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BRIEF COMMUNICATION

No negative effects of a multi-factorial, intensified treatment on self-reported health status, treatment satisfaction, and diabetes-related distress in screen-detected type 2 diabetes patients. The ADDITION-Netherlands study

Maureen van den Donk · Kees J. Gorter · Guy E. Rutten

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Abstract
Purpose To examine the effects of a multi-factorial, intensified treatment on self-reported health status, treatment satisfaction, and diabetes-related distress in screen-detected type 2 diabetes patients.
Methods Cluster-randomised controlled trial; A total of 498 screen-detected type 2 diabetes patients from 79 general practices were assigned to intensified ($n = 255$) or routine treatment according to Dutch guidelines ($n = 243$). At baseline and after 3 years, patients completed the Short Form-36 and the European Quality of Life-5 Dimensions questionnaires. After 4.5 years, patients completed the Diabetes Treatment Satisfaction Questionnaire and the Problem Areas In Diabetes scale. We analysed the effects of intensified treatment on self-rated health status, treatment satisfaction, and diabetes-related distress, using random effects models to account for clustering at practice level.
Results Three to 5 years after type 2 diabetes was detected by screening, there were no differences between intensified and routine treatment in self-reported health status, treatment satisfaction, and diabetes-related distress.
Conclusions Multi-factorial, intensified treatment did not influence self-rated health status, treatment satisfaction, and distress in screen-detected type 2 diabetes patients. Therefore, health care professionals do not have to fear negative effects of an intensified treatment on these psychological outcomes.

M. van den Donk (✉) · K. J. Gorter · G. E. Rutten
Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Str. 6.131, P.O. Box 85500, 3508 GA Utrecht, The Netherlands
e-mail: m.vandendonk@umcutrecht.nl

Keywords Randomised controlled trial · Diabetes mellitus, type 2 · Intensified treatment · Primary health care · Health status · Treatment satisfaction

Abbreviations

T2DM	Type 2 diabetes mellitus
UKPDS	UK prospective diabetes study
ADDITION study	Anglo-Danish-Dutch study of intensive treatment in people with screen-detected diabetes in primary care
IT	Intensified multi-factorial treatment
RC	Routine care
SF-36	Medical outcomes study 36-item short form health survey
EQ5D	European quality of life-5 dimensions
DTSQ	Diabetes treatment satisfaction questionnaire
PAID	Problem areas in diabetes scale

Introduction

Type 2 diabetes mellitus (T2DM) is related to worsened psychological outcomes, especially in case of complications [1, 2], but the effects of intensive treatment are not known. Intensive treatment of hyperglycaemia, hypertension, and dyslipidaemia can reduce cardiovascular disease in T2DM patients on the long run [3] and thus may improve psychological outcomes. However, T2DM patients may experience the need to take large quantities of medication as a burden, which can lead to psychosocial stress [4] and presumably less satisfaction with

treatment. This may especially be so in screen-detected patients, who do not have complaints, but still have to take medication. Examination of psychological outcomes showed that in screen-detected patients, intensified treatment led to more anxiety and less self-efficacy in the first year after diagnosis [5]. The UK Prospective Diabetes Study (UKPDS) found no impact of intensified treatment on perceived health in screen-detected patients, although health status was affected by complications of the disease [6].

In the ADDITION study (Anglo-Danish-Dutch Study of Intensive Treatment in People with Screen-Detected Diabetes in Primary Care), an intensified, multi-factorial treatment of screen-detected T2DM patients is compared with usual care according to national guidelines [7]. In the current study, we investigated the effects of 3–4 years of intensified pharmacological treatment combined with lifestyle advices on self-reported health status, treatment satisfaction, and diabetes-related distress in screen-detected T2DM patients in the ADDITION-Netherlands study. The follow-up period might be too short to detect differences in complications. Treatment targets are stricter than in the UKPDS, which may lead to more hypoglycaemic events and a larger burden of treatment and thus might influence psychological outcomes negatively.

