

## Emergency Department Clinicians Share Perspectives on Treating Lower Back Pain

Giuliana Grossi

**LOWER BACK PAIN AFFECTS** up to 4 million Australians and spans across all age and socio-economic groups. Approximately 80% of people can expect to experience lower back pain at some point in their life.

Lower back pain was the 5th most common reason for visiting the emergency department in Australia in 2017-2018 despite the recommendations of international guidelines that state it's best to receive care in primary or community care settings.

About half of all patients with lower back pain who seek treatment in the emergency department are discharged with a non-musculoskeletal diagnosis. It's not uncommon for lower back pain to be a symptom of an underlying problem.

### Identifying the Obstacles

Investigators including Simon Davidson, School of Medicine and Public Health, The University of Newcastle, Population Health, Hunter New England Local Health District, wanted to know why patients with lower back pain present to emergency departments and are then admitted to the hospital; what barriers and enablers do providers face when caring for these patients; and what are some strategies to improve the care of patients with lower back pain and associated care processes in the emergency department.

In order to optimize service delivery and improve patient care, it's critical to explore the perspective of clinicians. Co-designing the interventions with the end-users increases the likelihood of it being accepted and implemented.

Qualitative research has been conducted covering a range of topics related to the emergency department and patients with general chronic pain. Although, no studies have specifically focused on issues that clinicians face while treating lower back pain.

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## New Study Shows the Benefits of Gla-300 Treatment for Type 2 Diabetes Patients

Armand Butera

**IN DATA PRESENTED AS A** late-breaking poster at the 2021 American Diabetes Association Virtual Meeting, Eugene Wright, MD, and team studied people with type 2 diabetes (T2D) who switched from basal insulin (BI) to second-generation (2nd-gen) BI, Gla-300 or a first-generation BI (Gla-100, IDet) during the course of their treatment.

The change in insulin treatment in participants was recorded between April 1, 2015 and August 31, 2019. The team noted that patients with type 2 diabetes may

change BI therapy for clinical, personal, and financial reasons. Formulary changes are also common.

There were 3077 participants in each cohort, with a mean age of 68 years. Roughly half of the participant group were female, and data on each participant was collected using the Optum Clinformatics claims database.

Participants were followed for 12 months or until planned disenrollment or death. Cohorts were propensity score matched (PSM) on baseline demographic/clinical characteristic, and the outcomes evaluated during the study were persistence (days on treatment without discontinuation), adherence (proportion days covered), healthcare resource utilization and costs.

The investigators found that participants with T2D who switched to Gla-300 showed a greater persistence and adherence to therapy than those who switched to a 1st-generation BI. A change in A1C from baseline to 12 months was also significantly greater with participants who switched to Gla-300.

Additionally, while participants who switched to Gla-300 did have significantly higher pharmacy costs, they also had lower all-cause hospitalization and hypoglycemia-related ER costs. In general, lower total health costs were recorded in Gla-300 patients.

Total healthcare costs for participants who switched to Gla-300 were \$41,255 (\$22,613 of which was diabetes related), while the total healthcare costs for participants who switched to 1st-generation BI were \$45,316 (\$25,165 of which was diabetes related).

Additionally, persistence and adherence in the former group were also recorded as being higher than 1st-generation BI participant. Persistence and adherence were recorded as 45.5% and 42.8% for Gla-300 participants, and 42.1% and 38.2% for 1st-generation participants.

“Switching to Gla-300 was associated with significantly better persistence, adherence, and—despite these associated costs—lower all-cause healthcare resource utilization vs. switching to a 1st-generation BI, in people with T2D previously treated with BI therapy,” the team wrote. “This is the first study to assess these outcomes in tandem.”

Wright and colleagues lead the charge in terms of studying diabetes and diabetes management. As they noted in the study, patients may switch to different insulin treatments for a variety of reasons.

However, their study shows that while Gla-300 patients might have higher pharmacy costs, their overall health costs were significantly lower, while their overall commitment to diabetes treatment was significantly higher.

The study, “Real-World Persistence, Adherence, Health Care Resource Utilization, and Costs in People with Type 2 Diabetes (T2D) Switching from Basal Insulin (BI) to Second-Generation BI (Insulin Glargine 300 U/mL [Gla-300]) vs. First-Generation BI (Insulin Glargine 1)”, was published online by ADA. ■

## Seeking Out Solutions

Emergency department clinicians were able to identify internal and external factors that they believe drive presentations of lower back pain to the emergency department. Factors included difficulty accessing appointments with general practitioners, along with a patient’s assumption that emergency departments provide the highest and fastest level of care for a patient.

