Quality of diabetes care in general practice

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Quality of diabetes care in general practice

Kwaliteit van diabeteszorg in de huisartspraktijk

(met een samenvatting in het Nederlands)

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Aan mijn echtgenote en kinderen
Ter nagedachtenis aan mijn ouders

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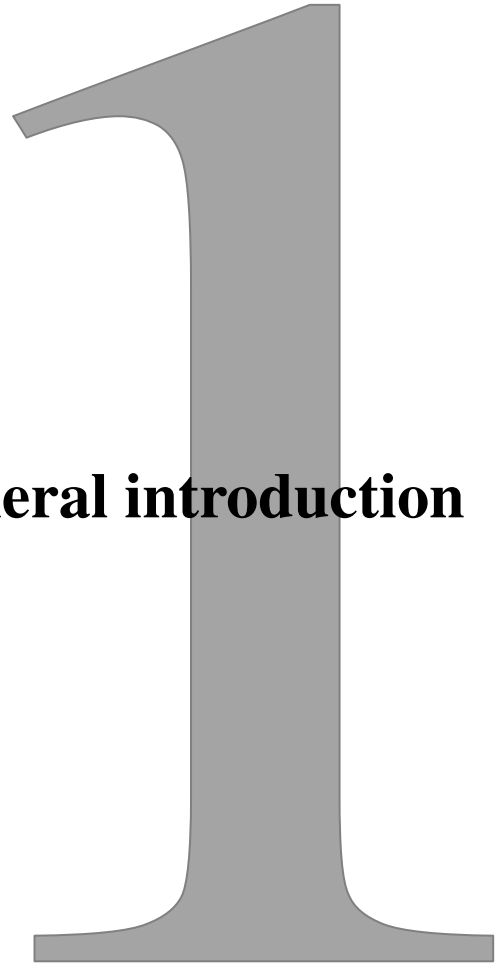

General introduction

Type 2 diabetes is an important, chronic condition notorious for its costly and disabling complications. All over the world diabetes prevalence and disease related costs are rising rapidly. In the Netherlands, the number of patients diagnosed with diabetes is likely to increase between the year 2000 and 2020 with approximately 35% and annual disease related costs are expected to be 430 million Euro.[1,2] The last decades there has been a transition of diabetes management from secondary to primary care. This so called substitution of care was greatly urged by policy makers, in an effort to reduce costs and maintain adequate care. Nowadays, about 75% of the patients with type 2 diabetes are being treated in general practice.[1]

At the end of the twentieth century, clinical trials provided evidence that tight control of blood glucose, blood pressure and cholesterol decreases the risk of developing diabetes related macro- and microvascular complications, and cardiovascular death.[3-7] Knowledge on the importance of stringent diabetes control is reflected in current diabetes guidelines recommending ambitious treatment goals for HbA1c, blood pressure and cholesterol levels.[8,9] Unfortunately, these guidelines are inadequately translated into daily practice and treatment remains substandard in many patients with diabetes.[10-13] Non-compliance with guidelines has been attributed to many different factors, like insufficient knowledge about the content of the guidelines, lack of time or motivation, inadequate support, and lack of collaboration or financial means.[14-17] Multiple strategies have been developed to improve physicians' guideline adherence. Successful implementation strategies are well designed, well prepared and preferably pilot tested before use.[18] Such strategies are targeted at different levels of care (professional, team, patient and organisation), adequately resourced, and include systems for training and evaluation.[19,20] It has been argued that the involvement of end-users in the development process and adaptation of national guidelines to local circumstances, will give rise to an increased uptake.[21] However, a randomised controlled trial involving local guideline adaptation was unable to demonstrate an additional effect of the adaptation process itself.[22] It remains, therefore, unclear whether adaptation of national guidelines is of importance.

Given this uncertainty we performed a randomised controlled trial comparing usual care with care in accordance with locally adapted shared care guidelines. The results of this trial are at the base of this thesis. Their description is intended to contribute to the evidence-based care for patients with type 2 diabetes and to the knowledge on what constitutes the quality of diabetes care.

Sharing and delegating diabetes care

The last decades, increasing numbers of general practitioners in the Netherlands as well as in other countries like the United Kingdom have assumed responsibility for the routine review of their patients with diabetes. Already in 1994, it became apparent that just shifting care to disinterested and unsupported general practitioners was ineffective and wasteful of resources.[23] On the other hand, if a system included a register, protected time for diabetes care, a practice nurse with some diabetes experience, a written management and education protocol agreed with the local consultant diabetologist and a system for auditing standards of care, effective diabetes care could be achieved in general practice.[23] The large scale introduction of this structured and shared care for patients with diabetes has not been unsuccessful: at present, it is generally recognised that prompted general practice care of people with diabetes, can be as good as or better than hospital care.[24] Notwithstanding this success, a treatment gap still exists when best practice is compared with usual care.[10,11,13,25] Clearly, other care concepts are needed to further enhance the quality of diabetes care.

In the Netherlands, general practitioners, specialists and paramedics are called upon to develop and implement multidisciplinary guidelines to minimise the risks for chronically ill patients.[26] A quality incentive is expected to ensue particularly from improved collaboration between professionals and arguments in favour of sharing and delegating care tasks are being made. In addition, the introduction of disease management is expected to succeed were other approaches have failed.[27] However, whether these arguments for closer collaboration and disease management are based on sufficient scientific evidence is questionable. The first study included in this thesis is therefore a literature study with the following research question at its base: *Does the sharing and delegation of care tasks improve the quality of diabetes care and reduce the cardiovascular risks in patients with type 2 diabetes?*

Quality measurement in a defined geographic region

Early studies on shared care clearly demonstrated the need for structure in all aspects of care. It has become apparent that high quality diabetes care requires the systematic delivery of care and the objective measurement of performance against predetermined standards.[23] Consequently, there is a need for an objective method to assess the quality of diabetes care, both in general practice and at the outpatient clinic. The Quality of Care and Outcomes in Type 2 Diabetes (QuED) Study Group developed a quality score based on process and intermediate outcome indicators.

This score has proven to be a strong predictor of major vascular events. After adjusting for patient case-mix and clustering, a linear relationship between the quality score and the incidence of cardiovascular events was found.[28] To our knowledge similar quality scores have not yet been used to evaluate the quality of diabetes management in a primary or secondary care setting. Therefore, in the second study included in this thesis, *we aim to evaluate the quality of diabetes management, both in general practice and at the outpatient clinic of a regional hospital using a QuED like multi item score.*

Local adaptation of national guidelines on type 2 diabetes

Development and implementation of clinical practice guidelines is considered an effective method to improve the quality of diabetes care. Evidently, these guidelines do not implement themselves and complex strategies are often needed to promote their uptake. A Cochrane Review of interventions to improve the management of diabetes mellitus in primary care, out-patient and community settings concluded that multifaceted interventions can improve the management of people with diabetes, as can organizational interventions that improve the recall and tracking of patients.[29] A randomised trial in Denmark demonstrated the potential in general practice to achieve successful outcomes after a complex intervention that fulfilled these criteria.[30] On the other hand, a complex multifaceted intervention to promote the introduction of a structured diabetes shared care in North Dublin, did not produce significant improvements in glycaemic control or other biophysical outcomes.[31] In the Netherlands, randomised controlled trials involving the effectiveness of multifaceted interventions to promote the uptake of diabetes shared care guidelines are lacking still.

Often clinical guidelines are produced nationally, with little or no participation of local end-users. Lately, however, growing attention has been paid to the involvement of end-users in the development and implementation of guidelines. Whilst there is some evidence that end-user involvement in the development process will promote guideline uptake, there are concerns about the cost effectiveness of this approach. Therefore, a more sensible strategy may be the adaptation of nationally produced guidelines to local circumstances. A systematic review by Grimshaw suggested that the use of a local consensus process was more likely to lead to implementation of clinical guidelines.[32] On the other hand, a recent study did not find any additional effect from the local adaptation process itself.[22]

Hence, it is questionable whether local adaptation is a prerequisite to ensuring changes in the quality of diabetes care in daily practice.

In light of the uncertainties described above, we aim to evaluate the effects of a multifaceted intervention to implement locally adapted guidelines on the shared care for patients with type 2 diabetes. Therefore, the research question of the third study of this thesis is: *Does the multifaceted implementation of a locally adapted national guideline improve the cardiovascular outcome of primary diabetes care?*

Diabetes care and clinical inertia in general practice

The discordance between best practice and usual care can be attributed partially to the inability of physicians to adjust their medical regimen in time. Grant and others demonstrated that although the testing rates for HbA1c, blood pressure and total cholesterol in a national sample of U.S. academic medical centres were very high, few untreated patients with high blood pressure or elevated LDL-cholesterol levels were started on corresponding drug therapy and only the minority of patients with increased HbA1c levels received adjustment of their anti-hyperglycemic regimens.[11] Apparently, high rates of risk factor testing did not necessarily translate into effective metabolic control. A recent Canadian study confirmed these results. Less than one-half of the patients with high HbA1c levels had intensification of their medications, regardless of the specialty of their physician. However, specialists were more aggressive with insulin initiation than primary care physicians, contributing to the lower HbA1c levels seen with hospital care.[33] In a prospective observational study comparing diabetes management in primary and secondary care, intensification of therapy was independently associated with improvement in HbA1c%.[34] Failure of health care providers to initiate or intensify therapy when indicated has been called clinical inertia.[35] Clinical inertia seems to be widespread and is probably a major barrier to better diabetes care. Although it has been attributed to many different reasons including lack of education, training and practice organization aimed at achieving therapeutic goals, our understanding of clinical inertia is still far from complete.

In the fourth study of this thesis *it is our aim to examine the incidence of clinical inertia in general practice, to investigate the relationship between inertia and the outcome of diabetes care and to explore the determinants of inertia within the scheme of the trial described in the third study.*

Polypharmacy and drug adherence in primary diabetes care

Many evidence-based clinical guidelines have been produced and implemented in an effort to improve the outcome of diabetes care. Nevertheless, cardiovascular risks of patients with diabetes remain too high. This has been attributed to different factors including physician's failure to initiate or intensify therapy when indicated, and patient's non-adherence with prescribed medications. Recently, the World Health Organisation stated that only fifty percent of the patients diagnosed with diabetes were fully compliant with their treatment regimens. Generally, adherence to prescribed medications is crucial to reach metabolic control as non-adherence with blood glucose and cholesterol lowering drugs is associated with higher HbA1c and LDL cholesterol levels.[36-39] Poor patient's adherence has been associated with increasing numbers of tablets, multiple daily dosing schedules, the concurrent use of several types of oral hypoglycaemic agents and increasing numbers of co-medications.[40-43] On the other hand, multiple drug therapy is often unavoidable to achieve recommended treatment goals. Consequently, polypharmacy is common among patients with diabetes.[44,45] Given the relationship between polypharmacy and patients' adherence, the lack of change in cardiovascular risk factors after implementing diabetes shared care guidelines may have been a consequence of decreased compliance due to enhanced polypharmacy in order to comply with current treatment goals.

In light of the hypothesis described above, *we aim to investigate the occurrence of polypharmacy and patients' adherence in general practice, their mutual relationship and the association between adherence and the outcome of diabetes care.*

Outline of this thesis

In *chapter two* we describe the results of a literature study into the effects of sharing and delegating diabetes care tasks.

Chapter three describes the quality of diabetes management, both in general practice and at the outpatient clinic of a regional hospital. We used a multi item score based on the results of the QuED study group, to measure the overall quality of diabetes care.

In *chapter four* we present the results of a randomised trial involving the effects of a facilitator enhanced implementation of locally adapted diabetes shared care guidelines. The baseline and follow-up data of this trial are used in all following chapters of this thesis.

Chapter five describes the occurrence of clinical inertia in general practice and the relationship between inertia and the outcome of diabetes care. In this chapter we also explore the determinants of inertia within the scheme of the trial described in chapter four.

In *chapter six* we will give a description of the results of our study involving the occurrence of polypharmacy and patients' adherence in general practice, their mutual relationship and the association between adherence and the outcome of diabetes care.

Finally, a general discussion on the quality of diabetes care, partially based on the results of the preceding studies, is presented in *chapter seven*.

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2

Shared and delegated systems are not quick remedies for improving diabetes care: A systematic review.

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Abstract

Background: Type 2 diabetes is an important, chronic condition notorious for its costly and disabling complications. Enhanced cooperation is expected to improve the quality of diabetes care and reduce cardiovascular risks in patients with diabetes. It is, however, questionable whether this assumption is evidence based.
Methods: A structured literature search of systematic reviews, randomised controlled trials (RCT's), and other effect evaluations regarding sharing and delegation of diabetes care tasks was performed.
Results: 22 studies were included in this review. The process of care improved in all studies that investigated this quality aspect. HbA1c improved in seven reviews and in five other studies. All included reviews and four RCT's were unable to demonstrate a positive effect on the height of patients' blood pressure levels. Total cholesterol level improved in two reviews and five other studies.
Conclusion: Sharing and delegation of diabetes care tasks lead to a significant improvement of the process of care and a reduction in HbA1c percentage. However, up till now, this improvement has not led to better cardiovascular risk management. For a number of reasons, a truly accurate estimation of the effects of shared and delegated diabetes care within the Dutch healthcare system is not possible yet.

Introduction

Tight control of blood glucose, blood pressure and dyslipidemia reduce mortality and morbidity rates in patients with type 2 diabetes. Long-term treatment policies that encompass these aims are feasible in a primary care setting.[1] In recent years, particular progress has been made in reducing patients' HbA1c percentages. Nevertheless, cardiovascular risks remain too high in patients with diabetes.[2-4] This may be due to the fact that existing guidelines are not fully adhered to. Non-compliance with guidelines has been attributed to many different factors like insufficient knowledge about the content of the guidelines, lack of time, motivation, support, collaboration, and financial means. Another reason for exceeding treatment targets may be patients' limited treatment compliance.[5]

At present, a quality incentive is expected to ensue particularly from improved collaboration between general practitioners, specialists and paramedics. Sharing and delegation of care tasks is considered an effective method to achieve this enhanced collaboration. Furthermore, arguments in favour of the introduction of disease

management have been made.[6] Whether these arguments for closer collaboration and disease management are based on sufficient scientific evidence is, however, questionable. In order to answer this question, we conducted a literature study with the following research question at its base: does sharing and delegation of care tasks improve the quality of diabetes care and reduce the cardiovascular risks in patients with type 2 diabetes?

Method

Definitions

The concept of shared care encompasses comparable levels of expertise for all collaborating parties. Shared care involves the joint participation of hospital consultants and general practitioners in the planned delivery of care informed by an enhanced information exchange over and above routine discharge and referral notices.[7] Transmural care is a typically Dutch care concept that has been defines as: 'care, geared to the needs of the patient, provided on the basis of cooperation and coordination between general and specialised caregivers, with shared responsibilities and specification of delegated responsibilities'.[8] Delegation of care involves the allocation of responsibilities to someone with a lower level of training.[9] Shifting care tasks from a general practitioner to a practice nurse is an example of such task delegation. Disease management can be described as follows: 'the programmatic and systematic approach of specific diseases and health problems using management instruments to improve the quality and efficiency of care'. In addition to substitution (sharing and/or delegation), the care approach is businesslike with strong emphasis on working with protocols, not targeted at the individual patient but at the population at risk and focused on education and self-management instead of on treatment itself.[10]

In many studies, there seems to be confusion about what constitutes shared care, transmural care and disease management. Due to this confusion the same publication may be mentioned in reviews on task delegation as well as disease management or transmural care. As far as possible, we have tried to place articles according to the definitions made above.

Search strategy

We searched for systematic reviews, randomised clinical trials and other effect studies dating from 1990-2005 in Medline using the following combination of terms: ("Diabetes Mellitus, Type 2"(MESH) OR diabetes) AND ("Delivery of

Health Care, Integrated"(MESH) OR "Disease Management"(MESH) OR (("Primary Health Care"(MESH) OR "Family Practice"(MESH)) AND "Outpatient Clinics, Hospital"(MESH)) OR "Nurse Practitioners" (MESH) OR integrated care OR transmural care OR shared care OR substitution of care OR ((primary care OR general practice) AND (secondary care OR hospital care)) OR nurse specialist OR nurse care OR practice nurse). For this purpose, the following limits were used: "Abstracts", "English", "Clinical Trial", "Randomized Controlled Trial" en "Review". Subsequently, the registers of the National Institute for Public Health and the Environment (RIVM), the Netherlands Institute for Health Services Research (NIVEL) and the Dutch Journal of Medicine (NGTV), the journal of the Dutch College of General Practitioners and the Cochrane Central Register of Controlled Trials were searched for relevant literature. Finally, the reference sections of the selected articles were searched for any other possible relevant studies.

Inclusion and exclusion criteria

In order to be included in this review, the following five aspects had to be present: first, shared and/or delegated care; second, an unselected patient population; third, a systematic review, an RCT, a non-randomised controlled study or a preliminary and follow-up study; fourth, a follow-up longer than three months; and fifth, clear outcome and process measurements. Purely descriptive studies without effect measurements and summaries of dissertations were not included. A formal quality analysis of the selected studies was not conducted.

Results

Our search in Medline resulted in 2,406 hits. After applying the described limits, 232 reviews, 129 RCT's and 226 clinical trials remained. Ultimately, 11 reviews, seven RCT's, one trial and three non-controlled studies fulfilled our criteria. Out of these publications, five dealt with shared care (table 1) and 13 with task delegation (table 2). Four studies covered both shared care as well as task delegation (table 3).

