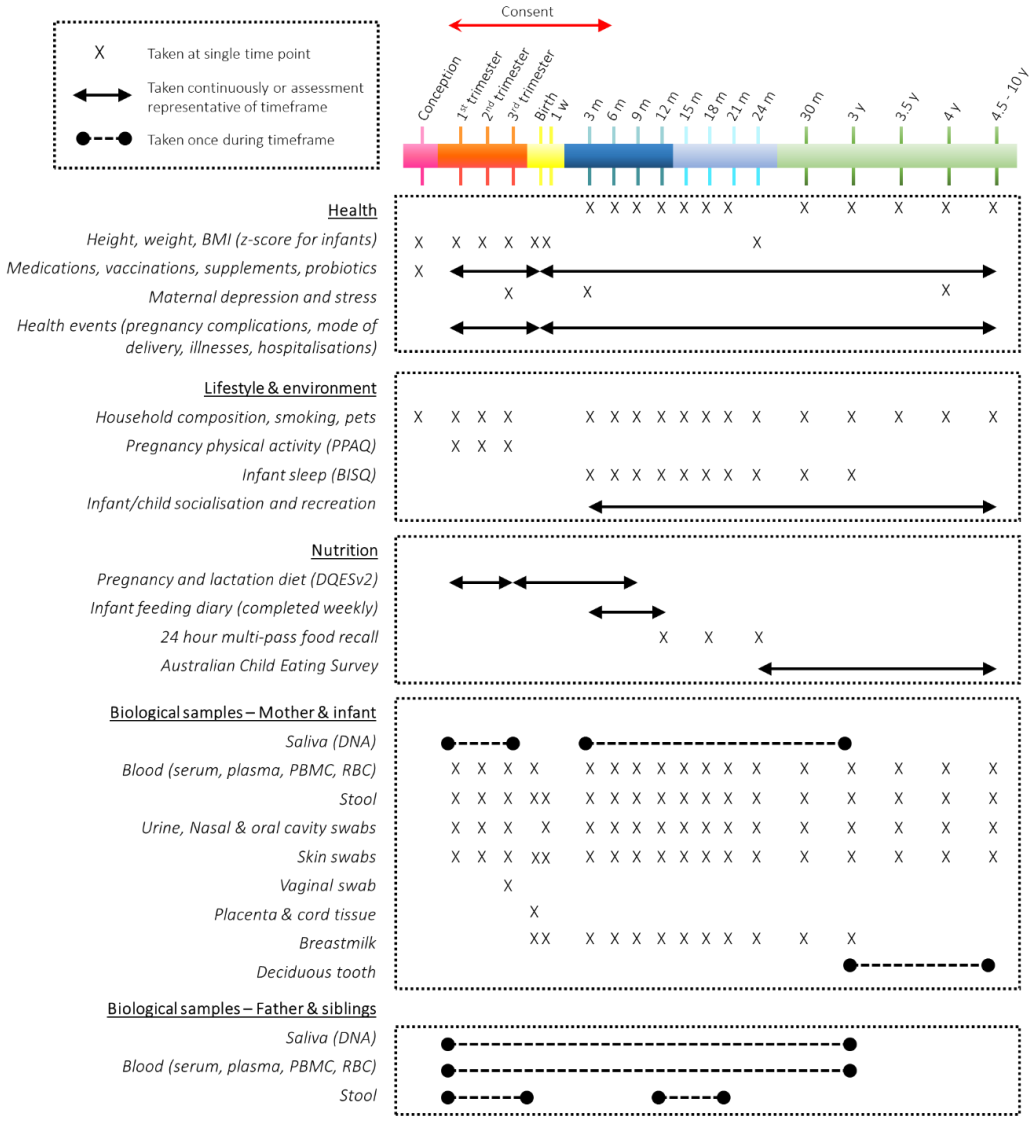
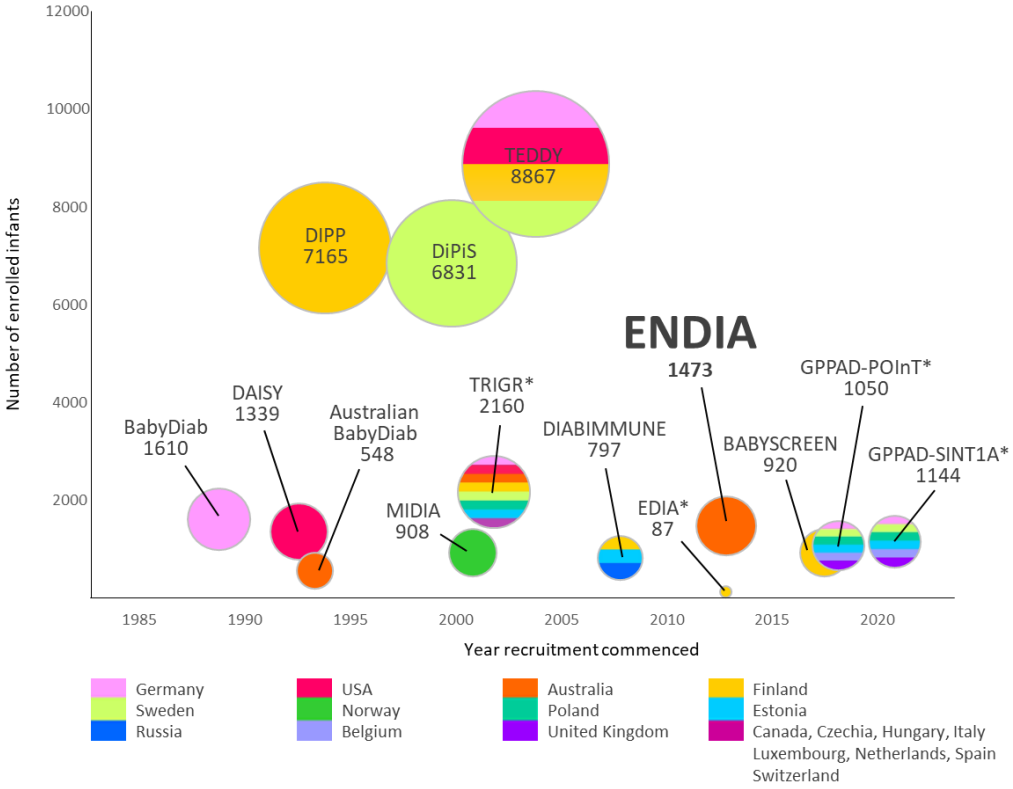
Supplementary Figures and Tables:



