# RETHINKING EARLY-PHASE CARDIOMETABOLIC DEVELOPMENT

From endpoints to execution

# Foreword

Progress in cardiometabolic research is rarely driven by a single study or dataset. It comes from understanding complex physiology, integrating diverse sources of evidence, and translating mechanistic insight into clinical decisions that genuinely change outcomes. Over the past decades, we have seen how rapidly the field can advance when scientific depth is paired with disciplined early phase execution — and this collection reflects that evolution.

Cardiometabolic development presents a unique challenge: multiple organ systems interacting simultaneously, heterogeneous patient populations, and endpoints that require both precision and clinical relevance. Across the industry, teams are re evaluating how early phase studies should be designed and delivered — how to characterise metabolic pathways more accurately, how to capture subtle pharmacodynamic signals, and how to generate data that regulators can rely on when assessing safety, efficacy, and long term risk.

A consistent theme running through this work is the importance of integrated early phase strategy. When clinical pharmacology, biomarker science, laboratory analytics, and regulatory insight operate in isolation, critical connections are lost. But when these disciplines work together — aligned from first in human through proof of mechanism — development becomes more efficient, more predictable, and more scientifically grounded.

This lookbook brings together perspectives from across the cardiometabolic continuum: metabolic phenotyping, biomarker strategy, clinical study design, and the operational frameworks required to run complex early phase trials with confidence. Each contribution highlights a practical way to strengthen decision making and reduce uncertainty in an area where clarity is often hard won.

For researchers, developers, and clinical leaders working to advance the next generation of cardiometabolic therapies, the message is clear: when scientific insight and operational excellence are integrated, progress accelerates. The tools and approaches outlined here are part of that acceleration.

*Thomas Forst*

## MEET THE AUTHOR

**Professor Thomas Forst, Chief Medical Officer, hVIVO**

Professor Thomas Andreas Forst is a board-certified physician in internal medicine and endocrinology with more than 30 years of experience in cardiometabolic research. He began his scientific career at the German Diabetes Research Institute and later held academic and clinical roles at the Johannes Gutenberg University Mainz, where he continues to contribute to medical training. Thomas has held senior positions at Eli Lilly, the Institute for Clinical Research and Development, and the Profil Institute Mainz, and has served as CMO at Clinical Research Services Germany. He has contributed to more than 300 clinical trials across obesity, metabolic disease, diabetes, lipid disorders, and cardiovascular disease, and is an active member of major diabetes associations. He has authored over 300 peer-reviewed publications and serves as Associate Editor of Endocrinology, Diabetes & Metabolism.

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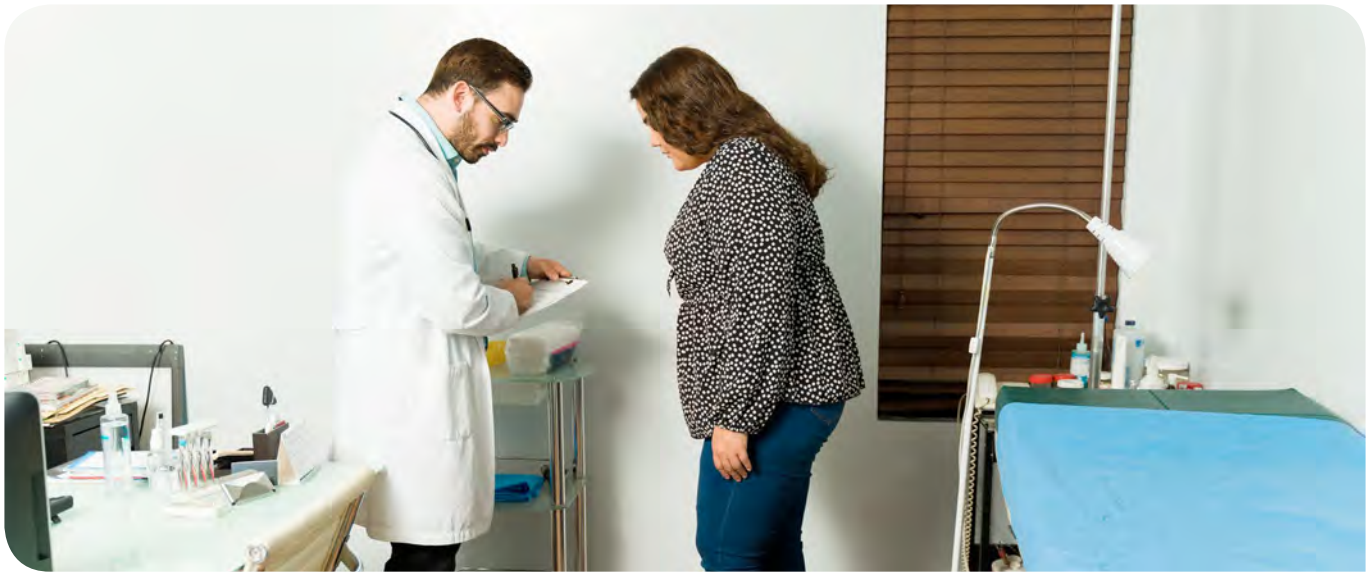


# Redesigning Obesity Trials for a Chronic Disease Era

**For much of its history, obesity research has occupied an awkward space within clinical development. Too medical to dismiss outright, yet, too entangled with lifestyle narratives to command the same seriousness as closely linked conditions like cardiovascular disease or diabetes, it has often been studied through a narrow lens – short trials, blunt endpoints, and a lingering assumption that weight loss alone was the outcome that mattered.**

That framing is now under sustained pressure. The rapid rise of GLP-1 therapies has transformed expectations of efficacy, and forced a broader reckoning with how obesity is understood, measured, and studied.

"Obesity is a chronic disease," says Professor Thomas Andreas Forst, chief medical officer at hVIVO. "It's a malignant disease and it drives a lot of other comorbidities like diabetes, fatty liver disease, hypertension, and lipid disorder – all together increasing the morbidity and mortality of these patients."

For contract research organisations (CROs) like hVIVO, that shift extends beyond simple semantics. It changes what a viable trial looks like. How long a study needs to run, what endpoints carry weight with regulators and payers and, critically, how patients experience participation – all areas where trials evolve along with our understanding of the disease. As such, obesity studies have begun to resemble the long, ethically complex trials more commonly found in the cardiometabolic space, including all the operational consequences that entails.

As Forst puts it, measuring weight loss on its own is no longer sufficient, particularly in a rapidly saturating market like GLP-1s. "If you develop a new drug and you see you lose body weight, that's fine," he explains. "But then everyone says, 'yes, we have other drugs doing exactly the same thing – what is special about your drug?"

That question now sits at the heart of obesity trial design.

## Retention, placebo, and the visibility problem

Retention has always been a central concern in long-term studies, but obesity trials present a particular challenge. For those assigned to receive the drug candidate in question, the effects are visible, rapid, and often dramatic, and participants do not need a medical degree to decipher whether or not something is happening. "They see others lose 10%, 15%, 20% of their weight and nothing happens with them," Forst says. "So, it is clear in the studies who's taking placebo and who is not."

In practical terms, that visibility erodes one of the foundational assumptions of placebo-controlled research. Even when formal blinding remains intact, experiential unblinding can quickly derail a study.

Consequently, CROs find themselves navigating a narrowing path. On one side sits the need for robust comparative data. On the other, a growing ethical discomfort with keeping patients on placebo for extended periods when effective therapies exist.

"In type 2 diabetes, it's no longer possible to run these kind of endpoint studies against placebo," Forst notes. "You want to treat patients for years with placebo while we have other drugs where we know they are cardioprotective – this is not possible anymore."

Obesity is moving in the same direction. Early cardiovascular outcomes data is already reshaping expectations and, with each new signal of benefit, the ethical justification for prolonged placebo exposure becomes harder to sustain. Some sponsors have responded by building extension phases into their programmes, allowing placebo participants access to the active drug once the core study concludes.

"If the core trial is completed, then everyone can get the real drug," Forst explains. "This is motivating some of the people."

That approach can help, but it also adds layers of complexity, requiring longer commitments, additional resourcing, and more demanding logistics. Retention, in this scenario, is increasingly bound up with study design itself.

