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General population screening for type 1 diabetes using islet autoantibodies at the preschool vaccination visit: a proof-of-concept study (the T1Early study)

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► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/archdischild-2023-326697).

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Received 28 November 2023
Accepted 8 June 2024

To cite: Scudder C, Townson J, Bowen-Morris J, *et al*. *Arch Dis Child* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/archdischild-2023-326697

ABSTRACT

Objective Type 1 diabetes (T1D) screening programmes testing islet autoantibodies (IAbs) in childhood can reduce life-threatening diabetic ketoacidosis. General population screening is required to detect the majority of children with T1D, since in >85% there is no family history. Age 3–5 years has been proposed as an optimal age for a single screen approach.

Design Capillary samples were collected from children attending their preschool vaccination and analysed for IAbs to insulin, glutamic acid decarboxylase, islet antigen-2 and zinc transporter 8 using radiobinding/luciferase immunoprecipitation system assays. Acceptability was assessed using semistructured interviews and open-ended postcard questionnaires with parents.

Setting Two primary care practices in Oxfordshire, UK.

Main outcome measures The ability to collect capillary blood to test IAbs in children at the routine preschool vaccination (3.5–4 years).

Results Of 134 parents invited, 66 (49%) were recruited (median age 3.5 years (IQR 3.4–3.6), 26 (39.4%) male); 63 provided a sample (97% successfully), and one participant was identified with a single positive IAb. Parents (n=15 interviews, n=29 postcards) were uniformly positive about screening aligned to vaccination and stated they would have been less likely to take part had screening been a separate visit. Themes identified included preparedness for T1D and the long-term benefit outweighing short-term upset. The perceived volume of the capillary sample was a potential concern and needs optimising.

Conclusions Capillary IAb testing is a possible method to screen children for T1D. Aligning collection to the preschool vaccination visit can be convenient for families without the need for an additional visit.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Screening children for type 1 diabetes by measuring islet autoantibodies (IAbs) may reduce life-threatening diabetic ketoacidosis. The optimal age for screening children at a single time point has been proposed as age 3–5. Routine immunisations are given at a similar age.

WHAT THIS STUDY ADDS

⇒ Aligning IAb testing with the preschool vaccination visit (ages 3.5–4 years) demonstrated 49% uptake and was acceptable to participants. Potential barriers and facilitators of this approach are explored.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The routine vaccination programme is a potential opportunity to screen children for future type 1 diabetes, offering improved engagement and potentially reducing the costs associated with a screening programme; all of which need exploration in a large and definitive study.

INTRODUCTION

Type 1 diabetes (T1D) is characterised by well-defined stages, with a preclinical phase preceding clinical symptoms.[1] Screening studies to date have been limited to at-risk populations and have demonstrated that the presence of two or more islet autoantibodies (IAbs) to insulin autoantibodies (IAA), glutamic acid decarboxylase (GADA), islet antigen-2 (IA-2A) and zinc transporter 8 (ZnT8A) confers >80% risk of children progressing to insulin requirement during childhood.[2 3]

In Europe and North America, 15–70% of children present with diabetic ketoacidosis (DKA) at diagnosis.[4 5] This typically requires hospitalisation and causes psychological and physiological morbidity.[6 7] Screening programmes measuring IAbs significantly reduce rates of DKA at diagnosis,[8 9] hospitalisation[10] and the presenting level of glycaemia.[11 12]

Adopting population screening for T1D requires a universal approach, since the majority (>85%) of children do not have a relative affected. It has been suggested that the optimal age to test for IAbs at a single time point is between 3 and 5 years,[13 14] since peak IAb development occurs between 9 months and 2 years.[2] Our aim was to explore, as a 'proof-of-concept' study, general population screening for IAbs in children attending their routine preschool vaccination in general practice. In this context, we