Methods

The current study is part of the ongoing international ADDITION study in 3,057 screen-detected T2DM patients, classified according to the 1999 WHO diagnostic criteria [8]. ADDITION consists of a screening study and a subsequent intervention study with a mean follow-up of 5 years, with a composite endpoint comprised of cardiovascular mortality and morbidity, revascularisations, and amputations as the primary outcome measure [7, 9]. The ADDITION-Netherlands study was approved by the medical-ethical committee of the University Medical Center Utrecht. In a stepwise population-based screening programme (2002–2004) in 56,978 non-diabetic patients, aged 50–70 years, from 79 general practices in the south-western region of the Netherlands, we detected 586 new T2DM patients [10]. Of them, 498 were included in a single-blind trial with practice level randomisation to intensified multi-factorial treatment (IT; $n = 255$) or routine care (RC; $n = 243$). The other 88 patients declined participation ($n = 69$) or did not meet the eligibility criteria ($n = 19$). Patients were blinded to which treatment arm their general practitioner had been randomised. Participants gave written informed consent [11].

The IT protocol was target-driven. The treatment targets are HbA_{1c} <7.0%, but alterations to glucose-lowering therapy when HbA_{1c} >6.5%; blood pressure ≤135/85 mmHg, but prescription of an ACE-inhibitor when blood pressure >120/80 mmHg; prescription of acetylsalicylic acid 80 mg per day for patients treated with an antihypertensive agent; total cholesterol ≤3.5 mmol/l [7, 11]. Treatment goals in the RC group, originally according to the 1999 guidelines of the Dutch College of General Practitioners, were revised in 2006, but still less strict than the IT protocol: HbA1c ≤7%, systolic blood pressure ≤140 mmHg, total cholesterol ≤4.5 mmol/l, and LDL-cholesterol ≤2.5 mmol/l; no acetylsalicylic acid had to be prescribed [12].

Prior to entry into the study and after 3 years, participants completed the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) [13] and the European Quality of Life-5 Dimensions (EQ5D) [14] questionnaires. The SF-36 is a 36-item questionnaire that measures perceived health, encompassing eight dimensions: general health, vitality, mental health, physical functioning, limitations due to physical difficulties (role physical), bodily pain, social functioning, and limitations due to emotional difficulties (role emotional) [13]. For each dimension, item scores are transformed to a scale ranging from 0 (worst health) to 100 (best health). The Dutch version has been shown to be valid and reliable [15]. The EQ5D is a measure of perceived health including five dimensions: mobility, self care, usual activities, pain/discomfort, and anxiety/depression [14]. Each dimension has three levels: no, some, and severe limitations. So, there are 243 (i.e., 3^5) possible sets of values for the EQ5D. All of these possible health states have been valued by the general public, ranging from −0.549 for severe problems with all dimensions to 1 for full health. Values found in the UK have been validated for the Netherlands.

After 4.5 years, participants completed the Diabetes Treatment Satisfaction Questionnaire (DTSQ) [16] and the Problem Areas In Diabetes scale (PAID) [17]. The DTSQ contains a six-item scale assessing treatment satisfaction. Each item is scored on a scale of 0–6; thus the total score of the DTSQ ranges between 0 and 36, with higher scores indicating greater satisfaction with treatment [16]. The PAID is a self-report measure of diabetes-related distress, consisting of 20 statements that were identified as common negative emotions related to living with diabetes [17]. Each item can be rated on a 5-point Likert scale ranging from 0 ("not a problem") to 4 ("a serious problem"). The total score is transformed to a 0–100 scale, with higher scores indicating higher emotional distress. The Dutch version of the PAID has good internal consistency and factorial validity [18].