## Redesigning obesity trials in real time

As the limits of placebo-controlled obesity trials come into sharper focus, alternative designs are gaining attention as potential replacements. Among them, active comparator studies and putative placebo approaches.

The logic behind these options is relatively straightforward, even if the execution is not. Rather than randomising patients to placebo, new therapies are compared against already approved treatments. Historical placebo data from earlier trials is then used to reconstruct a comparator arm through statistical matching.

"What we now do is we compare the new drug against an already registered drug that has done a placebo-controlled study," Forst says. "You can bring this data together and do some matching [...] We call that putative placebo."

The method itself is not new. Putative placebo designs have been prominently used in diabetes research for cardiovascular endpoint evaluation since the early 2000s. However, in obesity, it marks a significant departure from past practice.

From a CRO perspective, the implications are substantial. Putative placebo approaches are highly dependent on data quality, compatibility of inclusion and exclusion criteria, and careful alignment of endpoints across studies that were never originally designed to speak to one another.

"This is a complex statistical method," Forst acknowledges. "It's not against placebo groups, it's against single patients in the other database, which fit with the inclusion and exclusion criteria."

The burden does not end there. As therapies improve, demonstrating differentiation becomes even more complex. Superiority against an active comparator is now the gold standard, but achieving it often requires longer trials, larger populations, or highly specific endpoints.

"The best thing you can show is superiority against the active comparator," Forst says. "But the drugs are becoming better and better. Then, you need longer time periods, maybe five years instead of three, or more people in the studies."

## Reflect the whole patient, not just the scale

As trial designs evolve alongside our understanding of disease, so too does the question of what obesity studies are actually trying to measure. The options, Forst notes, are numerous; while weight loss remains a visible and meaningful outcome, it is only scratching the surface.

The use of BMI, in particular, has come under sustained criticism for oversimplifying the efficacy of a weight loss medication. As Forst explains, while BMI does correlate with risk at a population level, it tells clinicians little about vital metrics such as fat distribution, metabolic health, or individual vulnerability.

"BMI has an association with elevated risk, but it's not the best marker," Forst says. "It doesn't tell you about the kind of adipose tissue you have and the distribution."

The distinction matters. Visceral and ectopic fat carry far greater cardiometabolic risk than subcutaneous fat, yet, BMI doesn't differentiate between the two. Consequently, there is a risk of treating patients who look unwell, but who are metabolically stable, while missing others whose risk is higher, but less externally visible.

"We treat obese people who do not have a problem from a medical aspect," Forst explains, "and, on the other side, we miss people to treat who do not look obese."

Long-term outcomes complicate matters further. GLP-1 therapies have proven highly effective, but they are not curative, and lean muscle mass can be lost alongside adipose tissue. This means that patients who opt to discontinue treatment often experience weight regain, and not all tissue returns equally.

"A lot of people think that they can reduce their body weight, and when they reach the level they want, they can stop it. But in most cases, it doesn't work because they have weight gain again," says Forst. "This is not very good because during this treatment phase you lose weight, you lose adipose tissue, and you lose muscle tissue. And then, if you stop treatment and increase weight again, it's mostly adipose tissue."

Repeated cycles of loss and regain can risk leaving patients both obese and sarcopenic – a combination with serious functional consequences. It is one reason why Forst emphasises that lifestyle factors, particularly resistance training and protein intake, continue to matter, even in the era of highly effective pharmacotherapy.

Yet, the most striking insights are not always captured in traditional endpoints. Forst recounts a patient describing a constant "food noise" that dominated her waking hours, only disappearing after her first injection. Compared to the clear numerical and scientific evidence famous in clinical research, this anecdote is easy to overlook, but it highlights a core challenge in obesity research: appetite regulation, mental load, and quality of life influence adherence, retention, and long-term outcomes in ways the scale cannot capture.

## Shaping the next phase of obesity research

The pace of change in obesity research has been striking. New mechanisms, combinations, and targets are emerging faster than the field's traditional trial frameworks were built to accommodate. But, for Forst, this is part of what makes obesity such a rich landscape for research.

"It's fascinating how fast we are learning things that we had not even considered a couple of years ago," Forst says. "I'm absolutely convinced that we are at the very beginning."

Obesity trials are becoming longer, more complex, and more ethically scrutinised. They demand careful design, sustained patient engagement, and endpoints that speak to regulators, payers, and patients simultaneously. For CROs, the challenge is not simply to keep up, but to help shape how evidence is generated in a field that is redefining itself.

As obesity continues its transition from a marginalised condition to a core focus of metabolic medicine, the trials that underpin its therapies will need to reflect that seriousness.

"It's about becoming healthier. That's the important thing," explains Forst. "We now have the first studies with semaglutide in place, where it's also shown that for obese people you reduce the risk of cardiovascular events by 20%.

"It's not only making obese people leaner, it's treating a very, very malignant and dangerous disease; making really ill people much healthier."

# Q&A: Rethinking Obesity, GLP-1s, and the Future of Metabolic Care

**Obesity research is evolving quickly, and few areas have moved faster than incretin based therapies such as GLP 1 receptor agonists. To explore what this means for patients, drug developers, and the broader cardiometabolic landscape, we spoke with Professor Thomas Forst, Chief Medical Officer at hVIVO. In this conversation, he discusses the real drivers of obesity related disease, the promise and limitations of GLP 1s, and why a more nuanced understanding of fat biology is reshaping the field.**

## Q: When you look at the current obesity landscape, where do you see the greatest unmet need?

**TF:** We've learned that obesity is not simply a matter of excess weight. It's a complex, progressive disease with serious medical consequences. People living with obesity face elevated risks of type 2 diabetes, cardiovascular disease, heart failure, sleep apnoea, and even certain cancers. These complications are what drive morbidity and mortality—not the number on the scale.

Because of that, the need is twofold: we need therapies that meaningfully address the underlying metabolic dysfunction, and we need approaches that reduce the burden of these comorbidities. That's where the field has made real progress over the last decade.

## Q: GLP 1 receptor agonists have become central to that progress. What makes them so impactful?

**TF:** GLP 1s originally emerged as treatments for type 2 diabetes, and their weight lowering effects were almost a bonus discovery. Over time, we've seen that these drugs do far more than reduce appetite or body weight. They improve metabolic health in a broad sense.

Clinical studies have shown reductions in cardiovascular events, improvements in heart failure outcomes, benefits in renal disease, and positive effects on conditions like sleep apnoea. And importantly, these benefits extend to people with obesity even when diabetes isn't present.

So while the public conversation often focuses on weight loss, the real story is that GLP 1s help correct the metabolic disturbances that make obesity such a dangerous disease.

## Q: You've said before that "not all fat is equal." What do you mean by that?

**TF:** Body weight and BMI are crude measures. They tell us very little about the biological processes that actually cause harm.

The real issue is where fat is stored and how that fat behaves. When fat accumulates in places it shouldn't—like the liver, heart, pancreas, or skeletal muscle—we call it ectopic fat. This type of fat is metabolically active in the worst way: it promotes inflammation, secretes harmful adipokines, and disrupts normal organ function.

Ectopic fat is a much stronger predictor of cardiometabolic risk than BMI. Measures like waist circumference, waist-to-height ratio, or waist to hip ratio often tell us more about a patient's risk profile than weight alone.

So, when we talk about treating obesity, we're really talking about reducing this dysfunctional fat and the inflammatory environment it creates.

## Q: Given that complexity, are GLP 1s a complete solution?

**TF:** They're powerful tools, but they're not the whole answer—and they were never meant to be. GLP 1s are part of a broader class of incretin based therapies, and the field is already moving toward dual and triple agonists, as well as oral small molecules that target multiple pathways simultaneously.

These newer agents may offer even greater metabolic benefits, but none of them replace the fundamentals. Lifestyle modification still matters. Physical activity and nutrition remain essential, especially because weight loss—whether drug induced or not—can lead to loss of muscle mass. Preserving muscle is critical for long term health.

So it is always a combination of pharmacology and lifestyle, not one or the other.

