**Dr. Mariam Hanna**
Hello, I'm Dr. Mariam Hanna, and this is The Allergist, a show that separates myth from medicine, deciphering allergies and understanding the immune system.

I think one of the reasons mild asthma is so difficult to manage is that the patient often doesn't feel like they have asthma. They're not wheezing every day, they're not waking up every night, they're not using their inhaler on a regular basis. They're fine most of the time, right?

And then they get a cold, and suddenly the mild asthma means three weeks of coughing, maybe a nighttime cough, maybe a trip to urgent care, but hey, it was just a bad cold. And maybe an inhaler that they use repeatedly until they feel better.

Sound familiar?

Then they recover, then symptoms disappear, and by the time you see them in clinic, they're completely well. It's the mild asthma paradox is how I think of it.

The patient feels completely well most of their time, their lung function may be normal, their symptoms may be infrequent, but that doesn't necessarily mean that their asthma is low risk or that they're not going to get in trouble with it.

And sometimes the hardest part is not diagnosing that asthma properly. It's helping the patient understand that the fact that they feel well today does not mean that there is no asthma to treat.

That's what we're going to discuss today. How do we define mild and by extension moderate asthma? How do we treat patients whose disease seems mild, but whose asthma may still have important consequences?

There's a lot of territory to cover, history to explore, and we have the world expert in the field.

Our guest needs no introduction. Is Professor Paul O'Byrne. He's one of the world's leading authorities in asthma research. He's the Professor of Medicine at McMaster University, and his research has focused on the mechanisms of asthma and its treatment.

He's published more than 560 peer-reviewed papers. He's received some of the highest honors in respiratory medicine and academic medicine. These include election to the Royal Society of Canada, recognition as a giant of chest medicine, and appointment as an Officer of the Order of Canada in 2023. That's essentially like being knighted in respirology land, which is incredible.

Dr. Paul O'Byrne, thanks so much for taking time to join us, and welcome to the podcast.

**Dr. Paul O'Byrne**

Well, thank you so much for inviting me, but also for the very generous introduction. Very unwarranted, but but nice to hear, thank you.

**Dr. Mariam Hanna**
Oh, you're very welcome. I feel like knights are always very humble in their temperament. Okay, we're going to delve into this, because I really I do need help and support in in in mild asthma. I feel like it's the most important thing to recognize cause it comes so often in clinic.

But is the concept of mild asthma or the term mild asthma still have clinical value? Like are we doing these patients a disservice by calling it mild?

**Dr. Paul O'Byrne**
So, that's a very good way to start this discussion, Mariam, because I have spent much of my career grappling with exactly this issue. What is mild? When should we use the terminology?

And are we somehow giving people a sense of reassurance that is inappropriate or perhaps not balanced by using a terminology of that sort?

And we have very consistent evidence, many studies, to show that even if you make an effort to find the mildest asthma population you can, and I'll tell you what I mean by mild in just a moment, and you put those people into a clinical trial where you give them low doses of inhaled steroids, even once daily, they benefit immensely.

Their symptoms essentially disappear, largely, and particularly the risk of having a severe acute event that you describe, often following a viral upper respiratory viral illness, is greatly diminished. Very solid evidence, consistent study after study.

And the study that I perhaps like the most in regards to this, because it really did try to to formalize the definition of what mild asthma is, was a study called the START trial, which is now about 20 years old, but was the first study to large randomized study to ask the question whether early intervention with low doses of inhaled steroids, once daily, 400 micrograms in adults and 200 micrograms daily in children under the age of 12, and treated for three years, whether it could improve outcomes, particularly related to severe events as you describe, the need for going to hospital, being admitted to hospital or requiring oral steroids, as well as preventing what we thought was an important outcome, the decline in lung function over time in people with quote-unquote "mild asthma".

And to get into the study, these people had to have symptoms essentially less than every week. Although it turned out it was a large study, 7,000 patients were followed for three years in a double-blind, randomized trial, and they had to be steroid never previously treated with a steroid and have very, very infrequent symptoms, ideally less than weekly. Although some people did get in with symptoms more than one day a week, and that was a sub-analysis we did later on.

