“Breakthrough” treatments that we don’t really need (part four)

I couldn’t resist. Rather than leave these candidates for *“Breakthrough treatments that we don’t really need”* on the cutting room floor, I’m sallying forth with yet another (hopefully final!) installment.

The premise is that seemingly not a week goes by that we’re not regaled with news of a “game-changer” treatment—*beware of that word in health reporting!*

Each so-called breakthrough promises deliverance from one or another health peril—some real, some newly concocted. Most of these are expensive, and come with an array of harrowing side effects. The only true beneficiaries may be private equity investors who gamble on speculative medical start-ups.

Plus, fixes are often of marginal efficacy. Isn’t it time that we hit pause on our headlong rush to “progress” and call instead for refocusing on safe, reliable, economical solutions predicated on root causes?

So here goes:

Yet another anti-depressant drug?: The website for LifeStance Health, an online

purveyor of telemedicine psychiatry, heralds:

"Exxua represents a promising new antidepressant for Major Depressive Disorder (MDD) with a unique mechanism of action targeting the glutamatergic system . . . Potential benefits of Exxua include enhanced efficacy, a potentially faster onset of action, and a different side effect profile compared to traditional antidepressants . . . The FDA's 2023 approval of Exxua signals a significant milestone in this journey, potentially offering fresh hope for individuals who have found limited success with existing medications."

Indeed, Major Depressive Disorder (MDD)—in contrast to milder forms of the Blues—is notoriously hard to treat; even with the latest pharmaceutical options, the majority of patients achieve minimal relief of symptoms. MDD is said to afflict 8% of the U.S. population—21 million individuals.

Many patients hate the side effects of current drugs, which include sexual numbing, weight gain, and overall flattening of mood.

But is Exxua the breakthrough it's touted to be? It's worth examining Exxua's checkered development history.

Exxua (gepirone) is not new, according to a review published in *Pharmacy Times*. It was originally formulated in 1986 as a treatment for anxiety and depression. It knocked around attempting to gain approval until 1999, when the FDA denied its application *"due to a failure of the sponsor to provide 2 positive and well-controlled trials."*

Then followed two decades of equivocal trials resulting in more rejections from regulators, until a series of appeals and amended trial submissions culminated in Exxua's approval by FDA in 2023.

But of concern, according to *Pharmacy Times*, is "the number of negative trials, *which did not demonstrate benefit*." As with other drugs offering meager benefits to sufferers of challenging conditions:

"Supporters of gepirone argue that denying approval would send a negative message to drugmakers that could discourage further research and development, which could impact patients with unmet needs." In other words, even if it doesn't work that well, at least it's something!

Should pharmaceutical companies be awarded "participation trophies" like kids who fail to win athletic competitions?

Exxua blunts sexual responses less than commonly prescribed SSRIs, but has its own problems: Common side effects of gepirone are dizziness, nausea, light headedness, and QT prolongation.

A recent guest on *Intelligent Medicine*, U.K. psychiatrist Mark Horowitz, author of The Maudley Deprescribing Guidelines, decried U.S. over-reliance on long-term prescriptions of psychiatric medications. Recommendations from the National Health Service encourage mental healthcare practitioners to limit the duration of drug interventions for depression and anxiety, favoring low-cost lifestyle measures and counseling instead.

Overweight? Put a sock in it! Like Exxua, the EndoBarrier has experienced a bumpy regulatory history. It's a plastic sleeve that, when embedded in the small intestine, acts as a barrier to absorption of nutrients. The device looks like an

elongated clear plastic bag with hooks for attachment. *What could possibly go wrong?*

Billed as a cheaper and reversible alternative to gastric bypass surgery, the EndoBarrier is designed for temporary implantation over a period of up to 12 months. It produces dramatic weight loss, with documented improvements in blood sugar control and cardio risk.

But, as one might expect when attempting to fool Mother Nature, there are safety concerns. U.S. approval trials were set back in 2015 when patients experienced hepatic abscesses and GI bleeding. Trials have been resumed and proponents of EndoBarrier exude optimism over greenlighting stateside:

"It's not a dangerous device . . . the international data from the EndoBarrier worldwide registry suggest that the likely benefit of EndoBarrier treatment outweigh the risks."

But even if it eventually gains approval, EndoBarrier will likely only occupy a narrow niche between more definitive gastric bypass surgery and the ever more effective suite of popular new weight loss drugs.

Giving booze to alcoholics: A new program in San Francisco seeks to relieve the burden on emergency services by giving homeless alcoholics limited quantities of alcohol. The rationale is that, without a reliable source of booze, they might undergo withdrawal, requiring costly hospital admission. Like clean needle programs and consecrated places where addicts can obtain unadulterated drugs and safely shoot up, it's called "harm reduction".

It's said that this program has reduced pressure on city hospitals; but for a determined alcoholic, when was just *one shot* of vodka enough?

The high blood pressure shot: It's true that some people don't achieve optimal blood pressure control even with three or four medications; alternatively, many who most urgently need hypertension treatment can't be relied upon to take their medication regularly.

Enter the twice-yearly high blood pressure shot. *Healthline* reports:

"A new drug called zilebesiran may help lower blood pressure for as long as 6 months with just one injection."

They say it's dramatically effective, and produces few side effects other than injection site reactions. But I worry about the irreversibility of a long-acting shot. It's one thing to discontinue a blood pressure drug if the first dose makes you woozy; what if zilebesiran makes some users' heads swim for months on end until its effects wear off?

AI chatbots to supplant doctors: Artificial Intelligence is all the rage; according to *Scientific American*:

"Some researchers predict that within the year, a major medical center will announce a collaboration using LLM [large language model] chatbots to interact with patients and diagnose disease."

Tech start-ups are already vying for a potentially lucrative market. For example, docus.ai, scheduled to launch this July, promises consumers:

"Docus AI Doctor can be your first step toward an accurate diagnosis . . . Docus.ai

is an all-in-one diagnosis tool . . . If you have a Docus.ai subscription, you'll be able to use our Dr chatbot anytime, anywhere, and ask as many questions as you want."

A credulous media has hyped a recent study with headlines like: "The AI will see you now: ChatGPT provides higher quality answers and is more empathetic than a real doctor, study finds"

But a closer look reveals that the study did not rate ChatGPT answers for *accuracy*; moreover, the more comprehensive explanations regurgitated by AI lent the responses a misleading aura of "empathy" compared to doctors' curt answers.

There's even a danger that users might trust unreliable AI Chatbots *too much* because of their seeming authoritativeness; by comparison, try as I might, I can't replicate a chatbot's feat of regurgitating entire paragraphs of Harrison's Textbook of Medicine verbatim in answer to a patient's query.

AI developers have yet to tackle a fundamental flaw with LLMs: they "hallucinate", sometimes confabulating answers from entirely made up sources!

Robodocs are certain to quash innovation, too; medical LLMs are trained on orthodox medical texts and studies not congenial to integrative solutions.

BOTTOM LINE: While AI might help doctors crunch enormous quantities of disparate lab results, path findings, radiological images and clinical data, it'll be a long time before it supplants the judgment of seasoned physicians.

For a look at previous iterations of "Breakthrough treatments that we don't really need", see Part One, Part Two, and Part Three.

Be on the lookout for more useless "breakthrough" candidates—send us your suggestions via questions@drhoffman.net