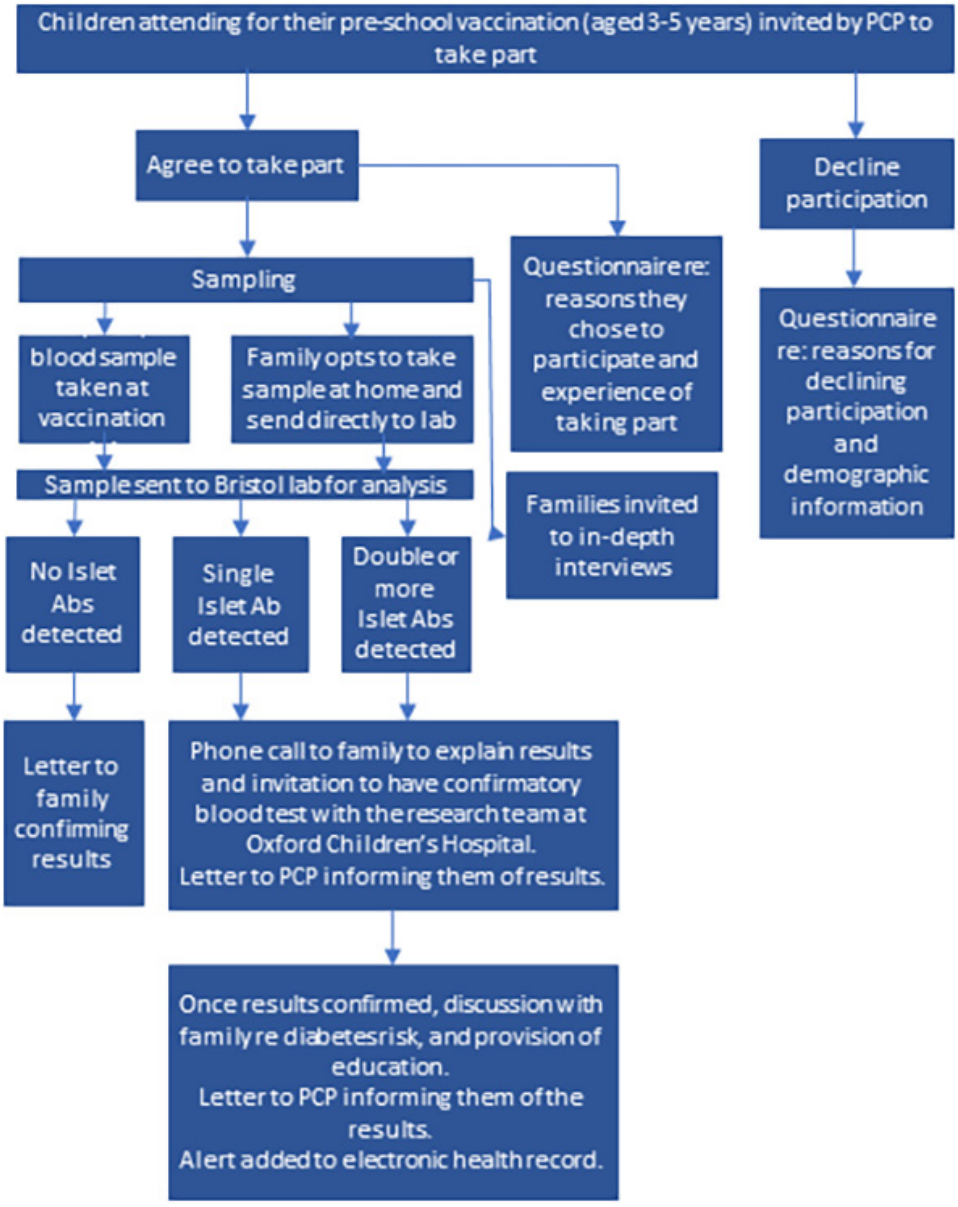

Figure 1 Study schema. Abs, autoantibodies; PCP, primary care practices.

define a 'proof of concept' study as providing the foundations of knowledge,[15] rather than assessing effectiveness.

The primary outcome was the uptake of capillary IAb testing in children attending their preschool vaccination. Secondary outcomes included (1) blood and serum volumes collected; (2) the ability to measure all four IAbs (IAA, GADA, IA-2A, ZnT8A); (3) acceptability from parents whose children were screened; and (4) feedback from non-responders.

