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# Individual Prediction of Insulin Therapy in Gestational Diabetes: Development of a Risk Calculator Based on Real-World Data from the GestDiab Registry

## Individuelle Vorhersage für eine Insulintherapie bei Gestationsdiabetes. Entwicklung eines auf Real-World-Daten aus dem GestDiab-Register basierenden Risikorechners

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ABSTRACT

**Introduction**

The prevalence of gestational diabetes mellitus in Germany is approximately 10%. One third of affected women require insulin therapy when conservative measures such as dietary changes and physical activity are insufficient to achieve target glucose levels. Timely initiation of insulin therapy is crucial for optimising obstetric outcomes. Early identification of high-risk patients at the time of diagnosis would facilitate prompt and individualised treatment adjustments.

**Materials and Methods**

A risk calculator was developed based on clinical parameters and medical history information to estimate the individual risk for insulin therapy. The models were derived from real-world data of the GestDiab registry, comprising 14157 pregnancies between 2018 and 2020, of which 4319 (30.5%) required insulin therapy.

**Results**

Various models incorporating maternal age, gestational age at diagnosis, parity, gravidity, body mass index, 75 g oral glucose tolerance test values, HbA1c levels, history of gestational diabetes mellitus, and family history of diabetes were developed. Validation using the GestDiab cohort from 2021 demonstrated that the model including all variables exhibited the highest predictive power (AUC 0.740).

**Conclusions**

The risk calculator is provided online to support both patients and physicians in making informed decisions. Individualised counselling based on personal risk assessments may

enhance therapy adherence and potentially reduce the necessity for insulin therapy.

## ZUSAMMENFASSUNG

**Einleitung**
Die Prävalenz des Gestationsdiabetes mellitus beträgt in Deutschland etwa 10 %. Bei rund einem Drittel der betroffenen Frauen ist eine Insulintherapie erforderlich, wenn konservative Maßnahmen wie Ernährungsumstellung und körperliche Aktivität nicht ausreichen, um die angestrebten Blutzuckerziele zu erreichen. Eine zeitgerechte Einleitung der Insulintherapie ist entscheidend für die Optimierung des geburtshilflichen Outcomes. Die frühzeitige Identifizierung von Hochrisikopatientinnen zum Zeitpunkt der Diagnosestellung kann eine umgehende und individualisierte Anpassung der Therapie ermöglichen.

**Material und Methoden**
Es wurde ein Risikorechner entwickelt, der auf klinischen Parametern und anamnestischen Angaben basiert, um das individuelle Risiko für die Notwendigkeit einer Insulintherapie zu schätzen. Die Modelle wurden anhand von Real-World-Daten des GestDiab-Registers erstellt, das 14 157 Schwangerschaften zwischen 2018 und 2020 umfasst. In 4319 Fällen (30,5 %) war eine Insulintherapie erforderlich.

**Ergebnisse**
Es wurden verschiedene Modelle entwickelt, die folgende Parameter einbeziehen: maternales Alter, Gestationsalter bei Diagnosestellung, Parität, Gravidität, Body-Mass-Index, Werte des 75-g-oralen Glukosetoleranztests, $HbA_{1c}$, anamnestischer Gestationsdiabetes sowie familiäre Diabetesbelastung. Die Validierung anhand der GestDiab-Kohorte von 2021 zeigte, dass das Modell unter Einbeziehung sämtlicher Variablen die höchste prädiktive Genauigkeit erreichte (AUC = 0,740).

**Schlussfolgerungen**
Der Risikorechner wird online bereitgestellt, um sowohl Patientinnen als auch behandelnde Ärztinnen und Ärzte bei fundierten Therapieentscheidungen zu unterstützen. Eine individualisierte Beratung auf Grundlage der persönlichen Risikoeinschätzung könnte die Therapieadhärenz verbessern und potenziell die Notwendigkeit einer Insulintherapie verringern.

