An active strategy to identify individuals eligible for type 2 diabetes prevention by lifestyle intervention in Dutch primary care: the APHRODITE study

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Background. Several trials have shown the potential of lifestyle intervention programmes for prevention of type 2 diabetes. The effectiveness of implementation of these programmes into daily practice is now being studied in several countries. The ‘Active Prevention in High Risk individuals of Diabetes Type 2 in Eindhoven’ (APHRODITE) study investigates whether type 2 diabetes prevention by lifestyle intervention is effective in Dutch primary care. In this article we describe the process of recruiting the study participants.

Objective. To assess the reach of an active strategy to recruit participants for a programme on type 2 diabetes prevention by lifestyle intervention in Dutch primary care.

Methods. A diabetes risk questionnaire was sent to general practice patients aged 40–70 years. Individuals with a risk score above threshold were invited for an admission interview with the GP and an oral glucose tolerance test (OGTT). All individuals with non-diabetic glucose levels were asked to participate in the intervention study.

Results. In total, 8752 (54.6%) of the individuals returned the questionnaire in time. Of all high-risk individuals (n = 1533), 73.1% contacted their practice to schedule a consultation with the GP. Response rates varied significantly among practices.

Conclusions. Using invitational letters, a substantial amount of individuals could be motivated to participate in a programme on type 2 diabetes prevention by lifestyle intervention in Dutch primary care. Further research is needed on what kind of strategy would be most effective and efficient to screen for individuals at high risk for type 2 diabetes in primary care.

Keywords. High risk, lifestyle intervention, primary care, screening, type 2 diabetes.

Introduction

Type 2 diabetes poses a great medical and financial burden to many nations worldwide.¹ It is estimated that globally around 240 million persons are diagnosed with the disease.²³ Furthermore, it is thought that at least an equal number of persons have pre-diabetes: impaired fasting glucose (IFG) levels, impaired glucose tolerance (IGT) or both.³⁴ Every year many of these persons with pre-diabetes develop full-blown diabetes.⁵ Early prevention of type 2 diabetes is therefore necessary to cope with this epidemic.

Several studies have shown the potential of lifestyle intervention programmes for primary prevention of type 2 diabetes in individuals with IFG, IGT or both.⁶ The Finnish Diabetes Prevention Study and the American Diabetes Prevention Program, for example, both demonstrated a reduction of diabetes incidence by nearly 60% in 4 years.⁷ In The Netherlands, similar results were found for individuals who completed a 3-year lifestyle intervention programme.⁸

In various countries, studies were launched to investigate the effectiveness of implementation of lifestyle intervention programmes in routine health care and community settings. In Finland, for example, the evidence regarding prevention of type 2 diabetes was translated into a nationwide prevention programme.⁹ In the DE-PLAN project, feasibility and cost-effectiveness of implementation of lifestyle modification programmes are systematically studied in 17 European countries.¹¹
Furthermore, reduction of the risk for type 2 diabetes by lifestyle modification has already shown to be feasible in several daily life settings.\(^{12-15}\)

In The Netherlands, a guideline for the prevention of type 2 diabetes in daily primary care practice has not yet been developed. The ‘Active Prevention in High Risk individuals Of Diabetes Type 2 in Eindhoven’ (APHRODITE) study investigates whether type 2 diabetes prevention by lifestyle intervention is effective in Dutch routine primary care. Furthermore, it aims to study which factors positively or negatively influence implementation of the lifestyle intervention programme. Primary care was chosen as the setting for implementation of APHRODITE because in The Netherlands, GPs are considered accessible and trustworthy and \(~99\%\) of the inhabitants are registered with a GP.\(^{16}\)

The APHRODITE study consists of three phases: recruiting study participants eligible for prevention of type 2 diabetes by lifestyle intervention, the lifestyle intervention programme itself and follow-up after the programme is completed. In this article, we aimed to assess the reach of an active strategy to recruit participants for a programme on the prevention of type 2 diabetes by lifestyle intervention in Dutch primary care. We describe the response rates at various stages of the screening protocol and their variation among practices. In addition, we describe the baseline characteristics of the participants in the lifestyle intervention programme.