METHODS

Participants

Between 22 June and 29 November 2022, across two primary care practices (PCP) in Oxfordshire, UK, the parents of children, aged 3.5–5 years, scheduled for their preschool vaccination (diphtheria; tetanus; pertussis; polio; and measles, mumps and rubella), were invited to participate (figure 1). Invitations were sent by text message attached to an automated preschool vaccination invitation and followed up by telephone.

Our approach was pragmatic and exploratory to align with each PCP. This allowed each PCP to decide on their recruitment method; sending invitation texts to either parents of children due vaccination or to those who had already booked a vaccination (online supplemental table 1: eligibility criteria). Informed consent was obtained from parents in person or remotely prior to screening (online supplemental methods 1: participant information sheet).

Sampling and laboratory methods

During or immediately after vaccination, research nurses collected a capillary sample of up to 200 µL (online supplemental methods 2: blood collection) and posted it to the University of Bristol Alistair Williams Antibody Facility, UK. Samples were processed for serum isolation on arrival. IAA, GADA, IA-2A and ZnT8A were measured by radiobinding assays (RBA)[16] for serum volumes >60 µL and by luciferase immunoprecipitation system (LIPS) assay if <60 µL.[17]

Qualitative methods

Interviews

Participants were approached by email, after their child's participation in screening, using a convenience sampling strategy. 51 parents were approached, and 15 took part (all mothers), 2 declined and 34 did not provide a response. Interviews were planned prior to receiving the test results. However, five participants had already received the results at the time of interview. Participants were remunerated for their time (£25 gift voucher).

Data collection

The interview schedule (online supplemental table 2) assessed the acceptability of the screening process. Interviews were conducted by CS, online, via Microsoft Teams or telephone, depending on the participant's preference, with oversight and training from JT, recorded verbatim and transcribed.

Postcards

Parents (n=66), and those declining participation, were provided with postcards containing up to six questions to complete anonymously immediately after the vaccination/screening appointment (online supplemental table 3), and which broadly mirrored the interview schedule. Postcards provide an opportunity to collect data with minimum burden to the participants while reducing the potential for recall, outcome and emotional bias.[18]

Analyses

The data were analysed inductively and deductively.[19] An established and defined process for developing a codebook in thematic analysis was followed.[20] CS and JT each applied initial codes to the raw, redacted data from the first three participant interviews using NVivo V.12. These initial codes identified by both researchers were discussed, with additional members of the study team (REJB, consultant paediatric endocrinologist and SG, medical sociologist). From this discussion, a coding framework was developed using hierarchical themes, subthemes and a description of the meaning of each code. A deductive approach was then applied to the coding of all data, including the postcard data, using the coding framework. Following coding by both researchers, consensus relating to specific themes was reached with the larger group. Finally, identification and interpretation of the emerging themes was discussed and agreed (JT, CS, SG, REJB).

Data collection

Demographic data were collected to allow assessment of deprivation score using the Index of Multiple Deprivation (IMD), where 1 is most deprived and 10 least deprived.

RESULTS

Population

Of 134 eligible children identified and their respective parents invited to participate, 66 (49%) were recruited (see figure 2). PCP 1 invited families that had already booked their child's vaccinations, and PCP 2 invited families whose children were due vaccination. More families responded and were recruited with the former approach (93% (54/58) vs 45% (34/76) response rate, 83% (45/54) vs 62% (21/34) recruitment). Of the 88 parents who responded, 9 (10%) declined the study, 4 (5%) refused vaccination and 9 (10%) were not recruited for other reasons (no reason provided (n=5), appointment availability (n=3), did not attend (n=1)).