And the evidence was, no matter how mild you define mild, the everybody benefited.

And the risk reduction went from about 20% of the patients per year requiring oral corticosteroids, which was real shock, because if you had have asked me before the study started, I would have said maybe 3 or 4%, 5% would per year would have had a severe event. It was 20% per year for each of the three years, and that that was reduced to about 4 or 5% of patients per year. So a 60 to 70% risk reduction. Very clear evidence.

So that then brings us back to your question. Does mild have any Is there any value in its use now?

And if you use those data, you would say, "Well, I suppose it it's useful in that it's maybe not severe or not very severe, but there's no patient with asthma who's not at risk. It just doesn't exist, in in my opinion."

And that then leads us to the question, even if they are have very infrequent symptoms, they're still at risk of having something untoward happening, as you described in your introduction, what to do about that?

And therein really lies the paradox, because, of course, despite this overwhelming amount of evidence, the likelihood of you or I or any of our colleagues convincing a mild patient to use steroids once a day, every day of their life, is vanishingly low.

**Dr. Mariam Hanna**
It is. Like I have a better job getting them on an aspirin or statin or stat- like and the risk reduction here is profound. Okay, yeah, keep going.

**Dr. Paul O'Byrne**
Exactly. Exactly so. Exactly so.

And so that led to the thinking around whether, in fact, we could get benefit by just changing the reliever from a SABA to a reliever that had a steroid. And that, of course, led to the SYGMA trials, which we conducted now about 10 years ago, and and I I I think have largely changed the face of what might be considered a mild asthma, because the risk reduction for severe events in again a quote-unquote "mild population", although about half the people were already on maintenance treatment, low-dose maintenance treatment in the studies, but still it was considered to be a mild population, the risk reduction with using a reliever that have has a steroid together with a a long-acting beta-agonist was actually equal, equivalent to the risk reduction with daily once daily inhaled steroids. And these people were in fact quite adherent in during the trial. We actually measured that. We measured every time the the inhaler was actuated, so we knew exactly what the patient was taking.

And so so now, coming all these years later on, I'm now asking myself, "Well, what do I mean by mild?" And what I mean by mild, and I do use the term in my clinic, I I will admit to you, Mariam, it's something I will say to patients, "You have mild asthma."

And mild asthma for me is a patient that I feel comfortable just using a reliever that has both an ICS as well as a long-acting beta-agonist as needed, only as needed.

And then moderate are patients who require maintenance combination treatment every day.

And then the discussion comes about, "Well, what differentiates those two? At what point do you say just PRN uses is acceptable versus when does the patient need a maintenance daily treatment?"

Right. Very long-winded answer, I apologize, but that's my sort of that's how I've arrived at where I am at the moment.

**Dr. Mariam Hanna**
No, I love that answer. I'm still listening. I'm like, "Yes, and when do we differentiate?"

Um, you know what, before you tell me about when we differentiate, mild asthma, number of symptoms per week, you kind of alluded to it. Um, yes, yes.

That definition also has changed over time over the different iterations. Can we talk a little bit about the why of that definition has changed and what is what we hold as definition today? And will that be changing in the next 5, 10 years as well?

**Dr. Paul O'Byrne**
I suspect it will, because over my years in following this area in in my research as well as my clinical life, it has gone from what might be considered mild, when, in fact, I was involved at one time in the GINA science committee and the GINA executive, and there was a lot of discussion about at what points should you try to insist that a patient requires a maintenance treatment.

And at that time, mild would be considered symptoms 2 to 3 days per week. If you needed treatment reliever treatment 2 to 3 days per week, that was sufficient to to at least recommend to the patient that they should be on maintenance inhaled corticosteroids.

At that time, we actually did not have a really good appreciation of risk associated with this. It was all symptom-driven, or indeed even lung-function-driven. If the patient had FEV1 less than, pick a number, 80%, or something of that, then they should be on a a daily maintenance treatment. So risk reduction really wasn't the it didn't really play any serious part in in thinking about how mild or moderate a patient would be.

That was why I think the START trial was so influential, because it indicated that it didn't matter how mild the patient was apparently at the time of entry into the study, some of them having essentially no symptoms at all during the weeks prior to randomization, they were still at about a 1 in 5 risk every year of having a severe exacerbation requiring oral corticosteroids.

