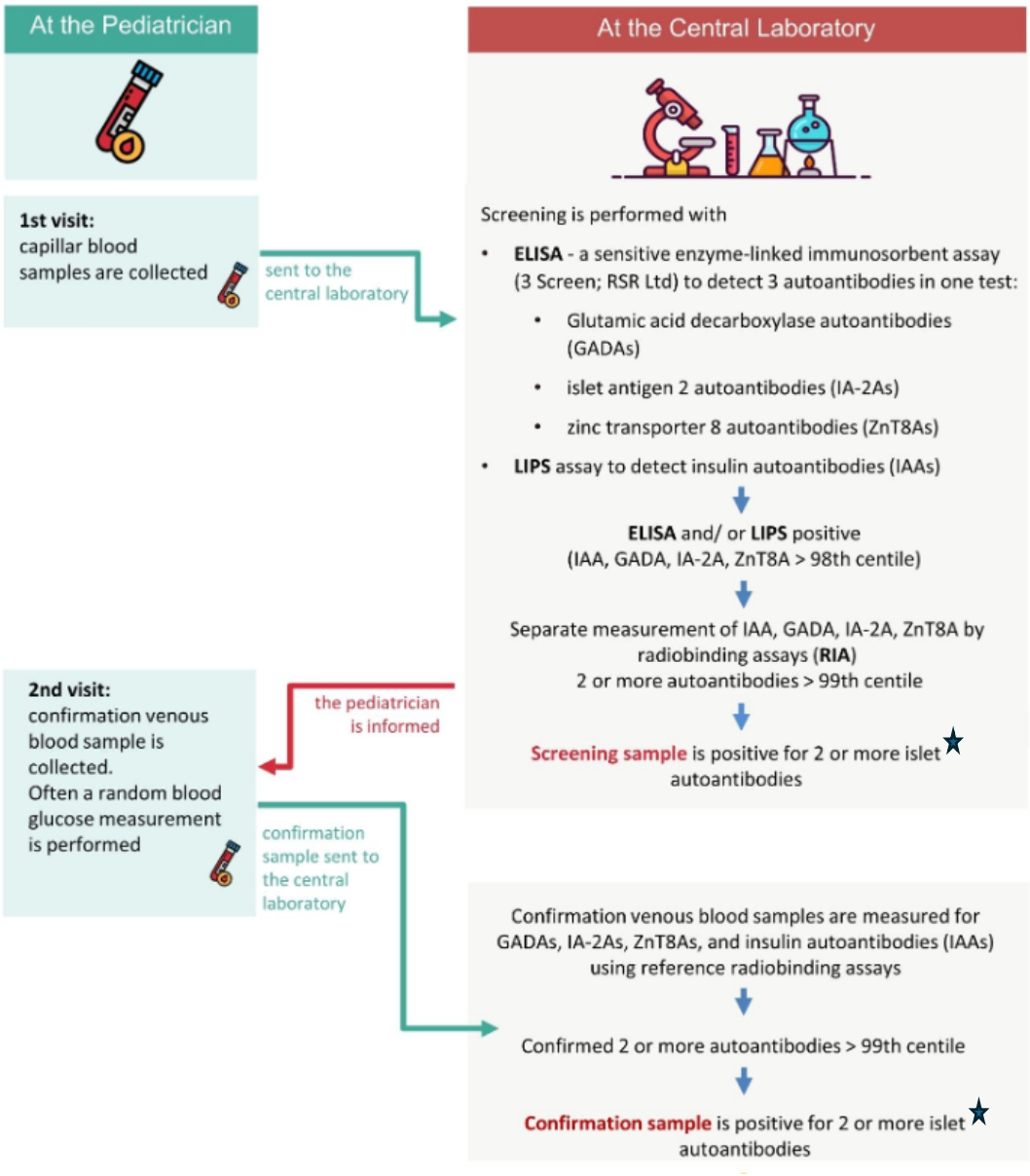
Abbreviations/Glossary

Abbreviation/term	**Explanation**
AB	Antibody
AB+	Antibody positive
T1D	Type 1 Diabetes
Early stage T1D/Frühstadium	Multiple AB positive in confirmation sample (>=2 single AB+); risk of progression to clinical T1D almost 100 %
single positive	If IAA or GADA or IA2 is positive in confirmation sample; low risk of progression to clinical T1D
FDR	First degree relative (mother, father, sibling); true, if at least one has T1D
GP	General population; true, if no FDR has T1D
FU	Follow-Up; Visits/Samples after Screening
hemolyzed	describes an abnormal blood condition; can happen for example if sample was not shipped fast enough or was exposed to hot temperatures
RIA	Radioimmunoassay; used for sinlge AB measurements
gada_trunc/GADA	T1D related Antibody; RIA measurement used to detect the GADA Antibody
ia2/IA-2A	T1D related Antibody; RIA measurement used to detect the IA-2 Antibody
znt8_c_arg/Zink	T1D related Antibody; RIA measurement used to detect the ZnT8R (arginine) Antibody
znt8_c_tryp/Zink	T1D related Antibody; RIA measurement used to detect the ZnT8W (tryptophan) Antibody
m_iaa/IAA	T1D related Antibody; RIA measurement used to detect the IAA Antibody
lips_unin_iaa	LIPS uninhibited measurement of the AB IAA; For Fr1da-Bayern from 18.02.2021-29.07.2025 as part of the first step in screening for detecting the AB IAA
lips_in_iaa	LIPS inhibited measurement of the AB IAA; tested in screening samples only if lips_unin_iaa not negative and in confiration samples
hbg_lips_in_iaa	High backgroud LIPS; LIPS: luciferase immunoprecipitation systems; Additional information to LIPS Inhibited IAA measurement
ELISA	Enzyme-linked Immunosorbent Assay; 3 Screen ELISA: first step in the screening process; screens for multiple beta cell autoantibodies in the blood (GADA, IA-2 and both ZnT8)
DBS	Dried Bloodspot (used for screening in Birmingham)

