# Improving preconceptional suboptimal glycaemic control in type 1 diabetes using RealTime Continuous Glucose Monitoring: a randomised trial

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This study is designed to investigate whether it is possible to achieve substantial improvement of HbA1c values in preconceptional suboptimal regulated type 1 diabetes mellitus (which is HbA1c 7.0-7.7%). Primary outcome- Absolute reduction in...

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| **Ethical review** | Approved WMO |
| **Status** | Will not start |
| **Health condition type** | Glucose metabolism disorders (incl diabetes mellitus) |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON36232

**Source**
ToetsingOnline

**Brief title**
Preconceptional Glucose Regulation in type 1 diabetes women using RT-CGMS

### Condition

- Glucose metabolism disorders (incl diabetes mellitus)

**Synonym**
Diabetes, Diabetes Mellitus

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum

**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** diabetes type 1, glucosemonitoring, preconceptional, real-time

## Outcome measures

### Primary outcome

Primary outcome

- Absolute reduction in HbA1c

### Secondary outcome

Secondary outcomes

- Incidence of severe hypoglycaemia

- Percentage of women with a fall in HbA1c of >= 0.5% (>= 5 mmol/mol)

- Percentage f women that reach target HbA1c (< 7.0% or < 53 mmol/mol)

- Time to reach target HbA1c

- number of consultations (by telephone, internet, on the out-patient clinic)

- Change in glycaemic variability

- Composite end point: reduction of HbA1 >= 0.5% (>= 5 mmol/mol) without an

episode of severe hypoglycemia

- Frequency of use RT-CGMS

- Fear of hypoglycaemia

- Quality-of-life

- Satisfaction with the device.

# Study description

## Background summary

Despite major advances in diabetes care the incidence of adverse pregnancy outcomes in women with type 1 diabetes mellitus is still significantly higher than in non-diabetic pregnancies. It is known that suboptimal glucose regulation is associated with adverse pregnancy outcomes: suboptimal control in the periconceptional period is associated with the development of congenital malformations.
There is general consensus that prepregnancy care and optimal glycaemic control is mandatory to achieve the best possible pregnancy outcome in these women with HbA1c as the parameter reflecting the quality of glycaemic control. The latest guidelines state that we should aim for a preconceptional HbA1c-level as near the normal range as possible to achieve the best outcomes but at least an HbA1c < 7.0% (53 mmol/mol).
With lowering of the HbA1c-level towards the normal range, the risk of hypoglycaemia and severe hypoglycaemia increases, currently posing a barrier to reach best control.
The current mainstay of monitoring glycaemic control (self-measurement of blood glucose levels by finger stick) only provides snapshot images, limiting the possibilities to improve glycaemic control.
Real-Time Continuous Glucose Monitoring System (RT-CGMS) allows instantaneous display of actual glucose values combined with an alert-function when glucose levels or changes in levels fall outside preset individualised limits. Studies have shown that RT-CGMS can improve glycaemic control in patients with type 1 diabetes but these were heterogenic and no studies have been done with RT-CGMS during the preconceptional or pregnant period in the specific patient group of preconceptional women with suboptimal regulated type 1 diabetes .
Glycaemic variability is a new concept in diabetes care and it has been suggested that the degree of glucose variability may be linked to adverse outcomes. Rt-CGMS may also decrease glucosevariability.

## Study objective

This study is designed to investigate whether it is possible to achieve substantial improvement of HbA1c values in preconceptional suboptimal regulated type 1 diabetes mellitus (which is HbA1c 7.0-7.7%).

Primary outcome
- Absolute reduction in HbA1c

Secondary outcomes
- Incidence of severe hypoglycaemia
- Percentage of women with a fall in HbA1c of >= 0.5% (>= 5 mmol/mol)
- Percentage f women that reach target HbA1c (< 7.0% or < 53 mmol/mol)
- Time to reach target HbA1c
- number of consultations (by telephone, internet and in out-patient clinic)

- Change in glycaemic variability
- Composite end point: reduction of HbA1 >= 0.5% (>= 5 mmol/mol) without an episode of severe hypoglycaemia
- Frequency of use RT-CGMS
- Fear of hypoglycaemia
- Quality-of-life
- Satisfaction with the device

**Study design**

Randomised controlled parallel-arm single centre trial for 16 weeks

This is a 16-week randomized controlled parallel-arm single centre trial comparing the use of RT-CGMS with standard extensive care in preconceptional setting in women with suboptimal regulated type 1 diabetes mellitus.

Setting:
The study will be carried out in the setting of the already longstanding collaborative group of the UMC Utrecht Departments of Internal Medicine and *Vrouw en Baby*. This group has founded in the nineties a joint Obstetrics-Internal Medicine clinic for pregnant patients with any kind of diabetes which has served as a role model for other institutions.

Recrutation:
Consecutively approach of patients: every women with suboptimal regulated type 1 diabetes mellitus who is treated at the out-patient clinic for Diabetology of the UMC Utrecht and who has a child wish will be approached for this study
Other centra will be asked to to tell patients, of this specific population, about this study. With aprovel of the patient the researcher will contact her for more explanation and potential inclusion.