And so even having one exacerbation a year, or one every two or three years for me, is unacceptable. In fact, I really try to tell the patient, "I'm going to work as hard as I can to make sure you're completely exacerbation-free," you know, with with the approaches that we have.

And to that end, one of the interesting post-hoc analyses from the SYGMA study, which which was published in Lancet Respiratory Medicine about three or four years ago, was that when you looked at the number of reliever medications used in any one day in the study, if in the SYGMA trial in one of the arms the reliever was a SABA only, and in another arm, there were three arms, in the one of the other arms it was only ICS-LABA, budesonide-formoterol in a in a single inhaler.

With the SABA, the more of the SABA you used in any given day, the greater the risk of requiring oral steroids or a hospital visit.

While with the ICS-LABA, the more you used, the lower the risk.

And, in fact, in people who used six or eight puffs in any given day, no patient during the entire year of the study needed oral steroids.

And so I'm actually fairly convinced by that, that using the PRN ICS-LABA combination, if they use it as they should, which is whenever they have symptoms, the more of it that's used at any given time, the less the risk of something bad happening, while it's exactly the opposite with the with the SABA.

So that again helps me feel, perhaps inappropriately reassured, that if I have this approach in my quote-unquote "mild asthmatic patients" to use an ICS-LABA as needed, that they actually are at very low risk of having a severe event, yeah.

**Dr. Mariam Hanna**
Okay. And how are you distinguishing the patient that comes in for consultation for them to go into mild versus moderate, let's say, at the time of consultation? What what what makes you decipher between those two?

**Dr. Paul O'Byrne**
So, honestly, if I think back in my own clinical experience, certainly in the past few years that we've had the anti-inflammatory reliever, which is the term that's now accepted for this approach, available, I would be very rarely asked to see a patient that didn't have symptoms very frequently.

So, you know, every day, or waking through the night, or have have reduced lung function. Um, so I I don't see many quote-unquote "mild patients", but I know that the vast majority of asthmatics that are managed in, particularly in primary care, have mild disease.

So with that in mind, if a if I have a patient that has has had an exacerbation requiring oral corticosteroids in the past two or three years, it depends a little bit on other things, then I will say, "That's not an acceptable asthma control. I think you need to have regular inhaled therapy." And for me, that makes the patient a moderate patient.

It's sort of based on how much treatment I feel the patient needs to keep them well. And if it's daily treatment, that for me is not a mild no longer a mild patient.

But with the understanding that still in that patient, there will be times, and I explain this to patients I'm using the anti-inflammatory approach in, there will be times when you may need that four or five times a day for a few days.

And you might call that an exacerbation, it probably is, but it's not an exacerbation requiring the kind of treatment intervention that I feel puts the patient at risk long-term, which is oral corticosteroids, or having such a severe event that they're actually put at risk of of some really bad untoward event requiring hospitalization or or or ICU care.

So so any exacerbation in the past three years, symptoms more than a day or two a week, I don't think are acceptable, frankly. Waking at night ever, I find is is would be unacceptable.

So these are the questions that I would be asking the patient. When when have you have you had an exacerbation, when was it, and how was it managed, and what happened when the exacerbation had occurred? Are you how often are you using your reliever medication, as least as a surrogate for how often symptoms are occurring? Are you ever waking at nighttime?

And if they are ever waking at nighttime, I don't think that's adequate control, and I would, at least to start with, recommend to the patient they use a maintenance treatment.

Now, the reality, Mariam, is that the adherence with this approach in somebody with the disease that is intermittent is still not going to be very good. And that's something we have to we have to sort of recognize. It's it's going to be poor.

There's a study I show when I'm giving talks about this, which I I it's a bit extreme, but I don't think it's that extreme. It was done in the um in California, at a HMO in California, I think it's the Kaiser Permanente system, and they took 5,000 asthmatic patients who were treated with a combination ICS-LABA inhaler as a maintenance, twice daily.

And to get into the study, everybody had to fill the first prescription. So 100% at the time of entry into the study. After one year, when they followed prescription renewals and they followed the patients fairly carefully, 12% of patients were using the inhaler every day still.

