Clinical Study Protocol

Impact of continuous glucose monitoring and patient education on patients with Prediabetes identified by Point-of-Care Tests in Community Pharmacies

Study short title

CGM-Pharm

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2 PROTOCOL SYNOPSIS

TITLE	Impact of Continuous Glucose Monitoring (CGM) and Patient Education on Patients with Prediabetes identified by Point-of-Care Tests (POCT) in Community Pharmacies					
OBJECTIVES	**Primary Objective** • *To investigate the effects of continuous glucose monitoring and patient education on HbA1c% concentrations in patients with prediabetes* **Secondary Objectives** • *To investigate the number of patients with elevated HbA1c levels in point-of-care screening tests in community pharmacies (>5.7%; 5.7-6.4%; ≥6.5%;)* • *To investigate the effects of continuous glucose monitoring and patient education on various glucose indices in patients with prediabetes (e.g. time in range, time above range, estimated HBA1c%, mean glucose, continuous overall net glycemic action (CONGA, 1h-, 2h-, 4h-based)), standard deviation, coefficient of variability, mean amplitude of glycemic excursions (MAGE), etc.).* • *To investigate the successful referral rate to treating physicians in patients with HbA1c levels compatible with diabetes (≥6.5%) when using short-message-service-based reminders* • *To investigate the successful referral rate to treating physicians in patients with HbA1c levels compatible with prediabetes (5.7-6.4%), when using short-message-service-based reminders* • *To semiquantitatively assess the patient experiences with continuous glucose monitoring and the consultation*					
DESIGN / PHASE	*Prospective, multicenter, cross-sectional study*					
STUDY PLANNED DURATION	**First patient** **First visit**	*Q2 2026*	**Last patient** **First visit**	*Q1 2027*	**Last patient** **Last visit**	*Q3 2027*
CENTER(S) / COUNTRY(IES)	*Up to 20 centers in 1 country.* *Austria*					
PATIENTS	*1000 Patients in Screening* *A minimum of 86 patients in the interventional study*					
INCLUSION CRITERIA	***For Screening part*** • ≥18 years of age • Screening is recommended by the Austrian Diabetes Society: >45 years of age, or >35 years of age with ≥ 1 risk factor: i) first-grade relatives with diabetes, ii) BMI ≥25 (or ≥23 for people with Asian descent, iii) metabolic syndrome, iv) arterial hypertension, v)					

	dyslipidemia, vi) steatosis hepatis, vii) history of gestational diabetes, viii) polycystic ovary syndrometo participate in the study ***For Interventional trial*** • HbA1c% of ≥ 5.7 and ≤ 6.4% • Willingness to participate in the study and comply with the study's requirements, i.e. o to wear a continuous glucose monitoring sensor for the projected time (maximum 14 days), o to share quantified glucose concentrations with the study team, o to participate in all planned visits within the planned time-frame o to document their food intake during CGM periods (e.g. via taking photos or notes) o To have a smartphone – to use the respective application and to view blood sugar measurements
EXCLUSION CRITERIA	***For Screening part*** • Prior diagnosis with prediabetes or diabetes • Treatment with antihyperglycemic drugs ***For Interventional Trial*** • Inability to comply with the trial's requirements • Skin conditions prohibiting the use of a glucose monitor (wounds, eczema, dermatitis, infections, sunburns, etc.) • Allergies or intolerances against the sensor or its materials/constituents, e.g. allergies against acrylic adhesive, isobornyl acrylate (IBOA), polyurethane, epoxy resins, plaster and tapes • Pregnancy or breastfeeding • Planned magnetic resonance imaging or computed tomography scans during the times when the CGM should be worn, • Planned treatment with diathermy • Intake of methyldopa or high doses of Vitamin C (>500mg/day or intravenous Vitamin C) • Intake of systemic corticosteroids
CONCOMITANT MEDICATION	**Allowed** This study will not interfere with the treatment of patients during the study.
ENDPOINTS	***Primary:***

	HbA1c% concentrations after 3 months compared to baseline between interventional group and control group. ***Secondary:*** • *Number of Patients with HbA1c% of 5.7-6.4% at screening* • *Number of Patients with HbA1c% of ≥6.5% at screening* • *Number of Patients with HbA1c% ≥5.7% at screening* • *Successful referral rate to treating physicians for patients with HbA1c of ≥6.5% using short-message-service-based reminders* • *Successful referral rate to treating physicians for patients with HbA1c of 5.7-6.4% using short-message-service-based reminders* • *Successful referral rate to treating physicians for patients with HbA1c of ≥5.7% using short-message-service-based reminders* • *HbA1c% concentrations after 6 months compared to baseline between interventional group and control group* • *in the control group: HbA1c% concentrations after 6 months (3 months after CGM Phase) vs baseline and vs. 3 months* • *Various glucose indices compared between CGM Phase 1 and CGM Phase 2 in the interventional group (Time in Range, Time in Tight Range, continuous overall net glycemic action (CONGA)-1h, CONGA-2h, CONGA-4h, mean glucose, median glucose, standard deviation of glucose, coefficient of variation of glucose, mean amplitude of glycemic excursions (MAGE), Mean of Daily Differences (MODD), time below range, time above range)* • *Various glucose indices within the CGM Phase 1 (in the intervention and control group) comparing the first 50% and the second 50% of the CGM duration (maximum 14 days, minimum to be eligible 7d, e.g. if the sensor is worn for 10 days – 5 vs. 5 days)* • To *semiquantitatively* assess the patient experiences with continuous glucose monitoring and the consultation
STATISTICAL METHODOLOGY	**Primary Endpoint** To evaluate the effects of the intervention (CGM + education) on HbA1c% over time, a linear mixed-effects model will be used. The model will include time (baseline, 3 months) as a within-subject factor, group (intervention vs. control) as a between subject factor, and the time x group interaction as the primary effect of interest. A random intercept will be included to account for the repeated-measures structure and within-subject correlation of HbA1c% levels. The time x group interaction will be interpreted as the differential change in HbA1c% between the intervention and control groups. Model assumptions (normality of residuals, homoscedasticity) will be evaluated visually and analytically. If assumptions are violated, robust standard errors of transformation will be considered.

	Secondary endpoints (number of patients, referral rate, semiquantitative feedback) will be described descriptively. Timepoints comparing trajectories of glucose indices between groups will be analyzed similarly to the primary endpoint. **Sample size calculation** *Yost et al. reported HbA1c levels for patients with prediabetes of 5.9±0.23% (mean ± standard deviation), which was confirmed by Bischof et al, who reported an HbA1c concentration of 5.9±0.21% for patients with prediabetes.* *We deem a difference in HbA1c levels of 0.2% between the interventional group and the control group within three months realistic and meaningful. Yost et al. reported in a non-controlled study a reduction in HbA1c with a similar intervention of 0.7±0.46%. Assuming a mean HbA1c of 5.9±0.2% at baseline in both groups, a two-sided alpha of 5% and a power of 80%, a group size of n=28 per group is required to show a difference of 0.2% in HbA1c as statistically significant, if the standard deviation increases to 0.3%, n=43 if the standard deviation increases to 0.4%. If the effect size increases to 0.3% then we could show a statistical significant difference for standard deviations of 0.5% (n=28) and 0.6% (n=38). These calculations assume a moderate correlation between baseline values and values after 3 months. To remain conservative and to account for up to some dropouts, we increase the sample size to n=43 per group with an option to include up to 100 patients. These calculations were done with a Wilcoxon Mann-Whitney test. The chosen statistical test (linear mixed-effects model) is efficient, which further increases the power.* *To include a minimum of 86 patients with HbA1c% levels compatible with prediabetes (5.7-6.4%) we will need to screen 500-1000 patients. In the study by Bischof et al. approximately 450 patients were screened, of which 75 had prediabetes. However, assuming that only 50% of these patients will agree to participate in this study, we may to screen more patients. Screening will be stopped after 1000 patients. As mentioned above, the sample size calculation is quite conservative and a minimum of n=28 patients could theoretically be sufficient to show the intended effects of the intervention.* **Statistical methodology** Descriptive statistics, linear mixed-effects model Interim analysis none Main analysis set(s) Main analysis: All patients who carry a CGM for at least 7 days Modified Per protocol: All patients who carry a CGM for at least 10 days **Other endpoints** Descriptive statistics will be applied for reporting demographics and baseline data. Descriptive statistics will be applied for the analysis of how many patients with HbA1c levels compatible with diabetes or prediabetes will be identified. Descriptive statistics will be applied for analysis of the referral rate to the treating physicians.

	Secondary endpoints of blood glucose indices will be analyzed analogue to the primary endpoint. Changes of HbA1c values within each group will be compared by a Wilcoxon test.

