CENTER FOR PUBLIC HEALTH LEADERSHIP

NATIONAL ASSOCIATION OF CHRONIC DISEASE DIRECTORS
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Additional Participant Questions

1. Can you please talk about issues of patients who achieve the ideal weight, and the insurance (or if change to a new insurance company) does not cover GLP-1 anymore?
    a. Justin – Currently, we don't know much (anything) about this in the context of insurance lapsing or the weight loss itself making individuals ineligible. I'm not aware of any research looking at GLP-1 RAs at maintenance dosages (not sure we know what those would be). However, there is a lot of interest and work looking at maintenance strategies for individuals who lost weight with Rx treatment and wish to maintain with lifestyle. Unfortunately, not a lot of that work has been completed to date. In short, it's definitely an issue, but it need more work before we can make recommendations specific for these patients (relative to individuals who lost weight through lifestyle interventions).

2. What data is there showing that titrating dosage of GLP-1s up slowly up help with side effects and reduce mental health adverse effects?
    a. Kristina - In the initial clinical trials conducted to earn FDA approval for semaglutide and tirzepatide, there was little flexibility around dosing – participants were on a standardized schedule to increase dose monthly and quickly reach the maximum dose to which they had been randomized. However, post-approval real-world studies have shown that, in clinical practice, many patients do not ever reach maximum doses, and uptitration is generally slower. Whether this is due to physicians trying to mitigate side effects, difficulty with getting patients back into clinic with a cadence to match clinical trial visits, patient preference, or dose shortages is unclear. It is likely a combination of all of these factors. I am not aware of clinical trials that have rigorously examined different dose escalation strategies, so for now we can only go on observational research. In my clinical experience, I often slow down uptitration for patients who are experiencing lingering GI upset at a particular dose of medication and this seems to help, but definitely another area where research is needed.

3. Have you taken into consideration the stage of menstruation in women? Have you addressed menopausal women and metabolic changes?
    a. Kristina - There is an active area of research focusing on the potential mediating effects of estrogen on the effectiveness of GLP1s. I am not involved in this research but if you are interested, I would suggest looking into publications by Matthew Hayes' group at UPenn. Here, also, is a link to a review article on sex differences with respect to GLP1 response: https://pmc.ncbi.nlm.nih.gov/articles/PMC11733500/. This line of work was initiated because it has been observed that reproductive-aged women seem to lose more weight on GLP1 medications than men.

4. Are people with gall bladder stones not a good candidate for GLP-1 medications?
    a. Kristina - Rapid weight loss (whether mediated by glp1-ra use, lifestyle change or bariatric surgery) increases risk for gallstone formation and cholecystitis. On top of this, GLP1-RA use seems to further increase the risk, perhaps due to impacts on reduced gallbladder contractility. I don't routinely screen patients for gallstones before starting a GLP1 medication, but if patients describe symptoms of biliary colic once on one of these medications (or in any weight loss program), it is a good idea to send them for an ultrasound to look for stones, and then, if needed, refer to surgery for evaluation for cholecystectomy.

5. Are the medications expensive to make? Or are they artificially high?
    a. Justin – All evidence suggests that these medications are expensive in the US due to market inflation that is not shared by other high-income countries. Some of this is due to America's willingness to pay, and the dire need for these drugs in the US relative to other high-income countries where they are less expensive (e.g., Japan). The other reason is the government's reluctance to negotiate drug prices collectively (think insulin) or to regulate pricing. These drugs are indisputably expensive to develop, but most of the 20+ year development pipeline research was funded by the US National Institutes of Health and subsidized by universities (e.g., the government doesn't build university labs, state taxes and private university endowments do that). As such, my person opinion is that they pharmaceutical companies are making

as much money as possible before generic versions are available in years to come and drug-specific profits fall.