

# Diabetes Type 2 in the Berlin Aging Study II: Prevalence, Incidence and Severity Over up to Ten Years of Follow-up

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## Research Article

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# Abstract

**Aim:** To describe the prevalence, incidence, and severity of diabetes mellitus type 2 (T2D) and antidiabetic medication in older people and to assess the prognostic value of diagnostic laboratory parameters.

**Methods:** Baseline data of 1,671 participants of the Berlin Aging Study II (68.8 ±3.7 years) and follow-up data assessed 7.4 ±1.5 years later were analysed. T2D was diagnosed based on self-report, antidiabetic medication use, laboratory parameters. T2D severity was determined by the diabetes complications severity index (DCSI). Prognostic capacity of laboratory parameters was evaluated by Receiver Operating Characteristics (ROC) and Areas Under the Curve (AUCs).

**Results:** The proportion of participants with T2D increased from 12.9% (37.3% women) at baseline to 17.1% (41.1% women) with 74 incident cases and 22.2% not being aware of the disease at follow-up. More than half of the 41 newly identified incident T2D cases were diagnosed solely by the 2h-plasma glucose test (OGTT) and diagnosis based on OGTT as the only criterion among incident cases was found more frequently in women (p=0.028). The OGTT assessed at baseline predicted incident T2D less accurate in men (AUC: 0.671, 95% CI 0.570-0.771) when compared to women (AUC: 0.7893, 95% CI 0.7036-0.8751). No sex differences were detected with respect to antidiabetic medication used and T2D severity.

**Conclusions:** A comprehensive picture of T2D with respect to prevalence, incidence, and severity in older people is provided. Clinically relevant sex differences in the capacity of the commonly used T2D diagnostic laboratory parameters to predict incident T2D on average 7.4 years later were detected.

## Introduction

The number of people diagnosed with diabetes has risen over the past decades, now reaching a prevalence of up to 10% in some countries (1), with an estimated average of 9.3% worldwide (2). In Germany this number has increased from <2% in the 1950s (3, 4) to 9.2% in 2010, including 2% undiagnosed cases (21.7% of the T2D patients) as reported from the German Health Interview and Examination Survey for Adults (DEGS1, 2008–2011) (5). As the risk of being diagnosed with diabetes increases with age, the globally estimated prevalence is almost 20% in the 65-79 year olds (2). Studies suggest that only 49.9% of patients worldwide and 60.3% of patients in Europe affected from diabetes mellitus are aware of their condition (2).

Besides genetic and demographic factors the following life style factors are associated in a significant way with diabetes mellitus type 2 (T2D): high body mass index (6), low physical activity (7), smoking (8), alcohol consumption (9) and an unhealthy diet (10). Being affected by diabetes results in a higher risk for comorbidities and a growing burden for the healthcare system, given that people diagnosed with T2D have healthcare expenditures 1.7 x higher than people without this diagnosis (11, 12). Micro- and macrovascular complications deriving from diabetes mellitus, including for example nephro- and neuropathy, and coronary vascular disease (13), are the main cause for these growing expenses (14).

Besides micro- and macrovascular complications, T2D is also associated with other diseases, such as depression (15) and dementia (16) to only give two examples. Early diagnosis and treatment of T2D are essential, as studies show that adequate glycaemic control in people who are affected by T2D lowers the risk for developing complications and improves the outcome for patients who had already developed them (15, 17–21).

To quantify the severity of diabetic complications and to better predict the risk of adverse outcomes, Young et al. developed the Diabetes complications severity index (DCSI) (22). The DCSI incorporates seven categories of diabetic micro- and macrovascular complications: *retinopathy, neuropathy, nephropathy, cardiovascular disease, cerebrovascular disease, peripheral vascular disease, and metabolic complication*.

The DCSI as well as its adapted version (aDCSI), which does not consider laboratory parameters (23), have been used as predictors of mortality, hospitalization, and healthcare use and cost in datasets of primary care and health insurances (22, 24–27). It has also been used as a valid measure for the severity of diabetes and its comorbidities in cross-sectional studies (28–30). The change of the DCSI and the aDCSI over time has been investigated several times using claims data (31–36). To our knowledge, longitudinal prospective data on the DCSI change have not yet been reported so far in a comparable German age group.

Aim of the current study was to describe the prevalence, incidence, and severity (DCSI) of T2D in a cohort of older men and women aged 60 years and above over the course of up to 10 years, since longitudinal data on this topic are scarce for this age group in Germany. The analyses additionally included the investigation of the criteria resulting in the T2D diagnoses, anti-diabetic medication, and also the capacity of three parameters of the glucose status, fasting glucose, HbA1c and 2-h-glucose (oral glucose tolerance test, OGTT), to predict incident T2D in both sexes.

## Methods

### **Berlin Aging Study II baseline assessments and follow-up as part of the GendAge study**

Participants of the Berlin Aging Study II (BASE-II) were recruited through an existing participant pool at the Max Planck Institute for Human Development and public advertisements from the Berlin metropolitan area. Baseline medical assessments took place between 2010-2014 and included 1,671 participants aged 60 years and older (range: 60–84 years, older BASE-II group). Follow-up data on 1,083 participants were assessed on average  $7.35 \pm 1.46$  years later (range 3.91 - 10.37 years) as part of the GendAge study. For further details on BASE-II and GendAge see Bertram et al. (39) and Demuth et al. (60).

In the current study we included a total of 209 participants with a T2D diagnosis at baseline. 185 participants had the diagnosis at follow-up. Of these 185, 111 had this diagnosis already at baseline or

were newly diagnosed on this occasion (prevalent cases). Seventy-four were newly diagnosed after baseline assessment (incident cases), of which 41 were diagnosed for the first time at follow-up (see Figure 1).