3 LIST OF ABBREVATIONS

ADR	Adverse Drug Reaction
AE	Adverse Event
ALT	Alanin Aminotransferase
ATP	Adenosine Tri-Phosphate
AST	Aspartate Aminotransferase
CRF	Case Report Form
CRO	Clinical Research Organization
CSR	Clinical Study Report
CTIS	Clinical Trials Information System
CTR	Clinical Trial Regulation (REGULATION (EU) No 536/2014)
DOH	Declaration of Helsinki
DSUR	Development Safety Update Report
ECG	Electrocardiography
EOS	End of Study
EU	European Union
EVWeb	Eudravigilance system
GCP	Good Clinical Practice
GGT	Gamma-Glutamyltransferase
HBsAg	Hepatitis B Surface Antigen
HBV	Hepatitis B Virus
HCG	Human Chorionic Gonadotropin
HVC	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
ICH	International Council for Harmonisation
IEC	Independent Ethics Committee
IMP	Investigational Medicinal Product
ISF	Investigator Site File
ISO	International Standardisation Organization
KKS	Koordinationszentrum für Klinische Studien
LLT	Lower level terms
mm	Millimeter
mmol/l	Millimol/Liter
RBC	Red Blood Cells
SAE	Serious Adverse Event
SAP	Statistical analysis plan

SAR	Serious Adverse Reaction
SOP	Standard Operating Procedure
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File
WBC	White Blood Cells
WHO	World Health Organization

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Table 1 VISIT AND ASSESSMENT SCHEDULE

Interventional Part of the Trial

PERIODS	**Name**	**SCREENING**		**Intervention**				
	Duration			**3 months**				
VISITS	**Number**	**1**	**2**	**3**	**3**	**4**	**5**	**6**
	Name	**Screening**	**Randomization**	**Counseling**	**Control 1**	**Control 2**	**Counseling 2**	**Control 3**
	Time	**Up to -14 days**	**Day 0**	**Day 4-9 after CGM placement**	**Week 4-6**	**Week 12-14**	**Day 4-9 after CGM placement**	**Week 24-26**
Informed Consent		X						
Inclusion / Exclusion Criteria		X						
Medical History		X						
Concomitant/change in medication		X						
Body weight and height		X				X		X
HbA1c Quantification		X				X		X
Counseling (Nutrition)				X (Intervention Group only)	X (both groups)		X (Control Group only)	
Randomization			X					
CGM Placement			X		X	X (Control Group only)		
Questionnaire						X (interventional group)		X (control group)

5 BACKGROUND INFORMATION

5.1 Background

Cardiovascular diseases are the leading cause of death worldwide (1). While diabetes is one of the key risk-factors for cardiovascular diseases (2), many type 2 diabetes mellitus cases remain undetected (3). The large Austrian LEAD study that included 7822 individuals recently reported an overall incidence rate of 63 (95% confidence intervals (CI) 60-66) for prediabetes and 8 (95% CI 7-10) for diabetes per 1000 person-years (4). In another recent study, we investigated the number of patients with HbA1c levels compatible with diabetes (≥6.5%) or prediabetes (5.7-6.4%) in Viennese community pharmacies. A total of 445 participants without prior diagnosis with diabetes or prediabetes were screened, of whom 17% (n=75) had HbA1c levels between 5.7 an 6.4% and 4% (n=18) had HbA1c levels ≥6.5% (5). These patients were all referred to treating physicians to undergo further diagnostic steps or receive respective treatment. Roughly 50% of these patients followed these recommendations and went to see their treating physician. Another 50% of these actually received treatment (5).

Continuous glucose measurement has been developed for the optimization of treatment of patients with type 1 diabetes. However, several studies showed positive effects of this measurement technique also for patients with type 2 diabetes with average reductions in HbA1c of 0.33% (6). However, several smaller studies investigated its use also in prediabetic patients. Yost et al. investigated its use in a small study in 15 prediabetic patients. However, HbA1c decreased from baseline to the first study period already by 0.7%. Hence, the authors did not observe further significant improvements in HbA1c concentrations, although positive trends in some blood sugar indices were observed (7). Other studies reported significant alterations of blood glucose indices in prediabetic patients (8). In a qualitative study, CGM was used in a diabetes prevention program and participants gave very positive feedback on CGM, i.e. user-friendliness, feedback on personal daily behavior, etc. Most participants reported to have changed their lifestyle by consuming more balanced meals and snacks (9). Liu et al. recently reviewed available evidence on CGM in prediabetes and emphasized its use in the detection of high-risk individuals and its ability to induce behavioral changes (10). Ma et al. reported that CGM in addition to a 2-week education session with metabolic assessments improved HbA1c significantly after 1 or 2 years compared with the control group, who received the same education session, but no CGM sensor. In this study, HbA1c dropped from a mean 5.86% to 5.68%, while it slightly increased in the control group (11).

5.2 Study rationale

CGM offers direct feedback to patients about individual blood glucose dynamics. Thus, it may indeed be used as an effective strategy to support life-style modification in patients with prediabetes. In Austria, CGM is currently only reimbursed in patients with type 1 diabetes and in patients with type 2 diabetes with insulin therapy. However, CGM is safe (12), and according to qualitative studies, patients highly recommend its use to other patients (9).

Several studies indicate that community pharmacies may successfully contribute to screening programs. First of all, within a healthcare system the most frequent patient-interactions take place in community pharmacies. This is especially important for a subgroup of patients, who does not use any other health services at all (13). Furthermore, pharmacies offer attractive opening hours, are often conveniently located and patients do not require appointments (14, 15). Our recent study corroborates these arguments: even though there is a universal healthcare system in Austria, we identified 21% or 93 of 445 individuals with elevated HbA1c levels (≥5.7%). However, we also noted a gap between risk identification during screening investigations and further diagnostic or therapeutic steps.

These findings motivated the current study. First of all, we will screen all-comers with an indication for diabetes screening according to the Austrian Diabetes Society with means of a POCT for HbA1c. All

patients with HbA1c levels compatible with diabetes mellitus type 2 will be referred to treating physicians, in order to facilitate further diagnostic steps or treatment of the disease. Patients not willing to participate in the interventional trial will likewise be referred to treating physicians. We will aim to improve the successful referral rate by implementing a short-message-service (SMS)-based reminder service to make appointments at treating physicians. Furthermore, in an interventional trial in patients with prediabetes we will investigate the impact of CGM and educational material on HbA1c% levels. The primary endpoint is defined as the change in HbA1c level after three months between the two groups. However, secondary endpoints include various blood glucose-based indices. After the end of the study, all patients will be referred to treating physicians to evaluate necessity of further diagnostic steps and or the need for treatment. However, for patients with prediabetes, guidelines mostly recommend lifestyle modification

6 STUDY OBJECTIVES (HYPOTHESIS)

In the screening part of the study, we aim to investigate the number of patients with elevated HbA1c levels (≥5.7%).

Furthermore, we will investigate the successful referral rate. To improve the referral rate of roughly 50% that we have observed in the previous study (5), we will implement an SMS-based reminder service.

The objectives for the interventional trial are listed in the following:

6.1 Primary objective (Hypothesis)

To investigate the effects of continuous glucose monitoring and patient education on HbA1c% concentrations in patients with prediabetes

6.2 Secondary objectives (Hypothesis)

- To investigate the number of patients with elevated HbA1c levels in point-of-care screening tests in community pharmacies (>5.7%, 5.7-6.4%, ≥6.5%)
- To investigate the effects of continuous glucose monitoring and patient education on various glucose indices in patients with prediabetes (e.g. Time in Range, Time above range, estimated HBA1c%, mean glucose, continuous overall net glycemic action (CONGA), standard deviation, coefficient of variability, mean amplitude of glycemic excursions (MAGE), etc.).
- To investigate the successful referral rate to treating physicians in patients with HbA1c levels compatible with diabetes (≥6.5%) when using SMS-based reminders
- To investigate the successful referral rate to treating physicians in patients with HbA1c levels compatible with prediabetes (5.7-6.4%), when using short-message-service-based reminders
- To semi-quantitatively assess the patient experiences with continuous glucose monitoring and the consultation

7 STUDY DESIGN

The screening part of the study is a cross-sectional trial, in which all-comers in participating pharmacies, in whom screening is recommended by the Austrian Diabetes Society, will undergo screening for HbA1c levels. Those with HbA1c levels compatible with diabetes (≥6.5%) will be recommended to make an appointment with treating physicians. An SMS-based reminder service will be implemented. Patients with HbA1c levels compatible with prediabetes (5.7-6.4%) will be invited to participate in the interventional trial. Those, who do not want to participate will be referred to treating physicians.