Table 1 Shared care

Study	Setting	Shared care Characteristics	Follow-up	Process	Outcome
Greenhalgh 1994	UK and Australia	Systematic review of 10 trials (5 randomised, 5 non-randomised, 2,185 patients) 12 descriptive studies and 3 non-published projects	1-5 years	Controls ↑ HbA1c test ↑ Podiatrist ↑ Dietician ↓	HbA1c % = Blood pressure =
Griffin 2000	UK and Australia	Systematic reviews of 5 RCT's (1,058 patients)	1-5 years	Controls ↑ HbA1c test ↑ Podiatrist ↑ Dietician ↓	HbA1c % = Blood pressure =
Struijs 2004	NL, Denmark, UK, US, Australia, Italy, Canada and Ireland	Systematic reviews of 22 studies (4 Dutch, 18 international, 31,760 patients)	1-6 years	Test HbA1c ↑ Measure blood pressure ↑ Lipids test ↑ Creatinine test ↑ Albumin test↑ Fundus control ↑ Foot control ↑	HbA1c % ↓ Blood pressure = Cholesterol = QI =
Rutten 2001	NL	Longitudinal study (336 patients)	3.2 years	Registration ↑	HbA1c %↓ Diastolic blood pressure ↓ Lipids ↓
Whitford 2003	UK	Repeated cross sectional study	10 years	HbA1c test ↓ QI test ↓ Cholesterol ↑ Fundus control ↑ Registration of smoking habits ↑	HbA1c % ↑ Blood pressure ↓ Cholesterol ↓ Creatinine ↑ QI =

= no changes, ↑ increase, ↓ decrease

Table 2 Delegated care

Study	Setting	Delegated care Characteristics	Follow-up	Process	Outcome
Vrijhoef 1999	US, UK, Ireland and Canada	Systematic review of 10 studies (3 for diabetes, 2 for diabetes and one other chronic disease, 5 for another chronic disorder)	3-12 months		HbA1c % ↓ Blood pressure = Cholesterol = QI =
Renders 2001	US, UK, Australia, NL and Germany	Systematic review of 41 studies (6 aimed at care providers and organisation of the care for which the efforts of nurses was part of the intervention and the outcome measures were reported)	6-36 months	HbA1c test ↑	HbA1c ↓ Cholesterol = Blood pressure =
Loveman 2003	Australia, US, and Canada	Systematic review of 6 RCT's (1,382 patients)	6-12 months		HbA1c % =
Frich 2003	US, UK	Systematic review of 7 RCT's	6-12 months		HbA1c % ↓ Cholesterol ↓ QI =
Ingersoll 2005	Australia, US, and Canada	Systematic review of 9 studies (1 review, 8 trials)	6-24 months		HbA1c % ↓ Cholesterol ↓
Groeneveld 2001	NL	RCT (246 patients)	1 year		HbA1c ≥8.5 % ↓ Systolic blood pressure = Cholesterol = QI =
Vrijhoef 2002	NL	Non-randomised study (198 patients, 175 delegated care, 23 control group)	1 year		HbA1c % ↓ Diastolic blood pressure ↓ Cholesterol ↓
Denver 2003	UK	RCT (120 patients)	6 months		HbA1c = Systolic blood pressure ↓ Cholesterol = Creatinine ↑

Table 2 continued

Litaker 2003	USA	RCT (157 patients)	1 year	Vaccinations ↑ Fundus control = Foot control ↑	HbA1c ↓ Blood pressure = LDL cholesterol ↓
Gabay 2006	USA	RCT (332 patients)	1 year	Albumin test ↑ Fundus control ↑ Foot control ↑	HbA1c = Blood pressure ↓ LDL cholesterol ↓ QI =
Van Son 2004	NL	RCT (111 patients)	1 year		HbA1c ≥8.5% % ↓ Blood pressure = Cholesterol =
Houweling 2005	NL	RCT (206 patients)	14 months	% Referred to ophthalmologist ↑ % Diabetes treatment ↑ % Blood pressure treatment ↑	HbA1c = Blood pressure = QI = Cholesterol =
Houweling 2005	NL	RCT (84 patients)	1 year		HbA1c = Blood pressure = QI = Cholesterol = Cholesterol/HDL cholesterol ↓

= *no changes,* ↑ *increase,* ↓ *decrease*

Table 3 Shared and delegated care

Study	Setting	Shared and delegated care Characteristics	Follow -up	Process	Outcome
Norris 2002	US, Sweden, NL, UK, Israel and France	Systematic review of 27 studies (1 Dutch, 26 international)	1-4 years	HbA1c test ↑ Fundus control ↑ Foot control ↑ Lipids test ↑ Albumin test ↑	HbA1c % ↓ Blood pressure = Cholesterol = QI =
Knight 2005	US, UK, Israel, Argentina, Australia, NL	Systematic review of 24 studies (19 RCT's, 5 non-randomised controlled studies, 6,421 patients)	3-30 months	HbA1c test ↑ Fundus control ↑ Nephropathy Screening = Foot control ↑	HbA1c % ↓ Blood pressure = Cholesterol =
Ubink-Veltmaat 2005	NL	Non-randomised prospective study (2,486 patients)	3 years	HbA1c test ↑ Measure blood pressure ↑ Cholesterol test ↑ Creatinine test ↑ QI measurement ↑ Fundus control ↑ Foot control ↑ Registration of smoking habits ↑	HbA1c≤7.0% = Blood pressure≤150/85 ↑ Cholesterol≤5mmol/l ↑
Rothman 2005	US	RCT (217 poorly controlled patients, HbA1c≥8.0 mmol/l)	2 years		HbA1c %↓ Blood pressure ↓ Cholesterol =

= no changes, ↑ increase, ↓ decrease

Shared care

We included three systematic reviews and two non-randomised studies regarding the shared care for patients with diabetes. Two reviews originated from England and one from the Netherlands. Diabetes shared care was the key element of the English reviews. The Dutch literature study covered transmural care. The English reviews had the same five RCT's in common, while the review by Griffin and Kinmonth[11] was one of the 22 studies included in the Dutch study.

Reviews

It became apparent from the results of the English reviews that shared care is not necessarily inferior to traditional hospital care. In these reviews, published in 1994 and 2000, the same five RCT's amongst 1058 patients were included.[11,12] Four trials originated from England and one from Australia. Two studies showed that patients in primary care were seen more often and that the HbA1c percentages of these patients were checked more frequently. Besides, more patients were referred to a podiatrist in general practice.[13,14] Metabolic control in patients with diabetes did not differ significantly between the primary and secondary care setting. The same applied to the effects on the patients' blood pressure levels as described in two publications.[13,15] The non-randomised studies included in the 1994 review, confirmed that structured diabetes care provided by GPs with a special interest in diabetes could be as good as specialist care.

The Dutch literature study clearly demonstrated that transmural care can lead to a significant reduction in HbA1c percentage. This review involved 15 controlled studies and seven cross-sectional evaluations of already implemented care concepts. The aspects covered were: multidisciplinary consultation, diabetes nurses working transmurally, or transmural protocols and guidelines.[16] Whilst most publications reported improvements to the process of care, transmural treatment produced positive results such as significant decreases in blood pressure, body mass index, and total cholesterol level in only a few of the studies.[17-21] However, 10 out of 15 studies found a significant decrease in patients' HbA1c percentages following the introduction of transmural care.[11,17-25] Out of the four selected Dutch studies, only two showed improvements to the patients' HbA1c percentages.[23,24]

RCT's and other effect evaluations

The Utrecht Diabetes Project (UDP) made clear that standardised information exchange could provide an effective infrastructure for the shared care for patients with diabetes. In this non-controlled study, patients who received shared care showed significant improvements to their metabolic status, lipid levels and diastolic blood pressure.[26]

In England, two cross-sectional studies were performed in 1991 (n = 2,284 patients) and 2001 (n = 5,809 patients). From these studies it appeared that over a period of 10 years both process and outcome measures of diabetes care improved when the primary and secondary care services worked closely together in order to plan care,

draw up protocols and share staff and funding. Smoking habits were registered more often and patients' cholesterol levels and retina's had been checked more frequently. Blood pressure and cholesterol levels dropped whilst HbA1c percentages and creatinine levels rose.[27]

Delegation of care

We selected five reviews, seven RCT's and one non-randomised study on the delegation of care tasks. Again, the reviews had a considerable overlap. The two Dutch reviews[28,29] included the same two trials[25,30] and two other reviews[31,32] had also two studies in common.[33,34] One of these other reviews[32] was included as a separate publication in the Ingersoll review.[35]

Reviews

The 1999 review clearly demonstrated that cardiovascular risk reduction in patients with type 2 diabetes is not self-evident when care is delegated to a specialised nurse who holds a central position.[29]. The authors included 10 studies. Over all 3,058 patients participated. Out of these 10 publications, only three were exclusively concerned with diabetes mellitus[30,36,37] and two with diabetes in addition to other chronic disorders.[38,39] Decreases in body weight, blood pressure as well as cholesterol levels were not reported in any of the studies. However, a reduction in HbA1c percentage was mentioned by one of the two studies included.[30]

From the 2001 review it has become apparent that HbA1c percentages in patients with diabetes can decrease significantly when care tasks have been delegated. This review included 41 publications from the US, England, Australia, the Netherlands and Germany. Of the included studies, 20 related to interventions that were aimed at both care providers and organisation of care. Whenever nurses participated in such an intervention, there were improvements to the outcome of diabetes care. Six studies showed a decrease in HbA1c percentage, one in two studies a decrease in blood pressure and one in three a decrease in cholesterol levels.[28]

The 2003 Cochrane review made clear that delegation of care tasks does not automatically lead to a decrease in HbA1c percentage. The authors included six studies on the effects of task delegation to nurses. A total of 1,382 patients from Australia, the US and Canada participated in these studies. After a follow-up of 12 months there were no significant differences in the HbA1c percentages between the

intervention and control groups.[32] Only one study showed a significant decrease in HbA1c percentage after six months.[34]

The review on the effects of nursing interventions in older patients or patients with a chronic disorder included seven publications that related to the care of 1,465 patients with diabetes.[31] The interventions were diverse and varied between the provision of routine care and the encouragement of changing behaviour. All studies showed positive clinical effects with the exception of one. HbA1c percentage decreased in three out of four studies[34,40,41] and cholesterol level in one out of two.[40] A decrease in body weight was not recorded in any of the publications.

The most recent review that included the 2003 Cochrane review as well as eight other publications from 2002 and 2003, confirmed the effectiveness of delegating care tasks. Only those studies with evidence at levels I (RCT, review of at least one RCT) or II (non-randomised trials, cohort studies, case control studies) were included.[35] The selected studies with a follow-up between six and 24 months, came from Australia, the US and Canada. Based on the evidence presented and the net effect of the interventions performed, interventions were classified as worthwhile, possibly effective, worthwhile considering, ineffective or insufficient. Four interventions were found to be possibly effective and the others worthwhile considering. HbA1c percentage decreased in four out of seven studies.[42-45]

RCT's and other effect evaluations

A Dutch RCT on the effects of task delegation to a specific diabetes service made clear that only those patients who were initially poorly controlled showed significant improvements to their glucose levels. This study involved 246 patients who were followed for one year. Any existing differences in blood pressure, body weight and lipid levels were not influenced by the intervention.[46]

From the results of three RCT's, different effects of task delegation on the height of patients' blood pressure levels became apparent. 120 patients where randomised to receive either usual care or care at a nurse-led hypertension clinic. After six months, systolic blood pressure levels decreased significantly more in the intervention group in comparison with the control group.[47] In 157 patients with type 2 diabetes who had been treated either by a primary care physician or a nurse practitioner in collaboration with a physician, no differences in blood pressure levels were found after one year.[48] An American study on the effects of case management in which

intervention group patients received support by a nurse who took responsibility for part of the treatment, showed a significant decrease in patients' blood pressure levels after one year. Most of the process measures also improved. There were, however, no differences in body weight, HbA1c percentages or cholesterol levels.[49]

A randomised Dutch study among 111 patients with diabetes made clear that delegation of care tasks could contribute to a reduction in the number of patients with HbA1c percentages exceeding treatment targets. After one year, mean HbA1c percentage, blood pressure, body weight and cholesterol levels did not differ significantly between the intervention and control group. However, the number of patients with a poorly controlled diabetes decreased by 27.3% in the intervention group in comparison with 5.7% in the control group.[50]

A recent study (RCT, 206 patients) demonstrated once and again that improvements to the process of care do not lead to better outcomes automatically. Due to the delegation of tasks from GPs to practice nurses the majority of the process indicators improved but after 14 months all investigated clinical parameters did not differ between the intervention and control group.[9] Also recently, the results were published of a RCT (n = 84) that studied the effects of task delegation from specialists to diabetes nurses. With exception to the cholesterol/HDL ratio, there were no differences in the outcomes of care between a diabetes nurse working with protocols and a specialist in collaboration with a diabetes nurse.[9]

In a Dutch non-randomised study on the effects of task delegation to a diabetes nurse, patients' HbA1c percentages decreased significantly after the delegation of the three-monthly check-ups. 198 patients participated in this study that was performed in 5 general practices. Diastolic blood pressure, total cholesterol and triglyceride levels equally improved although these results could not be compared with those of the control group.[51]

Shared and delegated care

Two systematic reviews, one RCT and one non-controlled trial involved both shared and delegated care. The reviews and the RCT looked into the effects of disease management in which sharing and delegating care tasks play an important role. The non-controlled Dutch study evaluated the effects of shared care with tasks delegation to nurses. The majority of the 47 studies included in the reviews originated from the US. The two reviews differed considerably. Whilst these two

studies were conducted within a short time span of each other, they only had four studies in common.

Reviews

From the 2002 review of 27 mostly American publications it became apparent that disease management could bring about both decreases in HbA1c percentages and improvements to the process of care. The follow-up of the included studies varied between one and four years. A decrease in HbA1c percentage was reported in 18 out of 19 studies. The median effect was -0.5%. Strong evidence was found for improvements in the percentage of care providers who checked the fundus and/or HbA1c percentage on a yearly basis. In addition, there was sufficient evidence to demonstrate improvements to foot care (control), screening for proteinuria and measuring patients' lipid profile. There was insufficient evidence of improvements to the participating patients' Body Mass Index, blood pressure or lipid levels.[52]

The 2005 review (24 publications, 6,421 patients) confirmed the limited effect of disease management on blood pressure and cholesterol levels. The results of 20 studies among 3,720 patients were used for a meta-analysis. This analysis showed that disease management significantly decreased mean HbA1c percentage by 0.5 percentage points.[53] A statistically significant decrease in systolic blood pressure was only described in one of the five studies.[54] Eight studies investigated the effects on total cholesterol or LDL cholesterol levels with one study showing a significant decrease in LDL cholesterol in the intervention group.[55]

RCT's and other effect evaluations

A Dutch non-randomised study into the effects of shared care with task delegation to a diabetes nurse involved two interventions that were applied simultaneously in two different groups.[56] Out of the two intervention groups, group A received extensive support from a diabetes nurse working in secondary care and group B received limited support on a consultation basis. Following the interventions, the process of care clearly improved. However, no improvements were seen in glycaemic control. The number of patients with a blood pressure of ≤150/85, or a total cholesterol of ≤ 5 mmol/l rose significantly in both intervention groups.

A recent American study involving 217 patients with an HbA1c ≥8.0 % showed that a disease management programme that is aimed at decreasing patients' cardiovascular risk factors can be successful.[57] The intervention consisted of a

programme using algorithms aimed at decreasing glucose levels and reducing cardiovascular risk factors. Following the intervention, considerably more patients in the intervention group were taking aspirin. Furthermore, achieved HbA1c percentages and blood pressure levels differed significantly between the intervention and control group.

Discussion

It has become apparent that shared care can be equally as effective as conventional hospital care and transmural care leads to significant improvements to the process of care and glycaemic control. There is, however, only little evidence in support of a decrease in patients' blood pressure or cholesterol levels. The non-controlled studies into the effects of shared care consolidate these conclusions. The positive effects of delegating care appear to be rather poor and inconsistent. At present, commitments made by diabetes nurses seem to result only in short term improvements of glycaemic control. There is, however, insufficient evidence for improvements in patients' lipid profile, blood pressure or Body Mass Index. The conclusion from the reviews on the combined aspects of sharing and delegating care is unanimous: disease management encourages improvements in glycaemic control and the process of care and possibly has a positive effect on blood pressure control. There is, however, insufficient evidence in support of a positive effect of disease management on body weight and lipid levels.

The conclusions of this literature study are limited by a number of factors. In the Netherlands, only a few controlled studies on the effects of shared and delegated care have been conducted. International studies can not be generalised completely due to differences in setting, funding and organisation of care. Consequently applying the findings of these studies to the Dutch situation is difficult. There is a considerable overlap between the different reviews and some of the publications do not describe the interventions in full detail. Moreover, the follow-up of most studies is limited meaning that long-term effects have not been clarified. Finally, as the aspects of shared and delegated care are often approached in combination with other interventions such as the introduction of guidelines or providing feedback, only a few studies cover just a single care aspect. These factors mean that an accurate assessment of the effects of shared and delegated care is not possible within the Dutch healthcare system. One other limitation of this review is the lack of a formal analysis of the quality of the selected studies. Considering the limited number of Dutch RCT's, we abandoned our original idea of only including randomised studies

or systematic reviews and decided to include any research material that we considered to be relevant.