## Introduction

The prevalence of gestational diabetes mellitus (GDM), defined as a glucose tolerance disorder first diagnosed during pregnancy using standardised testing methods, was reported to be nearly 10 % in Germany for the first time in 2021, according to perinatal statistics from the Institute for Quality Assurance and Transparency in Healthcare (IQTIG) [1]. In most cases, glucose tolerance disorders can be managed through conservative methods such as nutritional counselling, glucose monitoring, lifestyle interventions, and physical activity, thereby preventing maternal and fetal complications (e.g., preeclampsia, macrosomia, caesarean delivery and neonatal hypoglycaemia or admission to neonatal care units) [2, 3, 4, 5]. If target glucose levels cannot be achieved despite the full implementation of conservative measures, insulin therapy is indicated [6]. The proportion of women with GDM requiring insulin therapy has remained consistently around 30 % in Germany [7]. For optimising obstetric outcomes in GDM, the prevention of maternal hyperglycaemia and the prompt achievement of target glucose levels are essential [8]. Given the limited time window of pregnancy, insulin therapy should be initiated without delay once conservative measures are exhausted to ensure timely and adequate glycaemic control [6, 9]. Identifying high-risk patients enables close monitoring and the timely initiation of insulin therapy to achieve normoglycaemia as quickly as possible. Due to the heterogeneity of GDM, national and international publications recommend individualised treatment approaches based on risk stratification at the time of diagnosis of GDM [10, 11].

As indicators for the necessity of insulin therapy during pregnancy, these publications cite body mass index (BMI), a history of GDM, and glucose levels at diagnosis [10, 11, 12].

A personalised risk stratification based on a risk score can be used by both affected patients and healthcare providers to assess individual risk, allowing for targeted counselling, individualised monitoring intervals, and the joint establishment of intervention strategies. Awareness of one's own risk for requiring insulin therapy may ideally enhance patient motivation for consistent adherence to lifestyle modifications and help reduce frustration in cases where insulin intervention becomes necessary.

The aim of this study was to develop a practical and applicable risk score based on real-world treatment data from the GestDiab registry and to make it available to healthcare providers.

## Materials and Methods

The GestDiab registry is the largest German registry for pregnancies affected by gestational diabetes mellitus (GDM), type 1 diabetes mellitus, and type 2 diabetes mellitus. It collects healthcare data, perinatal outcomes, and follow-up results for GDM, which are documented in participating specialist diabetes practices ("Diabtesschwerpunktpraxen"; DSPs) and diabetes outpatient clinics. The GestDiab project is managed by the Scientific Institute of Office-Based Diabetologists (winDiab gGmbH). Initially launched in 2008 in North Rhine, GestDiab now includes data from 85 DSPs and diabetes outpatient clinics across Germany.

Patients whose data are entered into the registry provided written consent for the pseudonymised collection of their data within

the GestDiab registry. Participation in GestDiab as study centres is voluntary and largely uncompensated for the involved DSPs and diabetes outpatient clinics.

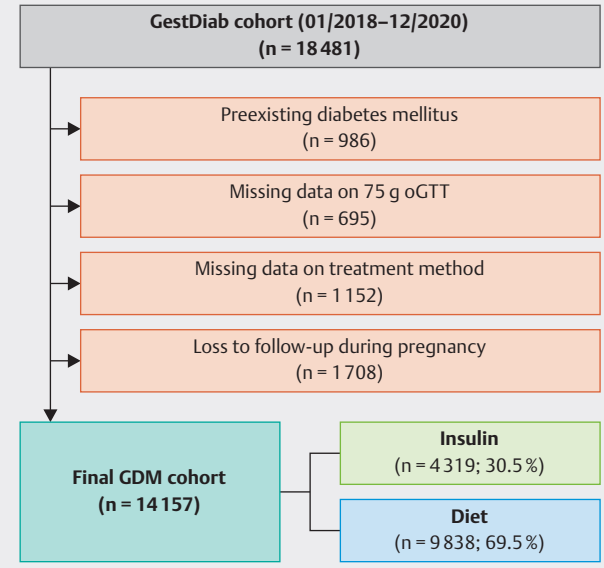
The project data collected as part of routine care were pseudonymised and recorded in the online database "secuTrial," developed by interActive Systems GmbH Berlin. SecuTrial is a professional, browser-based, and flexible software system for capturing patient data in clinical studies and registries, compliant with current data protection regulations.

The transmission of patient-related data (anonymised during processing by the various DSPs and diabetes outpatient clinics) occurs annually in a separate dataset, which is routinely analysed and provided to study centres in the form of benchmarking reports for internal quality control. The GestDiab registry has been approved by the Ethics Committee of the Medical Association of North Rhine (Ethics Committee No.: 2019272) and 15 additional ethics committees. The use of registry data complies with applicable data protection regulations.

## Cohort composition

Between 2018 and 2020, a total of 18481 pregnancies were recorded in the GestDiab registry. Our analysis excluded datasets from pregnant individuals with pre-existing diabetes mellitus (n = 986), those with missing data on the 75 g oral glucose tolerance test (oGTT) (n = 695), and cases lacking information on the treatment method (n = 1152). Additionally, patients who discontinued therapy or consultations at their respective DSP or diabetes outpatient clinic were not considered in this study (n = 1708) (▶ **Fig. 1**).