Supplementary Figure 1. Graphical summary of follow-up schedule in the ENDIA study.

Supplementary Table 1. Details of amendments to the ENDIA protocol following the publication of the original study protocol. *indicates new biospecimen collections introduced to the protocol.

Year	Details of amendment
2015	Addition of Barwon Health, Victoria and Monash Medical Centre, Victoria as recruitment sites
2016	Follow-up was extended until the child is 10 years of age. This was determined to be an appropriate time as the impact of insulin resistance in association with puberty may become increasingly relevant to disease progression beyond 10 years. Although early life exposures are not irrelevant in this older group, the numbers of children developing islet autoimmunity during the pre-pubertal and pubertal periods in ENDIA is likely to be at a slower rate.[1] Participants will have completed the study when they are 10 years old, or if they develop T1D, whichever occurs first.
	A retrospective preconception questionnaire was introduced to collect lifestyle data from the 3 months prior to conception for both parents (weight, supplements and medications, smoking, vaccinations, infections, stressful events, pets, exercise, sleep and diet).
	The Edinburgh Postpartum Depression Scale[2] and Perceived Stress Scale[3] were completed by the birthing parent during their third trimester and approximately 3 months postpartum.
	*Additional biospecimens were collected from all available immediate family members (stool and saliva from biological fathers and siblings for 'omics and genetics and postnatal blood samples from mothers to measure islet autoantibody levels and immune function).
	Modifications were made to sample collection protocols for participants living in regional areas.[4]
	Coeliac screen was expanded to include deamidated gliadin peptide immunoglobulin G and total immunoglobulin A as a more complete assessment of their risk for coeliac disease. Participants with a positive coeliac screen are referred to a paediatric gastroenterologist for follow up.
2017	A full blood count was introduced to be conducted in blood samples.
2018	*Collection of baby teeth was introduced. Deciduous teeth can be used to obtain information on exposures to during pregnancy and early life, including environmental toxins and stress hormones, to retrospectively reconstruct the dynamic exposome.[5] This is an emerging area and could help provide data on very early life exposures in a non-invasive way.
2019	The sample size was expanded from 1400 to 1500 infants in 2019 to include a minimum of 1200 infants recruited during pregnancy.
2020	Modifications were made to sample collection protocols in response to the COVID-19 pandemic.[6]
	A substudy was added to the protocol enabling ENDIA participants with persistent islet autoimmunity to undergo serial continuous glucose monitoring (ACTRN12620000947909).
2021	*Collection of an additional sample at the time of routine duodenal biopsy for ENDIA participants with coeliac autoimmunity.



Supplementary Figure 2. Bubble plot depicting the year of enrolment and size of established T1D risk cohorts that have followed children from early infancy or pregnancy. The colours indicate the country of enrolment. References are provided in Supplementary Table 2. *designates intervention studies.

Disclaimer: Information is based only on peer-reviewed published works and may not include cohorts' final number of participants.

Supplementary Table 2. Summary of the inclusion criteria for the early-life T1D risk cohorts.

Study name	ELIG	DR34	DR44	DR4X^	DR33	DR3X^	DRXX	GRS
BabyDiab[7]	FDR	yes#	yes#	yes#	yes#	yes#	yes#	-
DAISY[8]	COND	yes	yes	yes	yes	no	no	-
Australian BabyDiab#	FDR	yes#	yes#	yes#	yes#	yes#	yes#	-
DIPP[9]	COND	yes	no	yes	no	no	no	-
DiPiS[10]	COND	yes	no	yes	no	no	no	-
MIDIA[11]	COND	yes	no	no	no	no	no	-
TRIGR*[12]	FDR	yes	yes	yes	yes	yes	no	-
TEDDY[13]	COND	yes	yes	yes	yes	no	no	-
Diabimmune[14]	COND	yes	yes	no	yes	no	no	-
ENDIA	**FDR**	**yes#**	**yes#**	**yes#**	**yes#**	**yes#**	**yes#**	**-**
EDIA*[15]	FDR	yes	yes	yes	yes	no	no	-
BABYSCREEN[16]	COND	yes	yes	yes	yes	yes	no	-
GPPAD-POInT*[17]	COND & FDR	yes	yes	no	no	no	no	yes
GPPAD-SINT1A*[18]	COND & FDR	yes	yes	no	no	no	no	yes

ELIG refers to recruit eligibility requirements. ^indicates X represents genotypes other than 3 or 4. FDR refers to first degree relatives, and COND refers to conditional eligibility requirements based on HLA criteria where recruits are general population. For HLA genotypes “yes” indicates specific inclusion criteria while “no” corresponds to HLA types that were excluded from the studies. “yes#” indicates enrolment of these HLA types was incidental and not an inclusion or exclusion criteria. “-“ indicates the measure was not considered as part of the inclusion or exclusion criteria. GRS = genetic risk score. #personal communication with Jennifer Couper.

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