Others share our conclusion that sharing and delegation of care tasks does not automatically reduce the cardiovascular risks in patients with diabetes. A Cochrane review on the substitution of care from doctors to nurses brought to light that highly educated and well-trained nurses could equal the standard of care given by doctors.[58] However, the number of studies with enough statistical power to demonstrate this equality was very limited. The fact that delegation of tasks not automatically improves the quality of care is confirmed by a recent English review on the effects of disease management by nurses for patients with COPD. The authors concluded that there was insufficient evidence to support the widespread implementation of this innovation.[59]

So far, it has not been demonstrated that sharing and delegating diabetes care tasks makes an important contribution to the required reduction of patients' cardiovascular risks. However, the expectations are perhaps just too high on this point. Therefore, it is recommended that during the years to come, the effects of newly introduced care concepts are closely monitored (preferably by controlled studies). In literature, regular references are being made to the inability of clinicians to adjust medical regimens on time.[60,61] This phenomenon that is referred to as clinical inertia.[62] may partly explain the limited success of care programmes. Considering the association between clinical inertia and the outcomes of diabetes care, it is advisable to pay great attention to prescribing drugs timely and in sufficient dosages when introducing new care concepts.

Conclusion

The selected reviews and other effect evaluations demonstrate that sharing and delegating diabetes care tasks improves the process of care and glycaemic control. However, sharing or delegating care does not reduce the other cardiovascular risk factors of patients with type 2 diabetes. Disease management is not a panacea for the required augmentation of diabetes care.

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3

Overall quality of diabetes care in a defined geographic region: different sides of the same story

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Abstract

Objective: to evaluate the quality of diabetes management in primary and secondary care in a defined geographic region in the Netherlands using a quality score.
Methods: a cross-sectional study was carried out in 30 general practices among 2042 patients with type 2 diabetes,(1640 primary and 402 secondary care). Quality of diabetes management was assessed by a score comprising process and outcome indicators (range 0 to 40). Clustering at practice level and differences in patient characteristics (case-mix) were taken into account.
Results: at the outpatient clinic, patients were younger (mean 64.1 years, SD 12.5 versus mean 67.1 years, SD 11.7, $p<0.001$), had more diabetes related complications (macrovascular: 39.7% versus 24.3%, $p<0.001$ and microvascular: 25.9% versus 7.3%, $p<0.001$) and lower quality of life scores (EuroQol-5D: mean 0.60, SD 0.29 versus mean 0.80, SD 0.21, $p<0.001$). After adjusting for case-mix and clustering, there was a weak association between the setting of treatment and HbA1c (primary care: mean 7.1%, SD 1.1 versus secondary care: mean 7.6%, SD 1.2, $p<0.016$) and between setting and systolic blood pressure (primary care: mean 145.7mmHg, SD 19.2 versus secondary care: 147.77mmHg, SD 21.0, $p<0. 035$). The quality of care sum scores in primary and secondary care differed significantly with a higher score in primary care (mean 19.6, SD 8.5 versus mean 18.1, SD 8.7, $p<0.01$). However, after adjusting for case-mix and clustering, this difference lost significance.
Conclusion: general practitioners and internists are treating different categories of type 2 diabetes patients. However, overall quality of diabetes management in primary and secondary care is equal. There is much room for improvement. Future guidelines may differentiate between different categories of patients.

Introduction

In the Netherlands about 600.000 patients are known with type 2 diabetes.[1] Of these patients 75% are primarily being treated in general practice.[2] It has been emphasised that case-mixes in primary and in secondary care are unequal and that it is necessary to take these inequalities into account when comparing the outcome of care in different settings.[3,4] In general, there is as much variation in outcomes within disciplines as between them.[5]

Diabetes care is shared care and, consequently, close cooperation between hospitals and general practitioners is essential. Given the necessity to collaborate, knowledge about what is achievable in and outside the hospital is important, as this will influence the development and implementation of guidelines and the sharing of responsibilities. There is a need for an objective method to assess the quality of diabetes care, both in general practice and at outpatient clinics.

The Diabetes Quality Improvement Project has developed a comprehensive set of measures to assess quality of care accurately and reliably. Implementation of this set of measures is expected to bring quality improvement.[6] Recently the Quality of Care and Outcomes in Type 2 Diabetes study group developed a quality of care summary score based on readily available process and intermediate outcome indicators. Only indicators with a strong link with vascular complications were used. These measures were consistent with those adopted for the Diabetes Quality Improvement Project. After adjusting for case-mix and clustering, a linear relationship between quality score and the incidence of cardiovascular events was found.[7] Similar scores have not been used previously to evaluate the quality of diabetes management in a primary and secondary care setting simultaneously. The current study aims to fill this gap.

Research Design and Methods

In the Netherlands, everyone is registered with a general practice and insurance companies reimburse all diabetes-related expenses. By law, all inhabitants are insured by one of these companies and when needed, subsidiaries are given to pay for insurance costs. A cluster-randomized trial was performed comparing usual care with care according to locally adapted shared care guidelines near Apeldoorn, a city with 150,000 inhabitants. This paper describes the cross-sectional evaluation of diabetes management in primary and secondary care at the start of the intervention.

Study participants

All primary care practices (n=70) in the region and all internists (n=9) at the local hospital were asked to participate. All patients with diabetes (n=3357) on the lists of the participating practices were eligible for this project, both those cared for by a general practitioner and those treated at the outpatient clinic. In general practice, a computer search was performed to identify all patients known to have type 2

diabetes. Reasons for exclusion were the inability to complete a questionnaire, severe mental illness, unwillingness to attend the practice regularly, and a limited life expectancy.

Measures

General practice

At baseline, demographics, duration of diabetes, smoking habits, co-morbidity and the presence of macrovascular or microvascular complications were recorded. Standardised operating procedures were used to record bodyweight, height and blood pressure. Fasting blood and urine samples were analysed at the local hospital laboratory. HbA1c was determined by the Variant II Turbo Haemoglobin Testing System (Bio-Rad). Plasma glucose, total cholesterol, HDL cholesterol, triglycerides, albumin/creatinine ratio and microalbumen were determined with the Architect ci8200SR (Abbott).

Outpatient clinic

Specially trained nurses examined the records of all participants, extracted anthropometric data and checked the histories of these patients for duration of diabetes, smoking habits, co-morbidity and presence of macrovascular or microvascular complications. The records of the hospital laboratory were used to obtain the results of biochemical tests performed during the year preceding the start of the study.

Both settings

Health related quality of life was estimated with the EuroQol-5D (range -0.59 -1, where 1 indicates perfect health) and the validated Dutch version of the disease specific diabetes health profile (range 0 - 100, were 100 represents no dysfunction).[8,9] The overall health state of the participants and their treatment satisfaction were measured with the visual analogue scale of the EuroQol-5D (range 0 - 100) and the treatment satisfaction questionnaire (range 0 - 36) respectively.[10,11]

The files of all 18 pharmacists and those of three general practitioners having their own pharmacy were used to obtain a detailed medication profile of all patients using blood glucose lowering medication (ATC code A10), or those who had been diagnosed with diabetes by their general practitioner. Subsequently, these profiles were matched with our research data.

Yearly measurement of HbA1c, blood pressure, total cholesterol, albumin/creatinine ratio and the prescription of ATII-antagonists or ACE-inhibitors in case of microalbuminuria were identified as measures of the process of care The percentages of patients with HbA1c<8%, systolic blood pressure<140 mmHg, diastolic blood pressure<85 mmHg, mean cholesterol<6 mmol/l for non-smokers or <5 mmol/l for smokers and diabetes treatment satisfaction were used as outcome measures.

Because local shared care guidelines differed from those used by the Italian Quality of Care and Outcomes in Type 2 Diabetes study group, slight modifications had to be made to the original quality summary score. The threshold for diastolic hypertension was set at 85 instead of 90 mmHg. Total cholesterol was used as a substitute for LDL cholesterol. Instead of ACE-inhibitors only, both ACE-inhibitors and ATII-antagonist were recommended in cases of microalbuminuria. The quality score was, like the original Italian score, designed prior to the data analysis and was not based on weights derived from regression models. The lowest score was assigned if a patient was not effectively treated despite elevated values. An intermediate score was credited if treatment goals were met, but measurement of a parameter was not performed within the last 12 months. Finally, the highest score was given if patients were treated in line with both, process and outcome indicators (table 1).

Table 1 Quality of diabetes management scoring system

Quality of care indicator	**Score**
HbA1c ≥8.0%	0
HbA1c <8.0% but measurement less than 1/year	5
HbA1c <8.0% and measurement at least 1/year	10
Blood pressure ≥140/85	0
Blood pressure values <140/85 mmHg but measurement less than 1/year	5
Blood pressure values <140/85 mmHg and measurement at least 1/year	10
Cholesterol ≥5 mmol/l (non-smokers without vascular complications ≥6 mmol/l)	0
Cholesterol <5 mmol/l (non-smokers without vascular complications ≥6 mmol/l) but measurement less than 1/year	5
Cholesterol <5 mmol/l (non-smokers without vascular complications ≥6 mmol/l) and measurement at least 1/year	10
Not treated with ACE-inhibitors despite the presence of microalbuminuria	0
Treated with ACE-inhibitors or ATII-antagonists in the presence of microalbuminuria or microalbuminuria absent but measurement less than 1/year	5
Treated with ACE-inhibitors or ATII-antagonists in the presence of microalbuminuria or microalbuminuria absent and measurement at least 1/year	10
Score range	**0-40**

Analysis

The term 'case-mix' is used to describe the distribution of patient characteristics in different healthcare settings. These characteristics are hypothesized to remain the same if a patient is assigned to another unit of care.[12] As the distribution of such characteristics is not random it may lead to case-mix bias.[4] In this study sex, age, duration of diabetes, macro- and microvascular complications, education, insulin use and quality of life are considered case-mix variables. In the Quality of Care and Outcomes in Type 2 Diabetes study, the risk of developing a cardiovascular event was 89% greater in patients with a score of ≤10 and 43% higher in those with a score between 10 and 20, as compared to those with a score >20. The same cut-off points were used in the present study. To assess differences in baseline measurements between primary and secondary care, the Student's t-test, Mann-Whitney test and χ^2 test, were used where appropriate. A threshold value of at least

one measurement per year was considered to be desirable, whatever physicians' case-mix. Therefore, differences in the process of care between specialities were not adjusted for potential confounding by unequal case mixes. In the case of outcome measurements, multiple regression analysis was performed to account for confounding by case-mix differences between the primary and secondary care setting. Because multiple tests were involved, statistical significance was set at $p<0.01$. In both primary and in secondary care, generalized estimating equations models were used to adjust for clustering at practice level. Analyses were carried out using the statistical package SPSS (version 12.0) for Windows. SAS software (version 8) was used for generalized estimating equations. Analyses were performed for both summary scores: the original QuED score and, the adapted version.

The percentage of missing values per variable varied between 0% and 25.2%; mean 17.6%. Ignoring cases with a missing value may lead to biased results and loss of power.[13,14] Therefore, we imputed missing values using the regression method available in SPSS.

Results

Participants

In total 11 single-handed, 16 duo and three group practices agreed to participate. Reasons for non-participation were a lack of time, a dislike of research projects, a lack of confidence in the outcome of the study and the conviction that the practice performed well and did not need improvement. At the local hospital, all specialists agreed to participate. Overall, 2042 patients gave their informed consent. Of these patients, 1640 were treated in primary care and 402 were cared for at the outpatient clinic (figure 1).

Case-mix

Patients treated by general practitioners were older, had a shorter duration of diabetes and fewer macro- and microvascular complications. Patients cared for at the outpatient clinic were more likely treated with insulin and had lower EuroQol-5D, visual analogue and diabetes health profile scores (table 2).

Process of care

At the outpatient clinic, more patients were annually checked for their HbA1c and in cases of microalbuminuria, more patients were prescribed an ACE-inhibitor or

ATII-antagonist. Measurement of microalbuminuria was performed more often in general practice. After correction for case-mix and clustering, these differences became statistically non-significant (table 3).

Outcome of care

HbA1c percentage in secondary care exceeded that in primary care. In both settings, the percentage of patients that achieved adequate blood pressure control was equal. However, more patients in secondary care attained adequate lipid control). In general, patients were satisfied with their treatment. After correction for case-mix and clustering, differences in mean HbA1c percentage and the percentage of patients with HbA1c<8% reached borderline significance and weak evidence of an association between treatment setting and systolic blood pressure became apparent (tables 4 and 5).

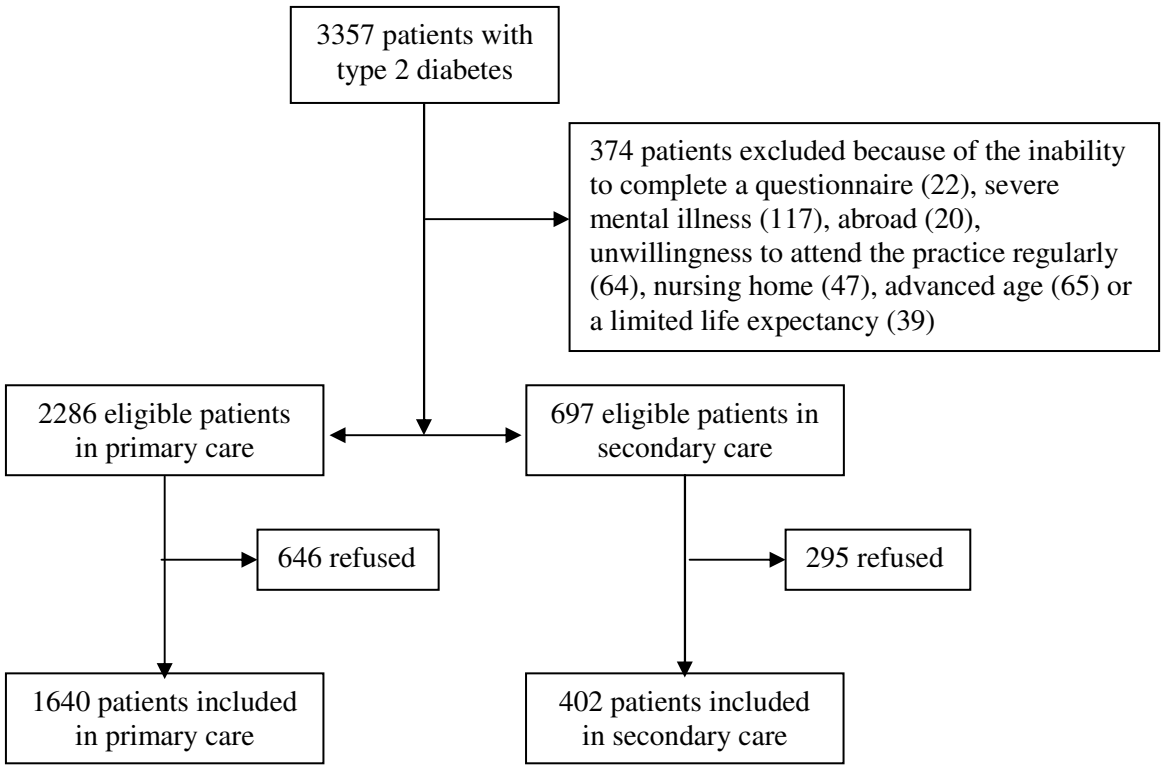

Figure 1 patient's flow sheet

Table 2 Case-mix variables in primary and secondary care

Case-mix	**Primary Care**	**Secondary care**	**P**
Male (%)	48.6	46.0	0.4
Age (yrs)	67.1 ± 11.7	64.1 ± 12.5	<0.001
Primary school and technical school (%)	57.9	54.0	0.2
Duration of diabetes (yrs)	6.6 ± 6.0	11.2 ± 7.7	<0.001
Macrovascular complications (%)	24.3	39.7	<0.001
Microvascular complications (%)	7.3	25.9	<0.001
Insulin use (%)	5.7	65.8	<0.001
EuroQol-5D	0.80 ± 0.21	0.70 ± 0.29	<0.001
EuroQol-VAS	75.3 ± 16.1	68.3 ± 18.3	<0.001
DHP	84.9 ± 9.8	79.5 ±11.1	<0.001

Table 3 Process of care in primary and secondary care

Process	Primary care	Secondary care	Odds ratio (95% ci)				ICC#
			Unadjusted		Full model adjustment*		
HbA1c measurement at least 1/year (%)	83.8	90.5	0.55	(0.38 to 0.78)	0.74	(0.36 to 1.52)	0.055
P value			0.001		0.416		
BP measurement at least 1/ year (%)	56.5	56.4	0.99	(0.80 to 1.24)	1.10	(0.63 to 1.92)	0.152
P value			0.950		0.740		
Lipid measurement at least 1/ year (%)	79.7	79.6	1.001	(0.76 to 1.31)	1.52	(0.91 to 1.30)	0.086
P value			0.992		0.111		
MA measurement at least 1/ year (%)	45.2	34.7	1.56	(1.24 to 1.95)	1.39	(0.74 to 2.61)	0.186
P value			<0.001		0.310		
Prescription of ACE-inhibitors or ATII-antagonists in the presence of microalbuminuria (%)	52.7	62.3	1.48	(1.08 to 2.03)	1.24	(0.77 to 2.01)	0.077
P value			0.014		0.368		