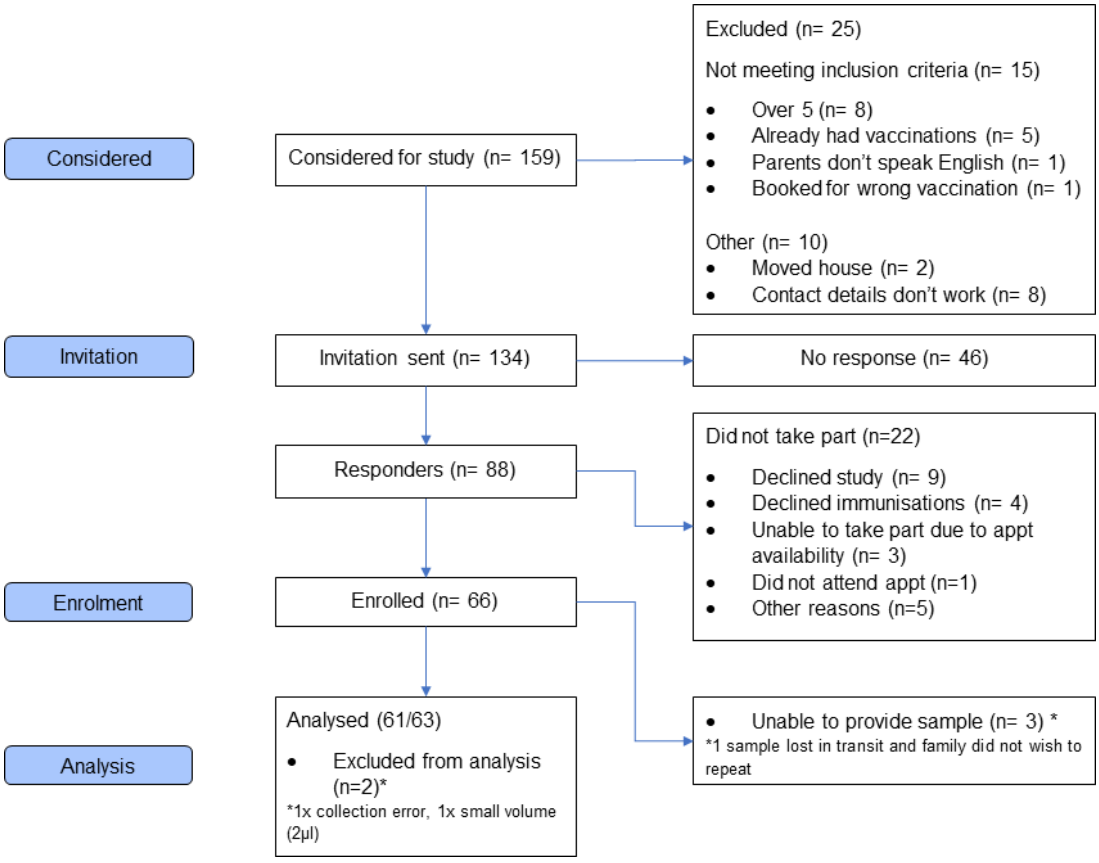

Figure 2 Consolidated Standards of Reporting Trials (CONSORT) diagram.

Table 1 Participant demographics (n=66) and baseline data from samples available for analysis (n=61)

Age, median (IQR), years	3.5 (3.4–3.6)
Female sex, n (%)	40 (61)
Ethnicity, n (%)	
English/Welsh/Scottish/Northern Irish	50 (75.8)
Other white background	4 (6.1)
Chinese	3 (4.5)
Indian	3 (4.5)
Gypsy or Irish traveller	2 (3.0)
White and Asian	1 (1.5)
Other mixed/multiple ethnic background	1 (1.5)
Other ethnic group	1 (1.5)
Not stated	1 (1.5)
Family history of type 1 diabetes, n (%)	3 (4.8)
IMD* decile, median (IQR)	8 (5–9)
Whole blood volume, median (IQR), µL	200 (150–220)
Serum volume, median (IQR), µL	100 (80–155)
Time to results, median (IQR), days	29 (25–46)

*Index of Multiple Deprivation (IMD) ranks small areas in England from 1 (most deprived) to 32 844 (least deprived) and divides into 10 equal groups: most deprived (1) to the least deprived (10).

