Collaborative Working Project executive summary

Project title	Evaluating current service provision for islet autoantibody positive pre-stage 3 type 1 testing and pilot implementation of early detection of First-Degree Relatives (FDRs) of diagnosed T1D patients cared for in centres across the UK.
Partner organisation/s	**Association British Clinical Diabetologists (ABCD) Diabetes Care LTD** 483 Green Lanes, London, N13 4BS **Sanofi** 410 Thames Valley Park Drive, Reading RG6 1PT
Project rationale	Type 1 diabetes is a condition caused by autoimmune damage to the insulin-producing pancreatic beta-cells leading to severe endogenous insulin deficiency. Autoimmune type 1 diabetes accounts for approximately 5–10% of all cases of diabetes worldwide and in the UK. (Maahs et al, Endocrinol Metab Clin North Am. 2010 Sep;39(3):481–497). In the UK, around 25% of those with newly diagnosed type 1 diabetes present with life-threatening DKA, with higher rates in the very young (up to 30% in those under 5 years of age) and in ethnic minority groups. (Besser REJ, Ng SM, Gregory JW, et al. Arch Dis Child 2022;107:790–795.) Diabetic ketoacidosis is a life-threatening but avoidable complication of diabetes mellitus requiring rapid assessment and is often managed in intensive care units. DKA at diagnosis is associated with adverse long-term glycaemia in some studies (Duca LM, Wang B, Rewers M, Rewers A. Diabetes Care. 2017 Sep;40(9):1249-1255.).

	It is now widely accepted that Type 1 diabetes is characterised by three stages: Stage 1: Initiation of the autoimmune process (presence of two or more islet autoantibodies); Importantly, currently early stage associated with normoglycaemia. In children stage 1 is associated with a 44% risk of progression to stage-3 within five years of developing stage-1. (Besser REJ, Ng SM, Gregory JW, et al. Arch Dis Child 2022;107:790–795.) Stage 2: Persistence of type 1 diabetes-related autoantibodies with further loss of βcell function and development of dysglycaemia. In children stage 2 is associated with a 75% risk of progression to a diagnosis of T1D within 4 to 5 years, and a lifetime risk nearing 100%. (Besser REJ, et al. Arch Dis Child. 2022-107(9)-790-795.) Stage 3: Stage 3 type 1 diabetes with hyperglycaemia which meets ADA criteria. In the absence of early testing, most patients present in this stage. Early detection of Stage 1 and 2 type 1 diabetes involves antibody testing from capillary and venous blood samples (stage-1) followed by oral glucose tolerance testing (OGTT) to confirm dysglycaemia (Stage-2). Although it is largely accepted within the clinical diabetes community that there are 3 stages of autoimmune type 1 diabetes, early detection and management of pre-symptomatic disease is not routine practice in UK diabetes clinical care.
Project period	Q4 2025 to Q4 2027

Project objectives	It is anticipated the collaborative working project will deliver the following benefits for Patients, Families, the NHS and Sanofi: **<u>Patients and Families</u>** • Identification of variation between centres may result in action to reduce variation and therefore improve equity of care for patients and family members in both the paediatric and adult age range. • For FDRs opportunity to learn more about pre symptomatic T1Ds from a specialist. • For those that are antibody negative, reassurance that their likelihood of developing T1Ds is low. • For those that are antibody positive education and monitoring to reduce their likelihood of experiencing DKA. **<u>NHS</u>** • Provide a template to standardise practice, aiming to reduce variation in care standards (improved equity of care) and promote collaborative working between adult and paediatric teams • Stakeholders will gain greater knowledge of current pathways enabling identification of gaps in current provision of care. • Understand the feasibility and cost of case finding via existing T1D population and ongoing monitoring of patients identified. • Understanding the level of uptake by the index patients and the FDRs • Potential for reduction in future unplanned care for those that are identified as presymptomatic T1Ds.

	Sanofi • An opportunity to learn about the variation in approaches to screening and management of patients with Type 1 positive antibody diabetes. • Improved corporate reputation with the associated partner organisations. • As Sanofi produce medicines within this disease area if overall patient care is optimised, there may be an increase in the usage of these products in line with national and local guidelines. • Sanofi has a product in At1D that is under regulatory and reimbursement review in 2024-25. **ABCD** • An opportunity to contribute to ABCDs national role in leadership in matters of emerging clinical importance. • To ensure that ABCD continues to encourage academic diabetes development and understanding. This project will be completed by pooling resources at a total cost of up to £1,133,220 Sanofi indirect and direct cost = £559,080 NHS indirect and direct cost = £574,139
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