Intra cluster correlation coefficient
* Adjusted for practice level clustering

Table 4 Outcome of care in primary and secondary care

Outcome	Primary care	Secondary care	Difference (95% ci) Unadjusted		Case-mix adjustment*		Full model adjustment**		ICC#
HbA1c (%)	7.1 (1.1)	7.6 (1.2)	-0.51	(-0.64 to -0.39)	-0.27	(-0.44 to -0.11)	-0.28	(-0.51 to -0.05)	0.067
P value			<0.001		0.001		0.016		
BP systolic (mmHg)	145.7 (19.2)	147.7 (21.0)	-2.01	(-4.15 to 0.13)	-2.15	(-4.90 to -0.60)	-3.50	(-6.75 to -0.25)	0.024
P value			0.066		0.127		0.035		
BP diastolic (mmHg)	82.7 (9.2)	79.6 (11.2)	3.05	(2.00 to 4.10)	3.14	(1.78 to 4.50)	1.78	(-0.28 to 3.84)	0.044
P value			<0.001		<0.001		0.090		
Cholesterol (mmol/l)	5.2 (1.0)	5.0 (1.1)	0.21	(0.10 to 0.32)	0.14	(-0.002 to 0.28)	0.02	(-0.19 to 0.24)	0.024
P value			<0.001		0.054		0.827		
BMI	29.4 (5.5)	30.2 (6.9)	-0.82	(-1.45 to -0.19)	-0.33	(-1.12 to 0.47)	-0.42	(-1.41 to 0.58)	0.009
P value			0.011		0.422		0.412		
DTSQ	31.6 (5.2)	30.4 (5.5)	1.23	(0.65 to 1.81)	0.03	(-0.68 to 0.73)	-0.19	(-1.01 to 0.64)	0.037
P value			<0.001		0.939		0.660		

Intra cluster correlation coefficient

* Adjusted for case-mix differences including gender, age, duration of diabetes, micro and macro vascular complications, education, insulin use and quality of life

**Adjusted for case-mix differences and practice level clustering

Table 5 Outcome of care in primary and secondary care

Outcome	Primary care	Secondary care	Odds ratio (95% ci)						ICC#
			Unadjusted		Case-mix adjustment*		Full model adjustment*		
HbA1c <8.0% (%)	82.9	65.6	0.39	(0.31 to 0.50)	0.64	(0.46 to 0.90)	0.63	(0.46 to 0.87)	0.037
P value			<0.001		0.009		0.004		
BP <140/85 mmHg (%)	24.7	25.1	1.03	(0.80 to 1,32)	1.11	(0.79 to 1.54)	0.94	(0.70 to 1.27)	0.011
P value			0.844		0.551		0.710		
Cholesterol <5 mmol/l or <6 mmol/l for non-smokers without vascular complications (%)	41.6	50.5	1.48	(1.19 to 1.85)	1.34	(0.999 to 1.80)	1.21	(0.88 to 1.67)	0.016
P value			<0.001		0.051		0.239		

Intra cluster correlation coefficient

* Adjusted for case-mix differences including gender, age, duration of diabetes, micro and macro vascular complications, education, insulin use and quality of life

**Adjusted for case-mix differences and practice level clustering

Quality Score

The overall quality of diabetes care in primary and secondary care was different. The mean quality of care summary score in general practice was higher (19. 6, SD 8.5 versus 18.1, SD 8.7 points, difference=1.41, 95% CI=0.472 to 2.352, p=0.003) and fewer patients within primary care had a score ≤10 points (21.3 versus 26.5%, OR=0.74, 95% CI=0.573 to 0.946, p=0.017). However, after accounting for case-mix and clustering the difference in quality of care score lost significance (difference=0.18, 95% CI=-0.247 to 0.612 p=0.406). Only a weak association between treatment setting and the percentage of patients with less than 10 points remained (OR=0.66, 95% CI=0.465 to 0.949, p=0.024). A repeated analysis with the original model by the Quality of Care and Outcomes in Type 2 Diabetes study group produced similar results (data not shown.)

Discussion

Summary of main findings

At the outpatient clinic, patients were younger, had more macro- and microvascular complications and perceived a lower quality of life. These case-mix differences are undoubtedly the result of the Dutch health care system, in which primary care physicians are advised to refer their patients with type 2 diabetes only for some well described indications, usually signs of advanced disease. Most differences in outcome measurements between primary and secondary care became non significant after adjusting for both case-mix differences and clustering. However, mean HbA1c and systolic blood pressure in primary care remained significantly lower, and more patients demonstrated an HbA1c<8%.

Study limitations

This study has some limitations. Firstly, general practitioners with a particular interest in diabetes may have been selected. However as approximately half of the primary care physicians in the study region participated, and some of them did not even keep a register of their DM2 patients, it can be assumed those selected were not only those paying special attention to diabetes care. Secondly, as the model used by the Quality of Care and Outcomes in Type 2 Diabetes Study Group was adjusted to the local guidelines, its validity to predict long-term outcomes may have been altered. Since the modifications made in the present study gave rise to even stricter targets, the adjusted model is still able to predict the long-term outcome of diabetes

care. Also, a repeated analysis with the original model produced similar results. Thirdly, baseline measurements in primary and secondary care were performed differently. Therefore, some differences in treatment outcome between general practice and outpatient clinic may be due to differences in data collection. However, as this study only used the most recent data available from the patient records in secondary care, this should not apply. Fourthly, as the present study has been performed in a defined geographic region, it is questionable whether the results of this study can be generalised. The findings of the present study regarding the quality of diabetes care in both general practice and outpatient clinic are in line with those of other studies performed in the Netherlands[15-18] Consequently, the results of this study can be considered representative for the quality of diabetes care in the Netherlands. Finally, the use of a single imputation procedure may have resulted in an underestimation of the standard errors or p-values that were too small.[13] Because it was not possible to demonstrate a significant difference in the overall quality of diabetes care between general practice and outpatient clinic, the results of our study are obviously not hampered by the use of a single imputation procedure

Relationship to the existing literature

The findings of this study are in line with studies performed in different healthcare settings. In both the US and in Italy, differences between specialities became non-significant after adjusting for case-mix differences and physician level clustering.[3,4] Control of cardiovascular risk factors in the Italian study was sub-optimal, as 65% of the patients showed total cholesterol and blood pressure levels above target.[3] These results are in accordance with the present study, as it also found insufficient blood pressure control, and cholesterol levels above target in the majority of the participating patients. A study in 2006 investigating the use of vascular risk-modifying medications for patients with diabetes demonstrated remarkable differences between specialities. Patients treated in secondary care were more likely to receive ACE-inhibitors and ATII-antagonists. Differences between study groups remained after adjusting for case-mix and clustering.[19] After taking case-mix and physician level clustering into account, the present study was unable to reproduce these results.

Implications for future guidelines and clinical practice

Using a slightly adjusted version of the QuED score, this study showed that the overall quality of diabetes care in a single geographic region did not differ significantly between specialities. As patients treated at the outpatient clinic

developed more macro- and microvascular complications despite their younger age, these patients may have a more severe course of diabetes. One might argue that these patients should be treated more aggressively. In that respect it should be kept in mind that in both care settings only one third of the patients showed a QuED score > 20 points, which is related to an important reduction in cardiovascular events.[10]

There is still much room for improvement; treatment should differentiate between patients, not only regarding the setting of their treatment, but also regarding the required intensity of disease management. Future guidelines should take these facts into consideration. The (adapted) summary score can be easily managed, and interpretation is relatively simple. If other studies confirm the results of the original QuED study the QuED score could be recommended on a large scale.

Funding body

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Ethical approval

The medical ethics committee of the University Medical Center Utrecht approved the protocol of the study and all participants gave informed consent.

Competing interest

The authors have stated that there are none.

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4

Implementation of locally adapted guidelines on type 2 diabetes: results of a cluster randomised trial in primary care

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Abstract

Objective: to assess the effects of a facilitator enhanced multifaceted intervention to implement a locally adapted guideline on the shared care for people with type 2 diabetes.

Methods: during one year a cluster-randomised trial was performed in 30 general practices. In the intervention group, nurse facilitators enhanced guideline implementation by analysing barriers to change, introducing structured care, training practice staff and giving performance feedback. Targets for HbA1c%, systolic blood pressure as well as indications for ACE/ARB prescription differed from the national guidelines. In the control group, general practitioners were asked to continue the care for people with diabetes as usually. Generalized estimating equations (GEE) were used to control for the clustered design of the study.

Results: in the intervention group, more people were seen on a three-monthly basis (88% versus 69%, $p<0.001$) and more blood pressure and bodyweight measurements were performed every three months (blood pressure: 83% versus 66%, $p<0.001$ and bodyweight: 78.9% versus 48.5%, $p<0.001$). Apart from a marginal difference in mean cholesterol, differences in HbA1c%, blood pressure, BMI and treatment satisfaction were not significant.

Conclusion: multi-faceted implementation of locally adapted shared care guidelines did improve the process of diabetes care but hardly changed intermediate outcomes. In the short term, local adaptation of shared care guidelines does not improve the cardiovascular risks of people with type 2 diabetes.

Introduction

Clinical practice guidelines are considered effective tools to improve the quality of diabetes care.[1] Their implementation, however, has not been straightforward. It has become evident that passive dissemination of guidelines is largely ineffective and only rarely induces a behavioural change.[2] Successful implementation strategies, therefore, are active and targeted at different levels of care (professional, team, patient and organization).[3] Such strategies must be adequately resourced and include systems for training and evaluation.[4] Recently, a Cochrane review concluded that multifaceted interventions can improve the treatment of people with diabetes, as can organizational interventions that improve the recall and tracking of these people.[5] In general, multi-faceted interventions targeting different barriers to change are more likely to be effective than single interventions.[6] Furthermore,

physician support and feedback by trained facilitators proved to be helpful in improving glycaemic control[7] and appeared to increase the rates of foot and eye examination in general practice.[8] Finally, it has been suggested that end-user involvement in the development and adaptation of national guidelines can result in an increased uptake.[9] A systematic review suggested that the use of a local consensus process was more likely to lead to the effective implementation of clinical guidelines.[10] A more recent study, on the other hand, did not find any additional effect from the local adaptation process itself.[11] Hence, it is questionable whether local adaptation of national guidelines is an essential prerequisite to ensuring improvements in the quality of care.

In an effort to improve the quality of diabetes care and reduce disease related costs, much attention is paid to different models of diabetes care, like shared care, integrated care and disease management. Especially disease management is expected to succeed were other approaches have failed. Systematic reviews support this view[12,13], but recognise important limitations of the original studies, including lack of consensus about what constitutes disease management. In the Netherlands, much attention is paid to the concept of shared care. Physicians, nurses and para-medics are called upon to implement multi-disciplinary shared care guidelines to minimise the risks for patients with chronic diseases. However, randomised controlled trials supporting this view are rare.

We report the results of a multifaceted facilitator enhanced intervention aimed at the implementation of a local guideline on the shared care for people with type 2 diabetes.

Research Design and Methods

The study was carried out in and around Apeldoorn, a city with 150,000 inhabitants in the Netherlands. It was a cluster randomised trial comparing usual care with care according to locally adapted shared care guidelines, taking clustering at a practice level into account.[14] The Medical Ethical Committee of the University Medical Center Utrecht approved the protocol and all participants gave informed consent.

Study participants

We asked all primary care practices in the greater Apeldoorn region (n=70) to participate. In the 30 participating practices, the lists of people diagnosed with

type 2 diabetes were updated prior to the start of the study. For this purpose a computer search was performed using the following terms: ATC code A10 (insulin and oral hypoglycaemic agents), ICPC code T90 (diabetes) and diabetes (text word). Then, the files of all tracked people were checked for the type of diabetes. Only people with type 2 diabetes (n=3357) were considered eligible for the present study. Exclusion criteria were the inability to complete a questionnaire, severe mental illness, unwillingness to attend the practice regularly or a limited life expectancy. As it was our aim to investigate the effect of the implementation of local shared care guidelines in primary care, people being treated at the outpatient clinic of the local hospital were excluded as well.

Randomisation

Participating general practices were randomised into an intervention and control group. Prior to randomisation, practices were divided into groups according to the following criteria: practice type (single-handed, duo or group practice) and presence of a specialised nurse. An independent researcher then carried out a restricted randomisation procedure using a random number table to ensure equal numbers of practices in each group.

Multifaceted interventions

Intervention practices were encouraged to treat people with type 2 diabetes in accordance with the locally adapted shared care guidelines. A working committee of four general practitioners, two internists from the local hospital, three diabetes nurse specialists and 2 dieticians based these guidelines on the national guidelines for the treatment of type 2 diabetes of the Dutch College of General Practitioners.[15] Due to new insights distinct differences arose between both guidelines (box 1). Control group practices were asked to continue to continue the care for people with diabetes in line with the national guidelines.[15]

In the intervention group practices, two nurse specialists interviewed practice staff, analysed barriers to change, discussed means to overcome these barriers and handed out abstracts of the guidelines on plasticized sheets. These nurses, trained as facilitators, visited all intervention practices two times per month for approximately three hours. During these visits, they trained the general practitioners, practice assistants and nurses in the use of the guidelines, encouraged the introduction of structured diabetes care, emphasized the need for three-monthly control and gave assistance in managing people with type 2 diabetes. Performance feedback was

Dutch College of General Practitioners guidelines	**Locally adapted shared care guidelines**
HbA1c > 8.5 % considered poor glycaemic control	**HbA1c > 8 %** considered poor glycaemic control
After diagnosis, all people are treated with **lifestyle intervention**. If necessary, oral hypoglycaemic agents after 3 months	After diagnosis, people with FBG > 15 mmol/l are immediately treated with **lifestyle intervention and oral hypoglycaemic agents.**
Recommended blood pressure < **150**/85	Recommended blood pressure < **140**/85
Patients with life expectancy > 5 years and a 10 years CV risk > **25**%, are treated with statins	Patients with life expectancy > 5 years and a 10 years CV risk > **20**%, are treated with statins
People with micro albuminurea < **50** years are treated with ACE inhibitors	People with micro albuminurea < **60** years are treated with ACE inhibitors or ATII receptor antagonists
No rules for referral back to primary care	**Explicit** rules for referral back to primary care

Box 1 Differences between the guidelines of the Dutch College of General Practitioners and the local shared care guidelines

given six months after the start of the intervention. We used the method described by Kiefe and others to formulate achievable benchmarks of care.[16,17] These benchmarks represent in essence the average performance for the top 10% of the physicians (practices) being assessed.

Measurements

Diabetes care providers examined all participants at the start of the study and approximately one year later at study completion. Demographics, duration of diabetes, smoking habits, co-morbidity and presence of macrovascular or microvascular complications were recorded. Standard operating procedures were used to record weight, height, waist and hip circumference and blood pressure. Fasting blood samples and urine samples were obtained and analyzed at the laboratory of the local hospital. HbA1c% was determined by the Variant II Turbo Haemoglobin Testing System (Bio-Rad Laboratories, Hercules, USA). Plasma glucose, total cholesterol, HDL cholesterol, triglycerides, albumin/creatinin ratio and micro albumen were determined with the Architect ci8200SR (Abbott Park,

Illinois, USA). The health related quality of life was estimated with the EuroQol-5D (range -0.59 - 1, where 1 indicates perfect health) and the validated Dutch version of the disease specific diabetes health profile (DHP) (range 0 - 100, were 100 represents no dysfunction).[18,19] To describe the overall health state of the participants we used the visual analogue scale (VAS) of the EuroQol-5D (range 0 - 100). The satisfaction of the participants with their treatment was measured with the Dutch version of the diabetes treatment satisfaction questionnaire (DTSQ) (range 0 - 36).[20]

All 18 pharmacists in the Apeldoorn region took part in our study. To obtain a complete medication file, we used their files and those of three general practitioners keeping their own pharmacy. We selected the complete medication histories of all participants using hypoglycaemic medication (ATC code A10), or being diagnosed by their general practitioner with type 2 diabetes.

Statistical analysis

Three-monthly measurements of fasting blood glucose (FBG), blood pressure and body weight and the prescription of ATII-antagonists or ACE-inhibitors in case of micro albuminuria were considered to be indicators of the process of care. As primary outcome measure, we used the percentage of people with poor glycaemic control at baseline that achieved an HbA1c of ≤ 8%. Mean HbA1c%, total cholesterol, diastolic and systolic blood pressure, quality of life, and treatment satisfaction were used as secondary outcome measurements. Participants' level of formal education was split into two categories. People who visited primary school only or primary and secondary school at a non-advanced level were considered to have a low level of formal education. All others were regarded as highly educated. Student's t-test and χ^2 test were used where appropriate. All analyses were by intention to treat. Based on literature and clinical reasoning, we identified the following potential confounders: age, gender, level of education, micro and macrovascular complications, insulin use and quality of life. Generalized estimating equations models (GEE's) were used to construct multivariable regression models, whilst controlling for potential confounders and the clustered design of the study. Statistical significance was set at $p<0.05$ two sided. Except for the GEEs, all analyses were carried out using the statistical package SPSS version 12.0 for Windows. We used SAS software version 8 (SAS Institute, Cary, NC) for the GEEs models.