Of the remaining 14157 pregnancies included in the analysis, 4319 (30.5 %) required insulin therapy during pregnancy.




▶ **Fig. 1** Cohort composition for the present analysis. Some cases met more than one exclusion criterion and are therefore represented in multiple categories. GDM: gestational diabetes mellitus; n: number of subgroup; oGTT: oral glucose tolerance test.

## Prediction models

To develop prediction models for insulin therapy, the clinical parameters available at the time of diagnosis were tested in four different models. Since GDM diagnosis in Germany is made both in obstetric-gynaecological practices and primarily in DSPs, different predictive models were designed. In addition to a comprehensive model incorporating all 11 relevant parameters (Model 1: "All Combined"), further models were created using either gynaecologically obtained parameters (Model 2: "Gyn") or primarily diabetologically obtained parameters (Model 3: "Diab"), as well as a model with a minimal set of data (Model 4: "Short"). For the development of the prediction models, SI units were used for HbA1c (mmol/mol) and glucose (mmol/l).

Model 1 ("All Combined") includes 11 discriminative variables that showed significant differences in the descriptive group comparison between women with and without insulin therapy: maternal age at the estimated due date (years), gestational age at diagnosis (weeks of gestation, WOG), parity (total number of births), gravidity (total number of pregnancies, including the current one), pre-pregnancy BMI (kg/m²), 75 g oGTT values in mmol/l (fasting glucose, 1-hour value, 2-hour value), HbA1c (mmol/mol), as well as the following dichotomous variables: history of GDM and a family history of diabetes (first-degree relatives).

Model 2 ("Gyn") includes eight of these 11 variables that are available to gynaecologists at the time of diagnosis (age, BMI, WOG, gravidity, parity, fasting glucose, 1-hour value, 2-hour value from the oGTT).

Model 3 ("Diab") includes seven of the 11 variables available to diabetologists (age, BMI, WOG, fasting glucose, 1-hour value, 2-hour value from the oGTT, HbA1c).

Model 4 ("Short") is limited to the minimum set of potentially available data, consisting of five variables (age, BMI, WOG, fasting glucose, HbA1c).

## Statistical methods

For the comparison of categorical data, the two-sided Chi² test or Fisher's exact test was used. Continuous data were summarised using the median and the 25th and 75th percentiles, as normal distribution was generally not present. Metric data were compared between groups using the two-sided Mann-Whitney U test.

Receiver operating characteristic (ROC) analyses were performed for individual predictors to assess the accuracy of predicting insulin therapy based on the area under the curve (AUC) with 95 % confidence intervals.

For insulin therapy, multiple binary logistic regression was applied using the predictors of each respective prediction model $x_1$, .... $x_k$ (where k represents the number of factors) as independent variables. The probability of requiring insulin therapy P(y = 1)) for individual patients was calculated using the following formula:

$$P(y=1) = \frac{1}{1+e^{-(\beta_0+\beta_1 \cdot x_1+\beta_2 \cdot x_2+\beta_3 \cdot x_3+\cdots+\beta_k \cdot x_k+\epsilon)}}$$

The parameters $\beta_0$, ..., $\beta_k$ are the estimators for the coefficients of the multiple binary logistic regression model. A ROC analysis was performed to discriminate the two groups using the patient-specific probability of insulin treatment determined in the model. The cut-off value for distinguishing the groups was determined by the maximum Youden index (4). To validate the prediction model, the discrimination of insulin-treated and diet-managed GDM was examined in an independent cohort using the cut-off.

The negative and positive predictive values (NPV and PPV) were calculated for the various prediction models. The level of significance was set at $\alpha = 0.05$, and no correction for multiple testing was made due to the exploratory nature of the study. The statistical analysis was performed using SPSS 29.0 (IBM Corp., Armonk, NY).

## Results

### Description of the GestDiab cohort

Women with insulin-treated GDM (iGDM) were significantly older, heavier (body weight and BMI), and had more prior pregnancies and deliveries than women with diet-managed GDM (dGDM) (▶ **Table 1**).

More patients with iGDM had a family history of diabetes and had had GDM in a previous pregnancy. No differences were found in terms of smoking status, height, multiple pregnancies, fetal sex ratio, or language barriers.