## Q: What should drug developers keep in mind as this therapeutic landscape expands?

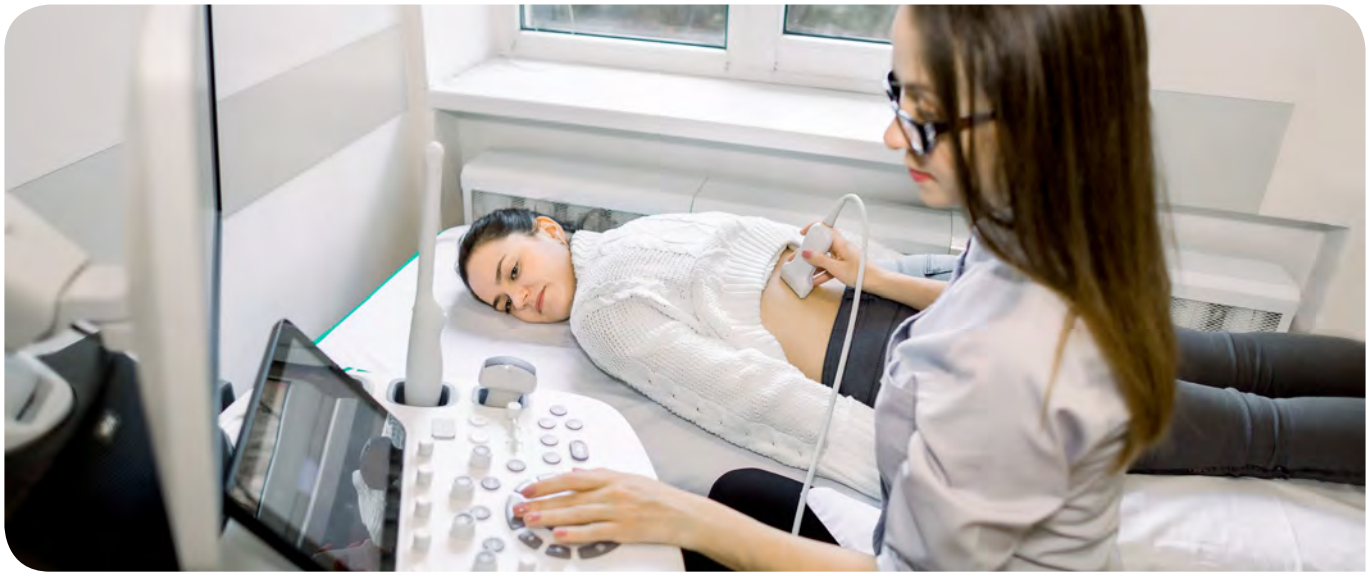
**TF:** The science is advancing quickly, but the underlying biology hasn't changed. Obesity is a metabolic disease with many downstream consequences, and the most successful therapies will be those that address the full spectrum of those complications—not just weight.

At hVIVO, we've spent years working in this space, helping sponsors understand how these drugs behave in early phase studies and how to design programmes that capture the right signals. The more we learn about fat biology and metabolic dysfunction, the more targeted and effective these therapies can become.

## Q: Any final thoughts for clinicians or researchers watching this space?

**TF:** We're entering a new era in obesity care. GLP 1s opened the door, but they're only the beginning. As more advanced incretin based therapies emerge, we'll have opportunities to treat not just obesity itself, but the full constellation of diseases it drives.

But even with these innovations, we shouldn't lose sight of the basics. Medication works best when paired with lifestyle changes that support metabolic health. That combination—science plus behaviour—will deliver the best outcomes for patients



# Obesity, Complexity, and the Lab: What 2025 taught us, and what comes next

**In recent years, we observed significant shifts in how obesity and cardiometabolic diseases are studied in early-phase research. Science is advancing, but the complexity of working with this patient population continues to challenge traditional trial design. The focus is no longer just on speed. It is on precision, reproducibility, and clinical relevance.**

Laboratories are no longer peripheral. They are central to modern clinical development - enabling earlier decision-making, more accurate endpoints, and better alignment between mechanism and outcome. This role became especially clear over the past year.

## What we observed in 2025: Labs are accelerating early-phase development

We saw more sponsors adopt parallel trial designs, combining elements of Phase I and II to reduce timelines. In metabolic disease, this increasingly includes the early introduction of patient cohorts – sometimes even in first-in-human studies, where traditionally only healthy volunteers were enrolled. Regulatory authorities and ethics committees are encouraging this shift, provided the infrastructure and safety protocols are in place.

Laboratories must be equipped to support this complexity. Imaging tools for reliable assessment of body composition and energy expenditure combined with validated metabolic laboratory assays like adiponectin, leptin, ghrelin, visfatin, but also inflammatory markers such as IL-6, TNF-alpha, or miRNAs, are becoming of essential interest. Without them, it is difficult to meet the expectations of both regulators and sponsors.

## Obesity trials are becoming more precise

The primary endpoint is no longer just weight loss. In 2025, the focus shifted to understanding what kind of weight is lost (fat versus muscle), fat distribution (ectopic versus subcutaneous) – and how that affects obesity driven comorbidities. This distinction is of important clinical relevance. Preserving lean mass is critical, especially as new therapies begin to influence energy expenditure in addition to food intake.

Answering these questions requires objective measurement. Imaging, metabolic profiling, and reproducible lab methods are necessary to generate data that can support regulatory and clinical decisions.

## A broader view of patient care

GLP-1 receptor agonists and incretin based treatments have shown to be effective in reducing body weight, improving glucose metabolism, and offering cardio-renal protection. With all these new therapeutic achievements in place, there is still a high need to develop new drugs. Not all patients react in the same manner; patients will achieve weight regain after stop of treatment, and body composition may underly significant redistributions. Patients require structured support – including high-protein diets, resistance training, and behavioural guidance – to maintain results and avoid muscle loss.

We observed that patients on these therapies often begin to make healthier food choices and change their overall lifestyle behaviour. However, this effect is not stable without reinforcement. For this reason, structured patient guidance and support is always part of the protocol and treatment, rather than treated as optional.

## Recruitment is more complex

Inclusion criteria are becoming stricter, particularly in comorbid populations such as those with cardiovascular comorbidities or MASLD. This makes recruitment more difficult. We have addressed this by expanding our patient database and strengthening our referral network with local physicians and specialists.

The goal is not only to find patients, but to find the right patients – those who best fit the study criteria and can generate meaningful data. Lab-enabled screening and structured data capture are essential to this process.

## What we expect in 2026: Personalised trial design will advance

We expect more trials to be stratified by phenotype, comorbidity profile, or predicted drug response. This is not gene therapy. It is a practical approach to matching patients with the drugs mode of action. As more therapies enter development – some targeting liver disease, while others focus on muscle preservation, or cardio-renal protection – this level of precision will become more and more critical.

This trend will extend beyond addressing body weight or body mass index. Infectious disease, immunology, and oncology will also require more personalised trial designs. Laboratories will play a central role in enabling this shift – not only by supporting biomarker-driven stratification and endpoint selection, but by providing the infrastructure to measure complex, multi-system responses with consistency and precision.

## Endpoints will expand

Weight loss is not enough. Sponsors will need to demonstrate muscle preservation, metabolic improvement, and behavioural sustainability. This will require new endpoints, new assays, and longer follow-up periods.

We expect more trials to include imaging, metabolic panels, and longitudinal data collection. These methods are already in use in obesity trials and will likely be adopted in other therapeutic areas where body composition is relevant.

## Multi-agonist therapies will increase complexity

GLP-1/GIP/glucagon combinations are already in development. These therapies affect multiple biological pathways and require more sophisticated trial designs. Measuring satiety, lipid metabolism, and hepatic function in parallel is not simple. It requires coordination between clinical and laboratory teams.

This complexity is not limited to obesity. As combination therapies become more common, the need for integrated lab support will grow across multiple indications.

## Patient support will be required

We expect more trials across the cardiometabolic sector to include structured patient support – including nutritional coaching and behavioural guidance – as part of the standard study protocols. This is not only an ethical consideration. It is necessary for efficacy, especially in chronic conditions where long-term outcomes depend on sustained behaviour change.