Patients with HbA1c levels between 5.7 and 6.4%, who are willing to participate in the study, will be randomized to the interventional group, in which they will receive a CGM sensor at baseline, one CGM sensor after 4-6 weeks and will undergo repetitive HbA1c% testing after 3 months. Screening must take place within 14 days of randomization and CGM sensor placement. Those patients randomized to the control group will be offered a CGM sensor following the HbA1c% testing after 3 months. All participants must agree to download the application to monitor blood glucose concentrations and to share the data with the study team. Patients will also receive educational material, i.e. short brochures, as well as access to educational sections of the respective apps. Furthermore, a consultation with a physician will be conducted to review blood sugar profiles and food and beverage intake.

7.1 Study population

Patients with HbA1c levels of ≥5.7% - ≤ 6.4% at screening, who have neither received prior treatment for diabetes nor been diagnosed with diabetes or prediabetes.

7.1.1 Subject population

7.1.2 Inclusion criteria

For Screening part

- ≥18 years of age
- Screening is recommended by the Austrian Diabetes Society: >45 years of age, or >35 years of age with ≥ 1 risk factor: i) first-grade relatives with diabetes, ii) BMI ≥25 (or ≥23 for people with Asian descent, iii) metabolic syndrome, iv) arterial hypertension, v) dyslipidemia, vi) steatosis hepatis, vii) history of gestational diabetes, viii) polycystic ovary syndrometo participate in the study

For Interventional Trial

- HbA1c% of ≥ 5.7 and ≤ 6.4%
- Willingness to participate in the study and comply with the study's requirements, i.e.
    - to wear a continuous glucose monitoring sensor for the projected time (maximum 14 days),
    - to share quantified glucose concentrations with the study team,
    - to participate in all planned visits within the planned time-frame
    - to document their food intake during CGM periods (e.g. via taking photos or notes)
    - To have a smartphone – to use the respective application and to view blood sugar measurements

7.1.3 Exclusion criteria

For Screening Part

- Prior diagnosis with prediabetes or diabetes
- Treatment with antidiabetic drugs

For Interventional Trial

- Inability to comply with the trial's requirements
- Skin conditions or prohibiting the use of a glucose monitor (wounds, eczema, dermatitis, infections, sunburns, etc.)

- Allergies or intolerances against the sensor or its materials/constituents, e.g. allergies against acrylic adhesive, isobornyl acrylate (IBOA), polyurethane, epoxy resins, plaster and tapes
- Pregnancy or breastfeeding
- Planned magnetic resonance imaging or computed tomography scans during the times when the CGM should be worn,
- Planned treatment with diathermy
- Pregnancy – Females with an ongoing pregnancy with prediabetes must not participate in the trial
- Intake of methyldopa or high doses of Vitamin C (>500mg/day or intravenous Vitamin C)
- Intake of systemic corticosteroids

7.1.4 Females of childbearing potential

Females of childbearing potential may participate in the study. However, in case of prediabetes and willingness to participate in the randomized trial, a pregnancy test must be conducted. In case of a positive result (pregnancy confirmed), females with prediabetes must be referred to treating physicians immediately and must not participate in the study.

7.1.5 Subjects in an emergency situation

Not applicable. These patients will not participate in the study.

7.1.6 Study duration

The screening part consists of a single visit in a participating community pharmacy. For those who are eligible for the interventional trial, the study lasts six months.

7.1.7 Withdrawal and replacement of subjects

Criteria for withdrawal

Subjects may prematurely discontinue from the study at any time. Premature discontinuation from the study means that the subject did not complete the final HbA1c% quantification as planned per protocol (after approximately 6 months).

Subjects must be withdrawn under the following circumstances:

- at their own request
- if the Investigator feels it would not be in the best interest of the subject to continue
- if the subject violates conditions laid out in the consent form / information sheet or disregards instructions by the study personal
- in case of allergies or intolerances to the CGM sensor

In all cases, the reason why subjects are withdrawn must be recorded in detail in the CRF and in the subject's medical records. Should the study be discontinued prematurely, all study materials (completed, partially completed and empty CRFs) will be retained.

Follow-up of patients withdrawn from the study

After study termination patients will be referred to treating physicians to undergo further diagnostic investigation to decide whether treatment and/or follow-up visits are deemed necessary.

Replacement policy

Patients in the interventional part, who do not complete at least 10 days of continuous glucose monitoring in the intended CGM periods (2 planned periods) will be replaced. Subjects in the control

group will not be replaced, unless they do not undergo the two HbA1c quantification at baseline and after 3 months.

7.1.8 Premature termination of the study

The sponsor has the right to close this study at any time. The IEC and the competent regulatory authority must be informed within 15 days of early termination.

The trial or single dose steps will be terminated prematurely in the following cases:

- If adverse events occur which are so serious that the risk-benefit ratio is not acceptable.
- If the number of dropouts is so high that proper completion of the trial cannot realistically be expected.

8 METHODOLOGY

8.1 Recruitment and Screening

All-comers with an indication for HbA1c Screening according to the Austrian Diabetes Society (for details please refer to the in the in- and exclusion criteria) will be invited to undergo a screening investigation for HbA1c% levels in participating community pharmacies by pharmacists. An informed consent form will be completed for the screening investigation. Personal data will be collected (including age, sex, height, weight, BMI, contact information, social security number) and point-of-care tests will be performed using spontaneous (regardless of the patients' fasting state) capillary blood samples. Local laboratory equipment will be used. Standard operating procedures must be closely followed.

Patients with HbA1c% levels of ≥5.7% and ≤6.4% will be invited to participate in the randomized trial.

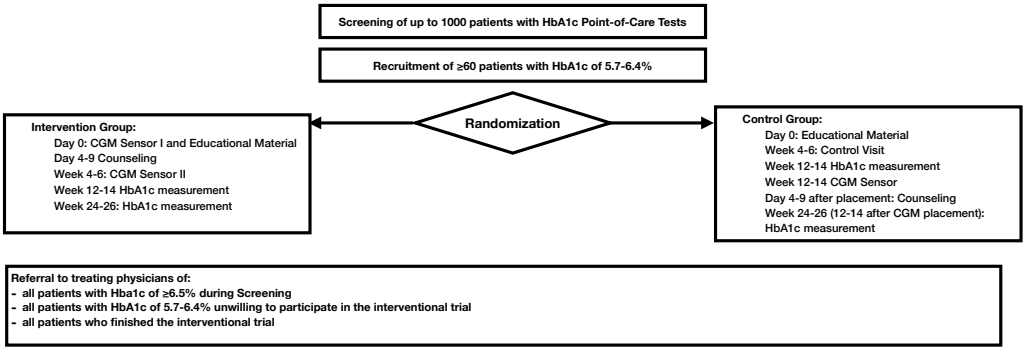
Patients with HbA1c% levels of >6.5% and those with HbA1c% levels of ≥5.7% and ≤6.4%, who do not want to participate in the interventional trial, will be referred to treating physicians. An SMS-based reminder service will be implemented that will send three monthly reminders to subjects to make an appointment with treating physicians. After a minimum of three months patients will be contacted by telephone and/or email to ask whether they have followed these recommendations.

8.2 Randomized Trial

If patients agree to participate in the randomized trial, another informed consent form will be completed. The informed consent process will take place in community pharmacies and will primarily be conducted by community pharmacists. However, in case of open questions and/or if patients wish to discuss this study with the investigators, they will of course be available for this process. In- and exclusion criteria will be checked. Screening may take place within 14 days of study start. Patients may be rescreened if the 14-day period is over. Patients will be randomized using a web-based randomization software. In the intervention group a CGM sensor will be placed according to the manufacturer's recommendations (=baseline). This might happen on the same day as screening or within at most 14 days. Participants will then download the application to their phone or tablet. They will receive instructions by community pharmacy staff with study-specific trainings and educational material (short brochure about prediabetes). Further appointments will be made: for a second CGM phase after 4-6 weeks, as well as for two more HbA1c quantifications and for measuring body weight after 3 months and after 6 months. At all appointments, study staff is available for questions and for advice with regards to technical issues, but also with regards to questions regarding blood sugar measurements, etc. Furthermore, between day 4-9 after placing the CGM sensor (ideally between day 4-7), a telephone or online discussion of their glucose measurements and respective food and beverage intake will take place with a physician, who is

part of the study team. In this short meeting (approximately 15 minutes) recommendations to improve food intake based on CGM results and the documented food intake will take place. This will be conducted in the first CGM phase only. In the control group patients will be informed that they will receive the CGM sensor after a three-month period and after a second HbA1c% control measurement. However, they will already receive an informative brochure after randomization. Baseline will be the first HbA1c quantification. After 4-6 weeks patients will be invited to the pharmacy or contacted via telephone to inquire about their lifestyle modification, to ask whether they have questions about the brochure and to remind them of their upcoming appointments. Furthermore, between day 4-9 after placing the CGM sensor (ideally between day 4-7), a telephone or online discussion of their glucose measurements will take place with a physician, who is part of the study team. In this short meeting (approximately 15 minutes) recommendations to improve food intake based on CGM results and the documented food intake will take place. After another 3 months (six months after baseline) a final HbA1c% quantification will take place, as well as weight measurement.