At the time of GDM diagnosis, all values of the 75 g oGTT (fasting glucose: 5.5 vs. 5.2 mmol/l [99 vs. 94 mg/dl]; 1 h value 10.1 vs. 9.6 mmol/l [181 vs. 173 mg/dl]; 2 h value 7.5 vs. 7.3 mmol/l [135 vs. 132 mg/dl] and HbA1c values [5.3 vs. 5.1 %] and 34 vs. 32 mmol/mol) were significantly higher in iGDM patients than in dGDM ($p < 0.001^*$).

Women with insulin had more inductions of labour (38.1 % vs. 28.6 %), had more caesarean sections (42.2 % vs. 34.5 %), fewer preterm deliveries (6.1 % vs. 7.5 %), more macrosomia (13.9 % vs. 10.4 %), and more children with postnatal hypoglycaemia (51.2 % vs. 40.2 %). The univariate analysis confirmed the significant influence of the discriminating parameters for insulin treatment (Online-Supplement **Table S1**).

First, the ROC AUCs were determined for all continuous variables (▶ **Table 2**). The best discriminatory properties were found for the fasting glucose value (AUC 0.680), followed by BMI (AUC 0.640) and HbA1c in mmol/mol at diagnosis (AUC 0.606).

### Predictive accuracy of the different prediction models

By combining different variables in the four models, the AUC and thus the prediction accuracy of insulin treatment could be further increased. The highest AUC (0.740; CI 0.729–0.752; < 0.01) and the highest NPV 82.8 % were achieved by including all 11 variables (model 1). In model 3 ("Diab"), the AUC was 0.735 (CI 0.724–0.747; $p < 0.01$; for model 2 ("Gyn"), the AUC was 0.732 (CI 0.721–0.744; $p < 0.01$) and for model 4, the AUC was 0.719 (CI 0.708–0.731; $p < 0.01$). PPV and NPV were almost the same for all four models at ~ 50 % and ~ 82 % (see ▶ **Table 3**).

### Validation of the different prediction models in an independent group

To validate the four models, they were tested using the GestDiab cohort from the following year, 2021 (n = 6651), with a comparable insulin treatment rate of 32.6 % (n = 2166). The determined prediction probabilities were confirmed and showed a clear correlation (see Online-Supplement **Table S2**).

### Risk calculator

The risk calculator can be found under the following link (https://tiny.uk-j.de/gdm-insulin). Depending on the data entered, the optimal model for the calculation is automatically selected in the background and the individual probability for an insulin treatment is then given as a percentage. With the minimum of the five clinical data for model 4, the individual risk for the patient can already be calculated (see ▶ **Fig. 2**). The conversion of the HbA1c and glucose values into the corresponding SI units (mg/dl into mmol/l or HbA1c % into mmol/mol) is done automatically.

## Discussion

### Summary of results

Based on data from the GestDiab pregnancy registry for women with GDM, we were able to create individual prediction models for the need for insulin treatment. This means that a publicly accessible risk calculator is now available for the first time for counselling by and for women with GDM (see ▶ **Fig. 2**) and can be used with just five clinical parameters (maternal age at the estimated date of delivery, pre-pregnancy BMI, gestational age at GDM diagnosis, fasting glucose and HbA1c).

Regardless of the number of variables included, only a positive predictive value of 50 % and a negative predictive value of 80 % could be achieved in the validation cohort of 2021. The present models only include patient characteristics that can be recorded at the time of diagnosis. Other factors influencing the indication for insulin therapy (e.g. ultrasound-based data on fetal growth) are not included in the model. These include patient-related influences such as compliance with and motivation for conservative therapeutic measures (dietary changes and exercise) that influence the need for insulin therapy, as well as practice-specific differences in management. For example, the insulinisation rate of the practices participating in GestDiab is 31 % on average, but the range is from 4 to 100 %. Even when considering only the practices with more than 10 treatment cases per year, the range is between 4 % and 68 %. In the analysis of the association between practice-specific insulinisation rates and the probability of individual insulin treatment, an AUC of 0.657 (CI 0.648–0.667, $p < 0.01$) was found, which was significant (data not shown). After fasting glucose (AUC 0.680), the practice-specific insulinisation rate thus showed the second-best correlation with the prediction model. The question remains as to whether this is due to a selected high-risk collective in the respective practice or to their treatment strategies.

It is likely that a standardised approach to insulin prescription would improve the model's predictive power. Conversely, calculating the individual risk of the patient can potentially harmonise insulin prescription.