The T2D diagnosis of 15 participants at baseline could not be confirmed at follow-up. Six of them had reached the cut-off for at least one of the diagnostic laboratory values (see below) at baseline, which was then close to the cut-off but not reaching it at follow-up. The remaining nine participants were considered to have T2D at baseline based on the medical history provided, which was differently reported at follow-up.

## Diabetes mellitus type 2 (T2D)

Diabetes mellitus type 2 was diagnosed based on American Diabetes Association (ADA) guidelines (61) when applying at least one of the following criteria:

- Anamnestic history of diabetes mellitus type 2 (self-report)
- Antidiabetic medication
- Fasting plasma glucose  $\geq 126$  mg/dl
- 2h plasma glucose during 75g-OGTT  $\geq 200$ mg/dl
- HbA1c  $\geq 6.5\%$

Prediabetes was diagnosed applying fasting glucose (100 – 125 mg/dl) and/or HbA1c (5,7 – 6,4%) and/or 2h plasma glucose during 75g-OGTT (140 – 199 mg/dl) according to ADA guidelines (61).

## Diabetes Complications Severity Index (DCSI)

The Diabetes Complications Severity Index (DCSI) is a score developed by Young et al. to evaluate whether the complications of diabetes and the degree of its severity determine mortality and risk of hospitalization (22). The score incorporates seven categories of complications deriving from diabetes, encoded according to the International Classification of Diseases, Ninth Revision (ICD-9-CM):

*Retinopathy, nephropathy, neuropathy, cerebrovascular disease, cardiovascular disease, peripheral vascular disease, and metabolic complication.* The index scale for each category ranges from 0-2 (0=no complication; 1=some complication; 2=severe complication), except for *neuropathy*, which is scored with 0-1, resulting in a maximum value of 13. Information on acute metabolic complications were not considered in our questionnaires and therefore this information is not available; thus, a maximum score value of 11 was achievable in our cohort. We computed the DCSI based on the data available in the BASE-II baseline and GendAge follow-up datasets and representing the DCSI categories as accurate as possible. A detailed description can be found in supplementary table 1. We included all 111 datasets of participants diagnosed with T2D at baseline and follow-up.

# Assessment of characteristics in the context of T2D

We evaluated physical activity using the Rapid Assessment of Physical Activity (RAPA) questionnaire. Body weight was measured to the nearest 0.1 kg and height was determined to the nearest 0.1 cm by using an electronic weighing and measuring station (seca 764, seca, Hamburg, Germany). The body mass index was calculated using the standard formula (weight in kilograms divided by height in metres squared). We used a modified version of the morbidity index originally described by Charlson (62), for details see (63).

## Statistical Analysis

The 'UpSet' plots (Figure 2 and 4) were produced with R 3.6.2 (64) and the "UpSetR" package (65). To analyze the intersection between the individual diagnostic categories or medication, we formed separate datasets that contained only participants who met the regarding criteria. Subsequently, the intersections between the individual datasets were analyzed and visualized as 'UpSet' plot. The bars on top of the columns represent the intersection size and the rows represent the individual datasets. All intersections are displayed and sorted by frequency.

Receiver Operating Characteristics (ROC) and Areas Under the Curve (AUCs) and its confidence intervals were calculated with the "pROC" package (66) in R. Logistic regression models were calculated by R's "glm" function.

## Results

In the current study, we used data from two waves of medical assessments of the older subsample of BASE-II participants, which represent up to 10.4 years of follow-up (mean follow up at  $7.4 \pm 1.5$  years). Data were available for 1,671 (mean age  $68.8 \pm 3.7$  years, 51.6% women) and 1,083 (mean age  $75.6 \pm 3.8$  years, 52.0% women) participants of baseline and follow-up assessments, respectively. Detailed characteristics are shown in table 1.

Two hundred and nine participants were diagnosed with T2D at baseline out of 1,625 for whom T2D data were available (12.9%,  $68.7 \pm 3.7$  years, 37.3% women), 52 of them were newly diagnosed (24.9%). One hundred eighty-five participants (out of 1,083) had this diagnosis at the time of follow-up (17.1%,  $75.6 \pm 4.2$  years, 41.1% female), including 111 prevalent and 74 incident cases (Figure 1). The corresponding incidence rate is 10.1 new T2D diagnoses per 1000 person-years. Of the 185 T2D cases at follow-up, 41 participants (22.2%, females N=21) were not aware of the disease, which resembles the proportion observed at baseline. At baseline, men had a T2D prevalence of 16.2% and women of 9.0% which increased at follow-up to 21.0% and 13.5%, respectively. Baseline and follow-up characteristics of participants with T2D are displayed in supplementary table 2. Details of the analytical sample of 111 participants diagnosed with T2D at baseline *and* follow-up, the prevalent cases, are displayed in table 2.

At baseline 38.9% of the participants had prediabetes. When focussing on the 74 incident T2D cases, for which 64 full laboratory datasets were available, 61 of 64 (95.3%) had prediabetes at baseline, and as expected they had significantly higher fasting blood glucose and HbA1c values at baseline when compared to the participants who had not developed T2D at the time of follow-up (both  $p < 0.05$ , Welch's t-test).

We next evaluated baseline HbA1c and fasting blood glucose in the 41 participants with incident T2D who were diagnosed at follow-up for the first time. This revealed that the mean baseline HbA1c was within the prediabetic range for both, men and women (both  $5.8\% \pm 0.3$ ), whereas this was the case for fasting glucose only in men ( $101.9 \text{ mg/dl} \pm 8.7$ ) and not in women ( $97.7 \text{ mg/dl} \pm 9.3$ ).