**Individuals, materials and methods**

**Study population**

Patients were recruited in January 2008 by 48 GPs from an association of primary care practices in Eindhoven and five surrounding towns and villages. All GPs in the association agreed to participate in the study. Each GP selected a random sample of his/her patients aged \(\geq 40\) and \(\leq 70\) years (n = 16 032), accounting for four exclusion criteria: known diabetes, terminal disease or physical or mental disabilities making active participation in the study impossible. Exclusion criteria were checked by the GPs making use of the electronic medical record.

As a tool to identify persons at high risk for developing future type 2 diabetes, a Dutch translation of the Finnish diabetes risk score (FINDRISC)\(^{17}\) was used. The FINDRISC is a validated questionnaire to identify individuals at high risk for type 2 diabetes. It contains items on age, body mass index (BMI), waist circumference, physical activity, fruit and vegetable consumption, use of antihypertensive medication, history of high blood glucose and family history of diabetes.

To adapt the FINDRISC questionnaire to the Dutch context, two changes were made with respect to the original version. First, in the question about family history of type 2 diabetes, the answer ‘grandparent, aunt, uncle or first cousin’ was extended with the phrase ‘not related by marriage’. Second, as berries are not commonly eaten in The Netherlands and they are regarded as fruit, the question ‘How often do you eat vegetables, fruit or berries?’ was replaced by ‘How often do you eat vegetables and fruit?’ As we wanted the question to be answered with ‘yes’ or ‘no’, it was then changed into ‘Do you eat vegetables and fruit every day?’ We did not validate the questionnaire again after these adaptations because we did not expect these adaptations to markedly influence the validity and reliability of the FINDRISC questionnaire.

The score on the FINDRISC questionnaire ranges from 0 to 26 points and a score of \(\geq 13\) points was chosen as a cut-off value for invitation to the APHRODITE programme. This cut-off value was chosen based on cut-off values used in previous studies in Australia (\(\geq 12\)),\(^{12}\) Finland (\(\geq 12\)),\(^{15}\) Austria and Spain (\(\geq 13\) and \(\geq 14\), DE-PLAN Study, personal communication).

The Dutch translation of the FINDRISC questionnaire was sent to all individuals selected by the GPs. The questionnaire was accompanied by a standard explanatory letter from the individuals’ own practice, a tape measure and a stamped addressed return envelope. Furthermore, a reply card was enclosed on which individuals unwilling to participate could specify their reasons. Individuals were asked to return the FINDRISC within 1 week. The final deadline for returning the FINDRISC was set at 1 month.

Risk scores were calculated from returned FINDRISCs and randomly double checked by an assistant. Missing information was enquired by telephone. Subsequently, individuals with a FINDRISC score above cut-off value received a letter from their own GP in which it was explained that they had an elevated risk of developing type 2 diabetes. Furthermore, they were invited to participate in the APHRODITE study and to make an appointment with their GP for an admission interview.

A chronological list of all high-risk individuals contacting their practice was kept by the practice assistants. Randomization was realized by assigning every second person on this list to the usual care group. The GP was blinded to which individual was assigned to which group until the start of the admission interviews. The maximum amount of admission interviews was set at 32 interviews per full-time working GP. If a GP had reached his maximum amount, the individuals were referred to a different GP in the same practice. If the total capacity of the practice was exceeded, the individual received an explanatory letter from the project assistant in which they were asked to plan a regular consultation with their GP.

During the admission interview (Fig. 1), the GP provided all individuals with general information about type 2 diabetes and the APHRODITE project and subsequently asked them to sign an informed consent form. After signing this form, the GP gave the individuals oral
and written information specific for the group they were assigned to (intervention/usual care) (Fig. 1). Furthermore, the GP invited the individuals to undergo an oral glucose tolerance test (OGTT). For the intervention group, 20 minutes were scheduled for the interview, for the usual care group 10 minutes. All GPs were instructed beforehand during a 2-hour training session. The protocol was registered with the Dutch Trial Register (TC = 1082).