▶**Table 1** Descriptive parameters of the total cohort (n = 14157) and presentation of group differences between patients with diet controlled (dGDM; n = 9838) and insulin-treated gestational diabetes mellitus (iGDM; n = 4319).

| Variables | Cases | Total Cohort (n = 14157) | dGDM (n = 9838) | iGDM (n = 4319) | p |
|---|---|---|---|---|---|
| Maternal age at delivery (years) | 14157 | 33 (29–36) | 33 (29–36) | 33 (30–37) | < 0.001* |
| Parity | 14116 | 1 (0–1) | 1 (0–1) | 1 (0–2) | < 0.001* |
| Gravidity | 14129 | 2 (1–3) | 2 (1–3) | 2 (1–3) | < 0.001* |
| Prepregnancy BMI (kg/m²) | 13954 | 27.2 (23.4–32.2) | 26.1 (22.8–30.9) | 29.6 (25.4–35) | < 0.001* |
| Prepregnancy weight (kg) | 13977 | 74 (63.9–89) | 72 (62–85) | 81 (69–96) | < 0.001* |
| Maternal height (cm) | 14114 | 165 (160–170) | 165 (160–170) | 165 (161–170) | 0.122 |
| Family history of DM (1st degree relatives) | 12851 | 4546 (35.4%) | 2896 (32.5%) | 1650 (42.0%) | < 0.001* |
| Smoking | 13192 | 1029 (7.8%) | 708 (7.7%) | 321 (8.0%) | 0.527 |
| History of GDM | 12784 | 2375 (18.6%) | 1280 (14.4%) | 1095 (28.3%) | < 0.001* |
| HbA1c at diagnosis (%) | 12822 | 5.2 (5–5.4) | 5.1 (4.9–5.4) | 5.3 (5.1–5.5) | < 0.001* |
| HbA1c at diagnosis (mmol/mol) | 12822 | 33 (31–36) | 32 (30–36) | 34 (32–37) | < 0.001* |
| GA at diagnosis (weeks) | 14157 | 26 (25–28) | 27 (25–29) | 26 (23–28) | < 0.001* |
| 75 g oGTT (mmol/l) | | | | | |
| ▪ Fasting glucose | 14119 | 5.3 (5.1–5.6) | 5.2 (4.9–5.5) | 5.5 (5.2–5.9) | < 0.001* |
| ▪ 1-hour glucose | 12557 | 9.8 (8.3–10.7) | 9.6 (8.2–10.6) | 10.1 (8.7–11.1) | < 0.001* |
| ▪ 2-hour glucose | 12348 | 7.4 (6.3–8.6) | 7.3 (6.3–8.6) | 7.5 (6.4–8.7) | < 0.001* |
| 75 g oGTT (mg/dl) | | | | | |
| ▪ Fasting glucose | 14119 | 95 (92–101) | 94 (89–99) | 99 (94–106) | < 0.001* |
| ▪ 1-hour glucose | 12557 | 176 (150–193) | 173 (147–190) | 181 (156–200) | < 0.001* |
| ▪ 2-hour glucose | 12348 | 133 (113–155) | 132 (113–155) | 135 (115–156) | < 0.001* |
| Multiples | 13150 | 288 (2.2%) | 213 (2.3%) | 75 (1.9%) | 0.083 |
| Fetal sex male | 9221 | 4932 (53.5%) | 3306 (52.9%) | 1626 (54.8%) | 0.094 |
| No or little language barrier | 14157 | 12392 (87.5%) | 8613 (87.5%) | 3779 (87.5%) | 0.935 |
| Induction of labour | 8167 | 2587 (31.7%) | 1587 (28.6%) | 1000 (38.1%) | < 0.001* |
| Mode of delivery | 9332 | | | | < 0.001* |
| ▪ Spontaneous | | 5448 (58.4%) | 3847 (60.6%) | 1601 (53.6%) | |
| ▪ Vaginal operative | | 437 (4.7%) | 309 (4.9%) | 128 (4.3%) | |
| ▪ C-section (planned or emergency) | | 3447 (36.9%) | 2187 (34.5%) | 1260 (42.2%) | |
| Shoulder dystocia | 782 | 41 (5.2%) | 29 (5.2%) | 12 (5.4%) | 0.861 |
| GA at delivery (weeks) | 9661 | 39 (38–40) | 40 (38–40) | 39 (38–40.0) | < 0.001* |
| Preterm delivery (< 37weeks) | 9725 | 684 (7%) | 494 (7.5%) | 190 (6.1%) | 0.012* |
| Length newborn (cm) | 9168 | 52 (50–54) | 52 (50–54) | 52 (50–54) | < 0.001* |
| Weight newborn (g) | 9358 | 3450 (3110–3760) | 3420 (3082–3730) | 3500 (3170–3820) | < 0.001* |
| Macrosomia (> 4 kg) | 9358 | 1082 (11.6%) | 662 (10.4%) | 420 (13.9%) | < 0.001* |
| APGAR 5 min < 5 | 5791 | 19 (0.3%) | 14 (0.3%) | 5 (0.3%) | 0.808 |
| pH umbilical artery < 7.1 | 5357 | 128 (2.4%) | 86 (2.3%) | 42 (2.6%) | 0.560 |
| Admission to NICU | 8718 | 886 (10.2%) | 577 (9.7%) | 309 (11.1%) | 0.58 |
| Fetal death | 8739 | 6 (0.1%) | 4 (0.1%) | 2 (0.1%) | 1 |
| Fetal hypoglycaemia | 842 | 336 (43.5%) | 237 (40.2%) | 129 (51.2%) | < 0.001* |