The 66 children recruited had a median age of 3.5 years (IQR 3.4–3.6, range 3.1–5.1 years), 40 (60.6%) female, and in the majority (95%) there was no family history of T1D. The study population was predominantly white British (75.8%) and of moderate to high affluence (IMD median decile 8 (IQR 5–9, range 3–10)).

Capillary IAb collection

Of the 66 participants enrolled, 63 (95%) provided a sample, 2 did not provide a sample and 1 provided a sample but was lost in transportation. Two samples were collected at home.

There was a 95% (60/63) success in sampling all four IAbs; one participant had a low serum volume resulting in only GADA, IA-2A and ZnT8 being analysed, and two samples failed, one due to low volume and the other due to collection error. The median serum volume collected was 100 µL (80–155), with 83% (52/63) >60 µL (table 1).

One participant was screened and confirmed positive by RBA for IAA. The family attended an appointment with the paediatric diabetes team to receive T1D education and were offered repeat IAb testing after 6 months. They also underwent random glucose and HbA1c measurement, which were normal.

The median time to receive results was 29 days (25–46).

Qualitative study results

15 parents participated in the qualitative substudy, interviews were 17–32 min long. 32 postcards were returned, 13 from participants attending PCP 1 and 16 from PCP 2 (online supplemental table 4).

Three hierarchical themes were identified (online supplemental table 5).

Prior to the vaccination/screening visit

All parents recognised the importance of childhood vaccination to protect against childhood illnesses. This positive attitude was reflected when considering undergoing screening for T1D. Parents described the benefits of knowing about risks to their child's health.

Reasons for participating

Being prepared

Overwhelmingly, parents recalled they would rather be prepared, allowing them to adjust to a potential diagnosis of T1D. Having time to mentally prepare, gather information and plan ahead was considered preferable to having to deal with the shock of a sudden diagnosis. Some parents related their opinions to their family background or general views on managing the health of their family.

Ruling something out and feeling reassured

Participants described wanting to know the outcome, stating that having the results provided reassurance.

Linked to the vaccination programme

The majority of parents reflected positively on having screening aligned to the child's vaccination programme, and the fact that it was conducted at the PCP surgery. Parents recounted busy lives, lack of transport and having to take their child out of nursery as reasons why they preferred the screening test to be conducted as part of a routine health visit. Some reflected they would have been less likely to agree to take part had the screening test been offered separately or in a different location.

Reflections on the whole process

Child's response

Parents described mixed experiences of their child's response to the process. Those reflecting positively described the ease of the process. Negative experiences included having to hold their child securely, and the stress caused to their child. Most parents reflected that their child was primarily upset due to the vaccinations, which were carried out first. Most parents stated that their child had recovered after 5–10 min.

Some parents were surprised about how well their child had reacted and that their child had not mentioned it afterwards, while others recalled their child mentioning their finger or arm hurting.

One parent related that they had been worried that the screening process might give their child a lasting fear of going to the doctors but was reassured that their child still seemed keen to attend afterwards.

In general, parents recalled their child's excitement over the stickers, plaster or treat they had received because of the visit.

Blood collection

Parents were surprised by the amount of blood required, and how much pressure the nurse needed to apply to their child's finger to collect the blood. There was concern over the length of time it took to collect the volume of blood required. Parents recounted feeling distressed and wishing the nurse would finish, and feeling sad on behalf of their child.

Waiting for results

In the main, parents had either forgotten about the results or expressed that they were not worried about them. Two parents recounted being nervous about getting the results, and one parent recalled attributing their child's behaviour as a potential indicator of the symptoms of T1D, acting as a reminder to check their results.

Benefits outweighing short-term upset

Overall, parents recalled satisfaction with the process, describing that the benefits outweighed the potential upset.

Parents were glad they had taken part and although, in some cases, the experience caused their child distress, overall, they felt positive about the experience and related that they would do it again and recommend it to others. All parents stated that they would want their child to take part in screening for T1D again if asked.

Postcard data from individuals who declined

Three postcards were returned from parents who had declined participation, and all went ahead with vaccinations. Two of the three parents stated that they felt undergoing the immunisations was difficult for their child and they did not want them to develop a fear of doctors and nurses. The other participant recounted they were not able to consider the information at that time.