And that's with an ICS-LABA combination given twice a day.

So however we think, right, how however good the advice we think we're giving, the reality is the patient will do what they think is best for them. And that's why, no matter what I do, I always insist they have an ICS-LABA as a reliever, because I think the only real mistake we can make in this instance is leaving them on a SABA as because they stop using their ICS-LABA as as the maintenance.

**Dr. Mariam Hanna**
So I get into this, it's a great segue, because I get into this discussion with my families to say like, "But we need the SABA, that's what the urgent care or the hospital has used, that's what feels like gives me relief. What if I max out my eight doses in 24 hours, you're going to leave me with no medications?" I mean, the list of excuses is expansive. Obviously.

But like, how do you address that discussion? And then the the lower age limit, sometimes I I worry that we've established a habit in our pediatric patients that it's the SABA juice that helps the most, and then you're trying to like flip them over. Um, can you comment towards that, please?

**Dr. Paul O'Byrne**
Yes. Oh, well, everything you've said, I've heard and heard and heard and heard. You're absolutely right.

And so what I have I've fallen back to a rather pragmatic approach to this, Mariam, and I will tell the patient, "Look, if you truly believe your SABA is what you say it is, and it it is your lifeline, and you've used it for 10 years, and on and on, sure, continue to have it with you. Carry it with you. Keep it in your handbag, keep it in your car, wherever you keep it. But please try my approach first. If this approach doesn't work, next time you come back and see me, you tell me, and you can, you know, you have your SABA there as your sort of your your lifeline if you feel you need it."

And I wouldn't say always, but pretty well always, next visit, 3 months, 6 months later, whenever I see the patient, basically the SABA is forgotten, because the ICS-LABA reliever approach works so well.

The only thing you have to be clear about though with the patient is that is the freon effect with the with the with the with the SABA. They get this sense of having something in the back of their throat because of the freon that carries the medication. So they know something has gone in.

While at least with Turbuhaler, there's no taste at all. You don't taste it, but it doesn't mean it's not not going in. So they they need to understand that's an important difference between the two two inhalers.

**Dr. Mariam Hanna**
Okay. Got it. Got it. And I like explaining the freon effect. It's like how I explain Buckley's. Just because it tastes bad doesn't mean it works. That works, too.

I now find that I have families that are increasingly concerned that they're getting too much ICS by putting it in a combo therapy. Are there, in fact, mild patients that are receiving more ICS or more medication than needed?

**Dr. Paul O'Byrne**
Yeah. Well, there's always there's always that risk. There's no doubt about that, and it's um it is in at least in tertiary practice that we would have where we were referred patients in with very difficult to manage disease. It is quite surprising how commonly how common vocal cord dysfunction is as a a cause of symptoms, even in people with diagnosed asthma, and it does take time and effort to sort that out and try to understand understand that.

I have a particular I've had a particular interest in the past in in in asthma in athletes, and I do get referred high-performance athletes with quote-unquote "poorly controlled asthma". And quite honestly, more than more than half the time, maybe even more than 70 or 80% of the time, it's actually not asthma that's the problem. It's it's the way the vocal cords are performing at in at very high intensity sport. So yeah, that's a that's a that's a real a real issue.

Now, with the PRN use, I suppose you you are at some risk that you're going to get some people who will overuse it, but it's likely to be less of a problem than if it's a maintenance twice-daily treatment, maybe.

And then if, in fact, the the patient is using it using the reliever medication more than once or twice, or maybe if you stretch it a little bit, perhaps three times a week, then the question is, well, why not use it as a maintenance? If you're having that if you need the inhaler that frequently through the week, then that is really no longer truly mild, quote-unquote "mild asthma".

And the final thing to say is that I think it's really important to reassure the patient, certainly those 12 and older, that the evidence of safety around the use of inhaled steroids is very compelling at the kinds of doses that 99% of patients need.

If you go over a milligram a day of most steroids, that's not a good thing. You will get increased risk of of some side effects, but you know, the doses we're using is less than that, and and uh with PRN use, it's often in the range of 100, maybe 200 micrograms a week, not a milligram a day, which is where the side effects begin to kick in.