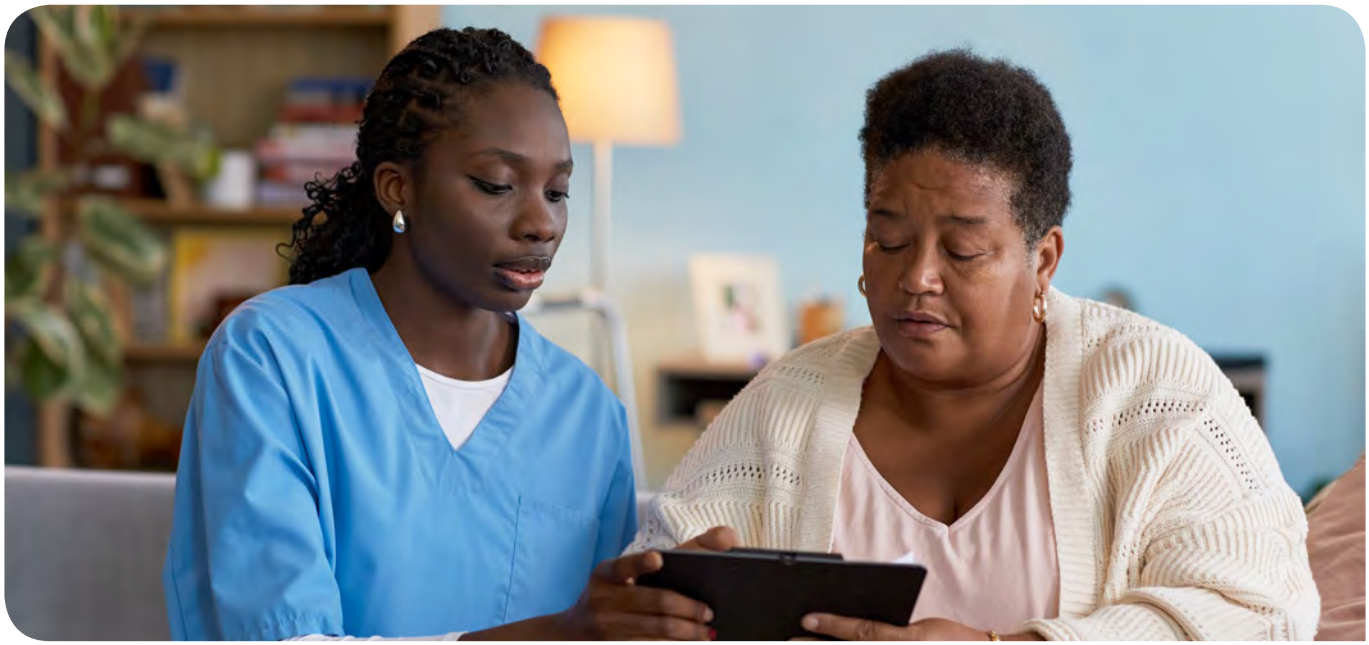
## Placebo-controlled trials will be reconsidered

In long-term studies involving effective therapies, placebo arms are becoming harder to justify. We expect more trials to use active comparators, supported by statistical methods that allow indirect comparison to historical placebo data. This change will require careful planning and robust lab data. But it is a necessary step toward more ethical and clinically relevant research.

## Looking ahead

Obesity is not a single disease. It presents in many forms, with different comorbidities and treatment responses. The same is true for many chronic conditions. This complexity requires a new approach to clinical research – one that is faster, more precise, and more personalised.

Laboratories will be central to this evolution. They are not just for sample processing. They are strategic partners in trial design, patient engagement, and scientific validation.



# Best Practices in Cardiometabolic Trial Design: Planning and Optimisation for Success

**Cardiometabolic disease is not a single entity. It is a broad spectrum of disorders that share common drivers such as obesity, ectopic fat deposition, insulin resistance and chronic inflammation. Under this umbrella sit diabetes, cardiovascular disease, fatty liver disease, heart failure, and even certain cancers. Each condition presents its own challenges, yet they are interconnected through overlapping pathophysiology. This complexity makes cardiometabolic research both scientifically compelling and operationally demanding. Designing and optimising trials in this space requires careful planning, flexibility, and a deep understanding of endpoints, recruitment realities and regulatory expectations.**

## The challenge of endpoints

One of the most persistent challenges in cardiometabolic trial design is the choice of endpoints. Hard outcomes such as cardiovascular events, stroke or mortality remain the gold standard, but they require long timelines and large patient populations. Surrogate endpoints — HbA1c for diabetes, weight reduction for obesity, MRI or biopsy for fatty liver, ejection fraction for heart failure — can provide earlier signals, but their acceptance by regulators varies. In most cases, authorities insist on hard outcomes, though strong surrogates may occasionally be accepted. This diversity of endpoints reflects the diversity of disease itself. A trial designed for diabetes will look very different from one designed for fatty liver or heart failure, even though all fall under the cardiometabolic umbrella. Sponsors must therefore tailor endpoints to the specific indication while keeping regulatory expectations firmly in view.

## Recruitment and retention realities

Recruiting and retaining patients for cardiometabolic trials is equally complex. Patients are often motivated when the trial offers access to therapies they would otherwise struggle to afford. In Germany, for example, obesity drugs are not reimbursed unless the patient is diabetic. This creates strong interest in anti-obesity trials, where participants can access medication free of charge. However, placebo arms remain a challenge. Once patients realise they are not receiving active treatment, retention becomes difficult. Sponsors often mitigate this by offering extension studies in which placebo patients later receive the active drug. Shorter trial durations — three to six months — are also more feasible, as patients can be motivated to remain engaged until they can access treatment. Multi-year placebo studies are increasingly impractical, both ethically and operationally.

## Optimisation through design innovation

To address these challenges, sponsors are embracing alternative trial designs. Adaptive designs allow interim analyses and modifications to improve efficiency. Active comparator trials are becoming more common, particularly where placebo arms are no longer acceptable. Statistical innovation now enables indirect placebo comparisons by linking new active-comparator data to historical placebo data. Regulatory agencies are beginning to accept these methods, though they remain relatively new. These innovations shorten timelines, reduce patient burden and provide more meaningful data for sponsors and regulators alike.

## The role of assays and early signals

Laboratory assays and biomarkers play an important role in early-phase cardiometabolic research. While they are rarely sufficient for regulatory approval, they provide valuable proof-of-concept signals. Sponsors are keen to see early evidence that a drug is moving biological markers in the right direction before committing to large, costly Phase III programmes. Assays can demonstrate changes in glucose metabolism, lipid profiles, inflammatory markers or renal function, offering reassurance that the drug is active. This early insight helps sponsors decide whether to invest further, reducing the risk of pursuing ineffective candidates. Assay planning should therefore be integrated into trial design from the outset, even if endpoints ultimately require hard outcomes.

## Leveraging broader infrastructure

Our experience in infectious disease and respiratory research has given us infrastructure that translates well into cardiometabolic trials. Decades of expertise in Phase I studies, volunteer management, and laboratory assay development provide a strong foundation. By integrating these capabilities with cardiometabolic expertise, hVIVO can offer sponsors a broader spectrum of services across indications. This breadth is increasingly important as many companies develop drugs that cut across therapeutic areas — for example, agents with both metabolic and cardiovascular benefits. A unified infrastructure ensures consistency, efficiency and quality across diverse trial designs.

## Looking ahead: optimism for the future

Despite the challenges, we are optimistic about the future of cardiometabolic research. The past decade has seen remarkable progress in obesity and diabetes therapies, with drugs that deliver rapid and visible results. Unlike cardiology trials, which may take years to demonstrate modest effects, cardiometabolic trials often show weight reduction or metabolic improvement within weeks. This immediacy benefits patients, who see tangible changes in their health; sponsors, who gain early confidence in their programmes; and payers, who can justify investment in therapies that deliver measurable outcomes quickly. For cost-conscious European health systems, the ability to demonstrate value within months rather than years is particularly compelling.

We believe the next generation of cardiometabolic trials will combine scientific rigour with operational agility. Endpoints will be carefully tailored to indications, recruitment strategies will reflect patient realities, and innovative designs will shorten timelines without compromising quality. Assays will continue to provide early signals, guiding investment decisions and de-risking development. Most importantly, new therapies will deliver rapid, meaningful benefits to patients, transforming lives and reducing the burden of disease. That is the promise of cardiometabolic research — complex, challenging, but full of opportunity.