**Oral glucose tolerance tests**
Lists of all individuals who had given their informed consent were kept by the GPs. Listed persons received an invitation for an OGTT directly from the laboratory. Two different laboratories were responsible for blood sampling and for analysing the blood samples. Blood glucose values of the first laboratory were calibrated on those of the second laboratory. All OGTTs were taken in the individuals' hometown according to internationally accepted standards. Diagnosis of pre-diabetes or type 2 diabetes was based on one fasting and one post-load blood glucose measurement according to the 2006 World Health Organization diagnostic criteria. Individuals with diabetic glucose values in either test were excluded from the study and were referred to the GP for a second blood test to confirm diagnosis and for further care.

**Measurements**
Body weight was measured without shoes and coats to the nearest 0.1 kg. Height was measured without shoes to the nearest centimetre. Waist circumference was measured at the midpoint between the lowest rib and the iliac crest to the nearest centimetre. Blood pressure was measured with a standard sphygmomanometer after at least 10 minutes of rest. All measurements were taken by the nurse practitioners, who were trained according to the standards of the Dutch Society of General Practitioners. The procedures described in these standards are concordant with the European Health Risk Monitoring protocol. BMI was calculated as the ratio of weight (kg) and squared height (m²).

**Data analysis and statistics**
Statistical analysis was performed using SPSS version 17.0. A P value of ≤0.05 was considered statistically significant. Differences between responders and non-responders and between high-risk individuals contacting or not contacting their practice were analysed with either an independent samples' t-test (continuous variables) or a chi-square test (categorical variables). Due to a change of electronic medical record system, sex and age of non-responders were not available for 1 of the 14 practices. This practice was left out of the analysis of sex and age of responders versus non-responders. To calculate the amount of variance explained by variables not on the level of the individual multilevel analysis for binary responses was performed on the data of the responders (level 1: individuals, level 2: practices) and on the data of the high-risk contactors (level 1: individuals, level 2: GPs, level 3: practices) using MLWin version 2.0. Variance percentages at higher levels were

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**Figure 1** Description of the content of the admission interviews given by the GP
estimated using $n^{2/3}$ as an approximation of the variance on the level of the individual. Both models were corrected for sex and age of the individuals. Differences between groups of different glycaemic status were analysed with either an analysis of variance (continuous variables) or a chi-square test (categorical variables).

Results

Reach of the APHRODITE screening protocol

Figure 2 shows the number of individuals in each phase of the APHRODITE screening protocol. A total of 8752 individuals (54.6%) returned the FINDRISC before the 1-month deadline. In addition, 72 individuals (0.4%) returned the FINDRISC after the deadline and 704 individuals (9.8% of the non-responders) sent back a reply card stating why they were not willing to participate. Reasons for non-participation are listed in Table 1. Responders were slightly older and more often of the female sex than non-responders (Table 2). Of the total variability between responders and non-responders, 1.7% was on the level of the practice. The percentage of individuals responding varied significantly among practices ($P < 0.001$), ranging from 39.7% to 62.0% (Fig. 3). The mean percentage of high-risk individuals contacting their practice was 73.4%, with a SD of 8.4%. There was no significant correlation between percentage of initial responders and percentage of high-risk individuals contacting their practice (Spearman Rho correlation coefficient 0.053, $P = 0.858$).

Of 1120 individuals who made an appointment for an admission interview, 15 individuals (1.3%) developed diabetes and two individuals died before the consultation could take place. One of the 14 practices had to reject 38 individuals (3.4%) because the maximum amount of interviews was reached. In total, 1065 individuals (69.5%) visited their practice for an interview with their GP. Sixteen individuals (1.5%) were not willing to participate in the study after the admission interview and 25 individuals (2.3%) did not show up at the laboratory, leaving 1024 individuals who had their blood glucose levels tested. In 99 of those 1024 individuals (9.7%), diabetic blood glucose values were detected, which left 925 individuals participating in the APRHODITE study.