Some barriers that providers face when caring for patients with lower back pain in an emergency setting extend beyond the patient presentation and decisions about what treatments to provide. Service level demands, like a patient’s length of stay, are important concerns that need to be addressed in order to optimize care.

Emergency department clinicians identified key strategies that could improve the care of patients with lower back pain. These strategies include a department-specific lower back pain pathway, modernized patient and clinician resources, better follow-up options post-discharge, and optimizing communication between the emergency department and primary care.

“Each professional group focussed their discussion on areas that are most relevant to them,” investigators wrote, “medical officers, clinical decisions and follow-up options; nurses, the provision of care to patients; and physiotherapists, optimizing function.”

## The Structure of the Study

Investigators conducted a qualitative exploratory study with emergency department clinicians (medical officers, nurses, and physiotherapists) at a tertiary-level public hospital in New South Wales, Australia. They used focus groups and individual interviews.

Participants included 21 clinicians with 2 individual interviews and 19 in focus groups. Investigators used thematic analysis on the participants’ responses to answer the predefined research questions.

Ultimately, they found that patient perception was suspected to be the driving motivator to these patients seeking treatment from the emergency department. Also, achieving optimal care included patient-, clinician-, and service-level factors.

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The study, “Perspectives of emergency department clinicians on the challenges of addressing low back pain in the emergency setting: A qualitative study,” was published in *Emergency Medicine Australasia*. ■

# Elena A Christofides, MD: Perspectives on Risk Factors, Care for Type 1 Diabetes Patients

Connor Iapoco

**AS THE 2021** American Diabetes Association Virtual Meeting concludes, important conversations have taken place surrounding diabetes prevention and treatment, as well as the makeup of at-risk patient populations.

*HCPLive* recently spoke with Elena A. Christofides, MD, Endocrinology Associates, on her thoughts about cardiometabolic medicine, patients with a predisposition for diabetes, as well as a highlight on the potential efficacy of teplizumab.

Check out part 1 of the interview below:

**HCPLive: Just to start, I was just hoping if you could maybe share some of your thoughts surrounding the larger conversation on cardiometabolic medicine, particularly in addressing obesity and diabetes and how important that larger conversation is when it comes to reduction and ultimately prevention of these conditions?**

**Dr. Christofides:** Right. So, I think what is an interesting element of this is I think that the conversation has been really segregated from the two conversations surrounding obesity and cardio-metabolic disease that have really not been talked about together for a long time. There's times when they come together, but I think that they really need to be talked about, the one core component.

You know, we used to talk about it in terms of metabolic syndrome, just metabolism, et cetera. But I think part of the problem is that there are a lot of clinicians, as well as researchers, who are out there talking about diabetes as a distinct and separate disease. And they really don't want to have to think about cardiometabolic disease because not everybody gets cardiometabolic disease who has diabetes. And there are people who have cardiometabolic disease who aren't diabetic, but they, for all intents and purposes look diabetic.

And I think part of the difficulty there is that people want diabetes to only be about the blood sugar problem. And it isn't only about the blood sugar and if you talk about diabetes, people want it to be all about the sugar, but it isn't about the sugar. And then when we talk about cardiometabolic disease, people are like well there's no diabetes, so it's not relevant, but in fact it is because they are exhibiting the same defects that we see in diabetics and the same similar outcome. So I guess that's kind of my thoughts on why they should be talked about together, but why people don't.

**HCPLive: Absolutely. So, following off of that, how would something like teplizumab, a preventative drug for type one diabetes, affect that sort of care if it were to be approved by the FDA?**

**Dr. Christofides:** Well, so here's the thing. Type 1 Diabetes has nothing to do with anything else in the world and should never be talked about in conjunction with other diabetes. So that's part of the difficulty. Teplizumab is great. I did some clinical trials on type one diabetes prevention drugs a while ago, and they were immune modulators, very similar to teplizumab. That's really the key feature of type one diabetes is that they're auto immune. They have a completely different problem. It originates differently. They're not one and the same, so it is inherently, ultimately unrelated to any other types of diabetes.

**HCPLive: A previous release had mentioned people having higher risk of type 1 diabetes based on nutritional factors, environmental exposures, and things like infections and viruses. Would something like teplizumab have a benefit for patients who are predisposed for T1D?**

**Dr. Christofides:**

Yes. If they are truly predisposed to type 1 diabetes, but the environmental factors that predispose someone to type one are not the same environmental factors that predispose people to Type 2. So it all depends on how you're defining it. So I do think that they defined it well in the study. I do think that the data on the mechanisms of type 1 diabetes at-risk individuals is well-described and well thought out. I just don't think that the world talks about it that way.