Sample size calculations were based on the assumption that at baseline 30% of the participants would have an HbA1c>8.0%. A sample size of 288 would provide 80 % power to detect a 30 % reduction in the number of these participants. In order to adjust for clustering at practice level we then multiplied this sample size by a design effect of 2.62 (based on an intra-class correlation coefficient of 0.034), thus requiring a total sample size of 817 people with type 2 diabetes in each study group.

Part of the participants had missing values. Ignoring cases with a missing value (complete case analysis) may lead to biased results and loss of power.[21] Therefore, we imputed missing values using the regression method available in SPSS. The imputation was based on the correlation between each variable with missing values and all other variables as estimated from the subjects with complete data.

Results

Participants

In total 11 single-handed, 16 duo and three group practices agreed to participate. Reasons for non-participation were a lack of time, a dislike of research projects, a lack of confidence in the outcome of the study and the conviction that the practice performed well and did not need improvement of diabetes care. In 45 percent of the participating solo practices, specialized nurses were concerned with diabetes care; in the duo and group practices this percentage was 56 and 67 respectively. Overall, 2983 people with type 2 diabetes were eligible. Of these people 2042 gave informed consent. 1640 participants were treated within primary care (figure 1).

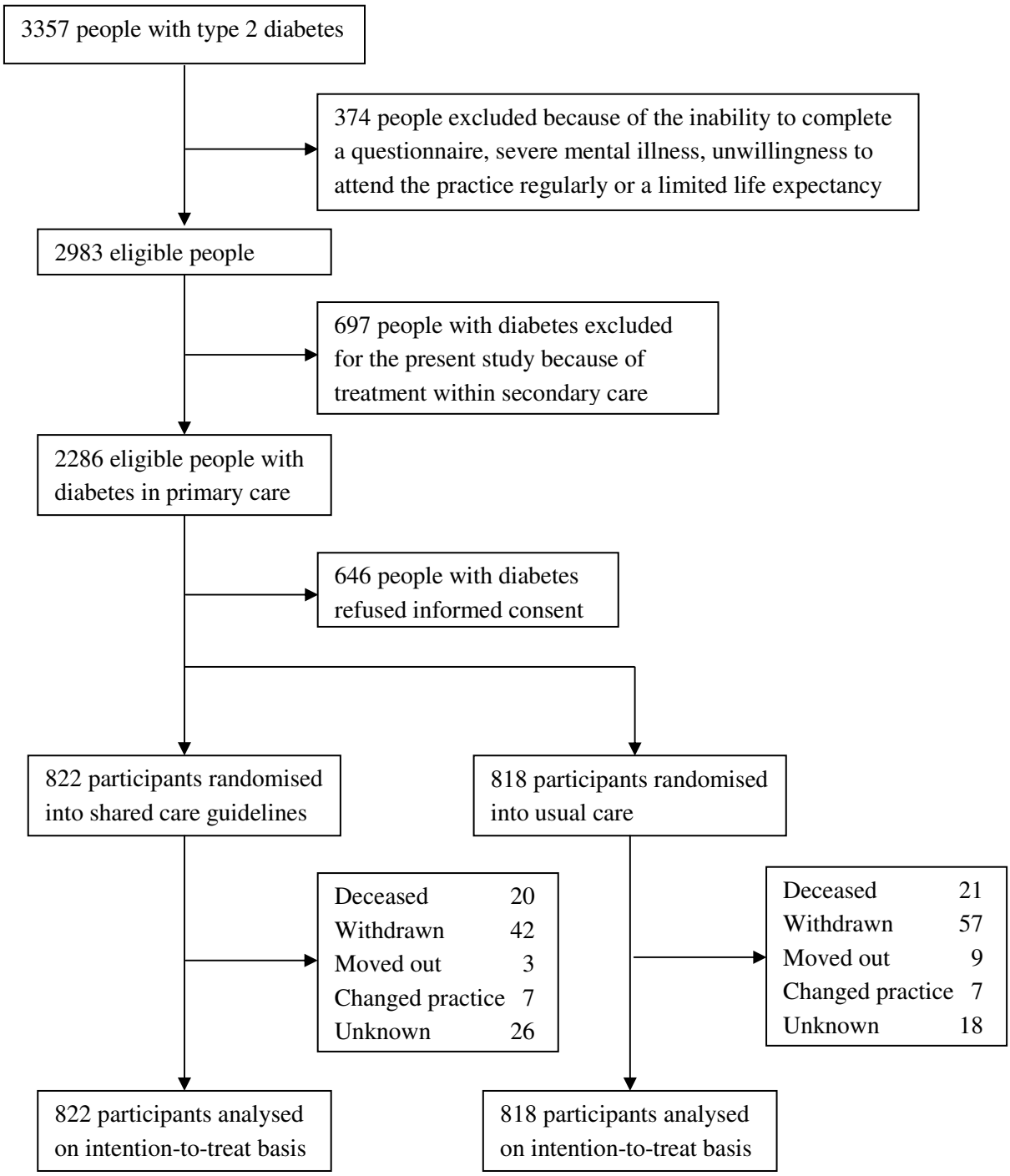

Figure 1 Flow sheet of the sampling process

Baseline characteristics

Except for education and the presence of macrovascular complications, patients' characteristics were highly comparable across study groups. In the intervention group, more participants had a low level of formal education. Controls were more often suffering from macrovascular complications. About 50% of the participating people with type 2 diabetes were men. Mean age of the participants was approximately 67 years (table 1).

Table 1 Patient's characteristics at baseline

	Intervention (sd)	**Control (sd)**
	N=822	N=818
Male (%)	46.8	50.4
Age (yrs)	67.1 (11.4)	67.2 (11.9)
Primary school and technical school (%)	62.8	53.1
Duration of diabetes (yrs)	6.6 (6.0)	6.6 (5.9)
Macrovascular complication (%)	20.6	28.0
Microvascular complications (%)	6.2	8.4
Insulin use (%)	4.0	7.3
HbA1c≤8.0 % (%)	84.7	83.2
Blood pressure<140/85 mmHg (%)	22.5	26.8
Cholesterol≤5 mmol/l (%)	42.2	46.6
HbA1c (%)	7.0 (1.1)	7.1 (1.2)
Systolic blood pressure (mmHG)	145.8 (18.4)	145.7 (20.0)
Diastolic blood pressure (mmHg)	82.5 (9.1)	82.9 (9.3)
Cholesterol (mmol/l)	5.3 (1.0)	5.2 (1.0)
BMI (kg/cm²)	29.7 (5.6)	29.0 (5.3)
EuroQol-5D	0.81 (0.20)	0.79 (0.22)
EuroQol-VAS	76.3 (16.0)	74.3 (16.2)
DHP	85.4 (9.4)	84.4 (10.2)
DTSQ	31.8 (5.3)	31.5 (5.2)

Process and outcome of care

After one year, process measures differed significantly between the intervention and the control group, except for the prescription rate of angiotensine blocking agents and ACE-inhibitors. These differences remained significant after we controlled for age, gender, level of education, micro and macrovascular complications, insulin use, quality of life and the clustered design of the study (table 2).

Table 2 Process measures in intervention and control group

	Intervention (sd)	Control (sd)	P	P*	P**
FBG every 3 months (%)	87.8	68.6	<0.001	<0.001	<0.001
Blood pressure every 3 months (%)	82.5	65.4	<0.001	<0.001	<0.01
Bodyweight every 3 months (%)	78.9	48.5	<0.001	<0.001	<0.001
ACE-inhibitor or ARB prescribed according to guideline (%)	67.4	65.1	0.7	0.4	0.6

P: unadjusted
P: controlled for age, gender, level of education, micro and macrovascular complications, insulin use and quality of life*
*P**: controlled for age, gender, level of education, micro and macrovascular complications, insulin use, quality of life and clustering at practice level*

In the intervention group, more initially poorly controlled participants reached adequate glycaemic control at the end of the study (70% versus 58%, p<0.05). This difference became non-significant after controlling for baseline value, potential confounders and clustering at practice level. After one year, we were unable to demonstrate significant differences in HbA1c, blood pressure, BMI and treatment satisfaction between both study groups. There was, however, a small but statistically significant difference in mean cholesterol after the implementation of the locally adapted guidelines. This difference remained statistically significant after we controlled for baseline value, potential confounders and the clustered study design. At study completion, the percentages of initially poorly controlled people that reached adequate blood pressure or lipid control were equal across study groups (tables 3 and 4).

Barriers

The barriers most commonly identified were: lack of time, lack of knowledge on the content of the guideline, lack of financial incentives, lack of motivation, and reluctance to prescribe multiple drug regimens. Training practice staff on the job, organising educational meetings and making comparisons with peers levelled these barriers. Furthermore, the nurses gave advice on insulin type and dosage in people with poor glycaemic control.

Table 3 Outcome measures in intervention and control group, all patients

	Intervention (sd)	Control (sd)	P	P*	P**
	N=822	N=818			
HbA1c≤8.0 % (%)	90.1	86.8	<0.05	0.07	0.1
Blood pressure<140/85 mmHg (%)	23.1	24.2	0.6	0.6	0.7
Cholesterol≤5 mmol/l (%)	46.4	46.0	0.9	0.3	0.3
BMI≤27 (%)	33.0	36.9	0.1	0.9	0.9
HbA1c (%)	6.9 (0.9)	7.0 (1.0)	<0.01	<0.05	0.1
Systolic blood pressure (mmHG)	146.3 (18.7)	146.8 (19.1)	0.6	0.4	0.9
Diastolic blood pressure (mmHg)	81.9 (9.3)	82.4 (9.7)	0.3	0.2	0.5
Cholesterol (mmol/l)	5.1 (1.0)	5.2 (1.0)	0.2	<0.01	<0.05
BMI (kg/cm²)	29.6 (5.1)	29.0 (5.1)	<0.05	0.8	0.8
DTSQ	32.4 (4.3)	32.1 (4.4)	0.1	0.3	0.3

P: unadjusted
P: controlled for baseline value, age, gender, level of education, micro and macrovascular complications, insulin use and quality of life*
*P**: controlled for baseline value, age, gender, level of education, micro and macrovascular complications, insulin use, quality of life and clustering at practice level*

Table 4 Percentages of initially poorly controlled people with type 2 diabetes that reached adequate control

	Intervention (sd)	Control (sd)	P	P*	P**
	N=125	N=139			
HbA1c≤8.0 % (%)	70.4	57.6	<0.05	0.1	0.2
	N=633	N=605			
Blood pressure<140/85 mmHg (%)	15.5	16.4	0.7	0.9	0.9
	N=472	N=441			
Cholesterol≤5 mmol/l (%)	29.7	26.3	0.3	0.2	0.2
	N=540	N=501			
BMI≤27 (%)	9.3	8.8	0.8	0.6	0.6

P: unadjusted
P: controlled for baseline value, age, gender, level of education, micro and macrovascular complications, insulin use and quality of life*
*P**: controlled for baseline value, age, gender, level of education, micro and macrovascular complications, insulin use, quality of life and clustering at practice level*

Referrals

Nearly 3% of all participants were referred to the outpatient's clinic to receive secondary diabetes care (intervention group 2.8%, control group 2.9%; p=0.9). From the outpatient clinic of the local hospital, many people were referred back to primary care (24.7% versus 23.3%; p=0.7).

Discussion

The facilitator enhanced implementation of a locally adapted guideline on type 2 diabetes led to a significant increase in the number of people with type 2 diabetes that were seen on a three-monthly basis. During the intervention, bodyweights and blood pressures of the participants were also registered more often. At the end of the study, there were no significant differences in the percentages of people that reached adequate control of their diabetes, blood pressure or BMI. Mean cholesterol improved 0.1mmol/l, while other cardiovascular risk factors remained unchanged.

Some limitations of this study need to be discussed. Firstly, as people under secondary care were excluded from this study, we are not informed about the effects of the implementation of the guidelines on the quality of secondary diabetes care. However, as randomisation took place within primary care, secondary care physicians were treating participants from both study groups and therefore had knowledge on the content of the guidelines. It would have been very difficult for these specialists to treat half of the participants in accordance with the local guidelines and the other half as usually. It is more likely that they would have treated all people with type 2 diabetes more ore less in accordance with the local guidelines. This would most certainly have diluted the effect of our intervention. Secondly, baseline measurements were performed in the intervention as well as the control group. These measurements necessitated the recall and registration of all people with type 2 diabetes. As registration and recall are fundamental to the quality of diabetes care, their introduction may have enhanced the quality of care in the control practices. Possibly, this strategy reduced the contrast between the intervention and the control group and thus the potential to detect a positive effect of the intervention. Thirdly, when selecting people we may have missed those receiving dietary treatment only. However, as we scrutinised the medical records not only for ATC code A10 but also for ICPC code T90 and the text word diabetes, we are confident that most patients on a diet were labelled as having diabetes. Furthermore, the percentage of patients on a diet in our study was 20 %. This

percentage is in line with the percentages found in several other Dutch studies.[22-24] Fourthly, the sample size calculation of our study was based on the assumption that about 30% of the participants would have an HbA1c of >8%.[22] At study completion, participants´ glycaemic control proved to be much better than expected. Therefore, our study might have been hampered by a lack of power. Finally, the use of a single imputation procedure may have resulted in an underestimation of the standard errors or too small p-values.[25]

The results of this study are in line with recent publications. Most large-scale quality improvement initiatives show only modest improvements in some process measures, but fail to demonstrate better intermediate or end-stage outcomes.[26] This may be illustrated by a recent study on diabetes shared care, a large scale controlled study on the effects of the Health Disparities Collaborative and a recent study on the impact of a quality improvement intervention on the quality of diabetes care at primary care clinics.[27-29] Notwithstanding, significant improvements in diabetes care delivery none or only minor improvements in intermediate outcomes were found. A Dutch study produced more optimistic results. After the introduction of structured shared care with task delegation to nurses, significant improvements in the process parameters and achieved target values at the individual patient level could be demonstrated.[24] However, as this was a non-randomised study, the results can only be indicative. Multiple studies have stressed the importance of local tailoring of an international or national guideline.[9,10,30-32] Local adaptation has been described as a key element in guideline implementation. However, randomised trials supporting this view are sparse. One randomised trial found significant changes in knowledge, attitude and reported practice as a result of disseminating guidelines, but it did not find any additional effect from the local adaptation process itself.[11] Our findings are in line with these results. As it was our aim to evaluate the effect of a locally adapted guideline under the best possible circumstances we thought it unwise to enhance usual care by employing nurse facilitators in control group practices. Therefore, these facilitators gave attention to intervention group practices only. Given the fact that we were unable to demonstrate significant differences in both primary and secondary outcomes of our study, it is unlikely that local adaptation under less optimal circumstances, will improve the intermediate outcomes of diabetes care.

One may wonder why our multi-faceted intervention did not induce any improvement in the cardiovascular risk factors. A Danish study into structured

personal diabetes care is a rare example of a randomised controlled trial showing a significant improvement in blood pressure at study completion.[33] This study lasted for six years, suggesting that a better outcome may follow an improved process of care over time. Clearly, the outcome of care is highly influenced by the ability of physicians to adjust the patients' regimen in time. Grant and others demonstrated that although the testing rates for HbA1c, blood pressure and total cholesterol in a national sample of U.S. academic medical centres were very high, only 10.0% of this cohort met recommended goals for all three risk factors.[34] Apparently, high rates of risk factor testing did not necessarily translate to effective metabolic control. A recent Canadian study confirmed these results: less than one-half of the people with high HbA1c levels had intensification of their medications, regardless of the specialty of their physician.[35] Failure of health care providers to initiate or intensify therapy when indicated has been called clinical inertia.[36] Clinical inertia seems to be wide spread and is probably a major barrier to better diabetes care. Therefore, the results of our study may be explained, at least partially, by the failure to intensify therapy appropriately. Implementation of diabetes guidelines is likely to be more effective if energy is spent to overcome clinical inertia instead of local adaptation of nationally agreed target values, prescription rules and referral indications.

Declaration

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Conflicts of interest: none

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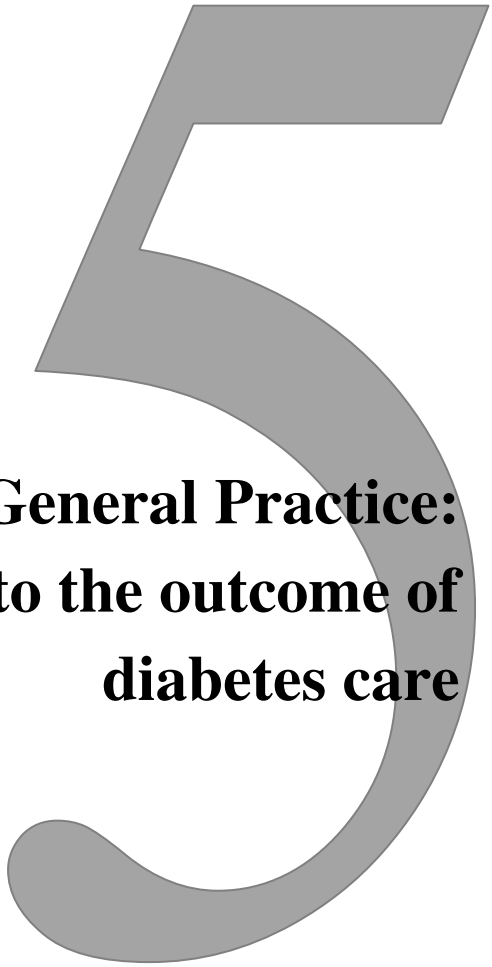

Clinical Inertia in General Practice: widespread and related to the outcome of diabetes care

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Family Practice (in revision)

Abstract

Background and aims: clinical inertia is considered a major barrier to better diabetes care. We assessed its prevalence, predictors and associations with achieved levels of HbA1c, blood pressure and cholesterol.