APGAR = a scoring system for assessing the clinical condition of the newborn (APGAR = Appearance, Pulse, Grimace, Activity and Respiration); DM = diabetes mellitus; Fetal hypoglycaemia = requiring either oral or intravenous glucose; GA = gestational age; NICU = neonatal intensive care unit; * = significant difference between iGDM and dGDM (p < 0.05)

▶**Table 2** Area under the receiver operating curve (AUC) for insulin therapy during pregnancy (descending order of the nine continuous variables of the model).

| Variables | AUC | CI (95%) | p |
|---|---|---|---|
| 75 g oGTT fasting glucose (mmol/l) | 0.680 | 0.669–0.691 | < 0.01 |
| Prepregnancy BMI (kg/m²) | 0.640 | 0.628–0.651 | < 0.01 |
| HbA1c at diagnosis (mmol/mol) | 0.606 | 0.594–0.618 | < 0.01 |
| GA at diagnosis (weeks)† | 0.589 | 0.601–0.577 | < 0.01 |
| 1-hour glucose (mmol/l) | 0.581 | 0.569–0.593 | < 0.01 |
| Gravidity | 0.564 | 0.552–0.576 | < 0.01 |
| Parity | 0.562 | 0.550–0.574 | < 0.01 |
| Maternal age at delivery (years) | 0.531 | 0.519–0.542 | < 0.01 |
| 2-hour glucose (mmol/l) | 0.530 | 0.518–0.542 | < 0.01 |

Presentation of the values = 1-AUC for a negative association between gestational age (GA) and insulin treatment (AUC 0.411; CI 0.399–0.423)

Another important factor influencing insulin sensitivity is the gestational weight gain of the pregnant woman [13]. In the group with false positive test (model 4, "short"), i.e. patients who did not receive insulin treatment despite the expected risk, the lowest weight gain of only 2.3 kg on median was observed. This confirms that with good compliance, the personal risk for insulin therapy can be reduced. This is also important information for counselling those affected. It is noteworthy that in the group that did not require insulin therapy despite an increased risk for it, as calculated, a lower increase in HbA1c was observed over the further course of pregnancy compared to all women without an increased risk (correct and false negative). This confirms that this group had good glycaemic control even without insulin therapy, despite an increased risk. It is also encouraging to note that a documented language barrier did not affect insulin treatment (Online-Supplement Table S3). This suggests that the possibility of under- or overprovision due to a lack of communication is ruled out.

## Comparison with the literature

As already described in the literature, we were able to confirm the typical risk factors for insulin treatment during pregnancy: maternal BMI, fasting glucose, 2-h glucose, HbA1c, history of GDM and family history of diabetes [12, 14, 15, 16]. Some studies have also identified fetal abdominal circumference as a predictor of insulin requirement in pregnancies affected by GDM [12, 14].

When validating our models using data from the GestDiab registry from 2021, we were able to achieve an AUC of 0.71 using model 1 by using all available variables. This is in line with the results of Rostin et al. on the predictive probability of insulin treatment with an AUC of 0.77 (95% CI 0.75–0.80; 0.75 in internal validation), which, however, was based on monocentric data [17]. Their optimal cutoff value at a score value of 9 had a 72% sensitivity, a 69% specificity and a NPV of 90%. Additionally, the large Korean study by Lee et al. (2023), which included 417 210 women, reported a similar AUC of 0.783 (95% CI: 0.766–0.799) [18].