After the final study visit, all patients will be referred to their treating physician to undergo further diagnostic steps and to assess if any kind of therapy is indicated.



Flowchart of the Trial

8.3 Continuous Glucose Monitoring

All participating pharmacists will be specifically trained to use and place a CGM sensor. The intended duration of the CGM period is 14 days per sensor. However, these sensors may be dislocated or there may be problems in their use. If this happens within the first 10 days, sensors will be replaced. If this happens on day 10-14, the CGM period will be truncated and the sensor will be removed. If a second CGM sensor is placed during a 14-day period, it will still be removed after 14 days to maintain the 14-day period of the intervention.

If there are any allergic or other adverse reactions to the sensor, it will be removed and the study will be terminated for the individual patient. Patients may be replaced, if the sensor worn for less than 10 days in the two CGM periods in the interventional group.

We will use the Roche Accu-Chek SmartGuide device and the Accu-Chek SmartGuide Predict app (Version 3) application. Both, sensor and application, are approved for use in humans. Data will be shared by means of a single-use password that is generated during installation and shared with the study team. Pharmacists will explain the app to study participants. A diary to enter food and beverage intake will support the biofeedback process.

8.4 Prediabetes brochure

Patients will receive an informative brochure on prediabetes (Appendix I).

8.5 Questionnaire

After completion of one CGM phase (control group) or two CGM phases (intervention group) a semiquantitative questionnaire will be handed to patients (Appendix II). The questionnaire has been specifically developed for this study, although it has not been validated.

8.6 Concomitant medication

The study will not interfere with the participants medical treatment. According to the guidelines lifestyle modifications are the recommended treatment for patients with prediabetes (16). However, if any antidiabetic medication is used, the study will be terminated in the individual patient.

8.7 Randomization and stratification

We will use a web-based randomization software (www.meduniwien.ac.at/randomizer). Block randomization with permuted blocks 8 will be used. We will only stratify randomization by age (<60 years; ≥60 years) and sex.

8.8 Blinding

This is an open-label study and blinding will not be performed.

8.9 Benefit and risk assessment

The screening part is characterized by minimal risks (capillary blood sample by trained personnel). The benefits are obvious: those with elevated HbA1c% levels are informed about these values and are referred to treating physicians to receive further treatment or to plan further diagnostic steps. Thus, the benefit/risk assessment of this part of the study is in our opinion positive.

For the interventional trial we decided to only include those with HbA1c% levels compatible with prediabetes. This has several reasons. First of all, the main therapeutic indication for patients with prediabetes is lifestyle modification. CGM and patient education are two means that may enforce this recommendation. Direct feedback of glucose kinetics as a response to food or beverage intake may inform patients about problematic behavior. The second CGM phase is thought to re-enforce these behaviors. The short discussion with a physician trained in the interpretation of these values should additionally support patients in adapting their lifestyle. After the study all participants will be referred to treating physicians. Thus, the time delay until further diagnostic work up is in our opinion acceptable. Furthermore, this study aims to support lifestyle modification as the main form of treatment, which means that necessary treatment is not withheld from participating patients. Furthermore, there is a realistic chance that patient education re-enforced by CGM may actually reduce the progress to diabetes in some patients. Of note, CGM sensors are currently not indicated and not reimbursed for patients with prediabetes.

The risks of wearing a CGM sensor is minimal. All study staff will be trained in the use of these sensors and in case of allergies or intolerances or other relevant side effects, the study will be terminated early.

In sum, we believe that the benefits clearly outweigh the risks of the study.

8.10 Study procedures

8.10.1 General rules for trial procedures

- All study measures like blood sampling and measurements have to be documented with date (dd:mm:yyyy).
- In case several study procedures are scheduled at the same time point, there is no specific sequence that should be followed.
- The dates of all procedures should be according to the protocol. The time margins mentioned in the study flow chart are admissible. If for any reason, a study procedure is not performed within scheduled margins a protocol deviation should be noted, and the procedure should be performed as soon as possible or as adequate. However, study staff should motivate patients to remain in the study, even if margins have to be violated due to unforeseeable situations.
- If it is necessary for organizational reasons, it is admissible to perform procedures which are scheduled for one visit at two different time points. Allowed time margins should thereby not be exceeded.

8.10.2 Recruitment procedure

All-comers will be asked to participate in the screening study. Those with prediabetes will be asked to participate in the main trial. Subjects may take their time to decide upon participation in the interventional part of the study. The screening must have taken place within 14 days of the study start (=randomization and CGM application)

8.10.3 Definition of the end of the trial

Last visit of the last patient or screening of 1000 participants.

8.10.4 Post-Trial provisions

At the end of the trial all patients will be referred to their treating physicians for further diagnostic workup and possibly to be included into a follow-up program (including SMS reminders). CGM sensors may be bought by patients in pharmacies, however, currently health insurances do not cover or reimburse their costs. For patients with prediabetes or diabetes that is not treated with insulin, there is currently no recommendation to wear these sensors.

9 SAFETY DEFINITIONS AND REPORTING REQUIREMENTS

9.1 Adverse events (AEs)

9.1.1 Summary of known and potential risks of the study drug

A risk-based approach will be implemented. The main risk of CGM regards local skin reactions (dermatitis, allergies, eczema, intolerances, infections). Other adverse events have not been described. We will document all adverse events and grade them. However, other AEs will not be systematically documented.

9.1.2 Definition of adverse events

An AE is any untoward adverse change from the subject's baseline condition, i.e., any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease which is considered to be clinically relevant by the physician that occurs during the course of the study, whether or not considered related to the study drug.

Adverse events include:

- Exacerbation of a pre-existing disease.
- Increase in frequency or intensity of a pre-existing episodic disease or medical condition.
- Disease or medical condition detected or diagnosed after study drug administration even though it may have been present prior to the start of the study.
- Continuous persistent disease or symptoms present at baseline that worsen following the start of the study.
- Lack of efficacy in the acute treatment of a life-threatening disease.
- Events considered by the Investigator to be related to study-mandated procedures.
- Abnormal assessments, e.g., ECG and physical examination findings, must be reported as AEs if they represent a clinically significant finding that was not present at baseline or worsened during the course of the study.
- Laboratory test abnormalities must be reported as AEs if they represent a clinically significant finding, symptomatic or not, which was not present at baseline or worsened during the course of the study or led to dose reduction, interruption or permanent discontinuation of study drug.

Adverse events do not include:

- Pre-planned interventions or occurrence of endpoints specified in the study protocol are not considered AE´s, if not defined otherwise (eg.as a result of overdose)
- Medical or surgical procedure, e.g., surgery, endoscopy, tooth extraction, transfusion. However, the event leading to the procedure is an AE. If this event is serious, the procedure must be described in the SAE narrative.
- Pre-existing disease or medical condition that does not worsen.
- Situations in which an adverse change did not occur, e.g., hospitalizations for cosmetic elective surgery or for social and/or convenience reasons.
- Overdose of either study drug or concomitant medication without any signs or symptoms. However, overdose must be mentioned in the Study Drug Log.

9.2 Serious adverse events (SAEs)

According to the Regulation (EU) No 536/2014 “Serious adverse event” means any untoward medical occurrence that at any dose

- requires inpatient hospitalization or prolongation of existing hospitalization,
- results in persistent or significant disability or incapacity,
- results in a congenital anomaly or birth defect,
- is life-threatening, or
- results in death.

9.2.1 Hospitalization – Prolongation of existing hospitalization

Hospitalization is defined as an overnight stay in a hospital unit and/or emergency room.

An additional overnight stay defines a prolongation of existing hospitalization.

The following is not considered an SAE and should be reported as an AE only:

- Treatment on an emergency or outsubject basis for an event not fulfilling the definition of seriousness given above and not resulting in hospitalization.

The following reasons for hospitalizations are not considered AEs, and therefore not SAEs:

- Hospitalizations for cosmetic elective surgery, social and/or convenience reasons.
- Elective treatment of a pre-existing disease or medical condition that did not worsen, e.g., hospitalization for chemotherapy for cancer, elective hip replacement for arthritis.