To learn more about partnering with hVIVO for cardiometabolic drug development and clinical trials, visit the **web site**.

# The New Reality of Early-Phase Diabetes Trials

**Diabetes drug development has changed more in the past decade than in the previous three combined. For years, progress was measured almost entirely by glucose control. A therapy that lowered HbA1c was considered successful, and early-phase trials were designed around that narrow objective. That era is over.**

Today, diabetes is recognised as a broad metabolic disease with implications that extend far beyond glycaemia. Cardiovascular risk, renal function, hepatic health, sleep, systemic inflammation, and body weight all sit within the same constellation. As a result, new therapies are expected to demonstrate benefits across this wider landscape. Lowering glucose is now the baseline; differentiation comes from everything else a drug can do.

This shift has raised the stakes for early-phase development. Sponsors must understand not only whether a drug is safe, but whether it shows early signs of delivering the broader metabolic effects that regulators, clinicians, and patients now expect. That requires a different mindset—and a different approach to early clinical research, one that includes patient involvement in the very early stages of clinical development.

## Early-phase trials now carry strategic weight

One of the most important changes in the field is the demand for meaningful signals earlier in development. Companies want reassurance that a drug is behaving as intended, and they want that reassurance before committing to large, expensive Phase II and III programmes. Equally, they want early clarity when a mechanism is unlikely to deliver. A fast, well-informed "no" is often more valuable than a slow, uncertain "yes."

This has led to a new model in which Phase I and Phase II thinking increasingly overlap. Early-phase studies now incorporate exploratory biomarkers, mechanistic readouts, and metabolic assessments that once belonged exclusively to later stages. The goal is not to prove efficacy in Phase I, but to understand whether the biology is moving in the right direction. When done well, this approach accelerates development, reduces risk, and gives sponsors the confidence to invest in the next step.

## Complexity has increased—but so have the opportunities

The expansion of therapeutic expectations means early-phase diabetes trials must be designed with a wider lens. It is no longer enough to track glucose and insulin. Developers need to think about cardiovascular markers, renal indicators, hepatic signals, and the interplay between metabolic pathways. They also need to consider how background medications, patient variability, and comorbidities influence early readouts.

Large pharmaceutical companies generally understand this complexity. They have internal teams who specialise in metabolic disease, and they come to early-phase units with clear expectations and well-defined biomarker strategies. Smaller biotechs, however—where much of today's innovation originates—often arrive with strong preclinical data but limited experience translating those findings into a clinical plan. They know what their molecule does in vitro or in animal models, but they need guidance on how to demonstrate that potential in humans.

This is where early-phase expertise becomes essential. The right partner can help identify which markers matter, which assessments are feasible, which patient populations are appropriate, and how to structure a study that generates meaningful insight rather than noise. Without that guidance, programmes risk stalling before they ever reach the clinic.

## What defines a strong early-phase metabolic environment

Modern diabetes development requires more than a clinical site capable of running a protocol. It requires an integrated environment—one that connects preclinical understanding, early-phase design, biomarker strategy, and patient-level execution.

A strong metabolic unit brings several elements together: deep experience in first-in-human and early patient studies, access to the right populations, validated methods for specialised investigations, and the scientific expertise to interpret early signals in context. It is not simply about collecting data; it is about knowing which data will matter six, twelve, or twenty-four months later when regulatory discussions begin.

This integration is what allows early-phase trials to function as strategic engines rather than procedural checkpoints. It is what gives sponsors the confidence to move forward—and the clarity to stop when necessary.

## A more holistic, more hopeful future

Despite the rising complexity, the trajectory of diabetes development is encouraging. The field is moving toward a more complete understanding of metabolic disease, one that recognises the interconnected nature of the systems involved. This creates opportunities for new mechanisms, new biomarkers, and new therapeutic strategies that address the full burden of diabetes rather than a single symptom or laboratory marker.

To realise that potential, early-phase trials must continue to evolve. They must be designed with intention, grounded in an overall physiological assessment, and supported by teams who understand both the science and the operational realities. When those elements come together, early-phase development becomes not just a gateway to later trials, but a source of genuine insight—and a foundation for better therapies.

# Rethinking Early-Phase MASLD Trials: A More Realistic Path Forward

**The landscape of fatty liver disease has changed rapidly, and the terminology has changed with it. What was once known as NAFLD or NASH is now recognised as MASLD—metabolic dysfunction-associated steatotic liver disease. The new name reflects a deeper truth: this is not an isolated liver condition, but a metabolic disease that sits at the crossroads of obesity, diabetes, cardiovascular risk, and systemic inflammation.**

For many years, MASLD was under-recognised by clinicians and almost invisible to patients. Most people who have it still do not know they do. Even among those with type 2 diabetes—where prevalence is extraordinarily high—awareness remains low. Yet the disease carries serious consequences. It can progress from simple steatosis to fibrosis, cirrhosis, and hepatocellular carcinoma, and it significantly increases cardiovascular risk. In fact, most people with MASLD do not die from liver complications, but from cardiovascular events.

This combination of high prevalence, low awareness, and significant morbidity creates a unique challenge for drug developers. It also makes early-phase clinical research more important—and more complex—than ever.

## A disease that is common, silent, and difficult to identify

One of the fundamental challenges in MASLD development is that the disease is both widespread and underdiagnosed. Traditional diagnostic tools are either too insensitive or too invasive to be practical for broad screening. Standard abdominal ultrasound only detects fatty liver once the disease is already advanced. MRI provides a far more accurate picture, but it is expensive and typically reserved for research settings. Transient elastography technologies such as FibroScan offer a sensitive, non-invasive alternative, but the equipment is costly and not universally available.

In recent years, clinical risk scores such as FIB-4, the Agile score, and the MASLD Risk Score have emerged as practical first-line tools to identify individuals who may warrant further evaluation. These scores are inexpensive, widely accessible, and useful for triaging large populations—but they are still imperfect. They can flag patients at risk, yet they cannot confirm disease stage or reliably distinguish

steatosis from fibrosis without follow-up imaging or elastography. As a result, sponsors still face a fragmented diagnostic landscape where no single tool offers both scalability and diagnostic precision.

This diagnostic gap has real implications for early-phase trials. Identifying suitable participants requires more than simply opening a study and waiting for referrals. It demands a deliberate strategy, an understanding of which tools are appropriate for which stage of disease, and the operational capability to screen efficiently without overwhelming patients or sites.

## Regulatory expectations are evolving—but not fast enough

The scientific community has made significant progress in developing non-invasive methods to assess liver fat, inflammation, and fibrosis. MRI-based techniques, elastography, and advanced ultrasound methods offer a clearer, more reproducible view of the liver than traditional biopsy. Yet regulatory expectations have not fully caught up.

Biopsy remains the standard requirement for many MASLD studies, particularly those aimed at demonstrating improvements in fibrosis. This creates a major barrier. Biopsies are invasive, uncomfortable, and carry a small but real risk of complications. Patients are understandably reluctant to undergo them repeatedly, and many physicians discourage their use outside of clear clinical necessity.

The result is a tension between what science can measure and what regulators still require. Sponsors often feel compelled to design biopsy-driven studies even when better tools exist, and this can make recruitment extraordinarily difficult. It is not unusual for programmes to struggle or stall simply because patients are unwilling to undergo multiple invasive procedures for research purposes.

## Why early-phase MASLD trials are uniquely challenging

MASLD sits at the intersection of several metabolic pathways, and its progression varies widely from person to person. This heterogeneity makes early-phase design particularly sensitive. Developers must understand not only the mechanism of action of their drug, but also how that mechanism interacts with the broader metabolic environment.

Early-phase studies need to capture signals that are meaningful, feasible, and aligned with the eventual regulatory path. That means selecting the right biomarkers, choosing the right imaging modalities, and defining endpoints that reflect both biological plausibility and operational reality. It also means recognising that MASLD patients often carry multiple comorbidities—diabetes, hypertension, dyslipidaemia—that influence both disease progression and study outcomes.