## Diabetes diagnostic criteria and antidiabetic medication at follow-up

We next focused on the diagnostic criteria and their combinations leading to the T2D diagnosis in the 185 participants with T2D at follow-up (figure 2). A total of 143 participants were diagnosed based on at least one laboratory parameter, fasting glucose, 2h-glucose (OGTT) or HbA1c, and 46 participants fulfilled the maximum of four diagnostic criteria (OGTT was only performed when T2D was not known): anamnestic information, antidiabetic medication, fasting glucose and HbA1c. In 42 participants the T2D diagnosis was based solely on anamnestic information on an existing T2D diagnosis and/or antidiabetic medication use without any of the laboratory parameters reaching the diagnostic cut-off. With 24 out of the 41 incident T2D cases at follow-up more than half of the newly diagnosed participants were diagnosed solely by the 2h-OGTT. Interestingly, the T2D diagnosis based on impaired glucose tolerance (OGTT) as the only criterion among the incident cases was found more frequently in women ( $N=16$ ) than in men ( $N=8$ ), a difference which was statistically significant ( $p=0.028$ , Fisher's exact test, supplementary figure 2 and 3).

We next evaluated the capacity of the three laboratory parameters, fasting glucose, HbA1c and 2h-glucose (OGTT), as assessed at baseline to predict incident T2D at follow-up ( $7.4 \pm 1.4$  years later, a dataset of  $N=860$  with all three parameters available was used for this analysis). Figure 3A shows the ROC curves from this analysis, which revealed that the AUCs for fasting glucose, HbA1c and 2h-glucose were comparable with overlapping 95% confidence intervals (CI) and can be classified as within the acceptable range: fasting glucose, AUC: 0.820, 95% CI 0.767-0.874; HbA1c, AUC: 0.792, 95% CI 0.735-0.850 and 2h-glucose (OGTT), AUC: 0.718, 95% CI 0.648-0.788. Stratification of this analysis by sex revealed that all three parameters of the glucose status tested are equally able to predict incident T2D with AUCs comparable to the values yielded from the not stratified analysis, with the exception of the 2h-glucose (OGTT) in men which predicted incident T2D less accurate (AUC: 0.671, 95% CI 0.570-0.771, Figure 3B and C).

Evaluating the antidiabetic medication of our sample in the follow-up dataset revealed that 100 out of the 185 participants diagnosed with T2D were treated with antidiabetic drugs. The majority (N=85) used metformin, 47 of them as the only antidiabetic medication and 38 in combination with another oral antidiabetic drug or insulin; the most frequent combination being metformin and a dipeptidyl peptidase 4 (DPP-4) inhibitor (N=15). There was no significant difference between women and men with respect to the antidiabetic medication, when considering each medication separately. For details see figure 4.

## Diabetes complications severity index (DCSI) at baseline and follow-up for prevalent cases

We computed the DCSI for both waves of assessments as a measure of T2D severity in prevalent cases and determined its change between the two assessments to evaluate T2D progression. The DCSI significantly increased in the  $7.3 \pm 1.5$  years between baseline and follow-up (mean DCSI  $1.1 \pm 1.2$  vs.  $2.0 \pm 1.8$ ; range 0-5 vs. 0-6). The mean DCSI in women (N=40) increased from  $0.7 \pm 0.8$  to  $1.8 \pm 1.7$  and in men (N=71) from  $1.3 \pm 1.4$  to  $2.1 \pm 1.8$  (all  $p < 0.01$ , Wilcoxon signed rank test). Thus, while the DCSI was higher in men at both time points, the increase of T2D severity as assessed with the DCSI was higher in women, but not statistically significant. The DCSI change per year was 0.12 in men and 0.14 in women. Results are displayed in figure 5 and 6.

In a next step we compared the different DCSI constituting categories (see supplementary table 3) with respect to their impact among the participants with prevalent T2D at both time points of assessment. This revealed that *cardiovascular* complications was the complication with the highest impact of 43.2% at baseline, and a steep increase to 67.6% at follow-up. This was followed by the DCSI categories *nephropathy* (21.6% and 61.3%) and *peripheral vascular disease* (27.9% and 28.8%). When looking at sex-differences, at baseline men were significantly more likely affected from cardiovascular diseases than women, but at follow-up this difference was not significant anymore ( $p < 0.05$  and  $p = 0.214$ , Mann-Whitney-U test). At follow-up *nephropathy* had the highest impact (60.0%) in women, followed by *cardiovascular diseases* (52.5%), whereas for men it was the other way around (76.1% and 62.0% respectively). When comparing the progression of each category, there was no significant difference between the sexes ( $p > 0.05$ , Mann-Whitney U test).

## Discussion

In the current study, we assessed the course of T2D over up to 10 years in terms of prevalence, incidence, and disease severity as reflected by the DCSI, as well as diagnostic criteria and antidiabetic medication. Epidemiological data on the prevalence and incidence of diagnosed, undiagnosed, and new-onset diabetes were lower, but basically in keeping with comparable nationwide data from the DEGS1 study (5). The prevalence of diabetes was lower in the current study (12.9% at baseline and 17.1% at follow-up) when compared to the nationwide reported 23.9% among 65-79 year olds. On average 23.6% (24.9% at baseline, 22.2% at follow-up) were undiagnosed cases compared to 17.6% when looking at 65-79 year-

olds in Germany (5). However, undiagnosed cases were only determined by HbA1c measurements in DEGS1, whereas we additionally considered fasting glucose and the OGTT. The incidence rate for diagnosed and undiagnosed diabetes in the current study was lower compared to nationwide data with 10.1 per 1000 person-years compared to 12.8 (37). On the one hand, these differences might be due to the fact that the nationwide data incorporate all types of diabetes and not only diabetes type 2, even though diabetes type 2 makes up over 90% of all diabetes diagnoses (38). On the other hand, the lower T2D prevalence in the current study might be explained Berlin Aging Study II participants being overall healthier at baseline when compared to nationwide data as described earlier (39).