Fr1da-Screening in general (for lab munich)



Result of the screening:

- **Multiple positive/early stage T1D**: If confirmation sample is positive for >= 2 Antibodies → children are invited to participate in a follow-up with multiple visits per year (frequency depends on glycemic values)
- **Single positive**: If confirmation sample is positive for 1 Antibody (IAA or GADA or IA2) → children are invited to send yearly follow-up samples
- **Negative:** if a screening sample was directly negative or if the confirmation sample was negative for all AB

★**Additional info:**

- since 14.10.2019 a confirmation sample is requested as well if only one AB (IAA or GADA or IA2) was positive in the screening sample and
- a final single positive report (one AB positive) is possible, too.

Cutoffs: see PowerPoint 2025-08-19_Fr1daPlus_antibody_evalutaion

Dataset 1: Use AI tools to elaborate suitable cutoffs that define 'true early stage T1D', and 'true single at risk AB+' by using the ELISA as first screen and 4 antibodies as confirmation in the same and in a follow-up sample

- file: **all_relevat_screenings_fu_fr1da.xlsx**
- Condition: Every participant that in one screening (Screening- and/or Confirmation-Sample) had at least **one elisa** measurement and at least **two single antibody** measurements:
    - lips_in_iaa and/or m_iaa
    - gada_trunc
    - ia2
    - znt8_c_arg and/or znt8_c_tryp
- Data source: Fr1da-Bayern and Fr1da-Antibody-Follow-Up-Project in Bayern
- Dataset contains all screening and follow-up data of the participants that meet the condition in at least one screening
    - Multiple rows per screening possible:
        - in general: first row screening sample and second row confirmation sample
            - exception: it is possible that one screening sample is represented in two rows
                - in our database the elisa and lips uninhibited measurements are stored in one row and the ria measurements are stored in another row
                - both rows should contain the sample_date if it is the same sample but some sample_dates are missing for the ria values
                - if the sample_dates match, the elisa, lips uninhibited and ria values are merged into one row
                - if the sample_date is missing only in the row with ria values, the registration date is used as the sample_date and because the samle_dates are not the same, the values are not merged into one row but are listed in two rows with a different sample_date (see sample_date logic)
                - this should mostly be the case for newer samples because we are cleaning/filling the sample_dates of the ria sample on a regular basis if the field is empty
            - another exception: if the blood volume was too low there can be more than two rows per screening because another additional sample was requested; in that case there should be a report resend_low_volume present
            - more exceptions: there can be more individual exceptions that don't follow the usual pattern
        - confirmation sample is requested only if screening sample was not evaluated as negative
    - rescreening: participants can participate officially twice in the screening, but there are some participants with three screenings in the dataset
    - some negative screened participants were invided for a control FU; for those data from the follow-up database is as well part of the dataset
- The dataset is arranged by uid and sample_date

- Columns (if additional information necessary)
  - Elisa (same for both files)
    - For lab = Munich: all elisa values that were >= 3900 were replaced with 3900
  - hemolyzed
    - True if sample arrived hemolyzed
    - Information is not complete because information is not filled out for every sample (meaning: samples not marked as hemolyzed = true could also have been hemolyzed)
  - sample_date and age_at_sample (same for both files)
    - sample_date and date_of_birth can be wrong, because of
      - Wrong information on questionnaire (filled out by pediatrician/parents)
      - Error at data entry (questionnaire data are typed in manually)
    - For Fr1da-Bayern and Fr1da-Extension: sample_date logic
      - *sample_date*: date of blood withdrawl that is written on the questionnaire that comes with the sample
      - *registration_date*: date when sample arrived in the laboratory
      - if sample_date <= registration_date → sample_date
      - if sample_date > registration_date → registration_date
      - if no sample_date present → registration_date
  - all_reports_screening and final_report_screening: explanation of the report types