## Strengths and limitations

A particular strength of this work is the large amount of data from the care sector throughout Germany, which allows for a high level of representativeness. Nevertheless, the register only reflects a fraction of patients with GDM in Germany. Therefore, this model might not be applicable to other cohorts that are not included in the GestDiab registry due to language barriers or other practice-specific decisions. A further limitation of the study is the lack of foetal ultrasound parameters (abdominal circumference, estimated weight), which are known to also influence the indication for insulin treatment. However, these are not recorded in the registry and therefore cannot be included.

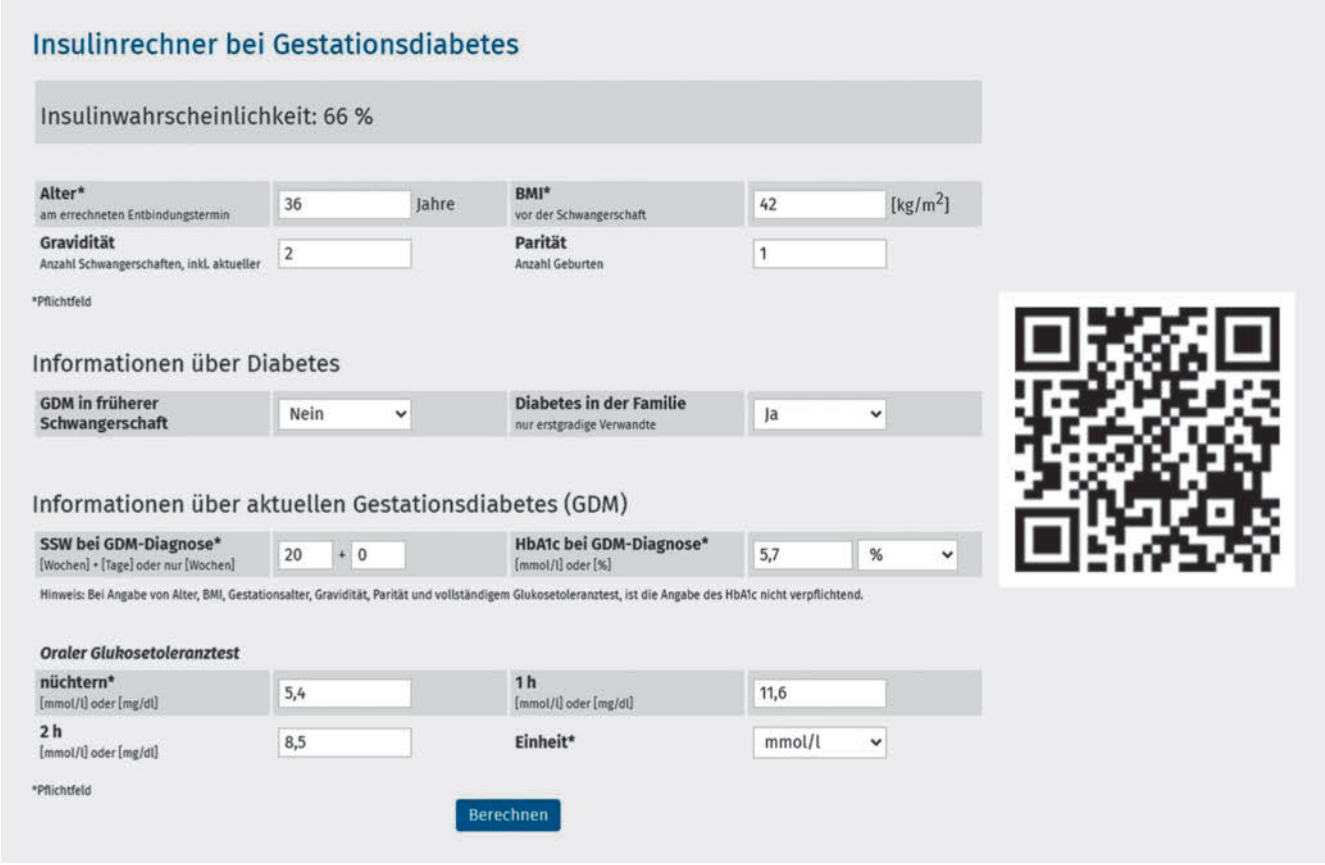
HbA1c is not recommended as a diagnostic parameter for GDM in the German guidelines [6]. However, the GestDiab registry shows that HbA1c values were available for 12 822 out of 14 157 women (approximately 90%). This is most likely because it is routinely used by DSPs as part of their standard practice.