Focussing on sex differences of diabetes prevalence in Germany, more men than women are affected from diabetes when considering the 18-79 year-olds (9.9% vs. 8.6%) (5) and also concerning 60-69 year-olds (14.5% vs. 10.0%) and 70-79 year-olds (21.9% vs. 16.9%); women “catch up” with and even overtake men when older than ninety years (40). The numbers reported here are comparable, with more men than women diagnosed with T2D (at baseline 16.2% vs. 9.0%; at follow-up 21.0% vs. 13.5%). As our cohort consists of participants that were on average younger than 80 years old, we could not determine conclusively whether women would overtake in terms of diabetes prevalence in older age.

When investigating T2D severity, the mean DCSI value increased from 1.1 to 2.0 between the two assessments. Men had a higher baseline and follow-up DCSI, whereas women had a stronger DCSI increase within the observation period, even though the latter difference did not reach statistical significance.

Women generally get diagnosed with diabetes later than men and at a higher BMI (41). Many studies have shown that natural menopause is not associated with a higher risk of T2D and that a higher postmenopausal diabetes incidence, if depicted, is rather due to chronological aging and physical inactivity than to the menopause per se (42-44). However, this research remains controversial, since there are studies that showed higher risk of metabolic syndrome in postmenopausal women independent of age (45, 46) and there is evidence that an early menopause increases the risk of T2D (47-49). Multiple studies suggest that women affected by diabetes are at higher relative risk for CHD than men with this diagnosis, pre- and postmenopausal (50-52). In our study, when looking at the absolute risk of the different DCSI categories on the subpopulation affected with T2D, *cardiovascular diseases* had the highest impact on T2D progression. At baseline, men with T2D were significantly more likely affected from *cardiovascular diseases* than women, but at follow-up this was no longer the case.

The ROSSO study observed 3,142 people with new-onset diabetes over a mean follow-up time of 6.5 years in Germany, focussing on diabetes mellitus complications and its treatment costs. Mean age of the participants recruited from primary care practices was  $62.5 \pm 9.6$  years (53). The complication rate increased linearly with time, coronary heart disease being the most common risk factor and complication, and neuropathy having the steepest increase after diagnosis. Men had more acute myocardial infarction events than women, in numbers of strokes and mortality there was no difference. A longitudinal study by Weng et al. investigated 16,950 people with newly diagnosed diabetes from a US administrative claims

database between 2006 and 2014, focusing on treatment and comorbidities of diabetes (31). They found that men had higher DCSI scores and the DCSI progression was in general faster at higher age. In the age group above 65 years, cerebrovascular diseases were most prominent, followed by cardiovascular diseases. The data reported by Hazel-Fernandez et al. support our finding of more diabetic complications in men than in women (27). In contradiction McCollum et al. found that women diagnosed with diabetes had significantly more comorbidities than men with this diagnosis (7.8 vs. 6.4 on average), but they did not distinguish between diabetes complications and comorbidities in general (54).

The investigation of the diagnostic criteria resulting in the T2D diagnoses at follow-up (N=185) showed that most of them are supported by four of the five criteria considered: anamnestic information, antidiabetic medication, fasting glucose and HbA1c (the 2h-OGTT was performed only when T2D was not known). Focussing on the newly diagnosed participants, 58.5% were diagnosed by 2h-OGTT only, of which 66.7% were women. This difference between the sexes is also reflected by the lower capacity of the baseline 2h glucose values to predict incident T2D in men at follow-up. These results are in line with earlier reports showing that women are more frequently affected from impaired glucose tolerance, whereas men more frequently show fasting glucose glycaemia (reviewed in (55)). With respect to the newly diagnosed participants at follow-up, only men's fasting blood glucose values (mean) at baseline were in the range indicating prediabetes, whereas the women's mean fasting glucose values were below the prediabetes cut-off. The HbA1c mean values, however, met the prediabetic range in both, women and men. This underscores the particular importance of diagnostic laboratory test(s) applied with respect to the chance of an existing T2D being diagnosed and its difference between women and men. Thus our data support the recommendations of the Deutsche Diabetes Gesellschaft of applying fasting blood glucose *and* HbA1c in combination when screening for T2D (56). When choosing to apply only one test, our findings suggest a sex-specific approach: for men, both tests can be equally applied, whereas for women, one would recommend to measure HbA1c. A 2h-glucose tolerance test (OGTT) should follow in case either of the two values, fasting glucose or HbA1c, were within the prediabetic range (56).

A recent study on antidiabetic medication showed a lower risk of cardiovascular complications when combining metformin with a GLP-1 receptor agonist or a SGLT2 inhibitor, with GLP-1 receptor agonists having a greater effect in women than in men (57). In our cohort these two antidiabetic drugs were only taken by a small proportion of the participants. With cardiovascular events being the most prevalent T2D complication, people diagnosed with T2D might benefit from these newer oral antidiabetic drug classes (58).

A limitation of the current study is that a proportion of T2D patients might actually be affected by latent autoimmune diabetes in adults (LADA). The prevalence of this type of diabetes which we were unable to distinguish here is estimated to range between 2 and 14 percent (overview in Hernández and Mauricio, 2021 (59)). The size of the dataset analysed here is another limitation particularly with respect to the comparably small number of incident cases.