9.2.2 SAEs related to investigational drug

Such SAEs are defined as SAEs that appear to have a reasonable possibility of causal relationship.

9.2.3 Suspected unexpected serious adverse reactions (SUSARs)

SUSARs are all serious adverse reactions with **suspected** causal relationship to the study drug that is **unexpected** (not previously described in the Summary of Product Characteristics or Investigator's brochure) and serious.

9.3 Pregnancy

Any pregnancy that occurs during study participation must be reported to the Investigator/sponsor. Pregnant subjects may terminate their participation in the trial, if they wish to do so. However, CGM is not contraindicated in pregnant women. In fact, in prediabetic women it may even be advantageous to reduce the risk of gestational diabetes or to decide about necessary treatment or a closer follow up with treating physicians. Pregnancy outcomes (including premature termination) will not be followed.

9.4 Severity of adverse events

The severity of clinical AEs is graded on a three-point scale: mild, moderate, severe, and reported on specific AE pages of the CRF.

If the severity of an AE worsens during study drug administration, only the worst intensity should be reported on the AE page. If the AE lessens in intensity, no change in the severity is required.

If an AE occurs during a washout or placebo run-in phase and afterwards worsens during the treatment phase, a new AE page must be filled in with the intensity observed during study drug administration.

Mild

Event may be noticeable to subject; does not influence daily activities; the AE resolves spontaneously or may require minimal therapeutic intervention;

Moderate

Event may make subject uncomfortable; performance of daily activities may be influenced; intervention may be needed; the AE produces no sequelae.

Severe

Event may cause noticeable discomfort; usually interferes with daily activities; subject may not be able to continue in the study; the AE produces sequelae, which require prolonged therapeutic intervention.

A mild, moderate or severe AE may or may not be serious. These terms are used to describe the intensity of a specific event (as in mild, moderate, or severe myocardial infarction). However, a severe event may be of relatively minor medical significance (such as severe headache) and is not necessarily serious. For example, nausea lasting several hours may be rated as severe, but may not be clinically serious. Fever

of 39°C that is not considered severe may become serious if it prolongs hospital discharge by a day. Seriousness rather than severity serves as a guide for defining regulatory reporting obligations.

9.5 Relationship to study intervention

For all AEs, the Investigator will assess the causal relationship between the study interven and the AE using his/her clinical expertise and judgment according to the following algorithm that best fits the circumstances of the AE:

Not related

- May or may not follow a temporal sequence from administration of the study product
- Is biologically implausible and does not follow known response pattern to the suspect study drug (if response pattern is previously known).
- Can be explained by the known characteristics of the subject's clinical state or other modes of therapy administered to the subject.

Unlikely

- There is a reasonable temporal relation between the AE and the intake of the study medication, but there is a plausible other explanation for the occurrence of the AE.

Possibly

- The AE has a reasonable temporal relationship with drug administration.
- The AE may equally be explained by the study subject's clinically state, environmental or toxic factors, or concomitant therapy administered to the study subject.
- The relationship between study drug and AE may also be pharmacologically or clinically plausible.

Probably

- There is a reasonable temporal relation between the AE and the intake of the study medication, and plausible reasons point to a causal relation with the study medication.

Related

- Reasonable temporal relation between the AE and the intake of the study medication and
- There is no other explanation for the AE and
- Subsidence or disappearance of the AE on withdrawal of the study medication and
- Recurrence of the symptoms on restart at previous dose (only applies for re-institution of mediation).

Not assessable

- The causal relationship between the study drug and the AE cannot be judged.

9.6 Reporting procedures

A special section is designated to adverse events in the case report form. The following details must thereby be entered:

- Type of adverse event
- Start (date and time)
- End (date and time)
- Severity (mild, moderate, severe)
- Serious (no / yes)
- Unexpected (no / yes)
- Outcome (resolved, resolving, not resolved, resolved with sequelae, unknown, fatal)

- Relation to study drug (Related/ Probably/ Possibly/ Unlikely/ Not related/ Not assessable)

Adverse events will be documented in the case report form in accordance with the above mentioned criteria. Adverse events will subsequently be summarized in the development safety update report of the trial (9.6.3)

9.6.1 Reporting procedures for SAEs

In case of a serious adverse event, the Investigator has to use all supportive measures for best patient treatment. A written report is also to be prepared and provided to the sponsor immediately (at least within 24 hours).

should at least contain the following:

- Patient number
- Patient: sex
- The suspected investigational medical product (IMP)
- The adverse event assessed as serious
- Short description of the event and outcome

If applicable, the initial report should be followed by the Follow up report, indicating the outcome of the SAE. The sponsor will report safety information as required.

9.6.2 Reporting procedures for SUSAR

All SUSARs are reported by the sponsor via Eudravigilance (EVWeb) within 7 or 15 days, depending on the event and will be included in the development safety update report (9.6.3)

Such reports shall be made by the sponsor and should content at least the following details:

- Patient number (study code/screening number)
- Patient: age in years, sex
- Name of Investigator and investigating site
- Period of administration
- The suspected investigational medical product (IMP)
- The adverse event assessed as serious and unexpected, and for which there is a **suspected** causal relationship to the IMP
- Concomitant disease and medication
- Short description of the event:
    - Description
    - Onset and if applicable, end
    - Therapeutic intervention
    - Causal relationship
    - Seriousness criteria or reportable reason

Electronic reporting should be the expected method for reporting of SUSARs to the competent authority. In that case, the format and content as defined by the regulatory requirements should be adhered to. The latest version of MedDRA should be applied. Lower level terms (LLT) should be used.

10 FOLLOW-UP

10.1 Follow-up of study participants including follow-up of adverse events

The investigators will support patients to receive adequate care for any local skin reactions and will follow-up on these. A risk-based approach will be implemented and severe and/or serious SAEs will be followed-up longer and closer than uncomplicated AEs of mild or moderate severity.

10.2 Treatment after end of study

CGM sensors may be bought by patients after participation in the study. However, these are not considered a "treatment" and therefore this will not be done by the sponsor or investigators.

11 STATISTICAL METHODOLOGY AND ANALYSIS

11.1 Analysis sets

Two different analysis sets are defined

(Modified) Intention to treat set

This analysis set includes subjects who were randomized (and received at least one CGM sensor).

Per-protocol set

This analysis set comprises all subjects who – in the interventional group - received at least two CGM sensor (and wore each of them for at least 10 days) and did not violate the protocol in a way that might affect the evaluation of the effect of the study drug(s) on the primary objective.

11.2 Sample size considerations

Yost et al. reported HbA1c levels for patients with prediabetes of 5.9±0.23% (mean ± standard deviation), which was confirmed by Bischof et al, who reported an HbA1c concentration of 5.9±0.21% for patients with prediabetes.

We deem a difference in HbA1c levels of 0.2% between the interventional group and the control group within three months realistic and meaningful. Yost et al. reported in a non-controlled study a reduction in HbA1c with a similar intervention of 0.7±0.46%. Assuming a mean HbA1c of 5.9±0.2% at baseline in both groups, a two-sided alpha of 5% and a power of 80%, a group size of n=28 per group is required to show a difference of 0.2% in HbA1c as statistically significant, if the standard deviation increases to 0.3%, n=43 if the standard deviation increases to 0.4%. If the effect size increases to 0.3% then we could show a statistical significant difference for standard deviations of 0.5% (n=28) and 0.6% (n=38). These calculations assume a moderate correlation between baseline values and values after 3 months. To remain conservative and to account for up to some dropouts, we increase the sample size to n=43 per group with an option to include up to 100 patients. These calculations were done with a Wilcoxon Mann-Whitney test. The chosen statistical test (linear mixed-effects model) is efficient, which further increases the power.

To include a minimum of 86 patients with HbA1c% levels compatible with prediabetes (5.7-6.4%) we will need to screen 500-1000 patients. In the study by Bischof et al. approximately 450 patients were screened, of which 75 had prediabetes. However, assuming that only 50% of these patients will agree to participate in this study, we may to screen more patients. Screening will be stopped after 1000 patients. As mentioned above, the sample size calculation is quite conservative and a minimum of n=28 patients could theoretically be sufficient to show the intended effects of the intervention.

11.3 Relevant protocol deviations

All major protocol deviations will be listed in the study report.

11.4 Statistical analysis plan

The statistical analysis will be done after completion of the trial (last visit of last patient). All data will be imported into an adequate statistical analysis software (IBM SPSS, R, etc.) and the analyses will be performed as indicated below.

11.5 Missing, unused and spurious data

Missing will not be imputed, spurious data will be removed. However, at least three investigators must agree to remove a specific value from the data set. This must be documented accordingly.

