Special ISSUE#2

The benefits of PRAESIIDIUM for clinical practice and research

Pablo Giraudi, Renald Mecani and Jelizaveta Sokolovska

A new approach to predicting pre-diabetes

How do clinicians and researchers address the growing need to integrate Artificial Intelligence (AI) and machine learning tools into the management of type 2 diabetes? How does clinical practice change when working side by side with computer scientists, technologists and AI specialists in an increasingly data-driven healthcare context, where data collection, selection and analysis becomes central?

The second special issue of this series is dedicated to the story of three experts involved in the European project **PRAESIIDIUM**, who deal with type 2 diabetes on a daily basis both in clinical practice and in research, actively

collaborating with professionals from the technological and computational world. At the center of their reflection, there is the need for earlier diagnosis: detecting pre-diabetes and its risk at an early stage enables timely intervention and more effective prevention strategies, acting when the risk is only beginning to emerge, before the condition fully develops."

Currently, clinicians lack reliable predictive tools to determine, based on available clinical data, who is likely to develop pre-diabetes within the next five to ten years. However, emerging predictive technologies, such as biomarker analysis, are paving the way for earlier and more accurate diagnostics. The added value of the PRAESIIDIUM project lies in its integration of multimodal data: beyond traditional clinical parameters, it incorporates information from wearable devices, continuous glucose monitoring (CGM) systems, physical activity levels, dietary habits, and more. Equally important for clinicians is the availability of advanced predictive models that can assess the effectiveness of therapeutic recommendations and lifestyle modifications, offering valuable feedback on patient progress and treatment impact.

Pablo Giraudi is a researcher at the Italian Liver Foundation (FIF), a research institute recognized by the Italian Ministry of University and Research (MUR) and founded in 2008 by Prof. Claudio Tiribelli. **Dr. Giraudi's** work focuses on identifying novel inflammatory biomarkers associated with the progression of pre-diabetes, particularly in relation to the liver, one of the organs most affected by complications linked to type 2 diabetes. Within the **PRAESIIDIUM** project, his research also includes *in silico* analysis of datasets and experimental proteomics. A key component of this work involves collecting biological samples, such as blood, liver tissue, and visceral adipose tissue, from patients with severe obesity undergoing bariatric surgery. These samples are used to identify early markers of inflammation and investigate its origin through detailed histopathological analysis.

Jelizaveta Sokolovska, an endocrinologist and research group leader at the University of Latvia in Riga, leads a data collection study involving individuals who are overweight or have first-degree obesity, but who show no clinical signs of impaired glucose metabolism. Her laboratory, which focuses on personalized medicine for metabolic disorders and diabetes-related complications, has recently expanded its scope to include the prevention and early detection of pre-diabetes. Through collaboration with developers of predictive technologies and models within the **PRAESIIDIUM** project, new opportunities have emerged to enhance personalized and proactive strategies for managing diabetes risk.

Renald Mecani a pediatrician by training and PhD student at the Medical University of Graz (Austria), conducts research in the diabetes technology unit led by **Prof. Julia K. Mader**. Within the **PRAESIIDIUM** project, **Dr. Mecani** is involved in a study focusing on a group of healthy individuals, some of whom have a family history of type 2 diabetes and are motivated to assess their risk and monitor their health proactively. He and his team are mindful of the potential recruitment bias common in clinical trials, where participants with greater health awareness or concerns (particularly those with a familial

predisposition) are more likely to enroll, often bringing specific anxieties and expectations regarding the outcomes.

Studies with participants: differences, commonalities and perspectives

As mentioned, the **PRAESIIDIUM** project included three studies conducted on different populations: one at **the University of Graz (Austria),** one at **the University of Latvia (Riga)** and one at the **Italian Liver Foundation (Trieste).**

The **Graz** study involved healthy subjects, some with a family history of type 2 diabetes, interested in knowing their health status. In general, these subjects were people who had not yet developed conditions that required major changes in their lifestyle.

The **study by the University of Latvia,** on the other hand, focused on individuals who were overweight or with first-degree obesity, a segment of the population already aware of their condition and therefore more motivated to participate in the study and initiate behavioral changes.