## Conclusions

The data on the studied cohort available allowed to describe a comprehensive picture of T2D with respect to its prevalence, incidence, and severity in older people in Germany. In addition, the combined use of cross-sectional and longitudinal data allowed us to detect clinically relevant differences in the informational value of the commonly used T2D diagnostic laboratory parameters between men and women. The study additionally provided a snapshot of the current anti-diabetic medication use in older people, an area that can be expected to undergo greater changes in the future due to available newer classes of medication such as GLP-1 receptor agonists and SGLT2 inhibitors.

## **Declarations**

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### **Competing interests**

The authors declare that they have no competing interests.

### **Author contributions**

NB, ID and JS conceived the study, discussed and interpreted data. JS analysed the data and wrote the first manuscript draft. ID, JS and VMV have prepared the illustrations. ID, VRZ and EST provided data. NB and I.D. supervised the study. All authors participated in drafting the paper or revising it critically, and provided final approval. ID 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 analyses.

### **Ethics approval**

The medical assessments at baseline and follow-up were conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Charité – Universitätsmedizin Berlin (approval numbers EA2/029/09 and EA2/144/16) and were registered in the German Clinical Trials Registry as DRKS00009277 and DRKS00016157.

### **Consent to participate**

Informed consent was obtained from all individual participants included in the study.

### **Availability of data and materials**

Due to concerns for participant privacy, data are available only upon request. External scientists may apply to the Steering Committees of BASE-II and GendAge for data access. Please refer to the BASE-II website (<https://www.>

base2.mpg.de/en/project-information/datadocumentation) for additional information. Please contact Ludmila Müller, scientific coordinator, at

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## Tables

**Table 1: Characteristics of BASE-II baseline (N=1,671) and follow-up (N=1,083) samples (older group).**

Variables	Baseline		Follow-up	
	Mean (SD) or %	Number of observations	Mean (SD) or %	Number of observations
Females	51.6	862	52.0	563
Chronological age (years)	68.8 (3.7)	1671	75.6 (3.8)	1083
Diabetes mellitus type 2	12.9	209	17.1	185
Diabetes mellitus type 2; new diagnosis*	3.2	52	3.8	41
Prediabetes	38.9	623	44.4	478
Fasting glucose (mg/dl)	96.3 (20.2)	1570	102.2 (22.3)	1070
2h-OGTT (mg/dl)	108.6 (36.0)	1382	117.3 (36.0)	822
HbA1c (%)	5.6 (0.6)	1568	5.7 (0.5)	1072
Anamnestic history of T2D (self- report)	9.3	150	12.1	131
Antidiabetic medication	6.9	111	9.2	100
Smoking (packyears)	10.4 (17.6)	1611	9,9 (17.7)	1003
Alcohol (4 times a week or more)	27.6	459	20.6	223
RAPA score	5.1 (1.5)	1588	4.8 (1.3)	1080
BMI	26.8 (4.2)	1638	26.9 (4.2)	1081
Morbidity index**	0.9 (1.1)	1495	1.2 (1.3)	940

2h-OGTT = oral glucose tolerance test (OGTT was only performed when T2D was not known); RAPA = rapid assessment of physical activity; BMI = body mass index; \*diagnosed during the course of the study either at baseline or follow-up; \*\*modified version of the morbidity index originally described by Charlson (62), for details see (63).

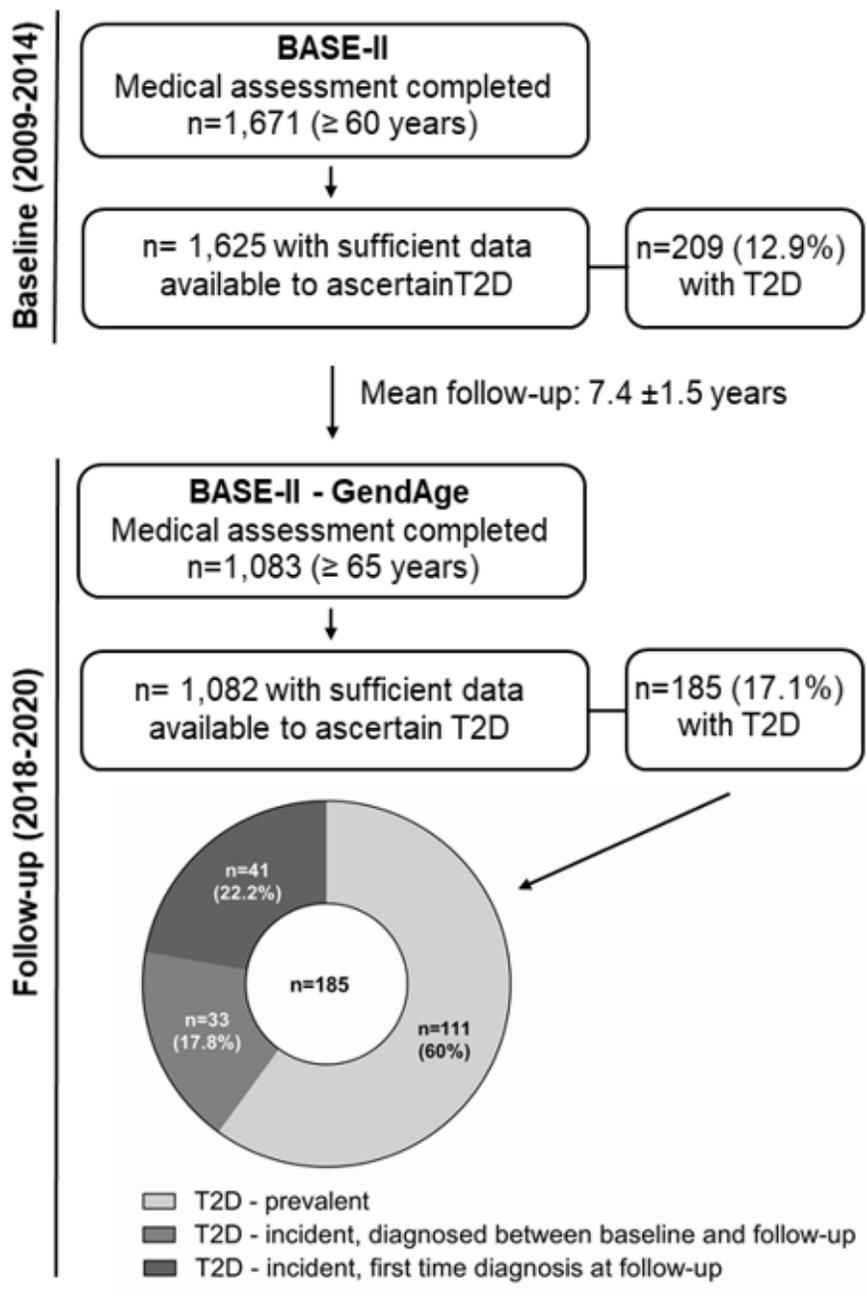
**Table 2: Characteristics of the prevalent T2D cases in BASE-II (N=111).**