Materials and Methods: we used the baseline and follow-up data of a RCT that compared usual care with care in line with a locally adapted national guideline. Duration of this study was one year. It took place in the Netherlands and involved 30 general practices and 1283 patients. Randomisation was at practice level. Treatment targets differed between study groups (intervention group: HbA1c $\leq$ 8.0% and blood pressure <140/85 and controls: HbA1c $\leq$ 8.5% and blood pressure < 150/85). Clinical inertia was defined as the failure to intensify therapy when indicated. A complete medication profile of all participating patients was obtained. Clustering at practice level was controlled for.

Results: in the intervention and control group, the percentages of patients with poor diabetes or lipid control that did not receive treatment intensification were 45 and 90 percent approximately. More control group patients with blood pressure levels above target did not receive treatment intensification (72.7% versus 63.3%, $p<0.05$). In poorly controlled hypertensive patients, inertia was associated with the height of systolic blood pressure at baseline (adjusted OR 0.98, 95% CI 0.98-0.99) and the frequency of blood pressure control (adjusted OR 0.89, 95% CI 0.81-0.99). If a practice nurse managed these patients, clinical inertia was less common (adjusted OR 0.12, 95% CI 0.02-0.91). In both study groups, cholesterol decreased significantly more in patients who received proper treatment intensification.

Conclusion: general practitioners were more inclined to control blood glucose levels than blood pressure or cholesterol levels. Inertia in response to poorly controlled high blood pressure was less common if nurses assisted general practitioners.

Introduction

Clinical trials have provided evidence that tight control of glycated haemoglobin, blood pressure and dyslipidemia decreases the risk of developing diabetes related macro- and microvascular complications and cardiovascular death.[1-6] In line with these findings, diabetes guidelines have set ambitious treatment goals for HbA1c, blood pressure and cholesterol levels.[7,8] Clinical guidelines may improve the quality of diabetes care and ensure the translation of evidence into daily practice.[9] However, a treatment gap still exists when best practice is compared with usual

care.[10-13] In part, this discordance may be a consequence of physicians' inability to adjust their medical regimen in time.[11,14] This failure to initiate or intensify therapy when indicated has been called clinical inertia.[15] It has been attributed to overestimation of care provided, use of "soft" reasons to avoid intensification of therapy and lack of education, training and practice organisation.[15] Although some progress has been made, our understanding of clinical inertia is still far from complete. Therefore, more attention should be devoted to understanding and ameliorating factors that contribute to clinical inertia.[16]

We performed a randomised controlled trial aimed at the implementation of a local guideline on the shared care for patients with type 2 diabetes. After one year there was proof of intensified diabetes care, but we were unable to show significant differences in HbA1c, blood pressure or BMI between the intervention and control group. Neither could we demonstrate a difference in the percentage of patients being treated to target.[17] We hypothesised that these results were at least partially a consequence of clinical inertia. To test this hypothesis we investigated the occurrence of clinical inertia in the intervention and control group and the relationship between inertia and the outcome of diabetes care. Furthermore, we studied possible predictors of clinical inertia.

Research Design and Methods

A cluster-randomised trial was carried out near Apeldoorn, a city with 150,000 inhabitants in the Netherlands. Participating practices were randomised to treat their patients either in accordance with local guidelines or in line with the 1999 guidelines for the treatment of type 2 diabetes of the Dutch College of General Practitioners.[18] In the local guidelines, stricter targets were agreed on for satisfactory glycaemic control (HbA1c $\leq$ 8% versus $\leq$ 8.5%) and adequate blood pressure control (BP < 140/85 mmHg versus < 150/85 mmHg). In both study groups, patients' total cholesterol levels should be $\leq$ 5.0 mmol/l (non-smokers without vascular complications $\leq$ 6 mmol/l). Furthermore, thiazolidinediones were recommended by the local guidelines if metformin was not tolerated, whereas these blood glucose lowering agents were not mentioned by the 1999 guidelines of the College.

Study Participants

All general practices (n=70) in the greater Apeldoorn region were asked to participate in the trial. All patients with type 2 diabetes on the lists of the participating practices were considered eligible. Exclusion criteria were the inability to complete a questionnaire, severe mental illness, unwillingness to attend the practice regularly and a limited life expectancy. Patients taking insulin at baseline were excluded for the present study, because we were unable to monitor changes in their insulin regimen. As it was our aim to investigate clinical inertia in general practice, patients being treated in the secondary care setting were excluded also. All 18 pharmacists in the Apeldoorn region took part in the study.

Randomisation

Participating general practices were randomised into an intervention and control group. Prior to randomisation, practices were divided into groups according to the following criteria: practice type (single-handed, duo or group practice) and presence of a specialised nurse. An independent researcher then carried out a restricted randomisation procedure using a random number table to ensure equal numbers of practices in each group.

Multifaceted interventions

Details on the intervention have been reported elsewhere[17] Briefly, in the intervention group practices, two nurse specialists interviewed practice staff, analysed barriers to change, discussed means to overcome these barriers and trained general practitioners, practice assistants and nurses in the use of the guidelines. Furthermore, they encouraged the introduction of structured diabetes care, emphasized the need for three-monthly control and gave assistance in managing people with type 2 diabetes. Practices in the control group were asked to continue the care for their patients with diabetes as usually.

Measurements

At baseline and about one year after the start of the trial, general practitioners and practice nurses examined all participating patients and recorded their demographics, duration of diabetes, smoking habits, co-morbidity, level of formal education and presence of macrovascular or microvascular complications. Fasting blood samples and urine samples were obtained and analysed at the local laboratory. HbA1c was determined by the Variant II Turbo Hemoglobin Testing System (Bio-Rad). Plasma

glucose, total cholesterol, HDL cholesterol, triglycerides, albumin/creatinin ratio and micro albumin were determined with the Architect ci8200SR (Abbott).

The electronic records of all 18 pharmacists and those of three general practitioners having their own pharmacy were used to obtain a detailed medication profile of all patients using blood glucose lowering medication (ATC code A10), or being diagnosed by their general practitioner with diabetes. Subsequently, these profiles were matched with our research data.

Prior to the start of the study general practitioners completed a questionnaire about different aspects of their practice, including number of enlisted patients, percentage of patients diagnosed with type 2 diabetes, location of the practice, practice type (solo, duo, group practice), presence of a practice nurse, role of the practice assistant (participating versus non-participating in diabetes care), involvement of the general practitioner in diabetes care, gender and age of the general practitioner and length of his/her professional career.

Clinical Inertia and Intensification of Therapy

In line with current views, clinical inertia was defined as the failure to intensify therapy when indicated.[15] In the intervention group, adjustment of drug therapy was required in patients with HbA1c levels > 8.0%, blood pressure ≥ 140/85 mmHg or total cholesterol > 5 mmol/ (> 6 mmol/l for non-smoking patients without microvascular or macrovascular complications). In the control group, intensification of therapy was indicated in patients with HbA1c levels > 8.5%, blood pressure ≥ 150/85 mmHg or total cholesterol > 5 mmol/l (> 6 mmol/l for non-smoking patients without microvascular or macrovascular complications). It should be kept in mind that both, the shared care guidelines and the guidelines of the Dutch College state that HbA1c should be < 7.0% whereas HbA1c between 7.0% and 8. 0% (8.5%) is acceptable. Glucose lowering drugs were categorised into three categories (metformin, sulfonylurea and thiazolidinediones), anti-hypertensive drugs into six (diuretics, beta blockers, calcium channel blockers, ACE inhibitors, AT2 antagonists and central working agents) and lipid lowering drugs into one (statins). For each patient at baseline and after six months, the defined daily dosages were determined of each of the drug categories mentioned above. By comparing the dosages used at the start of the study with those prescribed six months later, we established whether treatment had been intensified. Intensification of therapy was defined as an increase in the number of drug classes, increased dosage of at least

one medication, or a switch to another medication in a different drug class. A switch to medication in the same therapeutic class was only regarded as intensification of therapy if the defined daily dose of the new drug represented a higher bioequivalent dose compared with the previous agent. Patients receiving three maximally dosed medications for hypertension or two maximally dosed blood glucose lowering drugs and those receiving the maximal dose of a statin were classified as receiving maximal therapy.

Statistical Analysis

Patients' level of formal education was split into two categories. Patients who visited primary school only or both, primary school and secondary school at a non-advanced level were considered to have a low level of formal education. All others were regarded to be highly educated. For comparison of continuous and categorical variables, student's t-test and χ^2 test were used when appropriate. In an univariate analysis, we explored possible predictors of clinical inertia, including gender, age, duration of diabetes, education, microvascular and macrovascular complications, HbA1c% at baseline, systolic and diastolic blood pressure levels at baseline, total cholesterol level at baseline, the percentage of patients with an HbA1c% above target, the percentage of patients with a poorly controlled hypertension, and the percentage of patients with a poor lipid control. Significantly associated variables were entered into multivariable logistic regression models to determine adjusted odds ratios for predictors of clinical inertia. We constructed separate models for the failure to intensify blood glucose lowering, anti-hypertensive and cholesterol lowering treatment in the intervention as well as the control group, and in the group consisting of all poorly controlled patients from both study groups. The relationship between clinical inertia and practice related factors was analysed on practice level instead of patient level. After gradually increasing the cut-off level, it became apparent that best separation into two groups appeared at a level of 60%. Therefore, if in a practice more than 60% of the participating patients did not receive intensification of treatment, this practice was considered clinically inert. Generalized Estimating Equations were used to construct multivariable regression models to control for the clustered design of the study. Except for the GEE's, all analyses were carried out using the statistical package SPSS version 12.0 for Windows. We used SAS software version 8 (SAS Institute, Cary, NC) for the Generalized Estimating Equations models.

The number of missing values per variable varied between 0% and 25.2%; mean 17.6%. Ignoring cases with a missing value may lead to biased results and loss of power.[19] Therefore, we imputed missing values using the regression method available in SPSS. The imputation was based on the correlation between each variable with missing values and all other variables as estimated from the complete subjects.

Results

Participants

In total 11 single-handed, 16 duo and three group practices agreed to participate. Reasons for non-participation were lack of time, dislike of research projects, a lack of confidence in the outcome of the study and the conviction that the practice performed well and did not need enhancement of diabetes care. Overall, 2286 patients were eligible for the trial and 1569 patients gave informed consent. Of these 1283 were included in the present study (figure 1).

Baseline characteristics

In the intervention group, more patients had a low level of formal education and fewer patients were suffering from macrovascular complications. Almost 17% of the intervention group patients and 8.6% of the controls met the criteria for poor diabetes control. In both study groups poor blood pressure control and total cholesterol levels above target were highly prevalent (table 1).

General practitioners managing intervention group practices were younger and had more patients on their lists. In control group practices, more practice assistants were involved in the care for patients with type 2 diabetes (table 2).

Clinical inertia

The percentage of patients with poorly controlled diabetes who did not receive appropriate treatment intensification did not differ significantly between the intervention and control group (42.9% versus 46.4%, p=0.7). The same applied to the percentage of patients with cholesterol levels above target (89.8% versus 92.8%, p=0.2). There was a significant difference in the percentage of patients with a poorly controlled high blood pressure who did not receive treatment intensification between the intervention and control group (63.3% versus 72.7%, p<0.01).

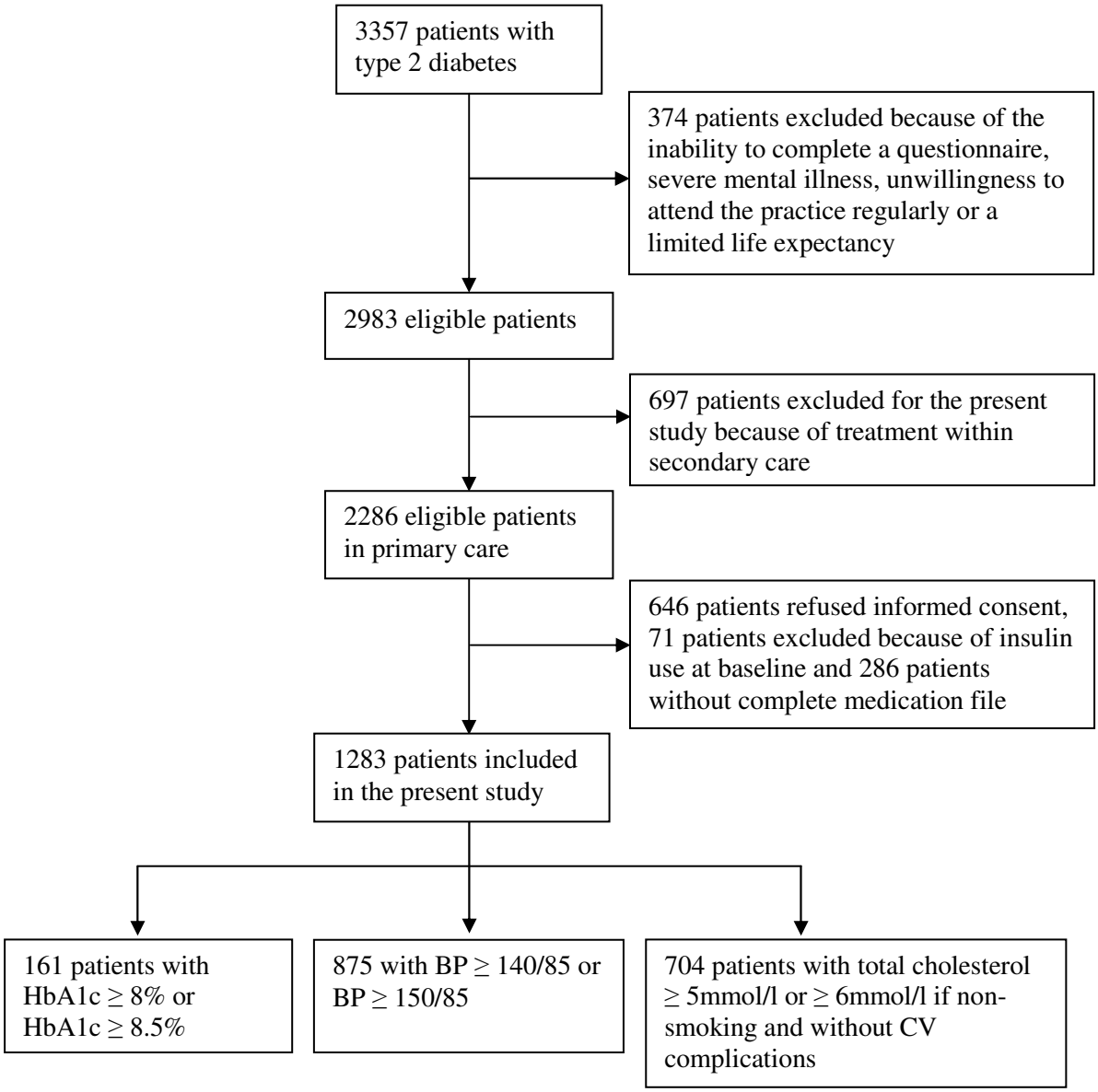

Figure 1 Flow of patients in the study

Using a 60% cut-off point, 35.3% of the participating intervention group practices were clinically inert regarding blood glucose lowering treatment. The same applied to 64.7% and 94.1% of the practices with regard to blood pressure and cholesterol lowering treatments. In the control group these percentages were 30.0%, 85.0% and 100% respectively. All differences between study groups were not significant.
In the intervention group, patients with poorly controlled diabetes and a high level of formal education were more likely to be confronted with clinical inertia (adjusted OR 2.17, 95% CI 1.03-5.04). In the control group, the failure to intensify treatment with blood glucose lowering drugs was associated with HbA1c% at baseline

Table 1 Patient characteristics at baseline

	Intervention (sd)	**Control (sd)**
	N=629	N=654
Male (%)	45.9	51.8
Age (yrs)	66.6 (11.2)	66.9 (11.6)
Low level of education (%)	63.1	53.1
Duration of diabetes (yrs)	6.6 (6.0)	6.5 (6.0)
Macrovascular complication (%)	19.2	26.6
Microvascular complications (%)	6.0	8.3
Poorly controlled diabetes* (HbA1c>8%) (%)	16.7	
Poorly controlled diabetes** (HbA1c>8.5%) (%)		8.6
Poorly controlled hypertension* (BP≥140/85) (%)	75.8	
Poorly controlled hypertension** (BP≥150/85) (%)		60.9
Poorly controlled total cholesterol*** (cholesterol>5.0mmol/l, non-smokers without vascular complications ≤ 6 mmol/l) (%)	57.1	52.8
HbA1c (%)	7.1 (1.1)	7.2 (1.1)
Systolic blood pressure (mmHg)	145.7 (18.9)	145.2 (19.6)
Diastolic blood pressure (mmHg)	82.5 (9.0)	82.7 (9.3)
Cholesterol (mmol/l)	5.2 (1.0)	5.2 (1.0)

** In line with local guidelines, ** in line with the guideline of the Dutch College of General Practitioners, *** in line with both guidelines*

(adjusted OR 0.44, 95% CI 0.25-0.75). In the group consisting of all poorly controlled patients from both study groups, there were no significant associations between clinical inertia and any of the tested factors

Factors associated with clinical inertia in response to poor blood pressure control

In the intervention group, there was a positive association between physicians' failure to intensify anti-hypertensive treatment and the height of systolic blood pressure at baseline (adjusted OR 0.99, 95% CI 0.98-0.99). In the control group, inertia was related to the frequency of blood pressure control visits (adjusted OR 0.83, 95% CI 0.74-0.93). In the group consisting of all poorly controlled patients, clinical inertia was associated with the frequency of blood pressure control visits (adjusted OR 0.89, 95% CI 0.81-0.99), and the height of systolic (adjusted OR 0.98, 95% CI 0.98-0.99) and diastolic blood pressure at baseline (adjusted OR 0.98, 95% CI 0.96-0.99).