Without careful planning, early-phase MASLD trials can become overburdened with assessments that are difficult to execute or interpret. The goal is not to replicate a Phase II study in miniature, but to generate early evidence that a mechanism is acting in the right direction and warrants further investment.

## The value of integrated early-phase expertise

Given the complexity of MASLD, early-phase development benefits enormously from an integrated approach. The most effective environments are those that connect preclinical insights with clinical strategy, and clinical strategy with operational execution. This integration allows teams to identify the most appropriate markers, anticipate feasibility challenges, and design studies that generate meaningful early signals without overwhelming patients or sites.

A strong early-phase metabolic unit brings together several critical elements: experience with first-in-human and early patient studies, access to the right populations, specialised investigations that have been validated and refined over time, and the scientific expertise to interpret early data in context. This combination helps sponsors move from preclinical promise to clinical proof-of-concept with greater clarity and confidence.

For smaller biotechs—many of whom are driving innovation in MASLD—this support can be transformative. They often arrive with compelling preclinical data but limited experience navigating the regulatory, operational, and scientific complexities of metabolic liver disease. Early guidance on study design, endpoints, diagnostic tools, and feasibility can prevent costly missteps and accelerate progress.

## A more realistic, more hopeful path forward

MASLD remains a challenging area of drug development, but it is also one of the most important. As understanding of the disease deepens and diagnostic tools continue to improve, the opportunities for meaningful therapeutic impact are growing. The key is to approach early-phase development with realism, scientific discipline, and a willingness to adapt to the evolving landscape.

By grounding early-phase studies in biology, aligning them with regulatory expectations, and designing them with operational feasibility in mind, sponsors can generate the evidence needed to move forward with confidence. The path is not simple, but it is navigable—and with the right expertise, it becomes not just feasible, but promising.

# What Sponsors Get Wrong About Renal & Hepatic Studies — According to the People Running Them

**Renal and hepatic impairment studies occupy a unique space in drug development: essential, tightly regulated, and deceptively simple at first glance. Many sponsors treat them as routine PK exercises — something to "slot in" once the programme reaches a certain point. But for the teams who run these studies every day, the reality is far more complex.**

At hVIVO's renal and hepatic impairment unit, years of hands-on experience have revealed a consistent pattern: sponsors often underestimate what these studies require, overestimate how quickly they can be delivered, and misunderstand the operational and clinical nuances that determine success.

Before any of that, though, there's an even more fundamental question: does the programme actually need a dedicated RI/HI study at all? Depending on the drug, its metabolism, the indication, and the available clinical and non-clinical data, sponsors may have several options — physiologically based PK modelling (PBPK), population PK approaches, or a standalone renal or hepatic impairment study. Choosing the right path early is critical. The wrong assumption, or a decision made too late, can create avoidable regulatory delays at the point of registration.

Here are the five most common misconceptions we see repeatedly — and what sponsors need to understand before they design or commission an impaired-population study.

## 1. "These studies are straightforward."

On paper, renal and hepatic impairment studies look simple: clear guidelines, defined patient categories, predictable PK endpoints. But that simplicity is misleading.

Recruitment is one of the biggest challenges. Stable moderate hepatic impairment patients are rare in Western Europe, and severe cases are even harder to find without specialised networks. Renal impairment cohorts require access to a full spectrum of CKD stages, dialysis capability, and clinicians who understand the subtleties of impaired-population PK.

In reality, these studies only look simple when the site has the right subjects, the right clinicians, the right study design, and the right infrastructure. Without that foundation, timelines slip and data quality suffers.

## 2. "Any early-phase unit can run these studies."

Not all early-phase units are equipped for impaired-population research — far from it. With more than 30 years of experience in planning and conducting RI/HI studies, hVIVO's renal/hepatic unit operates with a level of integration that is genuinely uncommon:

- rotating nephrologists from a university hospital
- shared recruitment pathways
- access to dialysis equipment
- hepatology and nephrology specialists embedded in the workflow
- cross-training between hospital and site staff

This kind of clinical network isn't a bonus — it's a prerequisite for reliable recruitment and high-quality data. Sponsors who assume any Phase I unit can deliver these studies often discover too late that specialised infrastructure is the difference between a smooth study and a stalled one.

## 3. "We already know what study design we need."

Many sponsors arrive confident in their scientific rationale but unfamiliar with the practical realities of impaired-population studies. One of the most common early missteps happens even before design discussions begin: assuming a standalone RI/HI trial is required when, in some cases, a waiver or an alternative approach (such as PBPK or population PK) may be acceptable. Misinterpretation of the guidelines is a frequent driver of last-minute requests — and it's not unusual for sponsors to find themselves planning an RI/HI study just before registration because an authority has asked for data they assumed they could avoid.

Once the need for a study is confirmed, additional design gaps often emerge, including:

- misunderstanding whether a single-dose or multiple-dose design is appropriate
- underestimating PK variability in impaired populations
- misinterpreting guideline allowances and restrictions
- overlooking the matching strategy for the control group with normal renal or hepatic function
- assuming unrealistic recruitment timelines

These issues surface frequently during protocol discussions. The truth is simple: impaired-population studies are specialised. Early consultation with an experienced unit prevents costly amendments and avoids avoidable delays — and timely planning is essential, because RI/HI studies form part of the registration package. When these decisions are left too late, they can directly impact approval timelines.

## 4. "Quality is a given."

Sponsors often assume that renal/hepatic studies are routine enough that quality "just happens." But quality is the result of deliberate, ongoing operational discipline. Over the past year, hViVO has modernised and strengthened our processes by:

- redesigning workflows
- tightening quality controls
- improving documentation pathways
- collaborating closely with regulators and QA

These changes were not about adding staff — they were about working smarter, not harder. High-quality data in impaired-population studies is not automatic. It is engineered through modern systems, disciplined processes, and continuous improvement.

## 5. "Recruitment will be fast — right?"

Sponsors frequently ask the same three questions:

1. Can you deliver this study?
2. Can you recruit eight patients per cohort?
3. Can you do it in six months?

The honest answer: it depends on the population. Recruitment is shaped not only by the availability of renal or hepatic impairment patients, but by the inclusion and exclusion criteria that determine who is actually eligible. Severe impairment patients are rarely "healthy," and designing criteria that are both clinically appropriate and operationally realistic — for both the impaired cohort and the matched control group — is essential.

Renal impairment recruitment is feasible when a site has a large, active nephrology network — which hVIVO does. Hepatic impairment is far more challenging, especially for severe cases. Geography, hospital partnerships, patient stability, and clinical relationships all influence timelines. Assuming uniform recruitment timelines across impairment categories is one of the fastest ways to derail a study plan.

## 6. "We don't need external expertise — we've got this."

This misconception causes more friction than any other. Some sponsors arrive convinced they know exactly what they need. Others recognise they need guidance. The difference between the two becomes clear the moment protocol discussions begin.

Impaired-population studies require clinical judgement, operational nuance, regulatory familiarity, and a deep understanding of impaired-population PK. But they also require clarity on a set of strategic questions that many early-stage teams haven't had to answer before: Do we need an RI/HI study at all? If so, should it be a full or reduced design? Is there an alternative approach that could satisfy regulators? And critically, when should the study be run — early enough to inform Phase 2 or 3, or closer to registration where it becomes part of the approval package?

These are not decisions most emerging teams can or should make alone. It's not a weakness to seek specialised expertise. The real weakness is assuming you don't need it — especially when the timing and design of RI/HI studies can directly influence regulatory outcomes.

## The Bottom Line

Renal and hepatic impairment studies are not routine box-ticking exercises. They are specialised clinical investigations that demand the right patients, the right clinicians, the right infrastructure, and the right operational discipline.

Sponsors who understand this — and who engage early with experienced teams — avoid delays, reduce risk, and generate cleaner, more reliable data. Those who don't often learn the hard way.

And this is exactly where an early-phase specialist ecosystem makes the difference. When clinical pharmacology, operations, laboratory science, and patient access sit under one coordinated approach, the entire programme moves with more confidence and fewer surprises — giving sponsors the support they need to deliver these complex studies well.