Variables	Baseline		Follow-up		p-value
	Mean (SD) or %	Number of observations	Mean (SD) or %	Number of observations	
Females	36.0	40	36.0	40	N/A
Age (years)	68.1 (3.7)	111	75.4 (4.1)	111	< 0.05
T2D new diagnosis (unaware of disease)	20.7	23	N/A	N/A	N/A
DCSI	1.1 (1.2)	111	2.0 (1.8)	111	< 0.05
Fasting glucose (mg/dl)	127.1 (31.2)	106	143.6 (34.5)	111	< 0.05
2h-OGTT (mg/dl)	218.8 (60.1)	21	N/A	N/A	N/A
HbA1c (%)	6.6 (0.7)	105	6.7 (0.8)	111	< 0.05
Anamnestic history of T2D (self-report)	77.1	84	91.0	101	< 0.05
Antidiabetic medication	56.4	62	76.6	85	< 0.05
Smoking (packyears)	14.7 (18.4)	103	15.3 (21.4)	100	> 0.05
Alcohol (4 times a week or more)	31.6	31	23.4	26	< 0.05
RAPA score	4.8 (1.5)	109	4.5 (1.2)	111	> 0.05
BMI	29.6 (4.4)	110	29.3 (4.2)	111	> 0.05
Morbidity index*	1.0 (1.2)	104	1.9 (1.7)	85	< 0.05

DCSI = diabetes complications severity index; T2D = diabetes mellitus type 2; 2h-OGTT = oral glucose tolerance test (OGTT was only performed when T2D was not known); RAPA = rapid assessment of physical activity; BMI = body mass index; \*modified version of the morbidity index originally described by Charlson (62), for details see (63); statistical analysis was performed by t-test or Wilcoxon signed test, as appropriate.