Table 2 Practice characteristics at baseline

	Intervention (sd)	**Control (sd)**
	N=17	N=20
Practice holder		
Male (%)	70.6	80.0
Age (yrs)	43.8 (8.2)	49.2 (6.8)
Duration of professional career (yrs)	12.4 (9.2)	16.4 (8.1)
Part time (%)	47.1	50.0
Practice		
Enlisted patients (number)	3281 (1045)	2814 (788)
Patients > 55 years of age per practice (number)	691 (325)	688 (263)
Patients diagnosed with type 2 diabetes (number)	71 (34)	70 (30)
Solo or duo practice (%)	70.6	80.0
GP's per practice (number)	1.9 (0.8)	1.6 (0.5)
Presence of practice nurse (%)	35.0	52.9
Practice assistant participating in diabetes care (%)	35.3	60.0
Initiation of insulin treatment in own practice (%)	43.8	40.0

Factors associated with clinical inertia in response to poor diabetes control

Factors associated with clinical inertia in response to poor cholesterol control

No significant relationships between clinical inertia in response to poorly controlled hypercholesterolemia and any of the tested factors were found.

Practice related factors associated with clinical inertia

There were no significant associations between any of the investigated practice related factors and the failure to intensify treatment with blood glucose lowering drugs or lipid lowering drugs. In the group consisting of all participating practices, clinical inertia in response to poor blood pressure control was less common if a practice nurse was actively involved in the care for patients with diabetes (adjusted OR 0.12, CI 0.02-0.91). We were unable to demonstrate this finding in the intervention or control group separately.

Table 3 Intervention group. Decrease in HbA1c%, blood pressure and total cholesterol in poorly controlled patients.

	Confronted with inertia during study		Not confronted with inertia during study		Decrease between baseline and end of study		P*
	Baseline (sd)	End of study (sd)	Baseline (sd)	End of study (sd)	Confronted	Not confronted	
	N=45		N=60				
HbA1c %	8.9 (1.3)	7.6 (1.2)	8.8 (0.8)	7.5 (1.2)	1.3 (1.8)	1.3 (1.3)	0.7
Systolic blood pressure	N=272		N=154				
mmHg	153 (14)	150 (17)	158 (15)	153 (18)	4 (18)	5 (19)	0.6
Diastolic blood pressure	N=168		N=108				
mmHg	90 (6)	85 (9)	91 (5)	86 (8)	5 (10)	5 (9)	0.3
	N=316		N=36				
Cholesterol mmol/l	5.9 (0.7)	5.6 (0.9)	5.8 (0.6)	4.8 (0.9)	0.3 (0.9)	1.1 (1.1)	<0.001

** Adjusted for baseline value and clustering at practice level*

Table 4 Control group. Decrease in HbA1c%, blood pressure and total cholesterol in poorly controlled patients.

	Confronted with inertia during study		Not confronted with inertia during study		Decrease between baseline and end of study		P*
	Baseline (sd)	End of study (sd)	Baseline (sd)	End of study (sd)	Confronted	Not confronted	
	N=26		N=30				
HbA1c %	9.3 (0.7)	8.1 (1.2)	10.0 (1.4)	8.4 (1.5)	1.2 (1.4)	1.6 (1.4)	0.1
Systolic blood pressure	N=193		N=82				
mmHg	162 (14)	155 (19)	170 (14)	155 (18)	7 (21)	12 (21)	0.5
Diastolic blood pressure	N=206		N=86				
mmHg	90 (5)	86 (9)	93 (7)	86 (9)	4 (9)	7 (10)	0.2
	N=310		N=24				
Cholesterol mmol/l	5.9 (0.7)	5.7 (1.0)	5.9 (0.7)	5.0 (1.0)	0.2 (1.0)	0.8 (1.1)	<0.01

** Adjusted for baseline value and clustering at practice level*

Clinical inertia and the outcomes of diabetes care

We were unable to demonstrate significant differences in mean HbA1c% and blood pressure levels between poorly controlled patients who were confronted with clinical inertia and those receiving appropriate treatment intensification. However, total cholesterol decreased significantly more in patients who received appropriate intensification of treatment (tables 3 and 4).

Discussion

This study confirmed that clinical inertia is widespread. The majority of the patients with a poorly controlled hypertension or cholesterol levels above target and about 45% of the patients with poor glycaemic control did not receive intensification of treatment. In the control group, significantly more patients with blood pressure levels above target were confronted with inertia. However, as we are not informed about the prevalence of clinical inertia prior to the start of the study, this result may not be attributed unambiguously to the successful implementation of the locally adapted guideline in the intervention group. Amongst diabetes patients with poor blood pressure control those with more severe systolic or diastolic hypertension and those with more frequent blood pressure control visits were less likely to be insufficiently treated, suggesting that general practitioners tend to treat at least those patients with the highest blood pressures. Of all investigated practice related factors, only the presence of a practice nurse was associated with more appropriate intensification of anti-hypertensive therapy. This finding is striking, because at present there is only little evidence that task delegation to nurses improves blood pressure control.[20] We were unable to demonstrate differences in HbA1c% and blood pressure levels between patients who received proper treatment intensification and those who did not. These results may be surprising, but are in line with previous studies. Possibly some stronger but unmeasured factors are operating to prevent an association between inertia, achieved HbA1c percentages and blood pressure levels. However, in patients with cholesterol levels above target, the failure to intensify treatment was associated with a significantly smaller decrease of total cholesterol levels.

Some of the limitations of this study need to be discussed. Firstly, as practices participated voluntarily, general practitioners might have been selected with a particular interest in diabetes. Therefore we may have underestimated the prevalence of clinical inertia. Secondly, as we were unable to monitor changes in

daily insulin dose, we could not verify whether patients already on insulin were treated adequately. Therefore, the results of this study are not applicable to these patients. Thirdly, we may have overestimated clinical inertia because our data did not permit to take into account some forms of treatment intensification, like increasing the dose of a medication the patient has already a supply of. However, as in the Netherlands by law, only a three-month supply of medications can be dispended and our follow-up was six months it is unlikely that many new, higher-dosed prescriptions were not accounted for. Fourthly, as we were not informed on the reasons for the lack of providers' response to elevated HbA1c%, blood pressure or cholesterol levels, clinical inertia may have been overestimated. If, for example, treatment was not intensified after taking patients' preferences into account, it is hardly justified to call this clinical inertia. After all, not adhering to a guideline after thorough discussion with a patient may well be an example of high quality care.[21,22] However, given the large percentages of inertia found in the present study, it is unlikely that these percentages were mainly a consequence of good clinical practice. One of the strengths of our study is ascertainment of drug coverage: we had complete knowledge on the prescribed medications, as all pharmacies in the greater Apeldoorn region participated. Furthermore, our study was conducted among insured patients who had no financial barriers to care. This design helps to isolate the relationship between clinical inertia and all predictors investigated but may limit generalisability to other populations.

The frequency of clinical inertia in our study was comparable with that found in previous studies. It should be kept in mind that most studies on clinical inertia were performed in the United States. Inertia occurred in 68% of the visits made by Veteran Administration patients with an HbA1c > 8% over 16 months.[23] In an academic medical centre, the failure to initiate or intensify pharmaceutical therapy among diabetes patients with poor glycaemic, blood pressure or cholesterol control, was equally high.[24] A recent study from Kaiser Permanente showed more optimistic results. A total of 66% of 48,568 patients with poor control of HbA1c experienced intensification of therapy within six months of observation. The same applied to 64% of patients with a poorly controlled systolic blood pressure and to 56% of those with LDL-cholesterol above target.[25]

In the present study clinical inertia in response to poor diabetes control was associated with patients' level of education and HbA1c at baseline. These findings are in line with the results of prior studies.[11,25] We could not find an association between the presence of a poorly controlled hypertension or hypercholesterolemia

and the failure to intensify blood glucose lowering drugs. These results are in contrast with those of the study from Kaiser Permanente, in which co-occurrence of one ore more of the three tested cardiovascular risk factors was independently associated with appropriate care.[25]

A recent study on the relationship between inertia and the outcome of diabetes care made clear that on average a 15% higher frequency of treatment intensification was associated with a 0.15% lower lever of HbA1c.[26] We were unable to confirm this result. In our study, blood pressure and HbA1c were not related with the failure to intensify therapy. We did find, however, that physicians' failure to intensify cholesterol-lowering therapy was associated with less decrease of mean total cholesterol levels. Generally, the use of statins is a powerful determinant of change in cholesterol level, whereas a complex web of patient factors modifies the impact of pharmacotherapy on blood pressure and HbA1c.[16] Therefore, the impact of inertia on blood pressure levels and HbA1c% is probably less predictable.

In conclusion, we demonstrated that inertia in response to poor glycaemic control was less common than inertia in response to a poorly controlled hypertension or hypercholesterolemia. Furthermore, poor blood pressure control and high lipid levels were far more common than high HbA1c percentages. Finally, inertia in response to a poorly controlled high blood pressure was less common if nurses assisted general practitioners. These findings may indicate a glucose centric view of general practitioners. In this respect it should be kept in mind that control of blood pressure and lipid levels is at least as important as glycaemic control to prevent cardiovascular complications and an increase in the associated communal costs.

Declaration

Ethical approval: The medical ethics committee of the University Medical Center Utrecht approved the protocol of the study and all participants gave informed consent.

Conflicts of interest: none.

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6

High refill adherence in general practice among patients with type 2 diabetes despite extensive polypharmacy

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Pharmacoepidemiology and Drug Safety (in revision)

Abstract

Background and aims: non-adherence is considered a major barrier to better outcomes of diabetes care. A relationship has been established between polypharmacy and patients' adherence. This study aims to investigate the occurrence of polypharmacy and non-adherence in general practice, their mutual relationship and the association between adherence and the intermediate outcomes of diabetes care.
Materials and Methods: we used the baseline and follow-up data of an RCT that compared usual care with care in accordance with a locally adapted national guideline. This study took place in the Netherlands and involved 30 general practices and 1283 patients. We obtained a complete medication profile of all participants and calculated the number of prescribed drugs and the adherence indices for oral blood glucose, blood pressure and cholesterol lowering drugs. Patients with an adherence index < 0.8 were considered non-adherent. Clustering at practice level and case-mix were taken into account.
Results: approximately 80% of the participating patients demonstrated an adherence index ≥ 0.8 for oral blood glucose, blood pressure and cholesterol lowering drugs. In the intervention group, increase of drug prescriptions exceeded that of controls (1.1 ± 2.0 versus 0.6 ± 1.5, $p<0.001$, adjusted $p<0.05$). There was evidence of a inverse relationship between the number of drugs that had been prescribed during the last six months of the study and patients' adherence to blood pressure lowering medications (adjusted OR 0.84, 95% CI 0.78 to 0.91). After one year, HbA1c and total cholesterol levels were significantly lower in adherent patients.
Conclusion: during the intervention the mean number of drug prescriptions increased in both study groups. This did not result in a lower adherence to blood glucose, blood pressure and cholesterol lowering medications. Given the relationship between the number of medications and patients' adherence to blood pressure lowering drugs, it may be wise to discuss adherence before prescribing multiple drug regimens.

Introduction

There is abundant evidence that tight control of glucose, blood pressure, and cholesterol levels decrease the risk of developing diabetes related macro- and microvascular complications and cardiovascular death.[1-6] Therefore, current

diabetes guidelines recommend stringent treatment goals for HbA1c, cholesterol and blood pressure levels.[7,8] Unfortunately, a treatment gap still exists when best practice is compared with usual care.[9,10] This gap has been attributed to different factors including physician's failure to initiate or intensify therapy when indicated and patient's non-adherence to prescribed medications. Recently, the World Health Organisation stated that only fifty percent of the patients diagnosed with a chronic illness were fully compliant with their treatment regimen.[11] Generally, adherence rates for medications for diabetes vary between 36 and 93%.[12] Adherence to prescribed medications is crucial to reach metabolic control as non-adherence with blood glucose lowering or lipid lowering drugs is associated with higher HbA1c and cholesterol levels respectively.[13-16]

To achieve recommended treatment goals in patients with type 2 diabetes, multiple drug therapy is often unavoidable. Consequently, polypharmacy is common among these patients[17,18] Compliance with fixed dose combination therapy is likely to be higher than adherence to dual therapy.[19,20] Increasing numbers of tablets, multiple daily dosing schedules and the concurrent use of several types of oral blood glucose lowering agents have been associated with poor adherence[12,21-23] Therefore, it has been hypothesised that polypharmacy and adherence to prescribed medications are contradictory.[23]

We performed a randomised controlled trial that involved the implementation of a locally adapted guideline on the shared care for patients with type 2 diabetes. Despite intensified diabetes care, we were unable to demonstrate differences in HbA1c, blood pressure and mean cholesterol levels between the intervention and control group.[24] Hypothetically, this may have been a consequence of a reduced adherence of the participating patients due to intensified care and a concomitant increase in polypharmacy. To test this hypothesis we evaluated the following research questions:

1. Does intensified care lead to increased polypharmacy?
2. Does intensified treatment lead to a difference in adherence to blood glucose, blood pressure and cholesterol lowering drugs?
3. Does increased polypharmacy lead to lower patients' adherence?
4. Is there a relationship between adherence and HbA1c, blood pressure and cholesterol levels?

Methods

Design

We carried out a cluster-randomised trial. Participating general practices were randomised to treat their patients either in accordance with locally adapted shared care guidelines or in line with the 1999 guidelines for the treatment of type 2 diabetes of the Dutch College of General Practitioners.[25] In the shared care guidelines, stricter targets were agreed on for acceptable glycaemic control (HbA1c $\leq$ 8% instead of $\leq$ 8.5%) and blood pressure control (RR <140/85 instead of < 150/85). The medical ethical committee of the University Medical Center Utrecht approved the protocol of this study and all participants gave informed consent.

Patients, practices and pharmacists

In the Netherlands, about 75% of the patients with type 2 diabetes are being cared for in the primary care setting. Almost everyone is registered with a general practice and insurance companies reimburse all diabetes related costs. We asked all general practices (n=70) in the greater Apeldoorn region to participate. All patients with diabetes on the lists of the participating practices were considered eligible for the present study. Exclusion criteria were the inability to complete a questionnaire, severe mental illness, unwillingness to attend the practice regularly and a limited life expectancy. Furthermore, we excluded patients taking insulin at baseline, as we were unable to monitor insulin use and thus treatment adherence of these patients. As it was our aim to investigate polypharmacy and adherence in primary care, patients being treated at the outpatient clinic were also excluded (figure 1). All 18 pharmacists in the Apeldoorn region participated. Their files and those of three general practitioners keeping their own pharmacy were used to obtain a complete medication profile. At the pharmacies, we used the ATC code for blood glucose lowering drugs (ATC code A10) to select all patients at risk and extracted the complete medication files of these patients. In the three general practices, we selected all participating patients being diagnosed with diabetes and extracted their medication files too.