In children, of course, it's a little different, because the evidence is pretty good, actually very good, that even very low doses of inhaled steroids do inhibit growth velocity in children.

And but, and it's important to reassure parents of this, as far as I can see, the evidence is pretty clear that it's not a it's not a um an additive effect. The effect is only seen in the first year or perhaps year and a half, and the the at absolute worst in in the CAMP study, it was about half a centimeter difference in height, although the study that Søren Pedersen published some years ago in the New England Journal where he followed children to adult adulthood showed no effect

on final height. So it's it's a very it's an effect, but it's a it's a small effect, and, of course, the the benefit is keeping these children well, active, in school, and you know, and so on.

**Dr. Mariam Hanna**
Perfect. And not on blasts of oral corticosteroids with their 10 colds a year. Yeah, no, I hear you.

Okay, biomarkers. Let's talk about biomarkers or combination of biomarkers. Do they change your management? What biomarkers are you following? Should we even follow them on a patient that we're classifying as mild to start out with?

**Dr. Paul O'Byrne**
Yeah. This is time for confession here, Mariam. I do not use biomarkers as a way to follow the mild to moderate patients who are well controlled.

I We have a routine here of measuring when the person comes in first of all to be certain the diagnosis is correct, because when you're seeing people with difficult to manage asthma, it's embarrassingly how embarrassing how often the diagnosis is actually not correct.

So we spend a lot of time measuring lung function, measuring methacholine if the lung function is normal, trying to demonstrate there's variable airflow obstruction, and measuring FeNO and eosinophils to see if we can come up with a a convincing set of investigations that support a diagnosis.

Um, in in people who are really poorly controlled and really with frequent exacerbations, the sort of the the standard severe quote-unquote "asthmatic patient" that one is considering a a biologic, then, of course, biomarkers become very important.

Blood eosinophils are the most widely used. They can be quite misleading in some people, because, first of all, the the variability in the measurement is very real, and so there are some studies that suggest that if you identify a population of what is colloquially known as T2-low asthma with severe asthma with low blood eosinophils, and you follow them for a year, something like 60 or 70% during that year will have elevated eosinophils. So it depends on when you make the measurement.

And FeNO, of course, is turning out to be quite useful, and then there are those who would make the case that uh that if you have both elevated FeNO and elevated blood eosinophils, you're what they call the hot-hot patient, that they will get the biggest benefit from many of the biologics or all the biologics that we have.

But in milder patients or those with more moderate disease who are just using inhaled medications and doing well, I don't see particularly any any benefit. I do measure lung function, because um I, as I mentioned a few minutes ago, always concerned about people who have variable lung function and don't know it, don't perceive it, and that I need to know about.

But their blood eosinophil counts I usually I would have it as a baseline measurement, and if it's elevated, then at least in my mind, that sort of ticks a box to say, well, at some point, first of all, they may be at higher risk of an exacerbation, that's true, I think, that elevated blood eosinophils is the only biomarker that predicts that.

Some studies would suggest that the eosinophil count and FeNO are both elevated, it's an even further increased risk.

Um, but would that allow would that um suggest I I change my treatment approach? At the moment, I don't know of any evidence to support that, as long as the anti-inflammatory reliever therapy is being used in in in the patient.

**Dr. Mariam Hanna**
That's great. I want your feelings about this step-up, step-down, more the step-down, because every single patient that comes back for follow-up is trying to convince me of how much better they are, and when are we weaning medications or stepping down.

So I think stepping up seems more natural to us as physicians, and we know what what triggers we would have for that, but much less information about stepping down. How do we safely reduce treatment in patients with mild and moderate asthma?

**Dr. Paul O'Byrne**
Yes. So, there have not been many studies, as you know, Mariam, on how best to step down, when to do it, how best to do it, what the right approach is. And...

**Dr. Mariam Hanna**
Well, why is GINA so focused on it then if they do don't...

**Dr. Paul O'Byrne**
Yes. They because they believe that the minimum treatment requirement should be identified.

But that would imply, if you're going to do that, you need to get the patient to a point where they begin to have symptoms again in order to say, "This is now the minimum to keep them well."