## Figures

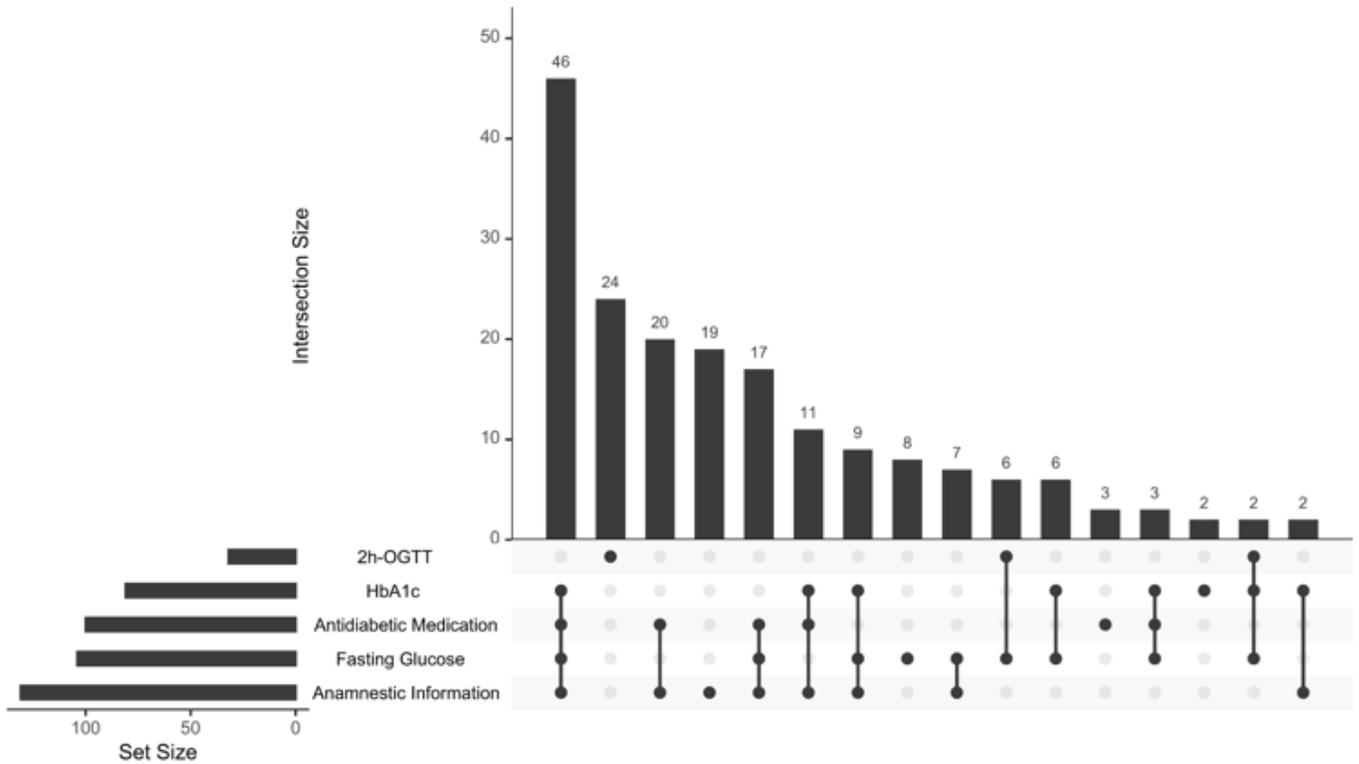
**Figure 1**



**Figure 1**

Diabetes mellitus type 2 at baseline (BASE-II) and follow-up (GendAge) The flow-chart shows the T2D prevalence among BASE-II participants at baseline and the number/proportion of prevalent and incident cases at follow-up 7.4 ±1.5 years later.

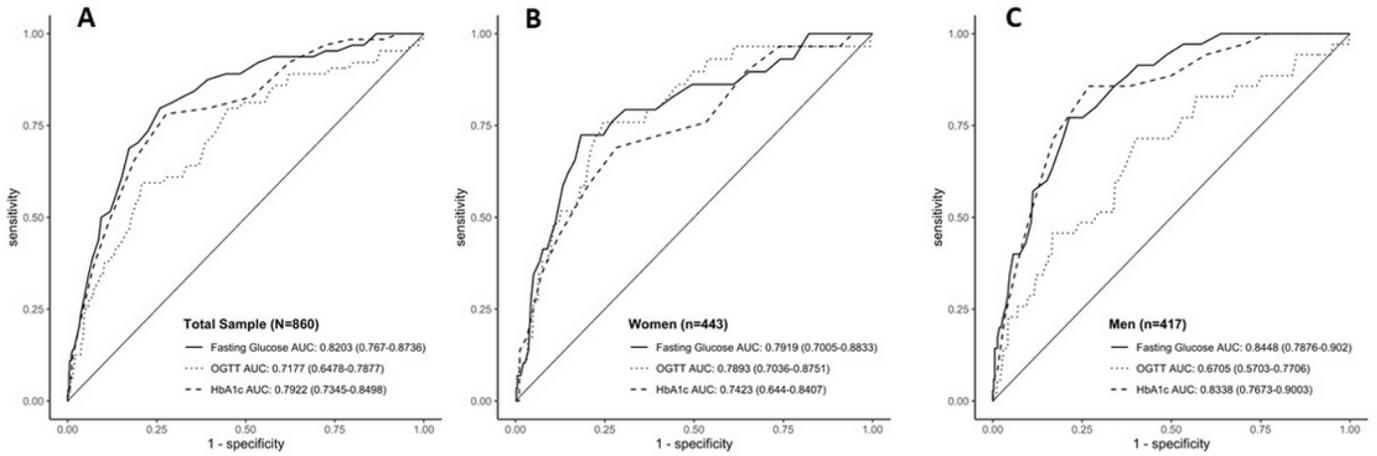
**Figure 2**



**Figure 2**

Type 2 Diabetes diagnosis at follow-up ( N=185). Diabetes diagnosis criteria at follow-up and their combinations are indicated with the number of cases above the bars (OGTT was only performed when T2D was not known). OGTT= oral glucose tolerance test.