**HCPLive: Could you follow up on that?**

For example, if you eat junk food, you drink soda, you don't exercise, you have obesity, you live in an urban environment where you're maybe micronutrient deficient, you're at risk for type two diabetes then. Because, you're at risk for all the ways that type 2 diabetes is caused and contributed to by lifestyle. None of those things have anything to do with type one, not a single thing. Type 1 is influenced by your genetics in terms of your genetic risk for autoimmune disease influenced by some micronutrient deficiencies, but not the same one that's type 2. To some degree, vitamin D is a commonality, but none of the other ones.

And then, we don't really know what the rest of the environmental factors are. We say that, but it is a lot of hand-waving, it is actually well described. Environmental factors that are well-described are interestingly a seasonality to type one diabetes. You're more likely to get diagnosed with type one diabetes in January through June, as opposed to June through December. And that's where vitamin D comes into play, you are outside more, children are out more, they're playing, they're more likely to be vitamin D sufficient.

But, obesity doesn't have anything to do with type one diabetes. Junk food doesn't have anything to do with type 1 diabetes, unless the person is nutritionally deficient. So that's what I'm getting at is that there are clear genetic risk factors, but those are hard to identify because it requires doing blood work, that requires doing genetic testing and people are universally afraid of genetic testing in the U.S. There's a lot of hand-waving about risk factors, but they're not common to either disease. ■

## Elaine M. Apperson, MD: Discussing Treatment in Pediatric Patients with Type 1 Diabetes

Connor Iapoco

**IN AN INTERVIEW WITH** *HCPLive* surrounding the 2021 American Diabetes Association virtual meeting, Elaine M. Apperson, MD, Prisma Health-Upstate, discussed the cost-benefit of a carbohydrate diet for pediatric patients with type 1 diabetes (T1D).

Apperson noted that she does not want to vilify carbohydrates, citing her adage is to fit diabetes into the life, rather than fitting life and diet around diabetes.

She mentioned her descriptions when talking with families about carbohydrates include describing glucose as Lego and encouraging families to choose carbohydrates in a smart way.

"I think you don't want to ostracize the child with diabetes in the household, you want to make it something that the family can do together, you want to make it simple," Apperson said. This is just a basic ideology. And so in terms of incorporating it as a treatment for diabetes, you just adopt the principle that minimizing simple sugars is the best way to go.

Apperson also touched on the effects of both the COVID-19 pandemic and the consequences of food deserts, where her attitude during care might shift.

She observed that judgment towards patients in these situations, particularly regarding diet options, will lead to less willingness to come in or a sense of fear if they do have to visit the office.

"I often feel like without even knowing it, we pass on an error of judgment, we take these blood sugars, we look at them, and we're like, no, this is kind of high, or you didn't check as much as today," Apperson said. "I try to exercise the utmost discipline to only focus on the positive. And maybe, as we're wrapping up, just find some areas of improvement."

She also mentioned that while her practice expected to have seen a diminishment of patient follow-up visits during COVID-19, patients have maintained follow-up visits.

However, she noted that there have been other factors at play, including an increase in stressors leading to mental health complications.

"I think the biggest thing I have noticed and my colleagues would say the same thing, is just the absolute profound increase in anxiety and depression in our adolescents with type 1 diabetes," Apperson said.

She noted the difficulties of isolation with virtual learning, a lack of mental health providers, and on top of that a chronic disease like Type 1 Diabetes have led to a drop off in adherence with diabetes management tasks.

Apperson also noted the teplizumab approval would be great if it was available, but does not consider it to be the end-all be-all agent.

"My understanding of the way that type one will be ultimately prevented from an immune standpoint is that it's not going to be a single agent, it's going to be like cancer therapy, it's going to be a concoction," Apperson said.

However, she expressed her excitement for the future of innovations in diabetes technology, including offering newly diagnosed patients an automated system for insulin and offering the ability to go through their day with a normal range of blood sugar, noting its positive effect on quality of life.