And I don't think anybody does that. I certainly do not do that.

Mind you, having said that, if the patient, let's take an example, if the patient has come in and I feel they need an inhaled ICS-LABA morning and night and as needed, which is often the approach for the more moderate patients, and they come back in six months, and their lung function is well-maintained, normal for them, and they're fully asymptomatic, having no symptoms, not requiring reliever hardly ever, then I will say to them, "Look, the best I can tell you, your asthma's extremely well controlled, I would be willing, if you are, to reduce the dose to one puff morning and night." So to cut the dose in half.

But with the caveat that if you start having symptoms every week, that you must put it back up to the previous dose that was keeping you well.

And very often that will be fine. The patient will do really well, because, again as you know, there's not a huge amount of evidence that doubling the dose of a steroid does very much. Certainly at higher doses, that's absolutely true.

And there's not a great deal of evidence that reducing the dose by half, halving the dose, does much harm in most patients. So if they're well controlled, I will at least discuss it with the patient and have them understand that I'm comfortable with it if they are, but but that they also must feel the uh they have a responsibility to go back up to the previous dose if they're not do doing very well.

Problem then becomes, and this is where it becomes a bit of a challenge, when they come back and they're doing really well, do I stop the maintenance and just have them on as needed, or insist they continue with the maintenance treatment?

And there, I think, because honestly there's virtually no data to base this decision on, that's where a discussion with the patient becomes so important.

Because, again, no surprise, if you really dig deep and you probe and you push, very often the patient's not doing that anyway. Once they're doing they're perfectly well, they feel terrific, they had no symptoms at all, say, "Well, I may forget the occasional dose at nighttime." Say, "Well, is that all you..." "Well, maybe it's some days I don't take it, you know."

And in fact, what they're doing is what you're sort of agonizing over: Should I stop the maintenance or not? And I I will find most of the time that is what what has happened, that they're actually reverting themselves to just using PRN reliever. And it emphasized to me again why the reliever should always be an ICS-LABA or an ICS-SABA, but something that has a steroid in it, because that's what the patient is is going to do.

But another area, despite all these years of research in asthma, Mariam, where we don't have really good evidence to say, "This is exactly the right approach one should one should take."

**Dr. Mariam Hanna**
Fair enough. I'm dissecting a little bit on GINA, but you can go after GINA or CTS or whatever guideline you'd like, but if there's if there's one one recommendation or one change in recommendation that you could put into GINA tomorrow, what would it be?

**Dr. Paul O'Byrne**
I would remove any recommendation that requires or implies the patient should be using a SABA.

I don't think SABA should ever I don't think any asthmatic in this world should have a SABA, ever.

**Dr. Mariam Hanna**
So many quotable moments, Dr. O'Byrne. Okay, yeah, yeah.

**Dr. Paul O'Byrne**
And it is for the reasons we've already discussed in some detail, that the GINA recommendations have the two tracks. They have a recommended track and they have a a preferred track and a second track. And the second track is, of course, low-dose ICS maintenance with the SABA as needed, or when the patient is symptomatic, the ICS and the SABA used as a reliever as separate inhalers.

It becomes so complicated and it's so dependent on good adherence, which I know is just not the case in most people.

And so I would, if I could, if I had all the power in the world, I would say SABAs probably maybe useful, continue using them in people with COPD. You know, that because I don't have any evidence to date they they could or should not be used there.

But in asthma, just because of that risk, I would prefer that no patient ever had access to a SABA.

**Dr. Mariam Hanna**
Fair. Fair. What's one GINA recommendation that we're not implementing well in primary care or subspecialty care at this point?

**Dr. Paul O'Byrne**
I think the one that is probably most problematic is around the diagnosis of asthma.

And you know, GINA spends a lot of time, as the CTS guide, around how best to make sure the patient has asthma, the diagnosis is correct. Um, in in primary care, again, you know this, lung function is rarely if ever measured, so measuring variability becomes essentially a a non-starter.

Um, this is such a concern that the um the the BTS and uh the SIGN guidelines that have been recently reported a few months ago have um recommended that the diagnosis could be made and perhaps should be made with just measuring FeNO and blood eosinophils. And if both are elevated in a patient with symptoms, the probability of having asthma is, I forget the number now, but it's it's very high.