Report name	**Meaning**
negative	if a screening sample was directly negative or if the confirmation sample was negative for all AB
resend_low_volume	if blood volume was too low to test for all required AB in screening or confirmation sample another sample is requested
call_for_2nd_sample	if a screening sample was not negative a confirmation sample is requested
single_positive	if only one AB (IAA or GADA or IA2) was positive in the confirmation sample
multiple_positive	if >=2 positive AB are present in the confirmation sample; that means the participant gets diagnosed with early stage T1D
multiple_positive_ after_single	if someone got a single_postive report and develops >=2 positive AB in the FU the status changes to early stage T1D
negative_after_single	if someone got a single_postive report and in the FU all AB are negative the status changes to negative

  - screening_info
    - some participants have rescreenings but screenings without any values were not included in this dataset (e. g. a participant has only one row in the dataset with the screening_info “third” and has no other data, because in the first and second screening no AB values could be measured)
    - it is defined manually who is a rescreener meaning this information is not complete and participants with different uids could be the same participant but we didn’t find the connection

    - fdr and any_fdr (same for both files)
        - information can differ for one uid if information is not idetnical in the database for first and rescreening
    - sample_empty
        - information if there is any sample left
        - true if sample was empty before all required measurements could be done and also true if sample is empty after measuring all required measurements
- 18.11.2025 added: last_contact_or_t1d_date and last_contact_date_type
    - T1D Onset date, Dropout date or current date
    - If T1D Onset date present
        - last_contact_or_t1d_date: t1d onset date
        - last_contact_date_type = **t1d_date**
    - If no T1D Onset date but Dropout date present
        - last_contact_or_t1d_date: Dropout date or the date of last contact if there was any contact after dropout; we don't expect the probands to let us know after the last contact about a potential T1D onset
        - last_contact_date_type = **dropout_date**
    - If no T1D Onset date and no Dropout date
        - last_contact_or_t1d_date: 18.11.2025
        - last_contact_date_type = **current_date**

Dataset 2: To elaborate differences in ELISA distributions between laboratories, relatives vs. GP, sex, age at testing and months/years

- file: **all_screening_elisa.xlsx**
- Condition: Every screening-sample with an **elisa** value is part of this dataset
- Data sources/studies and the site of the Lab where elisa was measured:

Study	Lab
Fr1da-Bayern and Fr1da-Antibody-Follow-Up-Project in Bayern	Munich
Fr1da-Extension in Hessen and Rheinland-Pfalz	Munich
Fr1da-Plex Hannover	Munich
Fr1da-Plex Dresden	Dresden
Edent1fi: Birmingham, Lisbon, Milan, Prague, Warsaw, Katovice (lab Warsaw)	Birmingham, Lisbon, Milan, Prague, Warsaw

- Fr1da-Antibody-Follow-Up-Project: Fr1da-Bayern participants that in a previous screening had an elisa >= 20 and with a negative end result were invited to send another screening sample to evaluate the elisa cutoff in the past
- In general there is only one row per screening (timepoint and participant) but there can be multiple rows per participant (different timepoints):
    - One participant is represented by one uid (same uid for all rows of one participant)
    - For participants that participated more than once in the Fr1da-Bayern study or in the Fr1da-Antibody-Follow-Up-Project there are two or more rows in the dataset
        - participants can participate officially twice in the screening, but there are some participants with more screenings in the dataset
    - For some participants measured in Prague there are two samples present in the dataset
- Columns (if additional information necessary)
    - Elisa (same for both files)
        - For lab = Munich: all elisa values that were >= 3900 were replaced with 3900
    - sample_date and age_at_sample (same for both files)
        - Sample_date and date_of_birth can be wrong, because of
            - Wrong information on questionnaire (filled out by pediatrician/parents)
            - Error at data entry (questionnaire data are typed in manually)
        - For Fr1da-Bayern and Fr1da-Extension: sample_date logic
            - if sample_date <= registration_date → sample_date
            - if sample_date > registration_date → registration_date
            - if no sample_date present → registration_date
    - screening_info
        - some participants have rescreenings but screenings without an elisa value were not included in this dataset (e. g. a participant has only one row in the dataset with the screening_info “third” and has no other data, because in the first and second screening no elisa value was measured)
        - it is defined manually who is a rescreener meaning this information is not complete and participants with different uids could be the same participant but we didn’t find the connection
    - fdr and any_fdr (same for both files)
        - information can differ for one uid if information is not idetnical in the database for first and rescreening
- The dataset is arranged by lab and sample_date

- last_contact_or_t1d_date and last_contact_date_type (change 18.11.2025)
    - T1D Onset date, Dropout date or current date
    - If T1D Onset date present
        - last_contact_or_t1d_date: t1d onset date
        - last_contact_date_type = **t1d_date**
    - If no T1D Onset date but Dropout date present
        - last_contact_or_t1d_date: Dropout date or the date of last contact if there was any contact after dropout; we don't expect the probands to let us know after the last contact about a potential T1D onset
        - last_contact_date_type = **dropout_date**
    - If no T1D Onset date and no Dropout date
        - last_contact_or_t1d_date: 18.11.2025
        - last_contact_date_type = **current_date**

Update 18.11.2025
Both files are the same as last time with the only difference in the two columns:
last_contact_or_t1d_date, last_contact_date_type