping the therapy.

Appropriate and purposeful use of biomarkers is another opportunity area. Use of biomarkers may be less widespread than actual use of biologics, particularly among clinicians who have smaller asthma caseloads. While most are using biomarkers to identify whether or not a patient is a good candidate for biologic therapy, there is less use of these tools to guide planning and evaluation of the therapy on an individual patient basis. Even among the "High Volume Adopter" segment, biomarkers do not appear to be fully leveraged to guide staging, dosing, and confirmation of the impact the therapy is having on severe asthma.

These results point to a need for greater education about biologics; the use of biomarkers as part of a treatment development and management plan; and the development and dissemination of protocols to guide treatment planning decisions, particularly as new options for therapy are coming online.

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RESPONDENT PROFILE

100% of respondents are physicians.

The average age of respondents is **50 years old**.

83% of respondents are **male.**
17% of respondents are **female**.

Respondents by Census Regions

Census Regions
■ Midwest Region
■ Northeast Region
■ South Region
■ West Region
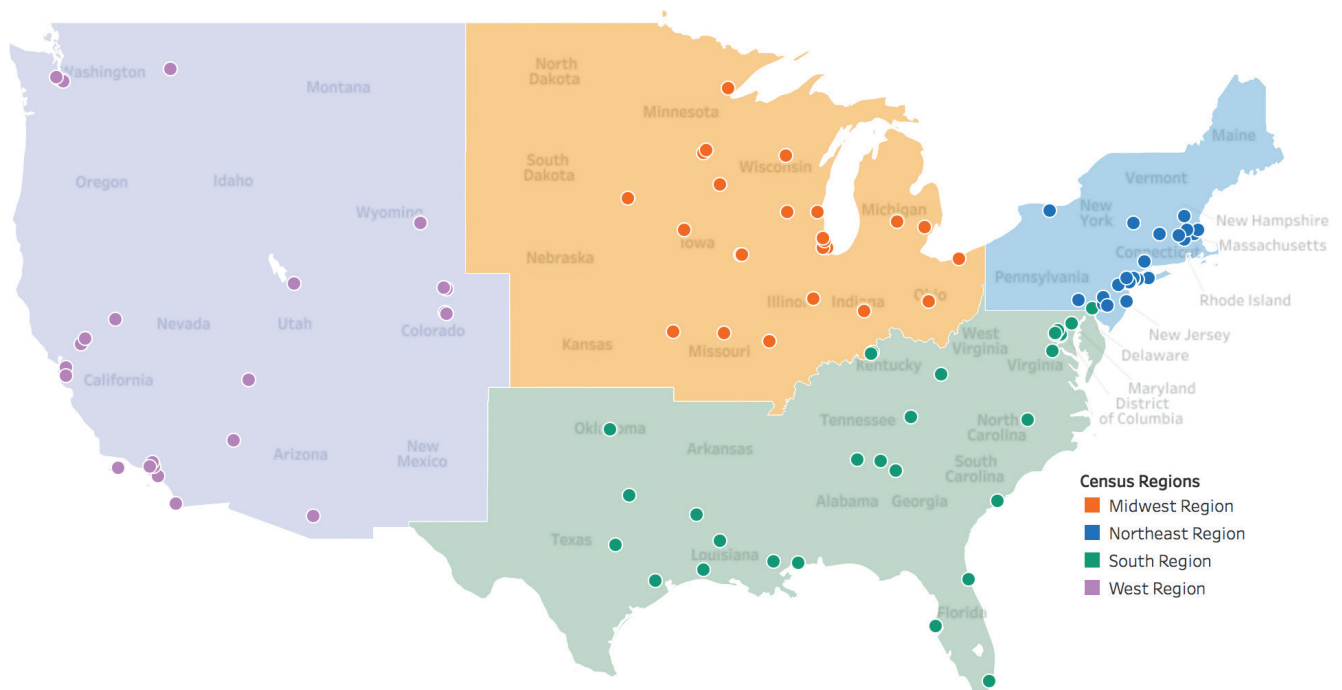
Of 103 respondents:

■ All respondents have the subspecialty of Pulmonary Disease/Respirology.

■ 88% of respondents have both the subspecialty Pulmonary Disease/Respirology and Critical Care/Intensive Care.