Finally, at the **Italian Liver Foundation**, the participants are people with severe obesity, some of whom suffer from full-blown diabetes, others still without clinical signs of the disease. All are waiting for bariatric surgery, having already tried other therapeutic paths without success. It is therefore a high-risk population and at an advanced stage of the clinical pathway. Some of these patients do not yet have signs of diabetes or pre-diabetes: will they get sick in the future, even after surgery? It is precisely on these questions that **PRAESIIDIUM**'s innovation is based**.**

A new frontier: beyond traditional risk factors

The goal of **PRAESIIDIUM** is to expand the scope of predictive factors beyond traditional indicators such as body weight and blood glucose levels. The project seeks to identify novel biomarkers and develop integrated predictive models that combine clinical, biological, and behavioral data through the use of Artificial Intelligence and machine learning.

In the laboratory in Riga, participant selection followed rigorous criteria. Individuals with grade 1 obesity were chosen in part because they often demonstrate greater awareness of the need to improve their lifestyle and are more inclined to take part in clinical studies. However, this can lead to a positive selection bias, making the study sample less representative of the broader population.

Participation required a substantial commitment: keeping detailed food diaries, attending follow-up visits, and using devices such as wearables and continuous glucose monitors (CGMs). Not all participants completed the study—some struggled to maintain these routines over time.

The experience also highlighted a fundamental challenge in prevention: the variability in personal attitudes. As outlined by **Dr. Jelizaveta Sokolovska**, a practicing clinician, some individuals, even when facing clear risk factors or a family history of diabetes, remain reluctant to change. Others, despite having no symptoms, actively seek early intervention. In some cases, patients already diagnosed with diabetes tend to minimize the condition, saying, for example, "*I don't feel the sugar, so I'm not worried.*"

Changing your lifestyle is crucial

A key component of the Latvian study was the promotion of targeted dietary changes: reducing the intake of high-glycemic-index foods and increasing the consumption of fiber, vegetables, and protein. One of the primary objectives was weight loss, as even a 5% reduction in body weight is associated with a significant decrease in the risk of developing diabetes. For individuals between the ages of 40 and 60, this also translates into a measurable reduction in cardiovascular risk.

However, researchers also highlighted important gaps in current clinical practice. In many cases, pre-diabetes is either underestimated or not treated as a clinically significant condition. As a result, patients often do not receive appropriate counseling or ongoing follow-up, missing a critical window for preventive intervention.

The added value of PRAESIIDIUM

One of the key strengths of the **PRAESIIDIUM** project lies in the use of innovative biomarkers, validated through methodologies recognized as Gold Standard Diagnostics, combined with integrated predictive models. This multifaceted approach enables a more comprehensive understanding of disease risk: some individuals with multiple risk factors may never develop diabetes, while others with few apparent risks might.

This underscores a growing consensus in the field: the future of medicine is translational, focused on turning scientific discoveries into tangible tools for clinical use. However, the widespread adoption of such innovations remains limited, largely due to high costs and the lack of large-scale validation. A telling example is the diagnostic use of HbA1c: although now a standard in diabetes diagnosis, it took years to be universally accepted, primarily due to initial challenges in achieving consistent measurements across laboratories

The limits of health systems and the challenge of the future

As **Dr. Jelizaveta Sokolovska** highlights, clinicians often face the challenge of justifying every medical intervention to national health systems or private insurers. In Latvia, for instance, continuous glucose monitors (CGMs) are still not reimbursed for adults with type 1 diabetes due to economic constraints, a striking example of the gap between scientific innovation and practical healthcare delivery.

While life expectancy has increased, it does not always equate to better health. Medications are becoming more effective, but also more costly, placing growing pressure on healthcare systems. As a result, even the most promising breakthroughs often face barriers to widespread clinical adoption.

There is still much ground to cover. Our understanding of diabetes is continually evolving, and there is a pressing need for robust data and long-term studies to clarify the disease's progression. The initial outcomes from the **PRAESIIDIUM project** are encouraging, even in the short term. What is needed now

are more advanced tools, intelligent technologies, and sophisticated predictive models to better support clinicians and patients in making informed preventive choices. Science is moving forward, medicine must be ready to keep pace

The Central Role of the Patient, and the Clinician

Within the **PRAESIIDIUM** project, a variety of digital tools were tested to monitor glucose levels, nutrition, physical activity, and lifestyle habits. These included continuous glucose monitoring (CGM) systems and devices like Fitbit, with the aim of improving data collection and offering patients firsthand insight into how recommended changes impact their health. This approach places the patient at the center of care, enabling personalized interventions tailored to individual needs and behaviors.

