aplasia. We identify *KISS1* as another gene associated with reversible hypogonadotropic hypogonadism.

Although its precise biological mechanism remains elusive, synapse formation or plasticity and re-establishment of neuronal connections have been proposed.[7] In the only family previously reported with *KISS1* mutation,[5] to our knowledge, four homozygous women showed complete GnRH deficiency, absent breast development, and primary amenorrhoea. Biochemical evaluation showed profound hypogonadotropic hypogonadism with undetectable LH concentrations.[5] As the authors reported only a single evaluation, we cannot rule out that spontaneous gonadotropic reactivation might have occurred during the follow-up in some of these patients.[5] Additional genetic events in the context of a consanguineous family could also have further fragilised their gonadotropic axis. As this is the first report in male patients, we cannot exclude the possibility of a sex-specific role of kisspeptin in maintaining the integrity of gonadotropic axis. When analysing murine studies, contrary to females, reproductive functions are preserved in males with approximately 5% of *Kiss1* transcripts.[8] Of note, however, is that mouse models with *Kiss1* invalidation do not fully recapitulate human findings,[9,10] which has generated scientific debate previously.[11] Reproductive abnormalities seem less pronounced in *Kiss1* than in *Kiss1r* knockout animals, raising the hypothesis of the presence of additional unknown Kiss1r ligands.[10] Additional complexity arises from the phenotype of mice with neurotoxic ablation of kisspeptin fibers, which remain cyclic and fertile.[12] Our findings contrast with those of the seminal report[5] and rather resemble those seen in kisspeptin knockout or ablated mice,[10,12] seeming to reconcile findings in humans with the literature reporting rodent models.

In summary, we show that abrogation of kisspeptin does not prevent GnRH late activation and hypogonadism reversal, indicating the pervasive and redundant nature of neuropeptides and mediators operating upstream of GnRH. The differential requirement for kisspeptin signalling in different phases of GnRH activation is intriguing. The presence of alternative KISS1R ligands, plasticity of neuroendocrine networks, or the potentiation of redundant biological pathways, including neurokinin B, glutamate, or other GnRH neuron afferents, have not been directly addressed by this study and need to be explored.

We declare no competing interests.

All authors had full access to the data, the data are available from the corresponding author by request.

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Artificial intelligence and diabetes: time for action and caution

Artificial intelligence (AI) has the potential to revolutionise medicine. Although substantial advancements have been made in diagnostic procedures across various medical fields, diabetes stands out as an area of AI-driven clinical management.[1] Notable examples include AI-driven insulin pumps and continuous glucose monitoring systems.

The potential of AI in diabetes care extends far beyond current applications. In the near future, AI could enhance early diagnostics and risk assessment for emergent subtypes of diabetes. The vast amounts of

available data will enable the early identification of at-risk populations and diabetes development in unimaginable ways.[2]

There is growing recognition that simple, cost-effective biomarkers and measurements can reliably and sustainably identify the early stages of the disease and groups who are at risk of developing diabetes.[3] This early identification could improve care globally, particularly in regions with not widely available or non-existent advanced medical care. AI could transform medicine by improving care for all patients, particularly as non-communicable diseases, such as diabetes, rapidly spread worldwide.[4] From a socioeconomic perspective, this approach is an egalitarian one that benefits not only individuals with the disease or those who are at risk, but also entire populations and their health-care systems.

It is time to call for coordinated global action to highlight and support efforts to leverage AI in diabetes care. Therefore, the International Diabetes Federation (IDF) has formed an international working group to develop the best strategies and guidelines to harness this opportunity.

Although AI promises considerable benefits for diabetes care, it also introduces new risks. As AI technologies, such as glucose and biomarker monitoring systems and closed-loop insulin delivery systems, become increasingly integrated, there is a real concern that these technologies, which are currently in their infancy, could lead to unforeseen consequences. The growing ability to influence human biology and lifespan might have implications we are not yet able to grasp.

Moreover, there are emerging concerns regarding the effect of AI on patients, particularly those who begin using these technologies at an early age.[5] Over-reliance on machine learning and advanced technologies could, in some cases, undermine their independence, self-confidence, and decision-making skills. Physicians should understand these risks and be prepared to offer informed guidance, recognising that once these systems are in place, they are not easily reversed.

AI-driven systems inherently lack ethics, social awareness, and humane qualities unless explicitly designed otherwise. The very strength of these technologies—their connectivity—also presents another risk: the potential for surveillance.[6] Governments, health insurance providers, and employers could gain unprecedented access to health data, with potentially harmful consequences for privacy and autonomy.

In response to these risks, the IDF AI Technology Committee advocates for a "human-in-the-loop" framework, ensuring that clinical judgment remains central in all AI-assisted decision making. These tools should be designed to amplify—not replace—the clinician's role, preserving patient trust and the therapeutic alliance.

These challenges can be mitigated by ensuring that the use of AI in diabetes care is guided by the principles of ethics, equity, and patient-centred care. While it is time to act, it is equally important to exercise caution and provide the appropriate guidance and leadership. The global diabetes community needs to coalesce around an action plan to generate real-world evidence, validate and monitor AI applications, and ensure equitable access. It is time to move from intention to implementation.

In the era of data-driven, intelligence-based diabetes care, clinical trials should coexist with continuously learning AI systems trained on real-world, multi-modal datasets. The promise of predictive, preventive, and personalised care can only be realised if supported by strong validation, ethical frameworks, and transparency.

We must set global regulatory guardrails. AI should be classified, regulated, and monitored as a medical intervention. Standards must go beyond accuracy to include explainability, fairness, privacy compliance, and bias mitigation. Privacy-preserving methods, such as federated learning, must be encouraged to protect individual data sovereignty.

Education and clinical preparedness are essential. The IDF is committed to training future diabetes professionals in AI literacy, ethics, and digital health, empowering them to interpret AI, raise concerns, and guide patients confidently.

Equity and inclusion should lead this innovation curve. AI tools should be validated in low-resource settings, with multilingual, culturally aligned deployment strategies. The true potential of AI will be realised only when it is available, accessible, and affordable for all patients—irrespective of geography, income, or digital literacy.

The IDF AI Technology Committee stands ready to guide this transformation—not merely as observers, but together with clinicians and front-line health-care providers as the "human-in-the-loop", acting as active architects of a future where intelligent systems serve with integrity, inclusivity, and global impact.

For more on the **IDF AI Technology Committee** see https://idf.org/

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