DISCUSSION

In this proof-of-concept study, we explore the methodology of collecting capillary blood for IAbs in children at the time of the preschool vaccination visit. We report that 49% of participants were recruited, although this was higher (83% (45/54)) in parents who were approached after they had booked their child's vaccination visit. Once the child attended, the success rate of measuring all four IAbs was high (95%). Although the data are limited and exploratory, we found that the experience of IAb testing was broadly positive.

T1D screening at the preschool vaccination versus other approaches

A single screen IAb test has been suggested between ages 3 and 5 years[21 22] with sensitivity around 40%. This approach was taken in the Fr1da study which initially screened children between 1.75 and 6 years, during the 'well child check' in primary care.[8] No such routine health visit exists in the UK but the preschool vaccination at ages 3.5–5 years offers a similar opportunity.

Of the 88 parents who responded, only nine actively declined participation. It is unclear whether the lack of response from individuals who were initially contacted via text messaging (n=46) was due to a lack of interest in the study or other reasons, such as not reading the information leaflet. A similarly low study uptake in response to primary care text messaging has been reported and should be considered when expanding recruitment.[23]

Several research groups are now testing non-targeted, opportunistic screening.[3 24] However, universal screening would allow population benefits in accordance with National Screening Committee criteria.[25] Improved patient-related outcomes have been demonstrated in screened children, including lower glycaemia, fewer diabetes-related symptoms, less hospitalisation and improved beta cell function at diagnosis, and in the longer term improved psychological stress and quality of life.[12 26 27]

Participant experience of T1D screening at the preschool vaccination visit

It was not clear whether parents fully understood that even if the screening result was negative at the time, that it was still possible that their child could develop positive IAb in the future, despite this information being available. This is consistent with the literature.[28] However, all parents stated that they would agree to having their child tested again and they would recommend it to others. The main concern was the perceived volume of blood needed and the time it took to collect. Two alternative approaches to the gold standard method of venous IAb sampling are currently being adopted in the research setting using capillary whole blood and dried blood spots (DBS). Both methods facilitate screening for GADA/IA-2A/ZnT8A but the DBS method does not usually include the more complex IAA test. As shown in our exploratory study, the new low blood volume LIPS approach[29] allowed screening for all four IAbs in the majority of lower blood volume samples. IAAs are often present in the very young child and peak before GADA, IA-2A and ZnT8A, and may not include ZnT8A, depending on the laboratory. For universal screening, excluding IAA in the first screen would mean that some young children, who have the highest rates of DKA, may be missed. The balance of acceptability and sensitivity will need to be considered, as well as the approach to improving recruitment before further expansion. One approach would be to request lower blood volumes and use LIPS testing or other ultra-low-volume technologies,[30] rather than RBA, to overcome the concerns raised over blood volume requirements.

Strengths

Qualitative interviews have been undertaken in antibody positive individuals,[31] but to our knowledge have not been undertaken in the general population undergoing screening. In this proof-of-concept study, we report the results from qualitative work undertaken to assess parents' real-life experience of participating in a potential screening programme. In combination with postcard data, this provided an understanding of the experience of parents on the whole study and will inform future study design.

Study limitations

Our study is small and likely biased by being limited to two PCPs from a relatively affluent and white demographic. Non-attenders were not invited for semistructured interviews.

Future studies should focus on including a larger and more diverse population where vaccination uptake is lower and address how to approach individuals who decline vaccination. Lower sample volume techniques are needed for the purposes of acceptability.

CONCLUSIONS

This proof-of-concept study shows the potential for screening children for T1D from the general population when aligned to routine preschool vaccination. Qualitative results indicate general acceptability of the technical aspects of the test when taken at the time of the vaccination visit by parents and will inform future expansion.

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Acknowledgements We thank Dr Eleri Shellens, who provided PPI input into the study, University of Bristol AWAF team members, Rachel Aitken, Anna Long, Kyla Chandler and Olivia Pearce for providing capillary collection kits, sample processing and testing, and the primary care practices in Witney and Bicester who supported the study.