# Improving Outcomes in Diabetic Kidney Disease

**Diabetic kidney disease (DKD), the leading cause of kidney failure and end-stage renal disease globally, will affect almost half of all patients with type 2 diabetes. With the prevalence of type 2 diabetes increasing, early identification and management of DKD is critical in clinical practice.**

This review provides a comprehensive clinical update on DKD in patients with type 2 diabetes, with an emphasis on novel treatment options.

Traditional DKD preventive and treatment measures, such as glycemic control and blood pressure management, have only minor benefits in reducing the decrease in glomerular filtration rate and progression to end-stage renal disease.

While cardiovascular outcome trials of SGLT-2i show a beneficial effect on various kidney disease-related endpoints, the effect of GLP-1 RA on kidney disease endpoints beyond decreased albuminuria has yet to be proven. Nonsteroidal mineralocorticoid receptor antagonists also have cardiovascular and renal protective properties.

With these novel medications and the prospect of further compounds in clinical development, doctors will be better equipped to customize DKD treatment in type 2 diabetic patients.

## The current state of diabetes

According to the International Diabetes Federation, 537 million people (20-79 years old) worldwide were living with diabetes mellitus in 2021, with the figure anticipated to rise to more than 780 million by 2045.[1]

Approximately 90-95 % of them have type 2 diabetes (T2D).[2,3] Nearly half of people with T2D develop diabetic kidney disease (DKD), formerly known as "diabetic nephropathy".[4,5]

DKD is the most prevalent cause of kidney failure and end-stage kidney disease (ESKD), requiring kidney replacement therapy (dialysis or transplant) worldwide.[6,7] Moreover, DKD is a major cause of cardiovascular disease and total mortality among diabetics.[8,9]

Given the rising prevalence of T2D, early identification and treatment of DKD are critical therapeutic considerations. This review offers an update on DKD pathogenesis, clinical symptoms, and current advances in DKD therapy.

## Pathophysiology

Multiple diabetes-related mechanisms, including hyperglycemia and accompanying metabolic abnormalities, glomerular hemodynamic alterations, and proinflammatory and profibrotic factors, all contribute to kidney damage in DKD.[10-13]

These pathways often result in glomerular hyperfiltration and hypertrophy, and evidence shows that this might progress to sclerosis, especially in the presence of concomitant hypertension.[11]

Obesity and systemic hypertension, which are frequent among T2D patients, increase glomerular hyperfiltration.[14]

Arteriolar hyalinosis, tubulointerstitial inflammation, and fibrosis are also prominent hallmarks of DKD (Figures 1 and 2).[11]

Progressive glomerular damage increases albumin permeability, leading to elevated albuminuria.[15] Albuminuria typically precedes filtration loss; in DKD, eGFR reduction can occur without albuminuria.[16-18]

People with reduced eGFR but no albuminuria often have extensive vascular lesions and interstitial fibrosis in their kidney tissue.[18] Table 1 describes the usual results of glomerular lesion biopsies in people with DKD.

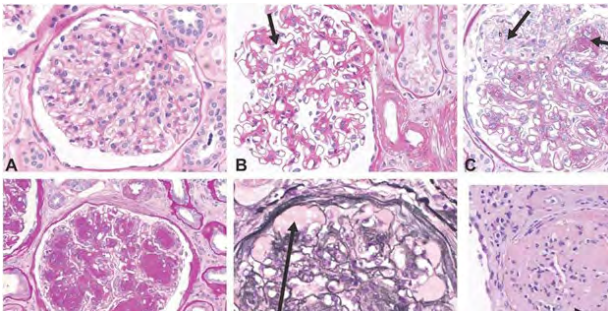



***Fig 1.*** *Histology images showing structural changes related to diabetic glomerulopathy.* ***A*** *Normal glomerulus.* ***B*** *Diffuse mesangial expansion with mesangial cell proliferation.* ***C*** *Prominent mesangial expansion with early nodularity and mesangiolysis.* ***D*** *Accumulation of mesangial matrix forming Kimmelstiel-Wilson nodules.* ***E*** *Dilation of capillaries forming microaneurysms, with subintimal hyaline (plasmatic insudation).* ***F*** *Obsolescent glomerulus.* ***A***–***D*** *and* ***F*** *were stained with period acid-Schiff stain.* ***E*** *was stained with Jones stain. Original magnification ×400. Reprinted with permission from American Society of Nephrology. Image Credit: Alicic, R.Z., et al. (2017)*[11]

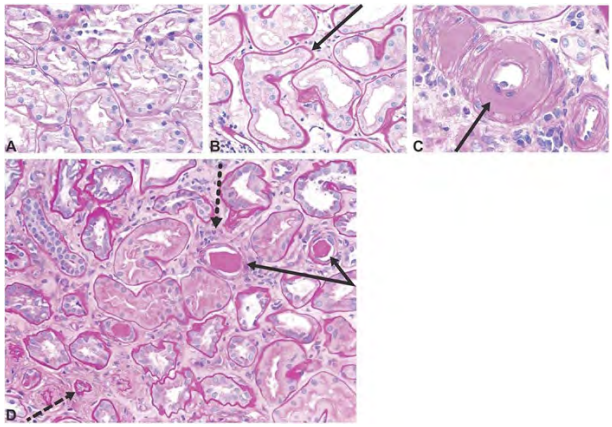



***Fig 2.*** *Histology images showing tubulointerstitial changes seen in diabetic kidney disease.* ***A*** *Normal kidney cortex. B Thickened tubular basement membrane and interstitial widening.* ***C*** *Arteriole with an intimal accumulation of hyaline material with significant luminal compromise.* ***D*** *Renal tubules and interstitium in advancing diabetic kidney disease, with thickening and wrinkled tubular basement membranes (solid arrows), atrophic tubules (dashed arrow), some containing casts, and interstitial widening with fibrosis and inflammatory cells (dotted arrow). All sections stained with period acid-Schiff stain, original magnification ×200. Reprinted with permission from American Society of Nephrology. Image Credit: Alicic, R.Z., et al. (2017)*[11]

## Clinical manifestations

DKD frequently escalates to renal failure or cardiovascular events, resulting in mortality in almost half of those affected.[11,20] As a result, early recognition, identification, and intervention are critical to improving clinical outcomes.

## Diagnostic tools and laboratory practices for DKD

A chronic rise in urine albumin-to-creatinine ratio (UACR, ≥ 30mg/g [≥ 3 mg/mmol]) and/or a persistent decline in eGFR (< 60 mL/min/1.73 $m^2$) in a diabetic patient are key indicators of DKD.[21] To qualify as DKD, these lesions must be caused solely by diabetes-related causes.[21]

The American Diabetes Association (ADA) Standards of Medical Care recommend that persons with T2D be checked for DKD at the time of diagnosis and then once a year after that.[21] As shown in Figure 3, there are three types of albuminuria.[22]

- *Stage A1, normal to mildly increased albuminuria:* < 30 mg/g (< 3 mg/mmol) UACR in urine sample
- *Stage A2, moderately increased albuminuria,* microalbuminuria: 30-300 mg/g (3-30 mg/mmol) UACR; occurring ≥ 2 times, 3-6 months apart.[21] This low-grade albuminuria is a less effective predictor of disease progression than macroalbuminuria.[23]
- *Stage A3, severely increased albuminuria,* macroalbuminuria: > 300 mg/g (> 30 mg/mmol) UACR; occurring ≥ 2 times, 3-6 months apart.[21]

The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation is the most widely used formula for estimating GFR from serum creatinine.

Recently, the American Society of Nephrology and the National Kidney Foundation recommended using race-agnostic approaches to diagnose and classify chronic kidney disease as a step toward more equitable healthcare.[24,25]

A significant development is the updated CKD-EPI 2021 eGFR equation. This new equation does not contain a word for race, with the goal of raising awareness of chronic kidney disease and encouraging more timely identification and treatment interventions for all populations.