"With further collaboration between all these pump in sensor companies and widening the collaboration and being able to offer more and more, I'm super excited," Apperson said. "I'm excited about the biological stuff too. But with the technology, if it's not working, or the patient's not tolerating it, you take it off, turn it off, try something else. So I find myself drawn more to what we can offer in the office to a patient, show them a demonstration, get them excited about it." ■

# Dennis Bruemmer, MD: Defining a New Era of Diabetes Care

Connor Iapoco

**AT THE 2021 AMERICAN DIABETES** Association Virtual Meeting, discussions were held surrounding the larger beneficial use of GLP-1 receptor agonists and SGLT2 inhibitors in patients with Type 2 Diabetes (T2D).

In an interview with HCPLive, Dennis Bruemmer, MD, Cleveland Clinic, discussed the use of these agents in patients with T2D at high risk of both cardiovascular and renal complications.

He noted both classes define a new era for diabetes and cardiovascular management, with extended indications ranging from CV event reduction to prevention of chronic kidney disease (CKD).

“The cardiovascular endocrinology spectrum of indications for both classes has been widely expanded,” Bruemmer said. “And as you’re well aware, these are comorbidities that frequently coexist in patients with diabetes. So we can have, essentially two classes of drugs that are quite appropriate for the vast majority of patients.”

Bruemmer also spoke on the possible slow adoption of these agents in the inpatient setting, noting the complications of diabetes management, slow adaptation of new habits for physicians, and

the newness of some of these agents, such as semaglutide.

“I think I think there’s a lot of work to do for us in terms of physician effort, patient education, discussion with payers, politics around medications, and I think time will tell, I think we’re getting better,” Bruemmer said. “And these medications are being used more by additional sub specialties. I think cardiologists, for example, become quite comfortable in writing prescriptions for SGLT2 inhibitors in patients with heart failures, they have taken that on very quickly.”

Bruemmer observed that there is a need in treatment for solving these overarching health problems in the country, including the prevalence of obesity and prediabetes.

He noted that physicians need to be more therapeutically alert and aggressive in controlling risk factors, which will ultimately benefit the patient.

“I think we need to change the way we educate, teach, and feed the nation,” Bruemmer said. “I think we need to aim for better coverage, we need to aim for preventive care and not reactive care.” ■

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# Phil Zeitler, MD: Risk Factor Development in Youth-Onset Type 2 Diabetes

Connor Iapoco

**HIGH RATES OF RISK FACTOR** development, including microvascular complications, were observed in patients with youth-onset type 2 diabetes (T2D) from the TODAY study.

The data was presented at the The Metabolic Institute of America (TMIOA) 2021 World Congress Insulin Resistance Diabetes & Cardiovascular Disease meeting this week in Los Angeles.

In an interview with HCPLive, the presenter of the data, Phil Zeitler, MD, Medical Director, Children’s Hospital Colorado Clinical & Translational Research Center, discussed the original TODAY study focusing on youth-onset T2D treatment, as well as the follow-up observational study on long-term complication rates in these patients entitled the TODAY2 study.

“What we found was very high rates of development of hypertension, dyslipidemia, and that really is despite pretty aggressive protocol driven treatment of risk factors during TODAY,” he said.

“In addition, what we found was a similarly high and increasingly rapid development of nephropathy and an increase in retinopathy from very little and almost exclusively mild retinal disease at the end of TODAY in 2011 to high prevalence and more severe retinal findings five years later, as part of TODAY2,” he continued.

He then went on to note that nearly 80% of the kids in the study developed  $\geq 1$  microvascular complication by 12 years from the time of randomization, which occurred within six months of diabetes diagnosis.

Then, he discussed improving outcomes for these patient populations, including more aggressive therapy for pediatric patients, pushing against the perceived default of treating children with the lowest dose of a drug.

“I think one answer is that we need to push back against the typical pediatric argument that you should treat with lower amounts of drugs, etc,” Zeitler said. “Argue that these kids need, if anything, more aggressive therapy than adults, because they appear to have aggressive onset of complications, at least as bad as the adults, if not more rapid.”

Zeitler noted that more presentations will look at data from TODAY, including topics such as diabetes distress in the population, healthcare usage, and vascular measures, including stiffness.

Additionally, he mentioned a collaboration with DPP and DCCT EDIC in order to compare complication rate outcomes in children with youth-onset type 1 diabetes (T1D) and adult onset T2D.

Lastly, Zeitler touched on the larger public health consequences of increasing rates of youth onset diabetes, noting his work in Denver saw a 50 - 75% increase in T2D diagnoses during the COVID-19 pandemic.