But it does mean you have to have a practice where you have a FeNO machine or have access to one, as well as the willingness to get blood eosinophils measured, and um and not rely on on on lung function.

I We had the uh individual who led those SIGN guidelines here visiting us a few weeks ago, and uh one of the things we discussed was a large would need a large prospective study in primary care to actually test that approach, because the recommendations are based on pragmatism rather than evidence.

And and I just don't know whether, in fact, asthma will be overdiagnosed if you have, for example, severe allergic rhinitis and maybe a cough, your FeNO will be up and your blood eosinophil count may be up, but the cough may not be related to asthma.

And and so I need to know what the risk is of mislabeling and therefore mismanaging patients if you don't try to measure variable airflow obstruction, which is the sort of for me the sine qua non for a diagnosis.

So I I worry a bit about that more perhaps more than anything else, that that um I think asthma is both, oddly enough, underdiagnosed and overdiagnosed. It's overdiagnosed likely particularly in in younger children where lung function's hard to measure, and and lots of kids cough and occasionally wheeze and hack and, you know, get cold after cold and they're labeled, and and then they have this label for the rest of their lives.

And and um and then sometimes, I think, there is a risk of uh of if you're not measuring what we should be measuring, perhaps labeling, particularly in adult-onset asthma, as something other than asthma when, in fact, it is. So it's a complicated process, but I I feel we're very poorly served at the moment by the quality of evidence we have.

**Dr. Mariam Hanna**
See? Another plug for research. Um, one paper, one paper you would point us to You've referenced a number of them actually during our conversation today, but what's one that you would think that every allergist should read this year?

**Dr. Paul O'Byrne**
Goodness. Wow, that's a great question.

If I may perhaps plug a paper, uh because I it certainly perhaps changed my thinking more than almost anything else that I've been involved with in the past few years. It's not published this year, but it's a paper that I was the first author on in Lancet Respiratory Medicine, which is the post-hoc analysis of the SYGMA data looking at the issue of how frequently somebody used a reliever and the risks associated with that in very mild patients.

And again, in in the in this study, we really did pick people who had very less than symptoms less than weekly.

And as I've already mentioned to you, when you use a SABA, the more you use, the greater the risk of something really bad happening. When you add the anti-inflammatory reliever approach,

the more you use, the less the risk. In fact, the risk disappeared completely at the higher daily doses.

And so for managing mild to moderate asthma, for me, that's a paper I think probably will stand the test of time.

**Dr. Mariam Hanna**
Calling all journal clubs! This is the one to review! Dr. O'Byrne, a perfect ending. Thank you very much. All right, time to wrap up and ask today's respirologist, Dr. Paul O'Byrne, for his top three key messages to impart to patients and physicians on today's topic, mild and moderate asthma. Dr. O'Byrne, over to you.

**Dr. Paul O'Byrne**
Well, thanks, Mariam, for the opportunity of doing this.

Um, the three things that I would like people to take away from this is, firstly, as again we've discussed in some detail, making sure the diagnosis is correct. It takes work, it takes effort, but this is a lifelong diagnosis, potentially, you're giving somebody, and I think it it's incumbent on us all to ensure that you don't just rely on symptoms to establish that the patient has has asthma.

Secondly, uh please do not start people when they are initially diagnosed on a SABA. For the reasons Mariam said, once you do that, the patient accepts that that is the right treatment approach, they become used to using it, and it's very difficult often to convince them that, in fact, while the SABA in the short term is very useful, when used overused, it can be very, very problematic.

And the third message is that for mild to moderate patients who need a reliever medication, it should always contain an inhaled steroid.

**Dr. Mariam Hanna**
Perfect. Thank you, Dr. O'Byrne, for joining us on today's episode of The Allergist.

**Dr. Paul O'Byrne**
I've enjoyed it immensely. Thank you for asking me and tolerating my my uh ramblings.

**Dr. Mariam Hanna**
We loved it.

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And remember, get the diagnosis right and get them on the right drug, not the bad juice!

Thanks for listening, sincerely, The Allergist.