11.6 Endpoints analysis

11.6.1 Primary endpoint analysis

To evaluate the effects of the intervention (CGM + education) on HbA1c% over time, a linear mixed-effects model will be used. The model will include time (baseline, 3 months) as a within-subject factor, group (intervention vs. control) as a between subject factor, and the time x group interaction as the primary effect of interest. A random intercept will be included to account for the repeated-measures structure and within-subject correlation of HbA1c% levels.

The time x group interaction will be interpreted as the differential change in HbA1c% between the intervention and control groups. Model assumptions (normality of residuals, homoscedasticity) will be evaluated visually and analytically. If assumptions are violated, robust standard errors of transformation will be considered.

Secondary endpoints (number of patients, referral rate, questionnaire) will be described descriptively.

Timepoints comparing trajectories of glucose indices between groups will be analyzed similarly to the primary endpoint.

11.6.2 Secondary endpoint analysis

Descriptive statistics will be applied for reporting demographics and baseline data.

Descriptive statistics will be applied for the analysis of how many patients with HbA1c levels compatible with diabetes or prediabetes will be identified.

Descriptive statistics will be applied for analysis of the referral rate to the treating physicians.

Secondary endpoints of blood glucose indices will analyzed analogue to the primary endpoint.

Changes of HbA1c values within each group will be compared by a Wilcoxon test.

11.6.3 Safety and tolerability endpoints

A table will present AEs that occurred during the study in a descriptive manner.

11.6.4 Baseline parameters and concomitant medications

Baseline parameters and concomitant medication will be documented and presented in a descriptive manner.

11.7 Software program(s)

IBM SPSS, Graphpad Prism, R.

12 DOCUMENTATION AND DATA MANAGEMENT

12.1 Documentation of study results

A subject screening and identification Log will be completed for all enrolled subjects with the reasons for exclusion.

12.1.1 Case report form (CRF)

For each subject enrolled, regardless of their participation in the interventional trial, an electronic CRF (eCRF) must be completed and signed by the Investigator or a designated sub-Investigator. This also applies to those subjects who fail to complete the study. If a subject withdraws from the study, the reason must be noted on the eCRF. Case report forms are to be completed on an ongoing basis.

ECRF entries and corrections will only be performed by study site staff, authorized by the Investigator.

Entry errors have to be corrected according the ICH-GCP Guidelines.

The entries will be checked by trained personnel (Monitor) and any errors or inconsistencies will be checked immediately.

The monitor will collect original completed and signed CRFs at the end of the study. A copy of the completed and signed CRFs will remain on site, while the original data are handed out to the sponsor.

Data Manager of the study will be Mag. Thorsten Bischof.

12.1.2 Data collection

Data collected at all visits are entered into an interactive form. The eCRFs will be source documents verified following guidelines established before study onset as detailed in the Monitoring Plan. Maintenance of the study database will be performed by Mag. Thorsten Bischof.

12.2 Safekeeping

The Investigator will maintain adequate and accurate records to enable the conduct of the study to be fully documented and the study data to be subsequently verified (according to ICH-GCP “essential documents”). These documents will be classified into two different categories: Investigator's study site file (ISF) with all essential documents regarding the study conduct, and subject clinical source documents.

The Investigator's file will contain all essential documents listed in ICH-GCP Guidelines section 8.

Subject clinical source documents include all patient hospital clinical records in original version, such as original laboratory reports, ECG, X-ray prints and other reports.

These two categories of documents must be kept on file by the Investigator for as long as needed to comply with the regulatory requirements.

12.3 Quality control and quality assurance

12.3.1 Periodic Monitoring

Monitoring will be performed on an ongoing basis and will focus on the primary endpoint of the study.

The designated monitor will contact and visit the Investigator on a regularly basis and will be allowed to have direct access to all source documents needed to verify the entries in the CRFs and other protocol-related documents provided that subject confidentiality is maintained in agreement with local regulations. It will be the monitor's responsibility to inspect the CRFs at regular intervals according to

the monitoring plan throughout the study, to verify the adherence to the protocol and the completeness, consistency and accuracy of the data being entered on them.

12.3.2 Audit and inspections

Upon request, the Investigator will make all study-related source data and records available to a qualified quality assurance auditor mandated by the sponsor or to competent authority inspectors. The main purposes of an audit or inspection are to confirm that the rights and welfare of the subjects have been adequately protected, and that all data relevant for assessment of safety and efficacy of the investigational product have appropriately been reported to the sponsor.

12.4 Reporting and publication

12.4.1 Publication of study results

The findings of this study will be published by the sponsor (Investigators) in a scientific journal and presented at scientific meetings. The manuscript will be circulated to all authors before submission. Confidentiality of subjects in reports/publications will be guaranteed.

13 ETHICAL AND LEGAL ASPECTS

13.1 Informed consent of subjects

Following comprehensive instruction regarding the nature, significance, impact and risks of this clinical trial, the patient must give written consent to participation in the study.

During the instruction the trial participants are to be made aware of the fact that they can withdraw their consent – without giving reasons – at any time without their further medical care being influenced in any way.

In addition to the comprehensive instructions given to the trial participants by the Investigator, the trial participants also receive a written patient information sheet in comprehensible language, explaining the nature and purpose of the study and its progress.

The patients must agree to the possibility of study-related data being passed on to relevant authorities.

13.2 Acknowledgement / approval of the study

The Investigator (or a designated CRO) will submit this protocol and any related document provided to the subject (such as subject information used to obtain informed consent) to an Ethics Committee (EC). Approval must be obtained before starting the study.

13.2.1 Changes in the conduct of the study

Protocol modifications

Proposed modifications must be submitted to the appropriate ECs. Substantial modifications may be implemented only after EC approval has been obtained. Modifications that are intended to eliminate an apparent immediate hazard to subjects may be implemented prior to receiving EC approval. However, in this case, notification must be done as soon as possible after implementation.

Study Termination

If the sponsor or the Investigator decides to terminate the study before the planned completion, they will notify each other in writing stating the reasons of early termination. Both the sponsor and the investigator will ensure the protection of the subjects' wellbeing. The sponsor will notify the ethics

committee about the premature termination. Documentation will be filed in the Trial Master File as well as in the Investigator Site File.

13.3 Insurance

Study participants will not be insured in this trial.

13.4 Confidentiality

The information contained in this document, especially unpublished data, is the property of the sponsor. It is therefore provided to you in confidence as an Investigator, potential Investigator, or consultant, for review by you, your staff, and an Ethics Committee or Institutional Review Board. It is understood that this information will not be disclosed to others without written authorization from the principal investigator or the sponsor representative.

13.5 Ethics and good clinical practice (GCP)

The Investigator will ensure that this study is conducted in full conformance with the principles of the "Declaration of Helsinki" (as amended at the 75 WMA General Assembly, Helsinki, Finland, October 2024) and with the laws and regulations of the country in which the clinical research is conducted.

The Investigator of the clinical trial shall guarantee that only appropriately trained personnel will be involved in the study. All studies must follow the ICH GCP Guidelines and the regulatory requirements.

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15 Appendix I – Information brochures

ÖDG Österreichische Diabetes Gesellschaft
helfen, heilen, forschen

Informationsbogen Prädiabetes

Was ist Prädiabetes?

Prädiabetes ist eine Vorstufe des Typ 2 Diabetes, der häufig auch fälschlicherweise als Alterszucker bezeichnet wird.

Warum ist Prädiabetes gefährlich?

Das Risiko innerhalb der nächsten Jahre an einem Typ 2 Diabetes zu erkranken ist sehr hoch (bis zu 10% der Personen mit Prädiabetes entwickeln einen Diabetes mellitus Typ 2 pro Jahr). Außerdem liegen häufig auch noch andere Erkrankungen vor, die das Risiko für Herz-Kreislauf-Erkrankungen erhöhen. Dazu zählen erhöhter Blutdruck, Übergewicht und Fettstoffwechselstörungen. Insgesamt ist das Risiko für Gefäß-, Nerven- und Augenerkrankungen bereits bei Prädiabetes im Vergleich zu Zuckerstoffwechselgesunden erhöht.

Wie wird Prädiabetes diagnostiziert?

Dazu gibt es mehrere Möglichkeiten:

1.) Anhand des Nüchternblutzuckerwertes, der mehrfach zwischen 100 und 126 mg/dl liegt

2.) Anhand des HbA1c-Wertes (5.7-6.4% bzw. 39-46 mmol/mol)

3.) Mittels eines Zuckerbelastungstests bei dem 75g Traubenzucker in Wasser aufgelöst getrunken werden und der Blutzucker 2 Stunden danach bestimmt wird (2h-Wert >=140 mg/dl und <200 mg/dl)

Besprechen Sie mit ihrer behandelnden Ärzt*in welcher der oben genannten Werte erhöht ist und ob weitere Laborbestimmungen notwendig sind.