“There’s no sign that this is decreasing, if anything, it appears to be accelerating gradually,” he said. “This is going to have enormous public health implications in the future.” ■



## Paul Sternberg, MD: Perspectives on Step Therapy in Wet AMD Treatment

Connor Iapoco

**ALTHOUGH THERE ARE QUESTIONS** on the rationale behind step therapy, particularly for neovascular (wet) age-related macular degeneration, a recent presentation at the American Academy of Ophthalmology 2021 Meeting aimed to balance how people feel with the rationale behind its use.

In an interview with *HCPLive*, Paul Sternberg, MD, G.W. Hale Professor and Chair, Vanderbilt Eye Institute, discussed his advocacy for step therapy, despite noting there are reasonable reasons to question its use.

“I think that that if it’s properly developed with physician input, that it can be an effective means to treating new vascular macular degeneration, and it can be much more cost effective,” Sternberg said.

He noted one of the critical questions is the definition of failure used, whether that is visual acuity or optical coherence tomography (OCT). For this study, they have chosen visual acuity.

“We choose if patients have not shown any improvement in visual acuity over at least one set of four injections and, and I usually wait

two sets of injections before I make that determination,” he said.

He mentioned that data from the clinical trials show that only about 40% of patients show any significant improvement in visual acuity that means 60% will be the same or worse.

According, he pointed out that compliance with treatment is then a result of a relationship with a patient, regardless if they are receiving step therapy or any other form.

“If we made the presumption that patients are going to stop coming in, if they don’t have improvement, we’d have a heck of a lot of patients that are not compliant with their treatment,” Sternberg said.

Then, Sternberg discussed reduced costs as a result of step therapy, as patients get to start off with the less expensive drug and move up, rather than beginning with the more expensive drug.

“I think that the I personally feel that the kind of global opposition to step therapy is really not well founded,” Sternberg said.

“What’s Wrong With Step Therapy for Wet AMD?” was presented at AAO 2021. ■

# Theodore Leng, MD: Characterizing the Definition, Rates of Intermediate Dry AMD

Connor Iapoco

**IN AN INTERVIEW WITH** *HCPLive*, Theodore Leng, MD, Department of Ophthalmology, Stanford University, discussed his presentation on the natural history disease progression among adults with dry age-related macular degeneration (AMD) in the IRIS registry.

His talk entitled “A Real-World Study of Prevalence and Natural History Disease Progression Among Adults With Dry AMD in the IRIS® Registry,” was presented at the American Academy of Ophthalmology 2021 Meeting.

Leng highlighted the benefit of the IRIS registry in this investigation, with longitudinal data from over 70 million unique patients and 412 million patient visits in the registry, encompassing 70 - 75% of all ophthalmology and retina visits in the United States.

“We wanted to see what the patient journey was for dry AMD patients when they showed up as a mild or intermediate, dry AMD patient,” he said. “Did they progress to advance disease with geographic atrophy or neovascular AMD and how long did that take?”

Then, Leng discussed the findings of the data set, analyzing 645,000 dry AMD patients where 90% of patients had mild to intermediate dry AMD. He noted this data shows that a large proportion of patients with AMD have early stages, which is not a main focus of current therapeutic treatments.

“I think the other major findings are that the probability of maintaining a dry AMD stage, so if you started out as a mild dry or intermediate dry, the probability of staying in that stage on an annual basis was about 80 to 90%, across all the disease stages,” he said.

However, Leng noted that the conversion from mild to intermediate, the rate was over 3 times higher for patients who are intermediate to an advanced stage. At a rate of per 100 person-years of progression to geographic atrophy, data show it was 3 times higher among those with intermediate dry AMD compared to mild dry AMD.

Then, he discussed the visual acuity component of the study,

explaining that visual acuity was shown to get worse faster if you had a more progressive stage of dry AMD.

“If you had geographic atrophy, those patients progress, as far as vision is concerned, more rapidly than those with mild, dry AMD,” Leng said. “And dry AMD progression to geographic atrophy and wet AMD were also faster once you reach the intermediate dry AMD stage.”

As a result, Leng noted that one of the key takeaways that he took from the study included a specific focus on intermediate AMD, as an area of huge unmet need.

“I think addressing the intermediate AMD population is going to be a key target next for us as a specialty, to really develop therapies that can prevent progression or stop progression, maybe even reverse disease in that population, because this study has shown that those intermediate AMD patients are at the highest risk of progressing to worse vision states, as well as more advanced disease states in AMD,” Leng said.

Additionally, Leng spoke on the impact of port delivery systems (PDS) on the future of care and how it will reduce both the treatment burden of patients with monthly injection visits. He also noted it may aid retinal physicians in addressing vision threatening diseases, particularly as the population ages and the bandwidth of clinicians is stretched thin.