We analysed differences (IT–RC) in changes from baseline to the 3-year measurement in the SF-36 and EQ5D scores. For effects on treatment satisfaction and diabetes-related emotional distress, we analysed differences (IT–RC) in the scores of the DTSQ and PAID scales after 4.5 years. We used random effects models to account for clustering at the level of the general practitioner. We calculated 95% confidence intervals for the differences between treatment arms and used a two-sided alpha of 0.05 to test significance. A formal power calculation was not carried out as these patient-reported outcome measures were not the primary outcome measures for the intervention study.

Results

Response rates for the different scores varied between 60 and 72% and did not differ for the IT and RC groups. The IT and RC groups are well comparable with respect to clinical, biochemical, and behavioural characteristics at baseline [11]. This did not change when only people who completed the questionnaires were taken into account, except for systolic blood pressure (mean IT: 167.6 mmHg; RC: 162.3 mmHg; $P = 0.03$) and mental health ($P = 0.03$; Table 1).

After 3 years (mean 2.97; SD 0.26), scores increased on the SF-36 scales general health, vitality, and mental health and decreased on the SF-36 scales role physical (statistically significant in IT), bodily pain (statistically significantly in RC), and social functioning. None of the changes in SF-36 or EQ5D differed significantly between IT and RC (Table 1).

Table 1 also displays the DTSQ and PAID scores at 4.5 years (mean 4.69; SD 0.62) in both treatment groups, showing no differences between IT and RC.

Discussion

This study showed no effects of intensified treatment on self-reported health status, satisfaction with diabetes treatment, and diabetes-related emotional distress. We examined a large group of screen-detected T2DM patients, who were followed until 3–5 years after diagnosis. The results address both diabetes-specific and generic outcomes [19] and are highly relevant for patients.

To our knowledge, the ADDITION study is the first randomised trial on the effects of an intensified, multi-factorial intervention in T2DM patients identified by screening. Until now, only few randomised controlled trials compared a multi-factorial treatment with a standard treatment of T2DM, [6, 20]. The UKPDS showed no effects of intensive treatment on perceived health [6]. Ménard et al. reported effects on quality of life in poorly controlled patients with a longer duration of diabetes using an adapted version of the Diabetes Quality of Life Measure [21], indicating an improvement after 1 year in general quality of life and life satisfaction, but not in diabetes-related worry [20]. However, due to the shorter follow-up period and different study population, these results are hard to compare with ours.

A limitation might be the response rates. However, these are in accordance with or even higher than in other studies in the Netherlands [22]. Response rates were comparable for IT and RC groups, and responders did not differ from non-responders (results not shown). With the included numbers of patients, we were able to detect differences up to 7%, which was reported as a moderate effect [15], on all of the reported scales except for SF-36 role physical and role emotional (each 10%).

Another limitation might be that it was not possible to include the DTSQ and PAID at baseline, as the patients were screen-detected and did not know that they had T2DM at that time. We cannot be sure whether patients in both groups are similar with respect to what they would have thought about treatment satisfaction or diabetes-related distress. However, as patients in the IT and RC groups were well comparable with respect to clinical, biochemical, and behavioural characteristics at baseline [11], we have no indications that there would have been large differences in baseline DTSQ and PAID values.

The scores on SF-36, EQ5D, PAID, and DTSQ indicate an overall good psychological state of the participants, probably because all patients are screen-detected. As a consequence, patients have diabetes for only a few years, with a few complications accordingly.

The finding that nor self-reported health status nor treatment satisfaction or diabetes-related distress was influenced by a multi-factorial intensification of treatment does imply that health care professionals do not have to fear negative effects of an intensive treatment starting immediately after diagnosing T2DM. Assuming that an intensified treatment may decrease the risk of complications compared to routine care, one could expect a difference between both groups on the long run in favour of the people who were treated intensively after their screen-detected diagnosis. Patients should be followed up for a longer period to assess the full impact on psychological outcomes of screening for T2DM immediately followed by intensified, multi-factorial treatment.

