Precision Medicine in Diabetes

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THE 59th Annual Meeting of the European Association for the Study of Diabetes (EASD) took place in Hamburg, Germany, as well as virtually. With exciting new developments in diabetes treatment in the forefront of our minds, as described by the EASD President, Chantal Mathieu, presenter Paul Franks from Lund University, Sweden, took to the stage to deliver 'ADA/EASD Precision Medicine in Diabetes Initiative: Executive Summary of the Second Consensus Report'. Franks provided the key updates to the consensus, published on 5th October 2023, only hours before the presentation.

WHY PRECISION MEDICINE IN DIABETES CARE?

Franks began his presentation by framing the issue faced today: living in an era where diabetes is a tremendous global burden. He emphasised that, although we have some excellent diabetes medications and an ever-growing understanding to prevent it, the prevalence of diabetes is rapidly increasing worldwide. "Over the next couple of decades, we will have something like 1.3 billion people on the planet with this disease we call diabetes," Franks stated, presenting an overwhelming urgency for new and effective treatments, that perhaps are not 'one size fits all'.

"Living in an era where diabetes is a tremendous global burden."

Franks explained that in trials of evidence-based medicine, we observe results based on a comparison arm, and researchers will often find that placebo cohorts obtain better responses overall compared with those undergoing active treatment. This is due to many different factors; however, he stressed that possible biological variation is likely driving a response to a treatment for the care or prevention of a disease. The biomarkers of this biological variation can be used to predict patients' responses to a preventative intervention or treatment, allowing doctors to optimise the treatment and patient outcomes, as well as to save resources in the long term. Franks highlighted a real-world example of this in the Look AHEAD trial,[1] which recently underwent a post hoc analysis, and emphasised the potential of a more personalised approach to diabetes treatment.

Franks went on to define precision medicine, and what it means in the context of diabetes care: "Precision medicine is essentially reducing error and improving accuracy in health recommendations and medical decisions." As error is relatively high in contemporary evidence-based medicine, many patients do not get optimal treatments, which might not be effective for the individual. "I would say that precision medicine is a reduction of that error," he explained.

AMERICAN DIABETES ASSOCIATION/EUROPEAN ASSOCIATION FOR THE STUDY OF DIABETES PRECISION MEDICINE IN DIABETES INITIATIVE

Established in 2018 by the American Diabetes Association (ADA) in partnership with EASD, the Precision Medicine Diabetes Initiative published its first consensus report in 2020. The 2023

"The 2023 International Consensus report was worked on by 200 academics from 28 countries and 196 institutions."

International Consensus report is a series of systematic evidence reviews, and was worked on by 200 academics from 28 countries and 196 institutions. Described as an 'herculean' effort, the report saw the experts conceive primary research questions that should be addressed, in order for precision medicine to be implemented into clinical practice by 2030.

Franks outlined the framework used throughout the evidence reviews, termed the pillars of precision medicine: precision diagnostics, prevention, treatment, and prognostics. He went on to share the strongest evidence for the clinical translation of precision medicine in different types of diabetes. In monogenic diabetes, which is a key focus area given that primary prevention is not an option, next-generation genome sequencing has been found to aid precision diagnostics and treatment decisions. In gestational diabetes, precision diagnostics have been shown to resolve heterogeneity in the condition for both the mother and offspring, and precision treatment has shown success in the mother. Further research is required for the development and validation of algorithms to predict treatment success and risk in gestational diabetes, likely in combination with metabolomics.

Franks stated: "There's some promise that in the next few years we will move into a more translational phase in Type 1 diabetes." Through precision prevention and diagnostics, polygenic risk assessment, in combination with islet autoantibody testing, has been shown to identify individuals at high risk of developing Type 1 diabetes for early prevention, as well as in predicting disease development. Precision diagnostics have also shown promise in Type 2 diabetes, allowing diagnostic subclassification; however, there is a need for further research to obtain clinically relevant approaches. This, alongside further development of diagnostic algorithms with the submission of new data, may see a translation of precision diagnostics into the clinical setting. Key evidence from the TriMaster trial[2] has also shown that simple clinical markers can be used to dictate treatment allocation in second- and third-line therapies.

RESEARCH GAPS TO ACCELERATE CLINICAL APPLICATION

The session moved on to establish a roadmap for the future impact of precision diabetes medicine. The initial focal point that Franks shared was accelerating the clinical application of precision medicine in diabetes, emphasising its remarkable potential to alleviate existing disparities in diabetes healthcare. However, he also cautioned that precision medicine could widen these gaps if it is exclusively viewed as accessible to well-funded settings, rather than as a tool to implement globally.

Franks stressed the urgency of prioritising diversity, equity, and inclusion in precision medicine, and the importance of not only including vulnerable groups in high-income settings, but also of ensuring their priority status for this treatment. The report advocates for monitoring disparity gaps to ensure their reduction rather than amplification.

The next critical aspect addressed the necessity for new prospective trials designed specifically to test hypotheses related to precision medicine in diabetes. The TriMaster trial[2] was presented as an example; however, it was stressed that incorporating such trials into drug development pipelines early is crucial for their clinical relevance and impact. Pregnancy, as a distinct area in diabetes, was revealed as the third focal point, due to its unique characteristics and potential for precision medicine interventions. However, as Franks shared previously, the existing evidence was flagged as mostly moderate or low in quality, urging a push for more robust studies, particularly focusing on pre-conception and impacting lifestyle behaviours before pregnancy.

The urgency of cost-effective, disease-modifying interventions in both Type 1 and Type 2 diabetes, particularly targeting microvascular and macrovascular complications, was outlined as the fourth focal point. Franks spotlighted the need to ensure that precision medicine is tailored to meet individual needs, rather than relying on single technologies like genomics. In the pursuit of a global precision medicine approach, emphasis was put on health equity and the mitigation of disparities, stressing the importance of developing solutions specific to target populations. The reliance on data predominantly from high-income countries and populations of European ancestry was highlighted, as it is not deemed reflective of the global burden of diabetes.

Furthermore, Franks stressed the importance of consistent reporting standards, and collaboration with regulators, such as the United States Food and Drug Administration (FDA) and European Medical Association (EMA), to ensure the seamless translation of precision medicine into clinical practice. Collaboration among various stakeholders was underscored as crucial to ensure that the best research is effectively applied in clinical settings.

CONCLUSION

Ultimately, this insightful session emphasised that the development of precision medicine in diabetes has been made possible through a huge collaborative effort. The dedication of 200 experts over 3 years, notably during the challenges of the COVID-19 era, formed the cornerstone of the progress made in the field. There is much excitement to come in this area, and we are one step closer to successfully tailoring diabetes treatment to each patient, optimising patient experience and quality of life. ●

References

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