Contributors REJB conceptualised the study. REJB, CS, JB-M, CMD, PE, NPBT and RF designed the study. JT, REJB and CS researched data, contributed to discussion and wrote the first draft of the manuscript. CMD, KG, JB-M, PE, NPBT, RF, SG and JAT contributed to discussion and reviewed and edited the manuscript. JS and SJ reviewed and edited the manuscript. All authors approved the final version of the manuscript. REJB is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Funding This study was supported by grants from the National Institute for Health Research (NIHR) Oxford Biomedical Research Centre (BRC) and from an NIHR Programme Development Grant (PDG) (NIHR203948). REJB, JT and CS are funded through the NIHR PDG. REJB, JAT and CS are also funded through the JDRF/Wellcome Strategic Award (4-SRA-2017-473-A-N; 107212/A/15/Z). LIPS testing was supported by a JDRF grant to KG (2-SRA-2020-964-S-B).

Disclaimer The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Competing interests REJB has been an independent advisor to Provention Bio. JAT consults for GSK, Vesalius Therapeutics, Precion and Immunocore. CMD has lectured for or has been involved as an advisor to the following companies: Novo Nordisk, Sanofi-Genzyme, Janssen, Servier, Lilly, AstraZeneca, Provention Bio, UCB, MSD, Vielo Bio, Avotres, Worg and Novartis. CMD holds a patent jointly with Midatech.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by North West–Preston Research Ethics Committee (21/NW/0340). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. Requests for data should be made via the corresponding author.