“I think having a sustained delivery device, like the port delivery system, is really going to help kind of unload our schedules a little bit so we can care for patients, with other indications and also new therapies that are coming to market,” Leng said.

When looking forward, Leng once more pointed to better characterizing intermediate AMD and narrowing the definition from mild AMD to geographic atrophy by determining those in-between stages.

“I think better characterizing this population will then lead to better studies, both for natural history and for potential therapeutics that are hopefully being worked on by our industry partners,” he said. ■

“We wanted to see what the patient journey was for dry AMD patients when they showed up as a mild or intermediate, dry AMD patient.”

# Not Just the Messengers: Carriers of X-Linked Diseases Can Be Patients Too

Kelli Williams, MD, MPH

**GENETIC DIAGNOSIS OF INHERITED DISEASE**, including many X-linked diseases, has increased dramatically in recent years with more advanced genetic testing options. After a genetic diagnosis is made, family member testing may be warranted. Family member testing can identify those who are carriers of disease, those who may be affected by disease, and add insight and guidance regarding the risk of future offspring being born with the disease. While this has fostered an improved understanding of genetic drivers behind these diseases, most of the medical community has considered the carrier population as simply the messengers of the genetic information, clinically unaffected by an abnormal gene; but we're learning this isn't always the case.

Increasingly, research has found that there are many X-linked diseases in which carriers show signs and symptoms of the disorder, in varying degrees of severity. Historically, these symptoms have gone largely unaddressed by the medical community. Studies show that the often-overlooked symptoms in X-linked carriers may negatively impact their physical and mental health if not properly addressed. A more holistic care approach for X-linked carriers of genetic diseases requires that we look at the carrier population as potential patients, too.

Chronic Granulomatous Disease (CGD) is a good example of this. CGD is a rare, genetic immunodeficiency that increases susceptibility to severe, recurrent and life-threatening bacterial and fungal infections and can produce abscesses in internal organs like the lungs, brain and liver.<sup>1</sup> Sophisticated diagnostic tools employed today, like the Dihydrorhodamine (DHR) assay, can accurately determine if someone has X-linked CGD, autosomal recessive CGD, or is an X-linked carrier of CGD, and also provides a prognosis for the severity of the disease. X-linked carriers of CGD can also present with recurrent skin infections and abscesses and may have DHR test values in the same range as patients with X-linked CGD.

In an essence, they phenotypically can have CGD and the providers who care for them may need to think of them like patients. We now know that DHR values of X-linked CGD carriers may change over time with age, and as a result the risk of serious infections may increase as carriers age.<sup>2</sup> The evolving clinical state of the X-linked CGD carriers demands that they be closely followed by medical providers, so that if and when their disease declares itself, they can be treated appropriately.

Follow-up and close monitoring are particularly important among this population, as case reports and large case series have shown that carriers of X-linked CGD may develop more symptoms as they age. Symptoms can include recurrent infections and abscesses, skin abnormalities (e.g. photosensitive rashes and discoid lupus), autoimmune thyroid disease, abdominal pain and diarrhea, and lupus-like symptoms (e.g. chronic fatigue and joint pain).

The impact of being a carrier isn't just physical – it's psychological, as well, and can greatly impact quality of life (QoL). In a survey of 75 X-linked CGD carriers, more than 40 percent reported experiencing moderate or higher levels of anxiety, which correlated to depression, lower self-esteem, presence of joint or bowel complications, and fatigue.<sup>3</sup> Like in many other diseases, it is well documented that these types of QoL indicators can carry a significant impact of health and quality of life, warranting closer monitoring and care for the carrier populations.

This phenomenon is assuredly not unique to CGD, but likely a consideration across many genetic diseases. It requires a fundamental shift in thinking among not only clinicians, but the entire healthcare team, including nurses, genetic counselors and other allied professionals. Holistic care for inherited genetic disease should involve family testing, identification and proactive monitoring; and disease management guidelines for X-linked genetic diseases should clearly reflect this to improve the care we provide for both diagnosed patient populations as well as the genetic messengers, the carrier patients. ■

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*Kelli Williams, MD, MPH, is a pediatric allergist-immunologist at the Medical University of South Carolina in Charleston, South Carolina, USA. She has cared for many patients and carriers with Chronic Granulomatous Disease (CGD) – a rare primary immunodeficiency that can cause serious, recurrent and potentially life-threatening infections, among other symptoms.*