*FIGURE 2  The number of individuals in each phase of the APHRODITE screening protocol*
Baseline characteristics

Table 3 shows the baseline characteristics of all individuals who had an OGTT stratified for their fasting and post-prandial blood glucose levels. Significant differences between groups were found for fasting and post-prandial glucose levels, FINDRISC score, age, BMI, percentage of obesity and systolic blood pressure. Groups were comparable for sex, percentage of overweight, diastolic blood pressure, education level and smoking behaviour. Women significantly differed in waist circumference between groups, whereas men did not.

Table 1  Reasons for not participating in the APHRODITE study (n = 647)

<table>
<thead>
<tr>
<th>Reason</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No confidence in the study</td>
<td>7 (1)</td>
</tr>
<tr>
<td>No confidence in my GP or nurse practitioner</td>
<td>7 (1)</td>
</tr>
<tr>
<td>I expect not to be able to hold on to the</td>
<td>102 (16)</td>
</tr>
<tr>
<td>programme</td>
<td></td>
</tr>
<tr>
<td>I expect the programme will not be successful</td>
<td>88 (14)</td>
</tr>
<tr>
<td>for me</td>
<td></td>
</tr>
<tr>
<td>Other reason, namely</td>
<td>443 (68)</td>
</tr>
<tr>
<td>No time</td>
<td>53</td>
</tr>
<tr>
<td>I moved to another city</td>
<td>29</td>
</tr>
<tr>
<td>My blood glucose levels are already regularly</td>
<td>47</td>
</tr>
<tr>
<td>checked</td>
<td></td>
</tr>
<tr>
<td>I am already diagnosed with diabetes</td>
<td>45</td>
</tr>
<tr>
<td>I am not interested in participation</td>
<td>67</td>
</tr>
<tr>
<td>I am already regularly checked for a disease</td>
<td>46</td>
</tr>
<tr>
<td>different from type 2 diabetes</td>
<td></td>
</tr>
<tr>
<td>I think my health is good</td>
<td>31</td>
</tr>
<tr>
<td>Other</td>
<td>125</td>
</tr>
</tbody>
</table>

Table 2  Characteristics of individuals returning or not returning the FINDRISC and contacting or not contacting the practice for an admission interview

<table>
<thead>
<tr>
<th></th>
<th>Individuals returning FINDRISC</th>
<th>Individuals not returning FINDRISC</th>
<th>P value</th>
<th>High-risk individuals contacting practice</th>
<th>High-risk individuals not contacting practice</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (%, male)</td>
<td>46.1</td>
<td>53.4</td>
<td>&lt;0.001</td>
<td>39.1</td>
<td>48.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Age (years)</td>
<td>54.5 (8.5)</td>
<td>52.3 (8.7)</td>
<td>&lt;0.001</td>
<td>58.2 (7.5)</td>
<td>57.2 (7.6)</td>
<td>0.02</td>
</tr>
<tr>
<td>FINDRISC score (points)</td>
<td>–</td>
<td>–</td>
<td></td>
<td>14.8 (2.0)</td>
<td>15.1 (2.3)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Data are means ± SDs unless otherwise indicated.

Discussion

Reach of the APHRODITE screening protocol

The APHRODITE study investigates whether a lifestyle intervention programme for the prevention of type 2 diabetes is effective in Dutch primary care. Furthermore, it aims to identify which factors positively or negatively influence implementation of the intervention programme. In this study, we evaluated the results of the recruitment phase. We described the response rates at various stages of the screening protocol and their variation among practices. In addition, we described the baseline characteristics of the participants in the lifestyle intervention programme.

In our study, 54.6% of the individuals returned the FINDRISC questionnaire within the 1-month deadline. Responders were slightly older and more often of the female sex than non-responders, a pattern that
is found in other screening studies as well. Only a small part of the variability between responders and non-responders was on the level of the practice. Response rates varied significantly between practices, which may partly be explained by practice variables such as the size of the practice, age and enthusiasm of the GPs in the practice and the community in which the practice is situated. Differences in primary response rate between practices may also be explained by variables on the level of the individual, like gender and age differences between the patient populations of the practices.