So far, this study relies solely on traditional statistical models. Incorporating machine learning could improve predictive accuracy

▶**Table 3** Area under the receiver operating curve (AUC) for insulin therapy during pregnancy.

| Variable | AUC | CI (95%) | p | PPV | NPV |
|---|---|---|---|---|---|
| Model 1 ("All Combined") | 0.740 | 0.729–0.752 | < 0.01 | 50.1% | 82.8% |
| Model 2 ("Gyn") | 0.732 | 0.721–0.744 | < 0.01 | 51.1% | 81.7% |
| Model 3 ("Diab") | 0.735 | 0.724–0.747 | < 0.01 | 47.3% | 82.6% |
| Model 4 ("Short") | 0.719 | 0.708–0.731 | < 0.01 | 47.3% | 81.1% |

Model 1–all 11 variables
Model 2–8 variables (maternal age at delivery, BMI, GA at diagnosis, gravidity, parity, fasting glucose, 1-hour and 2-hour glucose)
Model 3–7 variables (maternal age at delivery, BMI, GA at diagnosis, fasting glucose 1-hour and 2-hour glucose, HbA1c)
Model 4–5 variables (maternal age at delivery, BMI, GA at diagnosis, fasting glucose, HbA1c)




▶ **Fig. 2** Screenshot of the risk calculator with example (only German Version available).

by capturing complex, non-linear relationships between variables. This approach is being considered for future projects, particularly as the GestDiab registry continues to grow annually. However, Eleftheriades et al. employed a machine learning algorithm—specifically, the Classification and Regression Tree (CART)—to develop a predictive model for insulin therapy. Yet, the predictive value could not be improved, even with the use of machine learning and the inclusion of fetal ultrasound parameters (AUC 0.743; 95 % CI: 0.70–0.79) [12]. Instead of a cut-off value, we provide a tool that can be used to calculate the individual probability of receiving insulin as a percentage, depending on the risk factors present.

### User recommendations

Nevertheless, the calculator must be used with caution, as patients with a calculated low risk may tend to trivialise the problem of GDM. Since insulin resistance increases during pregnancy due to hormonal changes and thus the risk of hyperglycaemia, this fact must be included in the educational process. The individually calculated risk does not replace a medical assessment and repeated assessments during the pregnancy. Insulin treatment may become necessary during the course of the pregnancy, even at low risk, due to various effects.

## Conclusion

The prediction of insulin therapy requirement based on available and established risk factors represents a potentially valuable clinical decision support tool; however, its reliability should be interpreted with caution, given the influence of numerous additional individual-level determinants that are not captured by the model (PPV 50 %). An accessible online tool enables the estimation of individual insulin therapy risk as a percentage for patients diagnosed with GDM, based on the entry of a limited set of clinical parameters. Evidence indicates that the actual necessity for insulin can often be mitigated through adherence to lifestyle interventions. In this context, risk communication may serve as a motivational element within patient counselling. Personalised education regarding individual risk profiles can support patients and healthcare providers in the shared decision-making process, facilitating tailored therapeutic strategies aimed at enhancing adherence and potentially reducing insulin initiation rates.

## Supplementary Material

- **Table S1** Univariate logistic regression analysis to predict the need for insulin therapy in pregnancy in the case of gestational diabetes mellitus at the time of diagnosis.
- **Table S2** Area under the receiver-operating curve (AUC) for prediction of insulin therapy during pregnancy using the 4 models that combine different variables with PPV and NPV, based on the 2021 control cohort of the GestDiab registry.
- **Table S3** Representation of possible factors influencing the individual probability of insulinisation during pregnancy, calculated using model 4.

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## Conflict of Interest

FW is a member of the German Diabetes Association (DDG) and a member of the DDG's working group on diabetes and pregnancy. She is also a member of the working group on obstetrics and prenatal medicine of the German Society of Gynaecology and Obstetrics, section: diabetes/obesity and pregnancy. TG is a member of the German Diabetes Association (DDG) and spokesperson of the DDG's working group on diabetes and pregnancy. She is also a member of the working group for obstetrics and prenatal medicine of the German Society for Gynaecology and Obstetrics, section: diabetes/obesity and pregnancy. HA is a member of the German Diabetes Society (DDG) and on the board of the DDG's working group on diabetes and pregnancy and a member of winDiab (GestDiab Register steering committee) and the professional association of specialist diabetes practices in North Rhine. MK is managing director of winDiab, a member of the DDG and the DDG's working group on diabetes and pregnancy. He was honoured in 2022 for a presentation on gestational diabetes from ADS e. V. BD and DW declare that there is no conflict of interest. The GestDiab working group was a partner in the GestDina_basic project, which was funded by the Innovation Fund from 9/2019 to 2/2023 (funding no. 01VSF18009).

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