However, alongside the centrality of the patient, the critical role of the physician remains equally important. While technological innovation and access to more precise data are highly valued, many healthcare professionals emphasize the importance of grounding these tools in the lived experience of patients—ensuring they are both practical and sustainable in everyday life.

CGM systems have proven particularly effective for individuals with type 1 diabetes. With measurements taken every 5 to 15 minutes, they help to better adjust insulin dosing to patient's food intake and lifestyle, to prevent hypoglycemic episodes, and thus to improve quality of life. Their benefits are also evident in many patients with type 2 diabetes. However, when it comes to individuals with pre-diabetes or no diagnosis at all, the use of CGMs remains controversial—and is rarely covered by national health systems or private insurers.

As **Dr. Renald Mecani** points out, there is currently no established standard or widespread adoption of CGMs for people with pre-diabetes. Yet it is precisely in this area that CGMs could unlock new opportunities for personalized medicine. Evidence suggests that in people with diabetes, CGMs can lead to an approximate 0.5% reduction in HbA1c by providing real-time feedback on glucose fluctuations. Still, **Dr. Mecani** also notes some drawbacks, including the psychological burden that can come from frequent alerts and constant monitoring of one's health metrics.

One of the most promising avenues for CGM use in pre-diabetes is within clinical research. Thanks to machine learning algorithms, it is now possible to analyze large datasets generated by CGMs and identify glycemic patterns associated with the early stages of dysglycemia or the onset of pre-diabetes—paving the way for earlier, more targeted interventions.

Perspectives from Patients and Researchers

Experience from the University of Latvia's laboratory in PRAESIIDIUM project and other studies has revealed that the use of continuous glucose monitoring (CGM) can sometimes provoke anxiety. Some participants found wearing the sensor continuously uncomfortable, and notably, even some patients with type 1 diabetes discontinued its use due to the psychological stress caused by constant

monitoring. This reaction is understandable, as glucose levels naturally fluctuate, even in healthy individuals, such as after consuming a rich meal like tiramisu. Understanding these variations is crucial to distinguish between normal metabolic responses and true risk factors.

As **Dr. Jelizaveta Sokolovska** emphasizes, current CGM devices are primarily validated for people with diabetes, who experience significant glycemic swings. Manufacturers recommend that when CGMs are used by healthy individuals, testing should be performed after substantial meals or intense exercise to help the sensor properly calibrate. Moreover, any abnormal readings should always be confirmed with alternative methods, such as capillary blood glucose or venous blood glucose measurements. In some cases, inaccurate readings have been linked to accidental sensor compression—often occurring during sleep—highlighting the need for cautious interpretation of the data.

Beyond Glucose: Exploring New Frontiers in Continuous Monitoring

Alongside continuous glucose monitoring (CGM), new digital health devices are emerging. These include "digital stress sensors" that indirectly measure cortisol levels, and continuous lactate monitors. Lactate, produced during glucose metabolism, is typically cleared efficiently under normal conditions but can accumulate in diabetics, making it a promising biomarker.

However, the real challenge lies in usability: maintaining the devices, ensuring durability, interpreting results, and managing the emotional impact on users. Some patients—often those who favor self-monitoring and control—embrace these tools enthusiastically. Conversely, others prefer a lifestyle free from constant monitoring and find it difficult to incorporate these devices into daily routines.

Currently, there is no definitive evidence about whether frequent glycemic fluctuations in healthy individuals are harmful or predictive of future diabetes. While pronounced glucose spikes can be observed, this does not necessarily indicate inevitable metabolic disease. In fact, excessive monitoring might negatively affect quality of life, particularly in those prone to anxiety.

What we need today is more studies, more data, and greater awareness. Continuous monitoring can provide valuable insights, but it must be used thoughtfully and paired with proper interpretation. The question isn't simply whether CGM or other sensors should be used, but rather how, when, and for whom they are truly beneficial.

The future of personalized medicine depends on our ability to blend technological innovation with clinical wisdom and a focus on patient well-being.

