The Estimation of the Prevalent Presymptomatic Type 1 Diabetes Population in Germany Using a Patient Funnel Model

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Aymeric Mahieu[1], Abdul Jabbar Omar Alsaleh[2], Tom Clemmet[3], Hasan Basarir[3], Denis Azabdaftari[4], Klaus Bornholdt[4], Maja Hergl[5], Anette-Gabriele Ziegler[5]

[1]Sanofi, Paris, France; [2]Sanofi, Milan, Italy; [3]RTI Health Solutions, Manchester, UK; [4]Sanofi, Berlin, Germany; [5]Institute of Diabetes Research, Helmholtz Munich German Research Center for Environmental Health, Munich, Germany

OBJECTIVE

- **To develop a *de novo* patient funnel model that leverages stage 3 type 1 diabetes (T1D) incidence data.**
- **To estimate the prevalence of the stages of presymptomatic T1D in Germany.**

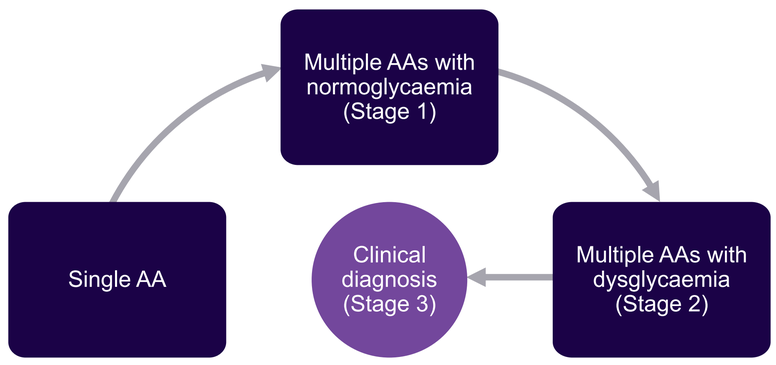
CONCLUSIONS

- **This epidemiological patient funnel model is driven by stage 3 T1D incidence data, which is often reported more widely and robustly than presymptomatic T1D prevalence data.**
- **The funnel provides estimates of population sizes by presymptomatic T1D stage in Germany. Such estimates contribute essential information to help optimise population-based screening programmes, enabling early identification of individuals in this disease continuum and facilitating timely interventions that may delay or modify the progression to symptomatic T1D.**

BACKGROUND

- T1D is a progressive disorder characterised by autoimmune destruction of insulin-producing pancreatic β-cells, leading to lifelong insulin dependence and substantial clinical and economic burden.[1]
- T1D screening enables the identification of individuals in early stage with no symptoms but have entered into the immune process of β-cell destruction, before clinical onset, which often go unrecognized as ~90% of new T1D cases have no family history to identify their risk.[2,3]
- T1D progresses through identifiable presymptomatic stages before clinical diagnosis (**Figure 1**),[4] offering a window of opportunity for early detection and intervention that may delay disease onset through therapies modulating the immune process.

Figure 1: T1D progression



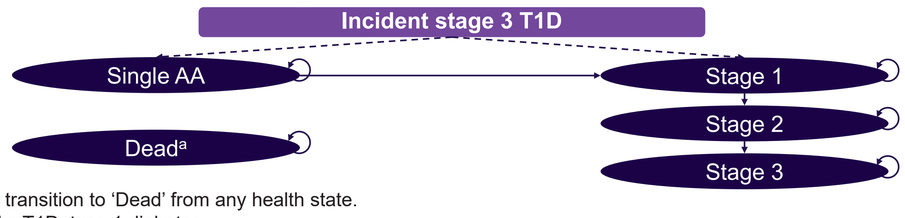
AA, autoantibody; T1D, type 1 diabetes

- The Fr1da study screened over 220,000 children for T1D-associated autoantibodies (AAs) in Germany, demonstrating the feasibility of large-scale early detection in the general paediatric population.
- Accurate prevalence data are essential for optimising screening programs. However, current estimates are primarily based on data from targeted screening initiatives, which limit their applicability to broader populations.[2]
- Therefore, it is essential to develop a robust approach to estimate the prevalence of presymptomatic T1D across diverse populations to inform comprehensive evaluations of screening strategies and their potential public health impact.

