Revolutionizing Weight Management and Diabetes Care

Part 1: THE GLP-1 MEDICINES IN 2025

Part 2: THE IMPORTANCE OF CLINICAL TRIALS

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Part 1: The GLP-1 Medicines in 2025

When people ask me what I do and I tell them I direct clinical research studies they're often surprised, "Aren't you a physician?" I don't blame them for the confusion; the role of clinical trials in medicine isn't discussed much. Yet most of us take medications as prescribed, forgetting each one of those drugs had to be studied for efficacy and safety before it was available for human use. Meticulous, real world clinical trials are essential to confirm scientific hypotheses, bench research and humane animal studies prior to human use. Clinical trials are the critical step in bringing FDA-approved, safe, useful medications to all of us! Yet many people do not understand the immense value of medical research studies in making new therapies possible and are unaware of opportunities to participate in clinical trials right here in Marin.

For example, let's talk about the tidal wave of interest in the GLP-1 "Wonder Drugs" for weight loss. How did the GLP-1 drugs get to celebrity status and what more do we need to know?

As an endocrinologist and clinical researcher here in Marin since the mid 1980's, I was a primary investigator in early research trials on the first drug in the GLP-1 class, approved and introduced in 2005, as a treatment for type 2 diabetes. I continue this work in 2025. Here's why…

THE FIRST GLP-1 DRUGS FOR PERSONS WITH DIABETES IN 2005

The whole notion of "gluco-regulatory" hormones produced in the normal gut was a revolutionary concept 40 years ago. Then an exciting discovery was that there were **hormones secreted in the gu**t called gluco-regulatory-peptides (GLPs) that were critically involved in metabolism and the utilization of glucose as fuel. These hormones were excreted in response to signals around eating and assisted insulin in keeping glucose levels stable after a meal and getting glucose from the gut into the cells of muscle, liver and other vital tissues. The GLP-1 drugs were developed to be look-alike compounds that could occupy receptors for naturally occurring GLP hormones and mimic their effects. They could lower blood glucose after meals by reducing gastrointestinal motility, limiting stored glucose release from the liver, and assisting insulin secretion from the pancreas. But the unanticipated effects were on the brain, markedly regulating the appetite center causing sensations of fullness and consequently weight loss. Without careful clinical research on thousands of people in real world clinical research studies, these effects might not have been realized so quickly.

Other GLP-1 drugs emerged rapidly as two more decades of simultaneous clinical studies

confirmed lowering the A1C in persons with type 2 diabetes and longer-term clinical studies showed additional benefits of highly significant weight loss, reductions of major adverse cardiovascular events (MACE), kidney disease (24%), and all-cause mortality (12%)! Recently trial results have confirmed benefits on sleep apnea and chronic kidney disease as well leading to further recent FDA approved indications for use.

THE EMERGENCE OF THE MAJOR GLP-1 MEDS FOR PERSONS WITHOUT DIABETES

Further research studies in individuals with overweight conditions who did **not yet** have diabetes showed even greater reductions in weight and adverse cardiovascular events leading to the emergence of the major GLP-1 meds now approved to treat obesity and overweight conditions in both people with type 2 diabetes and in persons without diabetes who are overweight and also have some cardiovascular risks.

Clinical research has shown the previous "eat fewer calories and exercise more" advice of the past three decades is wholly inadequate for treating significant weight disorders in most people. Regaining weight lost by just "dieting" or "starving" has been almost universal and frustrating for patients and their practitioners for years. We now see obesity not as patient failure or "non-compliance," a frequent erroneous diagnosis, but rather as a very complex chronic medical disease which can finally be treated successfully in many individuals by addressing underlying hormone imbalances in the GLP-1 gut hormone levels using the GLP-1medications and this can be achieved safely with an acceptable risk profile of adverse effects.

Part 2: THE IMPORTANCE OF CLINICAL TRIALS

The worldwide population that might benefit from the GLP-1 drugs is staggering. Without the crucial studies of the past three decades which is summarized in the November 2024 issue of Diabetes Care, we would not have the GLP-1 "Wonder Drugs." Kudos to the thousands of scientists, researchers, medical workers, monitoring institutions and patients for pursuing this transformative work!

At NorCal Medical Research, formerly Marin Endocrine Care and Research, in Greenbrae, we have conducted hundreds of protocols for over three decades. Our focus has been diabetes management and cardiometabolic compounds such as statins and anti-hypertensives, as well as many weight management studies using other drugs. The recent GLP studies have been most exciting in terms of their impressive benefits of dropping A1C into goal range, reversing diabetes and pre-diabetes in many, achieving weight loss of 10 to 30+ pounds and also improvements in blood pressure, chronic kidney disease, exercise tolerance, sleep apnea, osteoarthritis and other conditions. We are also conducting long-term (5 year) cardiovascular outcome studies on some of the already approved drugs in this class. We are grateful to be part of the emerging new GLP-1 and gluco-regulatory hormone drug story to learn more, and to improve options and availability for people with overweight, obesity and associated metabolic disorders of pre-diabetes, diabetes and cardiorenal risks. It's important that the community recognizes the vital need for clinical research and consider finding out more about their opportunities to participate.

Participants in well conducted clinical trials may benefit directly from the investigational product itself, as well as from the nutritional, exercise and lifestyle counselling that may be part of the protocol. No medical insurance is required, and personal identity and results are highly protected by codes. There is no cost to a participant in a clinical research study. Labs, medical visits, monitoring, and study drugs are free, and stipends are usually provided for patient travel and time.

Protocols are very carefully explained to interested persons as well as the possibility of receiving placebo (inactive comparators) in some study protocols as part of detailed and closely independently monitored Informed Consent procedures. Investigator physicians can communicate results with primary care practitioners as requested. In addition, many study participants enjoy the satisfaction of knowing that they are contributing to the body of international medical knowledge that may benefit others globally.

WHAT DO WE STILL NEED TO KNOW THAT WE MIGHT FIND OUT FROM CLINICAL STUDIES ON the GLP-1s?

- How **durable** are the results and what will happen if people discontinue use after some time?
- How about the results from **combinations** of GLP-1 meds with other glucoregulatory hormones that have since been discovered like GIPR, glucagon, amylin and others. Will they yield even better results? Will the side effects be reduced?
- Can we develop safe and effective **oral** preparations?
- What is the **long-term safety** profile of these preparations? Will they be found to have serious adverse events over time?
- Can new formulations **improve tolerability,** especially reducing the gastrointestinal side effects that some 50% of people experience on these meds?
- What about preservation of **lean body mass** and avoidance of **muscle wasting** (sarcopenia)?
- Will this group of drugs be useful to treat **other conditions**, like addictions, neurologic diseases?
- What about safety in **other populations**, children, adolescents, the elderly, hospitalized persons?
- Are cheaper **compounded products** effective? Safe?

We are confident that an **expanded choice** of effective GLP-1 medications will drive the **cost** of these drugs down so that their full potential can be realized globally.

There's a lot more work we must do together as a medical community, but our success depends on the generous participation of patients in these very meticulous, medically monitored clinical trials.

We're very excited to be screening people now for two new GLP-1 type weight loss studies. Please visit our **website** at NorCalMedicalResearch.com for more information on participation, sign up for our Newsletter and follow us on Facebook, LinkedIn and Next Door.