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REFERENCES

1 Insel RA, Dunne JL, Ziegler AG. General population screening for type 1 diabetes: has its time come? *Curr Opin Endocrinol Diabetes Obes* 2015;22:270–6.
2 Ziegler AG, Rewers M, Simell O, *et al*. Seroconversion to multiple islet autoantibodies and risk of progression to diabetes in children. *JAMA* 2013;309:2473.
3 Besser REJ, Bell KJ, Couper JJ, *et al*. ISPAD clinical practice consensus guidelines 2022: stages of type 1 diabetes in children and adolescents. *Pediatr Diabetes* 2022;23:1175–87.
4 Cherubini V, Grimsmann JM, Åkesson K, *et al*. Temporal trends in diabetic ketoacidosis at diagnosis of paediatric type 1 diabetes between 2006 and 2016: results from 13 countries in three continents. *Diabetologia* 2020;63:1530–41.
5 Große J, Hornstein H, Manuwald U, *et al*. Incidence of diabetic ketoacidosis of new-onset type 1 diabetes in children and adolescents in different countries correlates with human development index (HDI): an updated systematic review, meta-analysis, and meta-regression. *Horm Metab Res* 2018;50:209–22.
6 Whittemore R, Jaser S, Chao A, *et al*. Psychological experience of parents of children with type 1 diabetes: a systematic mixed-studies review. *Diabetes Educ* 2012;38:562–79.
7 Duca LM, Wang B, Rewers M, *et al*. Diabetic ketoacidosis at diagnosis of type 1 diabetes predicts poor long-term glycemic control. *Diabetes Care* 2017;40:1249–55.
8 Ziegler A-G, Kick K, Bonifacio E, *et al*. Yield of a public health screening of children for islet autoantibodies in Bavaria, Germany. *JAMA* 2020;323:339–51.
9 Winkler C, Schober E, Ziegler AG, *et al*. Markedly reduced rate of diabetic ketoacidosis at onset of type 1 diabetes in relatives screened for islet autoantibodies. *Pediatr Diabetes* 2012;13:308–13.
10 Barker JM, Goehrig SH, Barriga K, *et al*. Clinical characteristics of children diagnosed with type 1 diabetes through intensive screening and follow-up. *Diabetes Care* 2004;27:1399–404.
11 Chan CL, Taki I, Dong F, *et al*. Comparison of metabolic outcomes in children diagnosed with type 1 diabetes through research screening (diabetes autoimmunity study in the young [DAISY]) versus in the community. *Diabetes Technol Ther* 2015;17:649–56.
12 Hummel S, Carl J, Friedl N, *et al*. Children diagnosed with presymptomatic type 1 diabetes through public health screening have milder diabetes at clinical manifestation. *Diabetologia* 2023;66:1633–42.
13 Chmiel R, Giannopoulou EZ, Winkler C, *et al*. Progression from single to multiple islet autoantibodies often occurs soon after seroconversion: implications for early screening. *Diabetologia* 2015;58:411–3.
14 Parikka V, Näntö-Salonen K, Saarinen M, *et al*. Early seroconversion and rapidly increasing autoantibody concentrations predict prepubertal manifestation of type 1 diabetes in children at genetic risk. *Diabetologia* 2012;55:1926–36.
15 Kendig CE. What is proof of concept research and how does it generate epistemic and ethical categories for future scientific practice *Sci Eng Ethics* 2016;22:735–53.
16 Williams CL, Aitken RJ, Wilson IV, *et al*. The measurement of autoantibodies to insulin informs diagnosis of diabetes in a childhood population negative for other autoantibodies. *Diabet Med* 2022;39:e14979.
17 Liberati D, Wyatt RC, Brigatti C, *et al*. A novel LIPS assay for insulin autoantibodies. *Acta Diabetol* 2018;55:263–70.
18 Yee K, Kanstrup AM, Bertelsen P, *et al*. Collecting data in real time with postcards. In: Beuscart-Zéphir M-C, Jaspers M, Kuziemsky C, *et al*., eds. *Context sensitive health informatics: human and sociotechnical approaches*. IOS Press, 2013: 202–7.
19 Braun V, Clarke V. Reflecting on reflexive thematic analysis. *Qualitative Research in Sport, Exercise and Health* 2019;11:589–97.
20 Roberts K, Dowell A, Nie JB. Attempting rigour and replicability in thematic analysis of qualitative research data; a case study of Codebook development. *BMC Med Res Methodol* 2019;19:66.
21 Besser REJ, Ng SM, Gregory JW, *et al*. General population screening for childhood type 1 diabetes: is it time for a UK strategy? *Arch Dis Child* 2022;107:790–5.
22 Ghalwash M, Dunne JL, Lundgren M, *et al*. Two-age islet-autoantibody screening for childhood type 1 diabetes: a prospective cohort study. *Lancet Diabetes Endocrinol* 2022;10:589–96.
23 Pedder H, Sillero Rejon C, Jones T. How do patients respond to text messaging in primary care? 2020.
24 McQueen RB, Geno Rasmussen C, Waugh K, *et al*. Cost and cost-effectiveness of large-scale screening for type 1 diabetes in Colorado. *Diabetes Care* 2020;43:1496–503.
25 Sturdy S, Miller F, Hogarth S, *et al*. Half a century of Wilson & Jungner: reflections on the governance of population screening. *Wellcome Open Res* 2020;5:158.
26 Hummel S, Friedl N, Winkler C, *et al*. Presymptomatic type 1 diabetes and disease severity at onset. reply to Schneider J, Gemulla G, Kiess W et al [letter]. *Diabetologia* 2023;66:2389–90.
27 Schneider J, Gemulla G, Kiess W, *et al*. Presymptomatic type 1 diabetes and disease severity at Onset. *Diabetologia* 2023;66:2387–8.
28 Montalvo W, Larson E. Participant comprehension of research for which they volunteer: a systematic review. *J Nurs Scholarsh* 2014;46:423–31.
29 Bonifacio E, Weiß A, Winkler C, *et al*. An age-related exponential decline in the risk of multiple islet autoantibody seroconversion during childhood. *Diabetes Care* 2021;44:2260–8.
30 Cortez F de J, Gebhart D, Robinson PV, *et al*. Sensitive detection of multiple islet autoantibodies in type 1 diabetes using small sample volumes by agglutination-PCR. *PLoS One* 2020;15:e0242049.
31 Johnson SB. Psychological impact of screening and prediction in type 1 diabetes. *Curr Diab Rep* 2011;11:454–9.