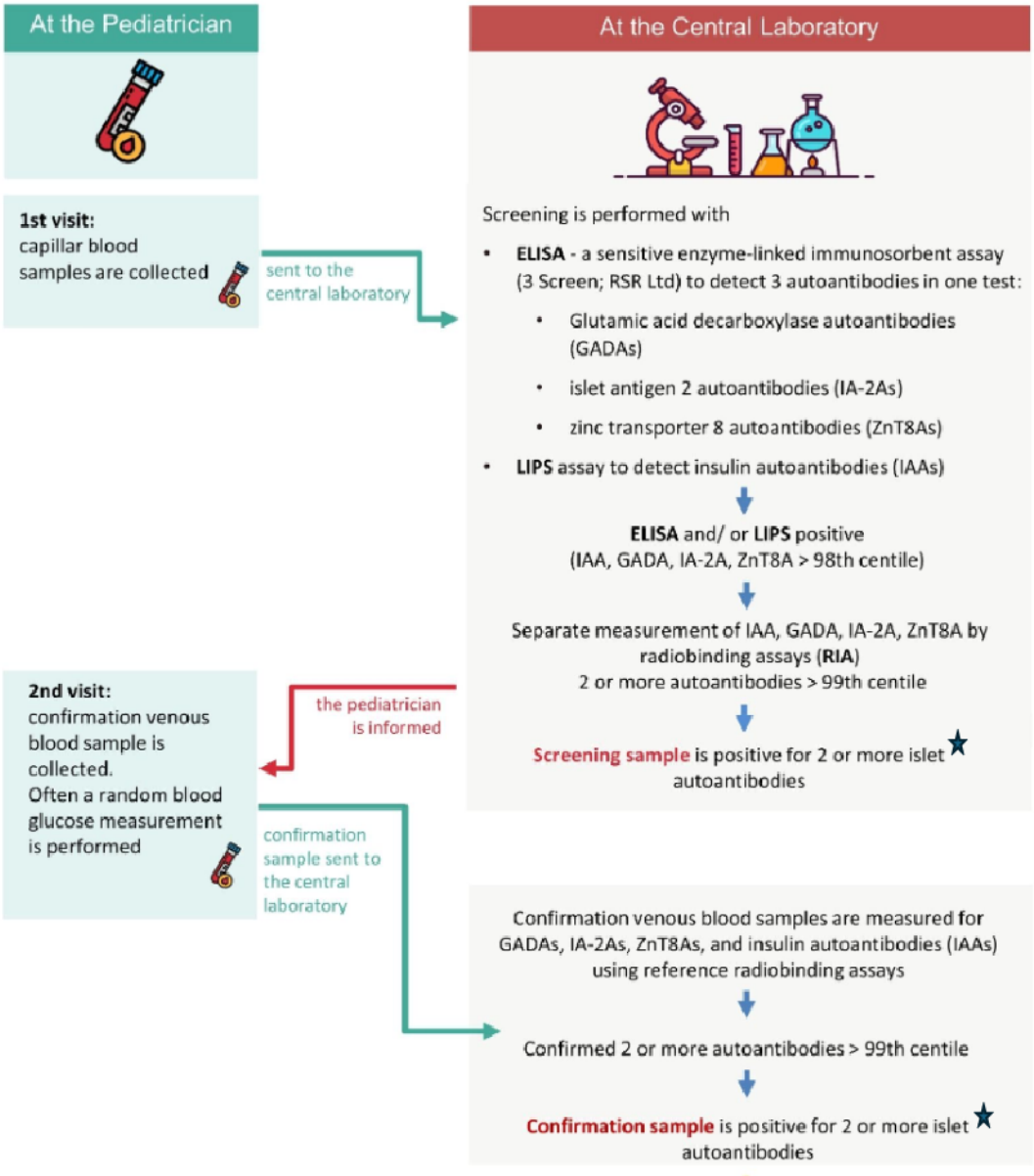
Abbreviations/Glossary

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

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
    - T1D Onset date or date of the last contact without T1D if no T1D onset so far
    - So far we only have the information about T1D onset for Fr1da-Bayern
    - The information about wheter anyone at Fr1da-Plex Dresden has developed clinical T1D will be added later
    - In other studies, the FU has generally not been long enough for participants to develop clinical T1D, and if they have already developed it, we can't currently tell because the information is not available in the database