METHODS

- A cohort-level model was developed using Microsoft Excel® to estimate the number of individuals at each stage of presymptomatic T1D in Germany.
- The model cycle length was 3 months, with a flexible time horizon that could estimate outcomes over a period of up to 20 years.
- The patient funnel model used data on T1D incidence (stage 3) and the time from seroconversion to T1D onset to estimate the number of people with stage 1 T1D or single AA at baseline. Subsequent progression through presymptomatic T1D stages to stage 3 T1D was modelled using a Markov approach (**Figure 2**).

Figure 2. Patient funnel model diagram



[a]Individuals can transition to 'Dead' from any health state.
AA, autoantibody; T1D, type 1 diabetes

- Relevant model inputs and their sources are summarised in (**Table 1**).

Table 1: Model inputs

Model inputs	Sources/references
Age-specific stage 3 T1D incidence rates	Reitzle *et al.*, 2023[5]
Median time between stage 3 T1D onset and seroconversion	Ghalwash *et al.*, 2022[6]
Transition probabilities between single AA and stage 1 T1D	Chmiel *et al.*, 2015[7]
Transition probabilities between stage 1 and stage 2 T1D	Fr1da data on file, 2025[8]
Transition probabilities between stage 2 and stage 3 T1D	Fr1da data on file, 2025[8]
Age-specific adjustment of transition probabilities	Wherrett *et al.*, 2015[9]

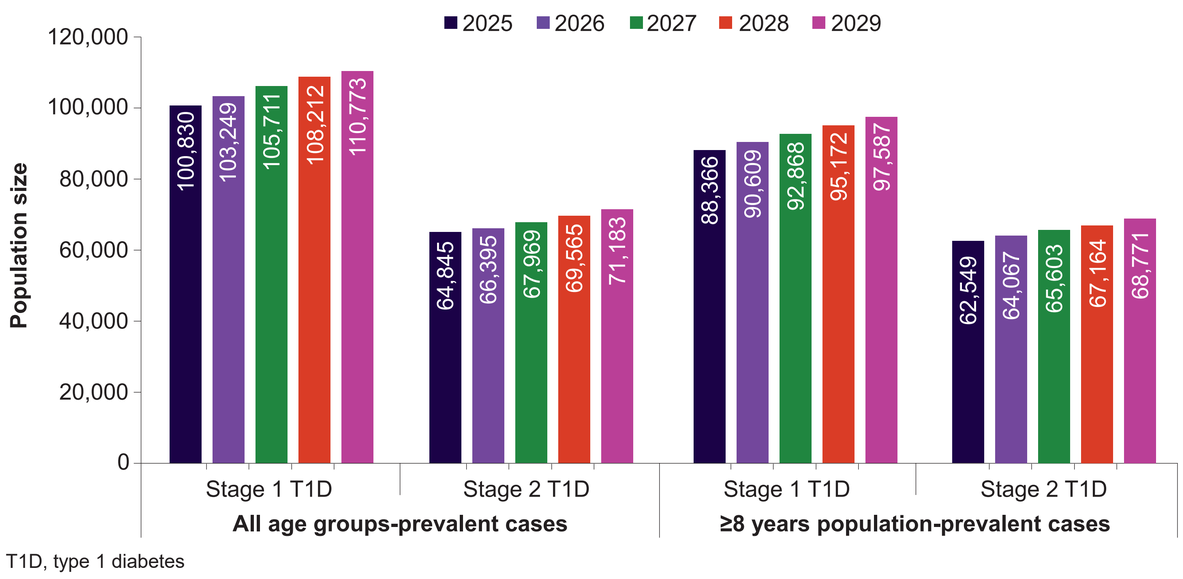
AA, autoantibody; T1D, type 1 diabetes

- The model was informed by national demographic data for Germany, including age distribution and birth trends.

RESULTS

- Across all age groups and in the ≥8 years population, the model results suggested an increasing prevalence of T1D over a 5-year period (2025–2029) driven by rising T1D incidence rates,[10] with stage 1 T1D having a larger prevalence than that of stage 2 T1D (**Figure 3**).