■ 18% of respondents have both the subspecialty Pulmonary Disease/Respirology and Sleep Medicine.

■ 3% of respondents have both the subspecialty Pulmonary Disease/Respirology and Interventional Pulmonology.

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RESPONDENT PROFILE *continued*

The employment types of respondents (percentages total to more than 100% because some have multiple employment types):

- Group Practice: 49%

- Teaching/Academic: 24%

- Private Hospital: 13%

- Not Identified: 12%

- Government/VA Hospital: 5%

- Solo Practice: 4%

Most respondents indicate that they are the primary clinician treating their patient with asthma (69%). This varies significantly, however, by patient volume; among respondents who see fewer than 10 patients with asthma per week, only 44% self-identify as the primary clinician while respondents with 10 or more patients are much more likely to play that role (84%). Respondents indicate that better than half of their patients with asthma are classified as moderate persistent or severe and that only half can be considered well-controlled.

Control of Asthma Amongst Patients

Poorly Controlled
18%

Well Controlled
55%

Not Well Controlled
27%
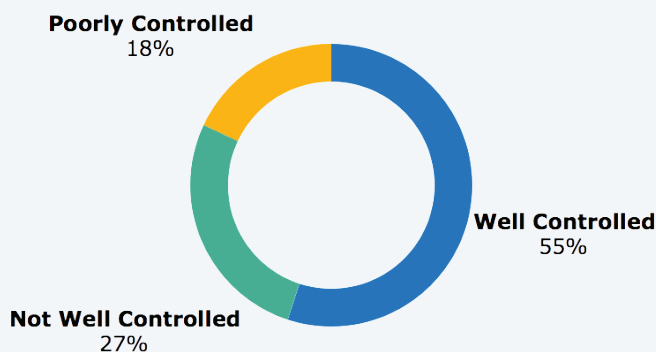
Severity of Asthma Amongst Patients

Severe
25%

Intermittent
16%

Mild Persistent
23%

Moderate Persistent
36%
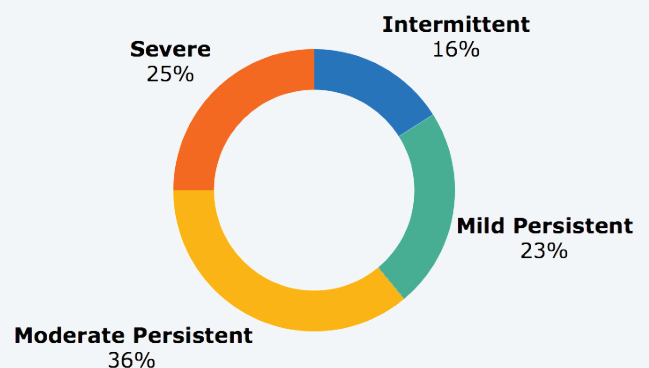
Q: Thinking specifically about your patients with asthma, approximately what percentage of your patients would you classify into the categories above?

Approximately what percentage of your patients with asthma would you classify into the categories above?

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ABOUT *CLINICAL PERSPECTIVES*

The CHEST mission is to champion the prevention, diagnosis, and treatment of chest diseases through education, communication, and research. With this goal in mind, CHEST has launched these quarterly *Clinical Perspectives* resources specifically designed to provide a lens to the experiences and attitudes of key opinion leaders and frontline practitioners who are defining the practice of chest medicine today.

CHEST conducts four unique *Clinical Perspectives* surveys each year, which cover compelling issues in pulmonary, critical care, and sleep medicine. An expert panel of thought leaders from the Mayo Clinic, Baylor College of Medicine, Medical University of South Carolina, Walter Reed Army Medical Center, and Emory University is helping guide the content of each survey and will lend their rich expertise and perspectives in interpreting the results. At the end of each year, a capstone report incorporating findings from all four surveys will be issued.

ABOUT CHEST ANALYTICS

CHEST Analytics is a new line of solutions and resources that helps industry partners and research entities to gain actionable, relevant, on-target insights, based on the input, ideas, experiences, and behaviors of CHEST's engaged and highly knowledgeable membership. We offer innovative approaches for custom research, data enrichment and mining, and ethnographic studies. With more than 80 years as a leader in clinical chest medicine research, and more than 19,000 committed members, we are poised to provide unparalleled insight into the practice of and research in chest medicine.

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