Worauf muss ich achten?

- Gehen Sie regelmäßig zu Kontrolluntersuchungen, bei denen unter anderem Ihr HbA1c Wert (Langzeitzuckerwert), die Blutfette und Ihr Blutdruck kontrolliert werden:
- **Zielwerte:** HbA1c Normalwert: < 5,7% (39 mmol/mol), ab 6,5 % (48 mmol/mol) liegt ein Diabetes mellitus vor
- **LDL-Cholesterinwert:** für viele Patient*innen mit Prädiabetes liegt der LDL-Cholesterin-Zielwert < 100 mg/dl - der Zielwert ist abhängig von anderen Erkrankungen und Risikofaktoren und sollte individuell mit Ihrer behandelnden Ärzt*in besprochen und festgelegt werden
- **Blutdruckzielwert:** für die meisten Patient*innen mit Prädiabetes liegt dieser < 130/80 mm Hg, kann aber bei Vorliegen von Nierenerkrankungen, Herz-Kreislauf-Erkrankungen oder höherem Lebensalter davon abweichen
- Befolgen Sie die allgemeinen Impfempfehlungen (insbesondere Covid-19, Influenza)

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Was kann ich gegen Prädiabetes tun?

Das Ziel ist es, das Fortschreiten zu einem Diabetes mellitus Typ 2 zu vermeiden und auch die Gefäße zu schützen.

Bewegen Sie sich regelmäßig

(Ziel: mindestens 150 Minuten pro Woche)

Es muss kein Spitzensport sein, jeder Schritt zählt. Integrieren Sie Bewegung in den Alltag, z.B. Treppensteigen statt Liftfahren, Radfahren oder Gehen statt Auto und Bus. Steigen Sie zum Beispiel eine Haltestelle früher aus und legen Sie den restlichen Weg zu Fuß zurück.

Rauchen Sie nicht

Da das Rauchen Stoffwechselprozesse stört und das Risiko für Herz-Kreislauf-Erkrankungen und Diabetes erhöht, sollte es vermieden werden.

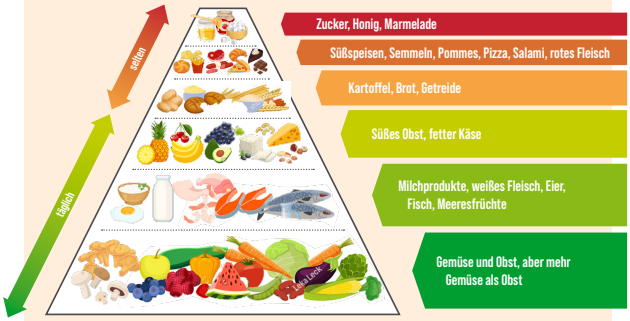
Reduzieren Sie gegebenenfalls Ihr Übergewicht

Radikaldiäten haben langfristig meist keinen Erfolg. Halten Sie sich an mediterrane Ernährung und reduzieren Sie die Energiezufuhr um etwa 500 kcal pro Tag in Kombination mit ausreichender körperlicher Bewegung.

Ernähren Sie sich gesund

Die gesündeste Ernährung ist eine mediterrane Kost. Vermeiden Sie Fertigprodukte, verzichten Sie auf zuckerhaltige Getränke und reduzieren Sie den Verzehr von rotem Fleisch und tierischen Fetten. Verwenden Sie Olivenöl, achten Sie auf ausreichende Zufuhr von Ballaststoffen, Hülsenfrüchten und Nüssen. Essen Sie regelmäßig Fisch, frisches Gemüse und Obst. Vermeiden Sie kalorienreiche Süßspeisen. (vorbehaltlich allfälliger Unverträglichkeiten, Allergien und anderer Erkrankungen)

Mediterrane Kost



Kann ich nicht einfach Medikamente nehmen und so leben wie bisher?

Nein, Lebensstilmaßnahmen sind die Basis aller Therapien zur Vorbeugung von Herz-Kreislauf-Erkrankungen und zur Senkung des Diabetesrisikos. Für die Blutzuckerkontrolle sind beim Prädiabetes meistens noch keine Medikamente notwendig.

Weitere Informationen zu Prädiabetes und Diabetes finden Sie unter

www.oedg.at

Impressum: Österreichische Diabetes Gesellschaft,
Währinger Straße 39/2/2, A- 1090 Wien, E-Mail: office@oedg.at

Kontinuierliche Glukosemessung (CGM) bei Prädiabetes – einfach erklärt

Ein **CGM-System** misst den Zuckerwert im Körper laufend über den Tag. So wird sichtbar, wie sich Essen, Bewegung oder Stress auf den Blutzucker auswirken – auch dann, wenn einzelne Messungen noch unauffällig sind.

So hilft kontinuierliche Glukosemessung bei Prädiabetes:

- Zuckerspitzen nach dem Essen erkennen
- den eigenen Körper besser verstehen
- Motivation für gesündere Ernährung und mehr Bewegung schaffen

CGM dient der Orientierung und Prävention, ersetzt jedoch keine ärztliche Diagnose. Ihre Apotheke berät Sie zur Anwendung von Glukose-Sensoren und hilft, die angezeigten Werte richtig einzuordnen. Bei auffälligen Ergebnissen wird zur ärztlichen Abklärung geraten.

Meine Apothekerinnen und Apotheker Wien

Die Diabetes-Gefahr

Mit Prädiabetes steigt die Wahrscheinlichkeit für damit verbundene Schäden an Gefäßen, Nerven und Augen. Außerdem ist das Risiko, innerhalb der nächsten zwei Jahre an Typ-2-Diabetes zu erkranken, deutlich erhöht. Bis zu 10 % der Menschen mit Prädiabetes entwickeln pro Jahr Typ-2-Diabetes. Oft kommen weitere Beschwerden dazu, die ein erhöhtes Risiko für Herz-Kreislauf-Erkrankungen darstellen, wie etwa Bluthochdruck, Übergewicht oder Störungen des Fettstoffwechsels.

Was kann Ihre Apotheke für Sie tun?

Schnelle Testung

In vielen Apotheken kann innerhalb weniger Minuten ein Blutzucker- oder HbA1c-Wert mittels Point-of-Care-Test bestimmt werden. Die Ergebnisse liegen sofort vor und können gemeinsam besprochen werden.

Einfacher Zugang

Flexible Terminvereinbarung, keine langen Wartezeiten – die Apotheke ist eine ideale Anlaufstelle für Menschen mit erhöhtem Risiko.

Individuelle Beratung

Apothekerinnen und Apotheker beraten, wie Risiken mit einer Verhaltensänderung minimiert werden können:

- Ernährung und Bewegung
- Gewichtsreduktion
- Rauchstopp

Früherkennung & Weiterleitung

Bei auffälligen Werten unterstützt Ihre Apotheke Sie dabei, frühzeitig eine ärztliche Abklärung einzuleiten.

Was tun bei Prädiabetes?

Eine Änderung des Lebensstils ist der wichtigste Schritt zur Vorbeugung von Typ-2-Diabetes. Apotheken begleiten Sie dabei im Alltag – praxisnah, individuell und langfristig.

Bewegung

Regelmäßige Bewegung muss nicht unbedingt Ausdauertraining oder Krafttraining bedeuten – auch kleine Einheiten machen einen Unterschied. Versuchen Sie, im Alltag mehr Aktivität einzubauen, etwa indem Sie Treppe statt Aufzug nehmen. Kurze Wege lassen sich oft gut zu Fuß oder mit dem Rad erledigen, anstatt das Auto oder öffentliche Verkehrsmittel zu nutzen. Bei mindestens 150 Minuten Bewegung pro Woche leisten Sie einen wichtigen Beitrag zu Ihrer Gesundheit.

Rauchstopp

Mit dem Rauchen aufzuhören, schützt Herz und Gefäße und reduziert das Herz-Kreislauf-Risiko deutlich. Bereits nach kurzer Zeit verbessern sich Durchblutung und Blutdruck.

Gewicht kontrollieren

Eine gute Gewichtskontrolle kann bei Prädiabetes den Blutzucker spürbar verbessern und das Risiko für Typ-2-Diabetes senken. Bei Übergewicht wirkt sich schon eine moderate Gewichtsabnahme positiv auf den Stoffwechsel aus. Wichtig sind realistische und alltagstaugliche Ziele in Kombination mit gesunder Ernährung und ausreichender Bewegung.