Of all high-risk individuals, 73.1% contacted their practice to schedule a consultation with the GP. High-risk individuals contacting their practice were slightly older, more often of the female sex and had lower FINDRISC scores than those that did not call. The amount of variance explained by variables on the GP and practice levels was larger in the data of the high-risk individuals than in the data of the responders. Therefore, it is conceivable that practice or GP variables play a more important role in the decision to participate in the programme than in the decision to return the FINDRISC questionnaire.

The amount of high-risk individuals contacting their practice varied significantly between practices. This variability may be explained by practice-level variables such as the location of the practice. However, in the ADDITION Netherlands study, it was recently found that individuals from rural practices were as likely to show up for OGTT screening as individuals from urban practices. Differences between practices in the amount of contactors may also be explained by GP-level variables such as the age and the enthusiasm of the GP and patient-level variables such as the individuals’ age and sex. There was no significant correlation between the percentage of responders in a practice and the percentage of high-risk individuals contacting that practice. Thus, practices with a high initial response may not necessarily attract more potential participants and vice versa.

**Comparison with previous research**

Our primary response rate of 54.6% is in line with the response rates found in other diabetes-screening studies using an invitation letter, ranging from 31.4% to 69.4%. Compared to our study, three studies had a higher initial response, that may partly be explained by a difference in screening aim. In these three studies, of which one was also performed in primary care, the aim of the screening was the identification of individuals with previously high-risk traits.
undiagnosed type 2 diabetes. In the APHRODITE study, the aim was to identify individuals willing to participate in a lifestyle intervention programme and this was already mentioned in the invitation letter. The prospect of having to change the diet, lose weight and exercise more may have kept people from responding. Other reasons for our lower response rate may be that our study population was younger than in previous studies and that we did not sent reminders, as for example was done in the study of Spijkerman et al.21

A lower primary response rate was found in five studies,20,24–27 of which three were also performed in primary care.20,24,27 The lower rates in these five studies may partly be due to a difference in the way the screening was organized. In three studies,24–26 individuals were directly invited for an OGTT, without prior calculation of the risk score from a questionnaire. In two studies, a risk questionnaire was also used as a first screening step.20,27 However, in these studies, the individuals had to calculate their risk score themselves and subsequently make an appointment for an OGTT if the risk score was too high.20,27 Both procedures are more demanding than returning a questionnaire.

Another approach to identify persons eligible for lifestyle intervention that has been used in several diabetes-related studies in primary care is opportunistic screening, i.e. case finding during regular encounters.12,15,29–31 Two of these studies reported the number of individuals willing to be screened: approximately two-thirds in the Greater Green Triangle study15 and 93% in the Irish diabetes detection programme.29 These response rates are high compared to ours and those found in other active screening studies in primary care.20,23,24,27

The higher primary response rates when screening during regular encounters may reflect the personal contact between the individual and the nurse or the GP in first instance. Therefore, the nurse or the GP can directly convince individuals of the importance of screening and lifestyle intervention. Furthermore, individuals having difficulties completing the questionnaire can easily be assisted by the nurse or the GP. Another possible reason for the higher response rate in the Irish diabetes detection programme may be that in this programme screening was not followed by a lifestyle intervention programme. Without the prospect of possibly having to change the lifestyle, people may be more willing to be screened.

Both with screening using invitational letters and with screening using case-finding individuals at high risk for developing type 2 diabetes may be missed. When screening using invitational letters, high-risk individuals may not respond, for example because they fear the results of the questionnaire or the blood test.27 When screening opportunistically individuals who do not come to the practice are not screened. Furthermore, during consultations, time or opportunity to discuss screening may sometimes be lacking.

Conclusions

Using invitational letters, a substantial amount of individuals could be motivated to participate in a programme on prevention of type 2 diabetes by lifestyle intervention in Dutch primary care. Response rates were in line with the rates found in other diabetes-screening studies using invitational letters but were lower compared to studies using an opportunistic approach. Further research is needed on what kind of strategy would be most effective and efficient to screen for individuals at high-risk for type 2 diabetes in primary care.

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Declaration

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Conflicts of interest: None.

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