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## AI-Supported Insulin Dosing for Type 2 Diabetes

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### A novel AI-based decision support system for insulin titration in type 2 diabetes reveals important considerations surrounding the feasibility of clinical implementation.

The landscape of type 2 diabetes (T2D) management has changed substantially over the past two decades, with innovations in non-insulin pharmacologic therapy and continuous glucose monitoring. New classes of antihyperglycemic medications have shaped diabetes management strategies, prioritizing cardiorenal and weight loss benefits alongside optimization of glycemic control.<sup>1</sup> Despite these advances, a large proportion of people with T2D continue to require multiple daily insulin injections. Owing to the numerous clinical and environmental factors that affect insulin requirements, achieving optimal glucose control through such injections is challenging and labor intensive for both patients and providers. This time-intensive effort often conflicts with time allotted for clinical appointments, leading to frequent and ineffective regimen changes perpetuating clinical inertia.

There is growing interest in the utilization of artificial intelligence (AI) to create digital health tools aimed at improving both patient- and provider-related outcomes in diabetes management.<sup>2–4</sup> In this issue of *Nature Medicine*, Wang et al.<sup>5</sup> explore the possibility of using a reinforcement learning (RL)-based dynamic insulin titration regimen (DITR) algorithm to guide management of insulin-treated T2D. Development of the RL-DITR algorithm is based on longitudinal electronic health records from patients with T2D hospitalized for glycemic control optimization. The algorithm provides insulin dosing

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Competing Interests:

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recommendations based on learning through iterative environmental interactions, while also invoking safety measures for dosing calculation using supervised learning. Testing of the algorithm was multifaceted — culminating in a feasibility trial addressing clinical implementation, in addition to quantitative and qualitative assessments of performance.

Initial validation testing of the proposed RL-DITR algorithm assessed multiple aspects of model prediction—such as glucose trajectory and time in target glucose range — as well as algorithm correlation with physician dosing recommendations. The authors combined these validation procedures with qualitative assessments of the RL-DITR algorithm by expert clinicians, offering insight into the adoption potential of algorithm-based dosing strategies. They further tested the feasibility of the RL-DITR algorithm for use in clinical diabetes management in a small cohort of 16 hospitalized patients with T2D. Over a 5-day study period, intervention with use of the RL-DITR algorithm was associated with a reduction in mean glucose ( $\pm$ standard deviation) from  $11.1 \pm 3.6$  mmol/liter during the first 24 hours to  $8.6 \pm 2.4$  mmol/liter during the last 24 hours of treatment. Post-intervention qualitative surveys supported overall satisfaction with the algorithm, with a high proportion (90.2%) of algorithm-based dosing recommendations being accepted by the treating physician. These preliminary findings suggest that clinical use of the proposed tool is feasible and that it would likely be accepted by end-users. However, pilot studies usually provide unstable estimates of efficacy and limited information about safety; therefore, further testing with randomized trials is needed.

In recent years, AI and machine learning (ML) have been integrated across various domains in diabetes care. These advanced technologies have ushered in transformative changes into multifaceted aspects of diabetes management. For example, harnessing AI and ML, mathematical equations were developed to predict and identify diabetes milestones, from disease onset to complications such as retinopathy, cardiovascular disease, renal impairment, and even dementia.<sup>6</sup> These tools enable improvements in screening and early detection along with more personalized, goal-oriented treatment. In addition, causal AI methods have been employed to delve into intervention mechanisms, enhance treatment personalization and inform strategic development for optimized outcomes.<sup>7</sup> There has also been a growing interest in recent years in using RL for glycemic management algorithms, including for use in closed-loop glucose controllers — but limited data exist on feasibility and clinical implementation.<sup>8</sup> The implementation strategy for the RL-DITR algorithm undertaken by Wang et al.<sup>5</sup> highlights the potential for RL-based AI not only to assist in insulin management, but to do so in a setting that bridges outpatient and inpatient care models, while also assessing adoption potential through physician trust in the algorithm.

The algorithm assessment by Wang et al. brings to light several interesting concepts surrounding the implementation, sustained meaningful use and future scalability of AI-based decision support. Although algorithm-informed tools for insulin titration have been developed for either dedicated inpatient or outpatient use,<sup>9–11</sup> evaluation of the proposed RL-DITR algorithm Wang et al. suggests that short-term inpatient algorithm-directed insulin titration may be useful for combatting outpatient clinical inertia. This could provide an alternative to longer term AI-based clinical management platforms that may not be financially feasible. Although multiple quantitative and qualitative evaluations of the RL-

DITR dosing recommendations revealed a high degree of concordance with expert physician opinion, further data are needed to understand how the algorithm may learn and evolve to improve glycemic control beyond what is currently achieved by more experienced diabetes care specialists. Additionally, given the potential for the algorithm to learn from ongoing interactions with dynamic patient factors, it will be important to explore whether there could be further application of dosing strategy recommendations for hospital discharge, informing the algorithm with anticipated outpatient factors that may affect insulin requirements at home. It is not yet known how this may be more broadly implemented within healthcare systems, but the promise of AI-based insulin dosing support is of growing interest as diabetes management continues to expand beyond specialist care.

The rapid proliferation of AI and ML-based tools has ignited a profound transformation in diabetes care, propelling it into an unprecedented era. AI models continue to expand in the form of apps and wearable devices, operating as real-time companions encouraging improved treatment adherence and behavioral change. The incorporation of AI, including large language models, into clinical practice holds promise for bridging medical expertise and patient comprehension—thereby bolstering education and communication between healthcare professionals and patients.<sup>12</sup> These tools offer opportunities to elevate the quality of diabetes care with respect not only to health outcomes but also to quality of life. As we stand at the intersection of technology and healthcare, the path ahead holds promise to revolutionize diabetes management and empower both patients and healthcare providers in ways previously deemed unattainable.

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