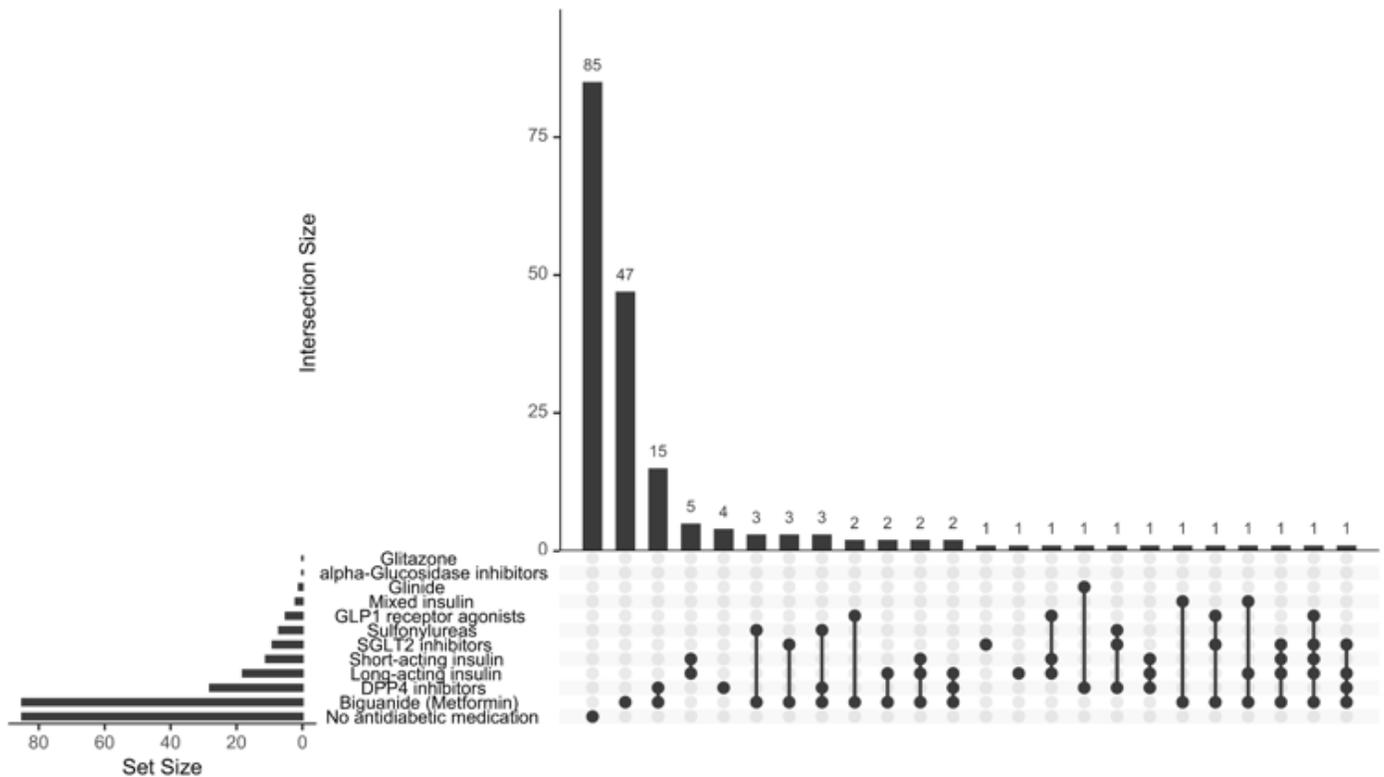
**Figure 3**



**Figure 3**

Capacity of glucose status laboratory parameters to predict incident diabetes. ROC curves showing the capacity to predict incident diabetes of fasting glucose, HbA1c and 2h-glucose (OGTT) in N=860 women and men (A) and separate for for N=443 women (B) and N=417 men (C) with data on all three tested parameters available. Data on a total of 64 incident diabetes cases of which 29 were women and 35 were men were available for this analyses.

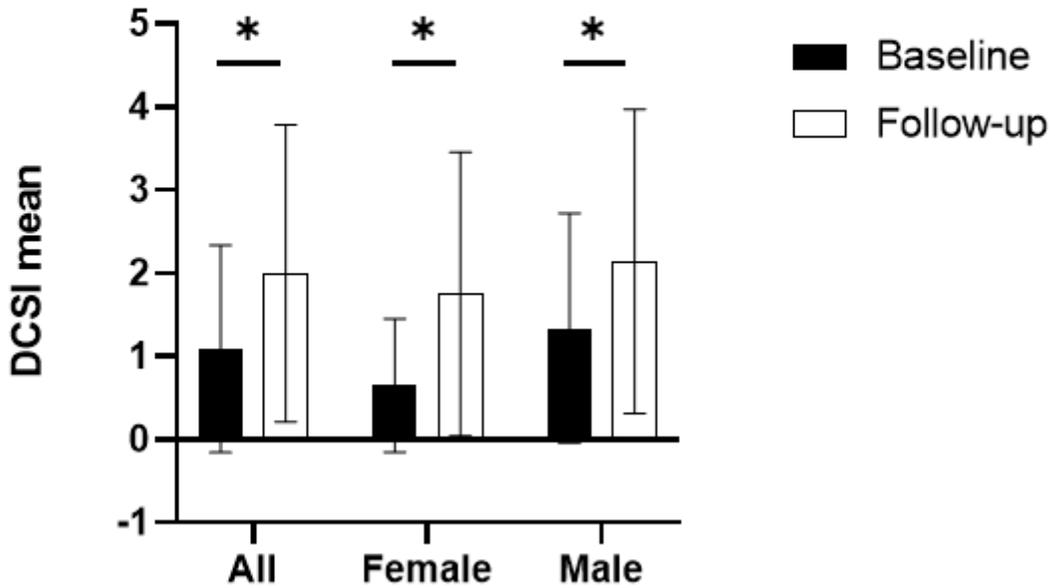
**Figure 4**



**Figure 4**

Antidiabetic medication at follow-up (N=185). Antidiabetic medication at follow-up and its combinations are indicated with the number of cases above the bars. DPP-4= dipeptidyl peptidase 4; SGLT2=sodium-glucose cotransporter 2. 41 of 85 participants without medication were newly-diagnosed incident cases.

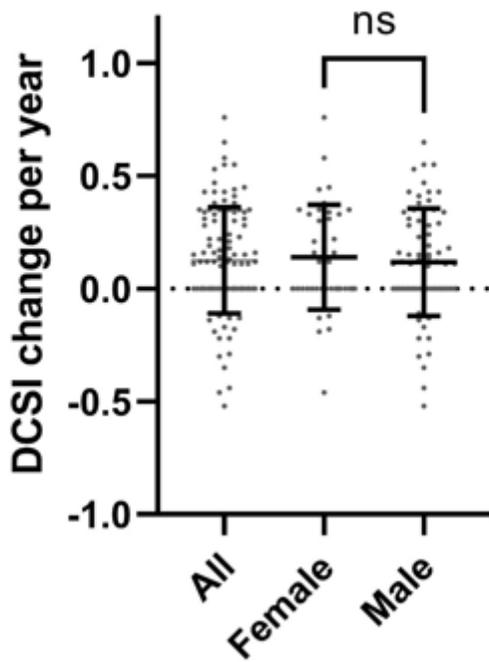
**Figure 5**



**Figure 5**

Severity of T2D as indicated by the DCSI The mean DCSI at baseline and follow-up is shown for all prevalent T2D cases (N=111) in the Berlin Aging Study II and separately for females (N=40) and men (N=71). Significant increase between baseline and follow-up for each group is indicated (\*, Wilcoxon test  $p < 0.01$ ).

**Figure 6**



**Figure 6**

DCSI change per year between baseline and follow-up in prevalent T2D cases The DCSI change per year over the  $7.4 \pm 1.5$  years of follow-up is shown. Mean and standard deviation is indicated. All: N=111; females: N=40; males: N=71. No significant difference (n.s.) between mean DCSI of female and male participants were detected by t-test.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Supplementarydata12112021id.docx](#)