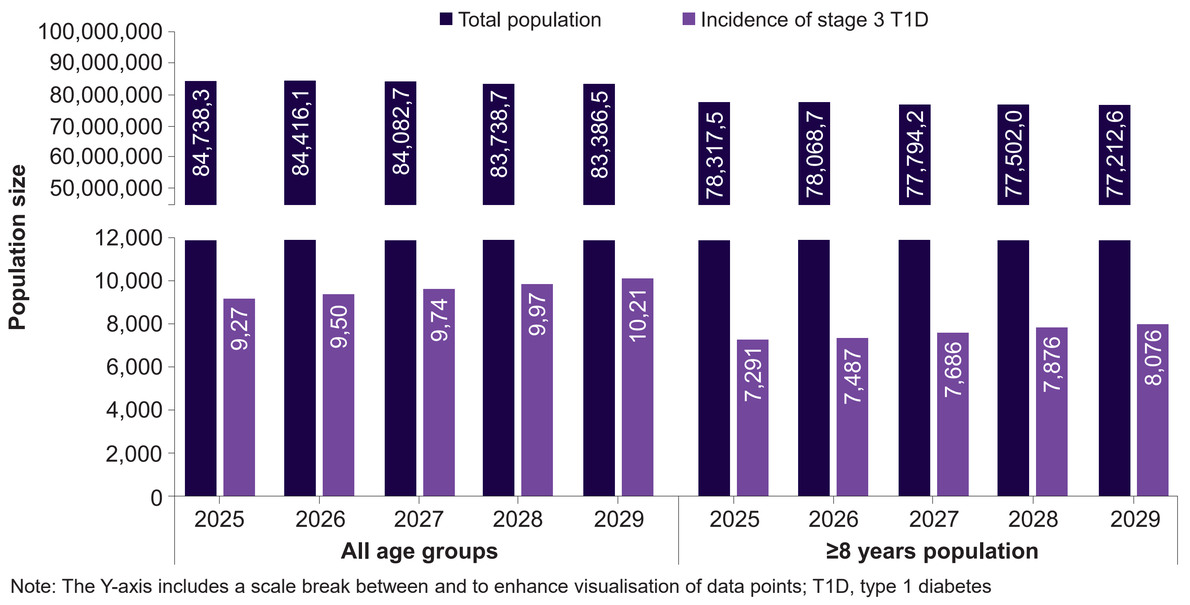
Figure 3: Estimates of presymptomatic T1D prevalent cases across all age groups and the ≥8 years population during 2025–2029



T1D, type 1 diabetes

- The total population in Germany and the incidence of stage 3 T1D cases across the age groups projected by the model for a 5-year period is illustrated in **Figure 4**.

Figure 4: Estimates of total population and incidence of stage 3 T1D cases across all age groups and the ≥8 years population during 2025–2029



Note: The Y-axis includes a scale break between and to enhance visualisation of data points; T1D, type 1 diabetes

DISCUSSION

- The patient funnel model results aligned with previous estimates for the prevalence of presymptomatic T1D in the general population (**Table 2**).[2]

Table 2: External validation

Validation study	Outcome	Age group screened (years)	Validation study value	Patient funnel model value
Fr1da	Prevalence of stage 1 or 2 T1D	1.75–10.99	0.3%	0.37%
Fr1dolin	Prevalence of stage 1 or 2 T1D	2-6	0.35%	0.26%
ASK	Prevalence of stage 1 or 2 T1D	1-17	0.52%[a]	0.38%[a]

[a]ASK estimates are based on a United States population, but the patient funnel model estimates were based on a German population.[2]

- The model estimates were comparable to estimates reported for the Fr1da and Fr1dolin studies.
- The stages 1 and 2 prevalence estimates were slightly lower in the patient funnel model than those reported for the ASK study, though these two estimates were informed by data for different countries, suggesting that considerable variability and potential uncertainty remains for these outcomes.

LIMITATIONS

- Critical knowledge gaps persist in presymptomatic T1D progression, particularly regarding the time between seroconversion and diagnosis in adults, and the proportion of stage 3 T1D cases without AAs. These uncertainties require clinical validation to enhance model accuracy and reliability.

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CONFLICTS OF INTEREST

AM, AJOA, DA, and **KB** are employees of Sanofi and may hold stock and/or stock options in the company. **HB** and **TC** are employees of RTI Health Solutions, which received funding from Sanofi to develop the model that informed this abstract. **AGZ** is a member of the data monitoring committee for 2 clinical trials for Sanofi and serves on an advisory board for Sanofi. **MH** has no conflicts of interest.

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