Table 1 SF-36 and EQ5D scores: changes within groups 3 years after screen-detection of diabetes and differences in changes between groups (IT-RC). DTSQ and PAID scores at 4.5 years after screen-detection of diabetes: differences between groups (IT-RC)

	Intensified treatment (IT)				Routine care (RC)				Difference
	N	Baseline	Follow-up	Change	*N*	Baseline	Follow-up	Change	
SF-36 PF	171	77.6 ± 1.7	77.3 ± 1.8	−0.3 (−3.4;2.8)	156	78.4 ± 1.8	79.1 ± 1.7	0.7 (−2.5;3.8)	−1.2 (−6.1;3.7)
SF-36 RP	171	83.8 ± 2.3	76.6 ± 2.7	−7.3 (−12.4;−2.1)‡	156	85.4 ± 2.4	83.4 ± 2.4	−2.0 (−7.0;3.0)	−5.3 (−12.5;1.9)
SF-36 BP	178	80.5 ± 1.7	78.0 ± 1.8	−2.5 (−5.7;0.7)	163	84.7 ± 1.7	81.1 ± 1.6	−3.6 (−6.8;−0.4)†	1.1 (−3.4;5.6)
SF-36 GH	161	59.5 ± 0.9	64.2 ± 1.5	4.7 (2.3−7.2)§	145	59.6 ± 1.0	65.8 ± 1.5	6.2 (3.7−8.7)‖	−1.5 (−5.0;2.0)
SF-36 VT	163	49.2 ± 1.1	65.6 ± 1.6	16.4 (13.0;19.7)‖	155	51.4 ± 1.1	67.7 ± 1.6	16.3 (13.4;19.2)‖	0.03 (-4.6;4.7)
SF-36 SF	160	89.3 ± 1.4	83.2 ± 1.7	−6.1 (−9.4;−2.8)§	150	90.0 ± 1.3	86.2 ± 1.6	−3.8 (−6.8;−0.9)†	−2.3 (−7.0;2.3)
SF-36 RE	172	89.3 ± 2.1	84.8 ± 2.4	−4.6 (−10.3;1.1)	157	87.9 ± 2.4	87.0 ± 2.4	−0.8 (−5.6;3.9)	−3.7 (−11.2;3.7)
SF-36 MH	172	68.1 ± 1.0	75.9 ± 1.4	7.8 (5.1;10.5)‖	160	71.1 ± 0.9*	79.7 ± 1.2	8.6 (6.1;11.1)‖	−0.8 (−4.5;2.8)
EQ5D	171	0.81 ± 0.02	0.81 ± 0.02	0.0002 (−0.03;0.03)	157	0.81 ± 0.02	0.82 ± 0.02	0.001 (−0.03;0.03)	−0.002 (−0.04;0.04)
DTSQ	184	n.a.	32.7 ± 0.3	n.a.	162	n.a.	32.7 ± 0.3	n.a.	−0.05 (−0.9;0.8)
PAID	177	n.a.	9.8 ± 1.0	n.a.	164	n.a.	8.4 ± 0.9	n.a.	1.4 (−1.2;4.0)

Data are mean ± SEM or mean (95% CI)

IT intensified multi-factorial treatment, *RC* routine care, *SF-36* medical outcomes study 36-item short form health survey, *PF* physical functioning, *RP* role physical, limitations due to physical difficulties, *BP* bodily pain, *GH* general health, *VT* vitality, *SF* social functioning, *RE* role emotional, limitations due to emotional difficulties, *MH* mental health, *EQ5D* European quality of life-5 dimensions, *DTSQ* diabetes treatment satisfaction questionnaire, *PAID* problem areas in diabetes scale, *n.a.* not applicable

* Statistically significant difference at baseline between IT and RC groups, $P < 0.05$

† Statistically significant difference between baseline and follow-up, $P < 0.05$

‡ Statistically significant difference between baseline and follow-up, $P < 0.01$

§ Statistically significant difference between baseline and follow-up, $P < 0.001$

‖ Statistically significant difference between baseline and follow-up, $P < 0.0001$

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