Medical Technologies, Big Data, and Personalized Medicine: Progress Still in Its Early Stages

We are only at the dawn of a more mature and conscious phase in the use of medical technologies for health data collection and monitoring. Wearable devices, smart sensors, digital platforms, and big data

hold great promise, but significant work remains to make their use reliable, widespread, and truly effective in everyday clinical practice.

As **Dr. Renald Mecani** highlights, maximizing the potential of these technologies requires careful calibration of instruments and thorough training for users. Each device comes with distinct functions, limitations, and applications—there is no universal solution. This is where the vision of personalized medicine becomes crucial. According to **Dr. Mecani**, while some individuals may greatly benefit from these tools, their impact at the population level remains limited.

This does not imply that these devices lack value, in fact, they can make a real difference on an individual basis. However, we cannot yet broadly recommend them as guaranteed solutions. Their effectiveness depends on multiple factors, including the user's digital literacy, personal motivation, sustained engagement, and the potential fatigue or frustration caused by constant notifications from these devices.

The Paradox of Information Overload

For clinicians and researchers alike, one major challenge is data overload. The vast amount of information collected, if not properly filtered and interpreted, can complicate rather than aid the decision-making process. This is a key issue to be tackled in collaboration with data scientists, who must determine the predictive value and weight of each variable: **Which parameters truly matter? Which data enhance clinical predictions, and which do not?**

Additionally, new approaches will likely be needed to manage the inherent inaccuracies in data, especially when working with small or heterogeneous cohorts.

Dr. Jelizaveta Sokolovska offers a concrete example with the use of continuous glucose monitoring (CGM) data in patients with type 1 diabetes. In such cases, the data prove extremely valuable: distinct patient clusters emerge, and certain variations in glycemic parameters may indicate liver conditions like fatty liver disease or the activation of inflammatory processes. Other pilot studies are exploring the use of wearable devices for remote monitoring of frail or elderly patients, revealing untapped potential.

According to **Dr. Renald Mecani**, the key to effectively using wearable technologies lies in asking a focused question before starting: *What am I trying to understand? What problem am I trying to solve?*

Many people own smartwatches or fitness trackers that record dozens of parameters but often end up overwhelmed by confusing and hard-to-interpret data by the end of the day. Conscious use begins with a clear objective: *Do I want to track how my heart rate changes during exercise? Or am I trying to figure out why I feel tired upon waking?* This way, the device becomes a means to answer a specific question, reducing the risk of being misled by irrelevant information.

Looking ahead, these tools could evolve into "digital health coaches"—devices or apps that provide personalized advice based on collected data, such as "*It's time to get up*," "*You've accumulated too much stress today*," or "*Move more*." However, acceptance of this type of feedback varies depending on the

user's personality. Some welcome guidance even from a watch, while others respond with frustration: "*Do I really have to listen to a device?*"

A Parallel with Molecular Biology

Dr. Pablo Giraudi offers an insightful comparison with the evolution of molecular biology. Years ago, the idea of studying thousands of molecules at the RNA level seemed overwhelming and overly complex. Yet, it was precisely from these early efforts that genetic sequencing technologies emerged—now a cornerstone of modern medicine. At that time, advanced analytical tools like artificial intelligence were not yet available. Nevertheless, progress came steadily. Today, we possess powerful tools to transform big data into actionable knowledge, but the challenge lies in applying them methodically, with vision and rigor

PRAESIIDIUM: a Bridge Between Different Worlds

In this regard, the **PRAESIIDIUM** project stands out as a unique initiative, a multidisciplinary consortium uniting clinicians eager to explore beyond traditional practice, researchers deeply attuned to real healthcare needs, and data scientists skilled at translating clinical challenges into analytical models.

Often separated by differing timelines, languages, and priorities, doctors and researchers came together in this project. Crucially, it became clear that no breakthrough can arise from big data without the combined expertise of physicists, mathematicians, and artificial intelligence specialists. Only through genuine interdisciplinary collaboration can truly innovative solutions emerge.

In this sense, **PRAESIIDIUM** was an inspiring endeavor, uncovering ideas, connections, and answers that no single field could have identified alone.

Contattaci:

Contattaci per maggiori informazioni

praesiidium.project@spindox.it

https://praesiidium.spindoxlabs.com

PRAESIIDIUM