Randomisation
By a list, made in forehand by a independent person (unknown to the researcher until the patient has signed for informed consent)

Intervention
Intervention group:
- Standard medical consultation by:
=> Diabetes nurse educator (scheduled every two weeks, plus possibility of 24h a day by telephone or email)
=> Diabetes specialist (scheduled week 0, week 1, week 4, week 8, week 12, week 16)
Every therapy change will be made under supervision (from nurse to research physician to supervising physician) and noted
- Standard therapy:
=> Insulin pump therapy (replaced by RT_CGMS: insulin pump and glucose sensor in one)

=> SMBG at least 5 times a day for at least 5 days a week
- Standard blood controls:
=> HbA1c and fructosamine every 4 weeks
TSH and FT4, cholesterol, Hb, Kreatinine and urinesediment at baseline
- Research related:
=> Questionnaires every 4 weeks
=> RT-CGMS during 7 consecutive days every other week (in total: 8 of 16 weeks)
Results will be used for counseling / treatment adjustments
=> 2 times blinded RT-CGMS for 48 hours conform the control group in week 1 and 12st
- Post study:
=> Patients will be offered to use RT-CGMS after end of study

Control group:
- Standard medical consultation as in intervention group
Every therapy change will be made under supervision (from nurse to research physician to supervising physician) and noted
- Standard therapy:
=> Insulin pump therapy continues
=> SMBG as in intervention group
- Standard blood controls:
=> Blood samples as in intervention group
- Research related:
=> Questionnaires as in intervention group
=> 2 times Blinded RT-CGMS as in intervention group. However, results will not be revealed to participating control group of women nor to the treating team except when CGMS analysis is clinically required.
- Post study:
=> Patients will be offered to use RT-CGMS after end of study

**Intervention**

Intervention group:
- Insulin pump therapy will be continued
RT-CGMS during 7 consecutive days every other week (in total: 8 of 16 weeks).
Results will be used for counseling / treatment adjustments
- 2 times blinded RT-CGMS for 48 hours conform the control group in week 1 and 12st (when patient is not using RT-CGMS)

Control group:
- Insulin pump therapy will be continued
- 2 times Blinded RT-CGMS as in intervention group. However, results will not be revealed to participating control group of women nor to the treating team except when CGMS analysis is clinically required.

**Study burden and risks**

Participation with this trial can be a burden on some fronts:
- Some patients have to change physician (namely the research-physician with supervision of the specialist who is concerned with the diabetic care of pregnant women). However, when they get pregnant (although not participating this study) they then also become under the supervision of the named specialist.
- The use of RT-CGMS can be a burden because the alert-function, besides the advantage of the warning possibilities, causes unpredictable disturbances of daily (meetings, visits, shopping etc) or nocturnal (sleeping) activities.
- Patients will have to connect the RT-CGMS themselves (every other week) and will have to replace the needle after 3 days of use
- Patients always have to confirm glucose values given from the RT-CGMS with SMBG before making therapy adjustments
- Former studies showed some possible skin irritative adverse affects from (RT-)CMGS use
- We will ask patients to fill in some questionnaires every 4 weeks

Risk of hypoglycaemic events
It is possible that the incidence of hypoglycaemic events increases during this trial compared to the period before participation. However, we expect that the incidence is as high (or even less high) in the intervention group as in the control group. Indeed the alertfunction of the RT-CGMS could theoretically prevent an hypoglycemic episode. The higher incidence is being expected because of the goals set by guidelines for women with diabetes type 1 who want to get pregnant: lowering HbA1c as far as possible but at least under 7.0% (53 mmol/mol).
A systematic review of 7 RCT studies using devices which are still on the market (not published yet) describes that 6 of 7 studies did not show an increase in hypoglycaemic events. One study did show an increase in severe hypoglycaemia (however the authors doubt if there was a relation with using the device. Two studies showed a decrease in HbA1c in absence of severe or non-severe hypoglycemia in the RT-CGMS group. No study was powered enough to demonstrate a decrease in hypoglycaemic events.

# Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

- diagnosed with diabetes mellitus 1 at least for one year diagnosis: diagnosis < 30 years of age AND anti-GAD antibodies AND/OR experienced ketoacidosis
- insulin pump (connectable with of changeable in a RT-CGMS device of Medtronic) for at least 3 months
- reliable performance of SMBG at least 5 times a day for at least 5 days a week
- child wish
- stable HbA1c 7.0 - 7.7 (53-61 mmol/mol): if consecutive values (two months) show a decrease, this decrease is accepted up to (including) 0.5% (5 mmol/mol).
- age 18-41 years
- willing to (patient herself) and capable of (as estimated by treating doctor) using RT-CGMS
- able to read and speak Dutch
- written informed consent
- internet access (uploading results sensor)

## Exclusion criteria

- co-existent medical problems that would interfere with study participation
- use of medication that could influence glycaemic control (for example corticosteroids) in last three months
- >=2 severe hypoglycaemia in the last 6 months (defined as an episode of hypoglycaemia resulting in seizure of coma or the use of glucagon and/or intravenous glucose for recovery)

# Study design

## Design

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|---|---|
| Study phase: | 4 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Treatment |

## Recruitment

NL

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|---|---|
| Recruitment status: | Will not start |
| Enrollment: | 20 |
| Type: | Anticipated |

## Medical products/devices used

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|---|---|
| Generic name: | RealTime-Continuous Glucose Monitoring System |
| Registration: | Yes - CE intended use |

# Ethics review

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|---|---|
| Approved WMO Date: | 23-02-2011 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 07-06-2011 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

ID: 26973
Source: NTR
Title:

## In other registers

| Register | ID |
|---|---|
| CCMO | NL33990.041.10 |
| OMON | NL-OMON26973 |

# Study results

**Summary results**
Trial never started