Gesunde Ernährung

Ernährungspyramide mit Fisch und Fleisch laut BMSGPK

Eine abwechslungsreiche Ernährung, die zu Ihrem Alltag und Ihrem Bedarf passt, unterstützt Körper und Gesundheit nachhaltig. Die Gesamtzusammenstellung Ihrer Mahlzeiten ist wichtiger als einzelne Lebensmittel. Achten Sie auf sinnvolle Portionen und ein ausgewogenes Verhältnis der verschiedenen Lebensmittelgruppen. Gemüse, Vollkornprodukte und hochwertige Eiweißquellen können dabei eine gute Basis bilden – auf hochverarbeitete Lebensmittel sollten Sie weitgehend verzichten. So lassen sich Energie, Blutzucker und Wohlbefinden leichter im Gleichgewicht halten.

16 Appendix II Patient Diary

MEDIZINISCHE UNIVERSITÄT WIEN

Österreichische Apothekerkammer

Ernährungs- und Aktivitätstagebuch
CGM-Pharm Studie – kontinuierliche Glukosemessung

Dieses Ernährungs- und Aktivitätstagebuch ist Bestandteil des Studienprotokolls „CGM-Pharm“ und dient der strukturierten Erfassung der Nahrungsaufnahme sowie körperlicher Aktivität während der jeweiligen CGM-Phase. Die Angaben werden gemeinsam mit den kontinuierlich gemessenen Glukosedaten ausgewertet. Die Führung dieses Tagebuchs ist insbesondere jeweils an den Tagen 4-9 nach Anbringen des Sensors wichtig, kann aber auch während der gesamten Messphase des Sensors (ca. 14 Tage) durchgeführt werden.

Datum: _____ CGM-Phase: Phase 1 Phase 2

Uhrzeit (Beginn)	Lebensmittel / Getränke	Menge (Schätzung ausreichend)

Bitte dokumentieren Sie alle Mahlzeiten, Snacks und Getränke (einschließlich zuckerhaltiger Getränke sowie Kaffee oder Tee mit Milch/Zucker). Relevant ist der Zeitpunkt des Beginns der Aufnahme.

Uhrzeit	Art der körperlichen Aktivität (z. B. Gehen, Sport)	Dauer

Schlafdauer letzte Nacht: _____ Std
Schlafqualität (subjektiv): gut mittel schlecht
Besondere Einflussfaktoren: Stress Erkrankung Alkoholkonsum

Hinweis: Die Glukosemessung erfolgt automatisch über den CGM-Sensor. Eine manuelle Dokumentation der Glukosewerte ist nicht erforderlich. Sofern technisch möglich, markieren Sie Mahlzeiten und körperliche Aktivität zusätzlich im CGM-System.

17 Appendix III Fragebögen

Kontinuierliche Glukosemessung

Bitte Ankreuzen: 1 Ich stimme überhaupt nicht zu

2 Ich stimme nicht zu

3 Ich stimme weder zu noch lehne ich ab

4 Ich stimme zu

5 Ich stimme voll und ganz zu

Teil A Zufriedenheit

	1	2	3	4	5
Insgesamt bin ich mit der Nutzung zufrieden	☐	☐	☐	☐	☐
Die Messung ließ sich gut in meinen Alltag integrieren	☐	☐	☐	☐	☐
Das Tragen des Sensors war angenehm	☐	☐	☐	☐	☐
Die Bedienung war einfach	☐	☐	☐	☐	☐
Die Nutzungsdauer war angemessen.	☐	☐	☐	☐	☐

Teil B Lernen & Feedback

	1	2	3	4	5
Ich habe durch die Messung neues über meinen Blutzucker gelernt	☐	☐	☐	☐	☐
Ich konnte Zusammenhänge zwischen meinem Verhalten und der Messung erkennen	☐	☐	☐	☐	☐
Ich habe gelernt wie meine Ernährung meinen Blutzucker beeinflusst	☐	☐	☐	☐	☐
Ich habe gelernt wie Bewegung meinen Blutzucker beeinflusst	☐	☐	☐	☐	☐

Die Messung hat mein Verhalten während der Messung beeinflusst	☐	☐	☐	☐	☐
Die Messung wird mein Verhalten in der Zukunft beeinflussen	☐	☐	☐	☐	☐

Teil C Motivation und Präsentation

	1	2	3	4	5
Die Messung hat mich motiviert mein Verhalten zu ändern	☐	☐	☐	☐	☐
Ich möchte auf Grund meiner Erfahrung mit der Messung bewusster auf Ernährung achten	☐	☐	☐	☐	☐
Ich möchte auf Grund meiner Erfahrung mit der Messung mehr Bewegung machen	☐	☐	☐	☐	☐
Ich glaube, dass die Messung mir helfen kann, Diabetes vorzubeugen	☐	☐	☐	☐	☐

Teil D Empfehlung und Akzeptanz

Wie wahrscheinlich ist es, dass Sie diese Messmethode weiterempfehlen?

0= sehr unwahrscheinlich 10 sehr wahrscheinlich

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

	1	2	3	4	5
Ich würde erneut eine solche Messung durchführen	☐	☐	☐	☐	☐
Die Messung ist auch für Menschen mit Prädiabetes sinnvoll	☐	☐	☐	☐	☐
Die Messung ist auch für Menschen ohne Diabetes oder Prädiabetes sinnvoll	☐	☐	☐	☐	☐
Der Nutzen überwog für mich mögliche Nachteile	☐	☐	☐	☐	☐

Fragebogen Beratungsgespräch

Bitte Ankreuzen:

1 Ich stimme überhaupt nicht zu

2 Ich stimme nicht zu

3 Ich stimme weder zu noch lehne ich ab

4 Ich stimme zu

5 Ich stimme voll und ganz zu

	1	2	3	4	5
Ich habe beim Beratungsgespräch etwas über Ernährung und Blutzucker gelernt	☐	☐	☐	☐	☐
Auf Grund des Beratungsgesprächs kann ich meinen Lebensstil anpassen	☐	☐	☐	☐	☐
Das Beratungsgespräch hat mich motiviert, meinen Lebensstil anzupassen	☐	☐	☐	☐	☐
Die Ratschläge, die ich erhalten habe, waren leicht verständlich	☐	☐	☐	☐	☐
Das Beratungsgespräch hat die kontinuierliche Glukosemessung sinnvoll ergänzt	☐	☐	☐	☐	☐
Ich kann das Beratungsgespräch in Kombination mit der kontinuierlichen Glukosemessung weiterempfehlen	☐	☐	☐	☐	☐
Diese Form der Beratung sollte anderen Patient:innen mit Prädiabetes zur Verfügung stehen	☐	☐	☐	☐	☐
Die Dauer des Gesprächs war angemessen	☐	☐	☐	☐	☐

Sonstige Anmerkungen:

18 Appendix IV List of participating Pharmacies

Apotheke Trillerpark, 1210 Wien, Trillergasse 4, PD. DDr. Philipp Saiko

Mariatroster Apotheke “Zum hl. Ulrich”, 1070 Wien, Burggasse 22; Mag.pharm Roswitha Kronemann

Siebenbrunnen Apotheke, 1050 Wien, Siebenbrunnengasse 32; Mag.pharm. Christoph Slatin

Marien-Apotheke, 1060 Wien, Schmalzhofgasse 1; Mag.pharm. Karin SImonitsch

Columbus Apotheke, 1100, Favoritenstraße 73; Mag.pharm Martin Heuberger

Ludwigs-Apotheke, 1110 Wien, Simmeringer Hauptstraße 128; Mag.pharm Dr. Dominik Kaiser

Apotheke zum Heiligen Joseph, 1120 Wien, Schönbrunner Straße 194-196; Mag.pharm Maria Wachouschek

Apotheke am Lainzer Platz, 1130 Wien, Lainzer Straße 139; Mag.pharm Karin Prinz

Apotheke Maria vom Siege, 1150 Wien, Mariahilferstraße 154; Mag.pharm Birgit Simersky

Linden-Apotheke, 1170 Wien, Hernalser Hauptstraße 155; Mag.pharm Viktor Hafner

Humanitas-Apotheke, 1210 Wien, Jedleseer 66/94; Mag.pharm Martin Mähr

Apotheke Neu Kagran, 1220 Wien, Erzherzog-Karl-Straße 84-88; Mag. pharm Gudrun Janka

Seestadt Apotheke, 1220 Wien, Maria-Tusch-Straße 12; Mag.pharm Silvia Marei

Vital Apotheke, 1230 Wien, Gatterederstraße 9; Mag.pharm Julia Wurm

Apotheke Schwenk zum heiligen Johann von Nepomuk, 1120 Wien, Schönbrunner Straße 259, Mag. Georg Sprinzl