The addition of serum cystatin-C to the CKD-EPI 2021 eGFR equation enhances both accuracy and precision.[25] Although the blood cystatin-C test is accessible in some parts of the world, it is not frequently utilized due to high prices and a lack of assay standardization.[26-29]

In both general and high-risk groups, albuminuria and lower eGFR are related to higher risks of cardiovascular events and death, as well as all-cause mortality.[30,31]

To assess renal and cardiovascular risks, individuals with diabetes and UACR > 30 mg/g (> 3 mg/mmol) and/or eGFR < 60 mL/min/1.73 $m^2$ should have these tests at least twice a year.[21]

In addition to monitoring kidney damage and function, people with T2D should have their glycated hemoglobin (HbA1c) checked every 3-6 months to ensure proper blood glucose management.[32]

**Table 1.** Overview of classes and biopsy findings seen in glomerular lesions associated with diabetic kidney disease (DKD). Source: Tervaert, T.W.C., *et al*. (2010)

| Class | Biopsy findings |
|---|---|
| I | Thickening of glomerular basement membrane > 430 nm in males ages 9 years and older, > 395 nm in females ages 9 years and older |
| II | Mild to severe expansion of mesangial extracellular material: width of interspace exceeds two mesangial cell nuclei in two or more glomerular lobules; also known as "diffuse diabetic glomerulosclerosis." |
| III | Nodular sclerosis, Kimmelstiel-Wilson lesions: focal, lobular, mesangial lesions with acellular, hyaline/matrix core. Generally, these lesions indicate a transition from early to later stages of diabetic kidney disease |
| IV | More than 50 % global glomerulosclerosis is attributed to diabetes: fibrotic lesions with a build-up of extracellular matrix proteins in the mesangial space. Presence indicates advanced diabetic kidney disease |
| Other changes, lesions | Interstitial fibrosis and tubular atrophy; hyalinosis of the efferent, and possibly the afferent, arterioles; insudative lesions known as "capsular drop lesions" when found in Bowman's capsule, as "hyalinized afferent and efferent arterioles when found in the afferent and efferent arterioles, and as fibrin cap lesions or hyalinosis when found in glomerular capillaries; "tip lesion" refers to abnormality in the tubuloglomerular junction, with atrophic tubules and no visible glomerular opening, and related to advanced DKD and macroalbuminuria |

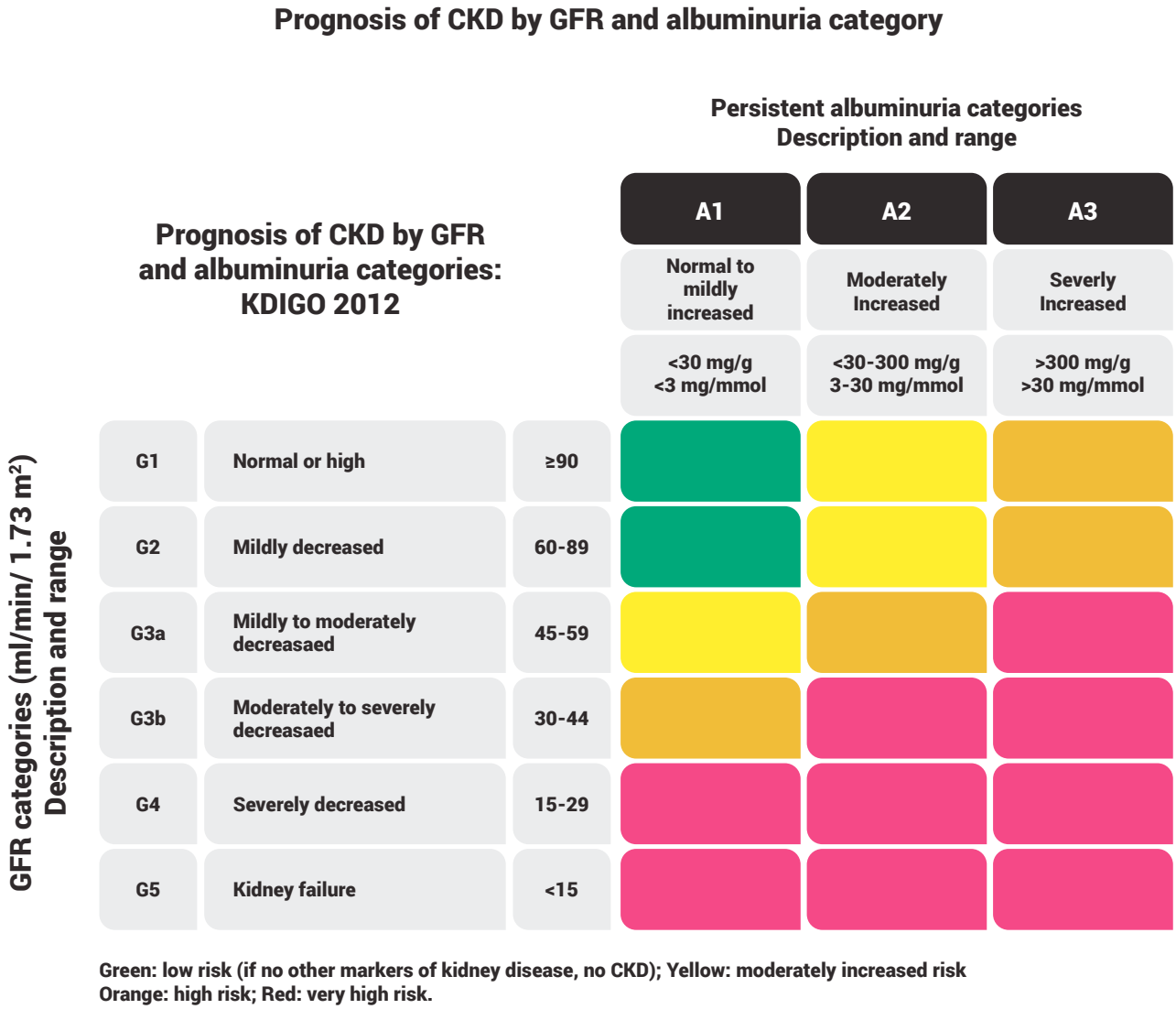



***Fig 3.*** *Prognosis of chronic kidney disease by GFR and albuminuria category. This figure was developed by Kidney Disease Improving Global Outcomes (KDIGO) and reproduced with permission from KDIGO. Image Credit: KDIGO (2012)*[22]

The ADA suggests that patients with T2D engage with their physician to develop a personalized objective for glycemic management, avoiding hypoglycemia while maintaining a general aim of HbA1c < 7 % (53 mmol/mol).[32]

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## Bringing together decades of scientific expertise to deliver a purpose built alternative to the traditional CRO model.

hVIVO is a science led early-phase drug development company that brings together decades of scientific expertise and is purpose built to deliver an alternative to the traditional CRO model.

Early phase drug development is undergoing a fundamental shift. Biology is increasingly complex, regulatory expectations are rising, and sponsors need decisive human data earlier than ever before. Traditional CRO models — built for scale, operational breadth, and late phase execution — were not designed for this environment. Early phase success depends on scientific depth, integrated capabilities, and the ability to move seamlessly from strategy to execution to interpretation, without the fragmentation that slows programmes and dilutes insight.

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Unifying our solutions and services under a single identity is not a change in direction but the culmination of a multi year evolution: the deliberate creation of a purpose built early phase ecosystem designed to deliver clarity, speed, and scientific continuity across the most critical stages of drug development.

Our integrated early-phase ecosystem combines specialist clinical sites, advanced virology and immunology laboratories, human challenge expertise, and early drug development consulting. This unified model enables sponsors to generate rigorous, decision-ready human data earlier in development, reducing uncertainty and accelerating progression through Phase I and II trials.

With industry-leading capabilities in respiratory and infectious disease, alongside expanding expertise in cardiometabolic and other high-growth therapeutic areas, hVIVO supports a diverse global client base that includes seven of the world's ten largest biopharmaceutical companies. Our London quarantine facilities are one of the largest purpose-built human challenge units in the world with specialist laboratory expertise on-site, complimented by additional early-phase clinical capacity in Germany and a specialist consulting team providing strategic, regulatory, and biometry expertise.

Our integrated approach delivers a seamless pathway from preclinical planning through early proof-of-concept, supported by continuous patient recruitment through FluCamp and a network of outpatient clinical sites for Phase II and III studies. By unifying scientific insight, operational control, and advanced laboratory capabilities, hVIVO provides sponsors with the clarity, speed, and reliability required to advance new medicines with confidence.