Measurements

At baseline and about one year after the start of the trial, general practitioners and practice nurses examined all participating patients and recorded demographics, duration of diabetes, smoking habits, co-morbidity, level of formal education, and the presence of macrovascular or microvascular complications. Standard operating

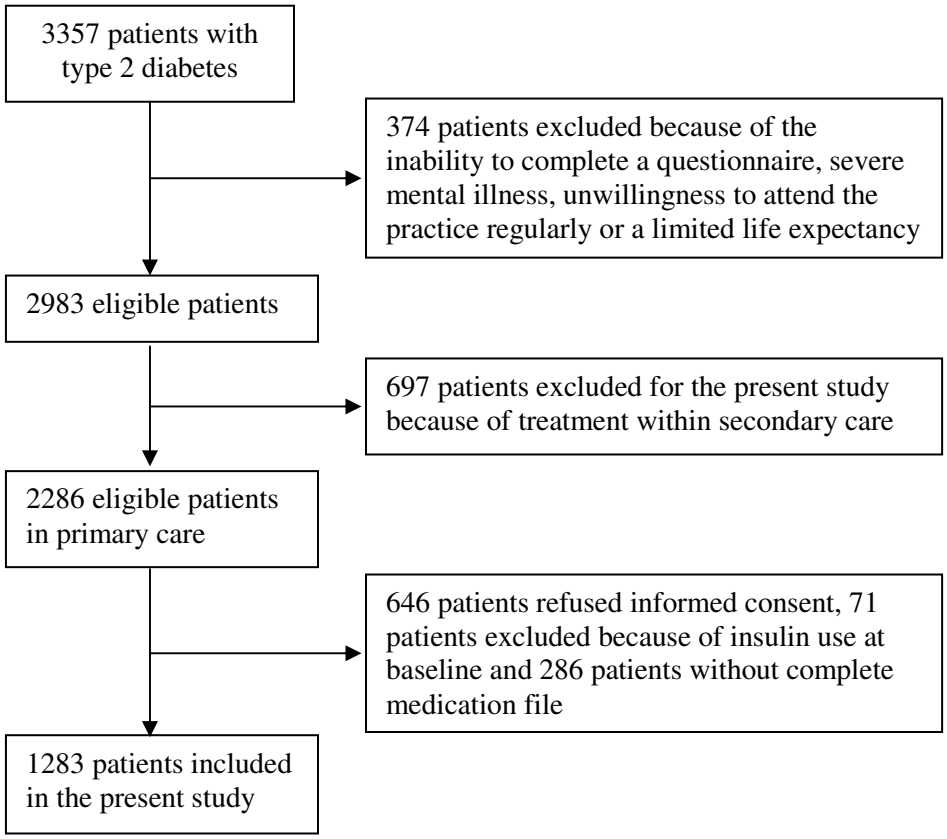

Figure 1 Flow of patients in the study

procedures were used to record weight, height and blood pressure. Fasting blood and urine samples were obtained and analysed at the local laboratory. HbA1c was determined by the Variant II Turbo Haemoglobin Testing System (Bio-Rad). Plasma glucose, total cholesterol, HDL cholesterol, triglycerides, albumin/creatinin ratio and micro albumin were determined with the Architect ci8200SR (Abbott). Health related quality of life was estimated with the EuroQol-5D (range -0.59 -1, where 1 indicates perfect health) and the validated Dutch version of the disease specific Diabetes Health Profile (range 0 - 100, where 100 represents no dysfunction).[26,27] The overall health status of the participants and their treatment satisfaction were measured with the visual analogue scale of the EuroQol-5D (range 0 - 100) and the Treatment Satisfaction Questionnaire (range 0 - 36), respectively.[28,29]

Polypharmacy and adherence

Polypharmacy was defined as minor (the chronic and concurrent use of 2-3 drugs), moderate (4-5 drugs) or major (> 5 drugs). In the Netherlands a new prescription is

required every three months for each drug. As not all prescriptions are refilled within this time frame, we used a period of six months to establish whether or not polypharmacy was present. Presence of polypharmacy was established twice, namely during the six months preceding the start of the study and during the last six months of the intervention. Generally, oral blood glucose lowering, cholesterol lowering, blood pressure lowering or anticoagulant drugs are used chronically. Therefore, if patients filled a prescription for one of these agents during the six months period, its use was considered chronic irrespective of the duration of drug coverage of the prescription. The use of all other drugs with a defined daily dose (DDD) was considered chronic if patients filled at least one prescription with total drug coverage of 90 days during the six months period. Drugs without a DDD in the form of ointments were not included.

At present, there is no generally accepted gold standard for measuring adherence.[30] Many drug adherence studies are based on self-reported adherence. However, self report is a subjective method that tends to overestimate patients' compliance.[30,31] In this study, adherence indices (AI) for oral blood glucose lowering, blood pressure lowering and lipid lowering drugs were calculated using prescription refill data. The sum of the number of days of therapy dispensed on all but the last prescription in the index period was used as the numerator of the adherence statistic and the number of days in the interval between the dates of the first and last prescriptions during this period served as the denominator. Al indices were calculated over the year before the start of the intervention and the year of the intervention.

Statistical analysis

To answer the first research question, we assessed differences in polypharmacy and in the number of prescribed drugs between the intervention and control group. Data on these variables were collected both during the six months preceding the start of the study and during the last six months of the intervention. Measures collected during the last six months of the intervention were specified as dependent variables and the corresponding pre-intervention measures were specified as covariates. Based on literature and clinical reasoning, the following potential confounders were identified: age, gender, level of education, micro and macrovascular complications and quality of life. Patients' level of formal education was split into two categories. People who visited primary school only or primary and secondary school at a non-advanced level were considered to have a low level of formal education. All others

were regarded as highly educated. As ignoring cases with a missing value (complete case analysis) may lead to biased results and loss of power[32], we imputed missing values using the regression method available in SPSS. The imputation was based on the correlation between each variable with missing values and all other variables as estimated from the subjects with complete data. To allow for the clustering of patients within practices, population averaged models were estimated using generalized estimating equations (GEE's). Analyses of continuous variables were done with the following settings: dist=normal, link=identity and type=exch and for categorical variables with: dist=multinominal link=cumlogit and type=indep (SAS Institute, Cary, NC). Pre-intervention measures and potential confounders were included in the models as covariates and all analyses have been performed at patient level.

Regarding the second research question, differences in adherence to blood glucose, blood pressure and cholesterol lowering drugs between the intervention and control group were assessed. Adherence indices were calculated over the year before the start of the intervention and over the year of the intervention. We found the distributions of the indices to be skewed and were unable to find a simple transformation. Therefore, adherence was split into two categories. Patients with an adherence index < 0.8 were considered non-adherent and all others adherent. Adherence over the year of the intervention was specified as the dependent variable whilst the corresponding pre-intervention adherence was considered a covariate. We used generalized estimated equations to allow for clustering at practice level. Analyses were performed with the following settings: dist=bin link=logit and type=exch (SAS Institute, Cary, NC). Potential confounders including age, gender, level of education, micro and macrovascular complications and quality of life were included in the models as covariates. Analyses were performed at the level of the patients.

With regard to the third research question, we evaluated the association between the number of drugs that had been prescribed during the last six months of the intervention and patients' adherence to oral blood glucose, blood pressure and cholesterol lowering drugs. Adherence was specified as dependent variable and the number of prescribed medications as independent variable. Generalized estimated equations were used to allow for clustering at practice level. Analyses were performed with the following settings: dist=bin link=logit and type=exch (SAS Institute, Cary, NC). We included intervention, age, gender, level of education,

micro and macrovascular complications and quality of life as covariates in the models.

Finally, we assessed differences in HbA1c, blood pressure and cholesterol levels between adherent and non-adherents patients. Patients from both study groups were analysed simultaneously and GEE's were used to allow for clustering at practice level. Intervention and potential confounders were taken into account. All analyses were performed at patient level.

Statistical significance was set at $p< 0.01$. Except for GEE, all analyses were carried out using the statistical package SPSS version 12.0 for Windows. We used SAS software version 8 (SAS Institute, Cary, NC) for the Generalized Estimating Equations models.

Results

Practices and patients

In total 11 solo-, 16 duo- and three group practices agreed to participate. Reasons for non-participation were lack of time, a dislike of research projects, a lack of confidence in the outcome of the study and the conviction that the practice performed well and did not need to improve diabetes care. In 45 percent of the participating solo practices, specialised nurses were involved in diabetes care. In the duo and group practices these percentages were 56 and 67 respectively. Overall, 2983 patients were eligible for the study and 2042 patients gave informed consent. Of these 1283 were included in the present study (figure 1).

Baseline characteristics

In most aspects, baseline characteristics were similar between the intervention and the control group. In the intervention group, more patients had a low level of formal education, whereas controls were more often suffering from macrovascular complications. In both study groups, the majority of the participants demonstrated blood pressure or total-cholesterol levels above target (table 1).

Polypharmacy

During the study, the increase in the number of drug prescriptions in the intervention group exceeded that of controls significantly. This difference, however, lost significance after we controlled for age, gender, level of education, micro and

Table 1 Patient's characteristics at the start of the study

	Intervention (sd) (N=629)	**Control (sd) (N=654)**
Male (%)	45.9	51.8
Age (yrs)	66.6 (11.2)	66.9 (11.6)
Low education (%)	63.1	53.1
Duration of diabetes (yrs)	6.6 (6.0)	6.5 (6.0)
Macrovascular complication (%)	19.2	26.6
Microvascular complications (%)	6.0	8.3
HbA1c (%)	7.1 (1.1)	7.2 (1.1)
Systolic blood pressure (mmHg)	145.7 (18.9)	145.2 (19.6)
Diastolic blood pressure (mmHg)	82.5 (9.0)	82.7 (9.3)
Cholesterol (mmol/l)	5.2 (1.0)	5.2 (1.0)
Poorly controlled diabetes* (HbA1c>8%) (%)	16.7	
Poorly controlled diabetes** (HbA1c>8.5%) (%)		8.6
Poorly controlled hypertension* (BP≥140/85) (%)	75.8	
Poorly controlled hypertension** (BP≥150/85) (%)		60.9
Poorly controlled hypercholesterolemia*** (total-cholesterol > 5 mmol/l, non-smokers without vascular complications ≥ 6 mmol/l) (%)	57.1	52.8
EuroQol-5D	0.82 (0.20)	0.80 (0.21)
EuroQol-VAS	76.7 (16.1)	74.8 (15.7)
DHP	85.2 (9.1)	84.6 (10.0)
Mean number of drugs	3.1 (2.5)	3.4 (2.2)
No polypharmacy (%)	30.8	20.8
Minor polypharmacy° (%)	30.1	37.3
Moderate polypharmacy°° (%)	22.5	24.0
Major polypharmacy°°° (%)	16.6	17.9
Percentage of patients taking oral blood glucose lowering drugs who are adherent to these drugs (intervention group n=501, control group n=586)	86.8	84.1
Percentage of patients taking blood pressure lowering drugs who are adherent to these drugs (intervention group n=358, control group n=425)	81.3	78.6
Percentage of patients taking cholesterol lowering drugs who are adherent to these drugs (intervention group n=197, control group n=258)	85.8	83.7

** In line with local shared care guidelines, ** In line with the guideline of the Dutch College of General Practitioners, *** In line with both guidelines, ° 2-3 drugs, °° 4-5 drugs, °°° > 5 drugs, N total number of patients, n total number of patients taking these drugs*

macrovascular complications, quality of life and clustering at practice level (1 ± 2.0 versus 0.6 ± 1.5, p<0.001, adjusted p<0.05). At the end of the study, the mean number of drug prescriptions and the percentages of patients belonging to the different categories of polypharmacy did not differ between the intervention and control group (table 2).

Table 2 Mean number of drugs in the intervention and the control group and percentages of patients in four polypharmacy classes at the end of the study

	Intervention (N=627)	**Control (N=654)**	**P#**	**P***
Mean number of drugs (SD)	4.2 (2.4)	4.0 (2.4)	0.4	<0.05
No polypharmacy (%)	11.2	13.0		
Minor polypharmacy° (%)	33.5	33.6	0.7	0.08
Moderate polypharmacy°° (%)	29.8	26.9		
Major polypharmacy°°° (%)	25.5	26.5		

*° 2-3 drugs, °° 4-5 drugs, °°° > 5 drugs, #Adjusted for clustering at practice level, *Adjusted for pre-intervention value, age, gender, level of education, micro and macrovascular complications, quality of life and clustering at practice level, N total number of patients*

Adherence

During the study, the percentages of adherent patients were comparable across study groups. Approximately 80% of the participants showed an adherence index of ≥ 0.8 (table 3). These results did not change after stratification for different levels of polypharmacy (data not shown).

Adherence and polypharmacy

There was an inverse relationship between the number of medications that had been prescribed during the last six months of the study and patients' adherence to blood pressure lowering drugs. This relationship remained significant after we controlled for the clustered design of the study, intervention, age, gender, level of education, micro and macrovascular complications and quality of life. There were no significant associations between the number of medications and patients' adherence to oral blood glucose or cholesterol lowering drugs (table 4).

Table 3 Adherence (AI ≥ 0.8) to blood glucose lowering agents, anti-hypertensive drugs and statins during the year of the study

	Intervention	**Control**	**P#**	**P***
Percentage of patients taking oral blood glucose lowering drugs who are adherent to these drugs (intervention group n=569, control group n=605)	83.8	81.2	0.6	0.9
Percentage of patients taking blood pressure lowering drugs who are adherent to these drugs (intervention group n=441, control group n=456)	81.0	76.5	0.2	0.6
Percentage of patients taking cholesterol lowering drugs who are adherent to these drugs (intervention group n=260, control group n=303)	87.7	85.5	0.6	0.9

*# Adjusted for clustering at practice level, *Adjusted for pre-intervention value, age, gender, level of education, micro and macrovascular complications, quality of life and clustering at practice level, n total number of patients taking these drugs*

Table 4 Relationship between the mean number of drugs during the last six months of the study and patients' adherence to oral blood glucose, cholesterol and blood pressure lowering drugs during the year of the study

	OR (95% CI)	**OR# (95% CI)**	**OR* (95% CI)**
	Adherence to oral blood glucose lowering drugs		
Mean number of drugs during the last six months of the study	1.03 (0.96 to 1.09)	1.02 (0.95 to 1.10)	1.01 (0.94 to 1.08)
P value	0.5	0.5	0.9
	Adherence to cholesterol lowering drugs		
Mean number of drugs during the last six months of the study	0.97 (0.87 to 1.07)	0.97 (0.85 to 1.11)	0.95 (0.83 to 1.09)
P value	0.5	0.7	0.5
	Adherence to blood pressure lowering drugs		
Mean number of drugs during the last six months of the study	0.86 (0.80 to 0.92)	0.86 (0.80 to 0.93)	0.84 (0.78 to 0.91)
P value	<0.0001	<0.001	<0.0001

*# Adjusted for clustering at practice level, * Adjusted for intervention, age, gender, level of education, micro and macro vascular complications, quality of life and clustering at practice level.*

Adherence and metabolic control, blood pressure and cholesterol level

Both at the start and at the end of the study, non-adherent patients demonstrated significantly higher HbA1c percentages and mean cholesterol levels. At the start of

Table 5 HbA1c%, blood pressure and cholesterol level at the start and the end of the study in adherent and non-adherent patients

	Adherence during the year preceding the start of the study				Adherence during the year of the study			
	Adherent (SD)	Non-adherent (SD)	P#	P*	Adherent (SD)	Non-adherent (SD)	P#	P*
HbA1c (%)	7.1 (1.1)	7.4 (1.2)	<0.001	<0.01	6.9 (0.9)	7.2 (1.0)	<0.0001	<0.0001
Systolic blood pressure (mmHg)	148.3 (18.4)	151.1 (20.7)	<0.05	<0.05	149.0 (18.9)	149.1 (17.9)	0.9	0.9
Diastolic blood pressure (mmHg)	83.9 (9.2)	83.0 (9.6)	0.3	0.9	82.9 (9.8)	83.1 (9.5)	0.7	0.4
Cholesterol (mmol/l)	4.9 (1.0)	5.3 (1.1)	<0.001	<0.01	4.8 (1.0)	5.2 (1.1)	<0.01	<0.01

*# Adjusted for clustering at practice level, * Adjusted for intervention, age, gender, level of education, micro and macro vascular complications, quality of life and clustering at practice level.*

the study, there was also evidence of a weak association between patients' adherence to their blood pressure lowering regimens and achieved systolic blood pressure levels (table 5).

Discussion

During the year preceding the start of the study, more than 80% of the participating patients showed an adherence index of ≥ 0.8 for oral blood glucose, blood pressure or cholesterol lowering drugs. During the intervention the mean number of drug prescriptions increased in the intervention as well as the control group. Notwithstanding this increase, refill adherence remained high. There was an inverse relationship between the number of drugs that had been prescribed during the last six months of the study and patients' adherence to their blood pressure lowering regimens. We were unable to demonstrate such a relationship between the number of drug prescriptions and patients' adherence to oral blood glucose or lipid lowering medications. Patients with adequate adherence to oral hypoglycaemic agents and cholesterol lowering drugs demonstrated lower HbA1c % and total cholesterol levels. The relationship between adherence to blood pressure lowering drugs and achieved blood pressure levels was less clear, as we only found evidence of a weak association between adherence and patients' systolic blood pressure levels at the start of the study.

Assessment of adherence to prescribed medications is difficult. Due to different methods (self report, pill count, refill data, Medication Event Monitoring Systems), settings and cut-off-points reported adherence to prescribed medications varies greatly. A study that used both pill count and Medication Event Monitoring Systems (MEMS) found significant differences between the methods applied. Pill count was only able to detect 40% of the non-adherent patients whereas MEMS detected 100% of those non-compliant with their medication regimen. Due to this difference the percentage of patients taking at least 90% of the drugs prescribed varied between 78.9 and 47.4%.[33] In studies using the same 80% threshold as we did, percentages between 53.9 and 71.1% were found.[13,15,34,35] These results are in line with those of a recent review. Among 11 retrospective studies adherence rates ranged from 36 to 93%. In five prospective studies with electronic dose monitoring, adherence rates were more consistent. In these studies, mean adherence with oral glucose lowering drugs was between 61 and 85%.[12] In our study, the percentages of patients showing adherence rates > 80% for oral hypoglycaemic agents, anti-

hypertensive drugs or statins were at the upper limit of those reported previously. There are at least two possible explanations for this finding. Firstly, as unwillingness to attend the practice regularly was an exclusion criterion, possibly less compliant patients were excluded. Secondly, as it has been demonstrated that limited access to pharmaceutical care contributes to poorer patients' adherence[36], the high percentages of adherent patients found in our study may have been a consequence of the Dutch healthcare system in which basic healthcare insurance is mandatory for all persons and all diabetes related costs are reimbursed. In this respect it should be kept in mind that still 20% of the participating patients were not adhering to their treatment regimens. Even if one takes into account that non-adherence can be rational in light of serious side effects or medical errors, the prescription of medications that are not refilled, is a waste of scarce healthcare resources and suggest a systemic problem.[37]

It has become apparent that an increase in the number of co-medications tends to decrease the adherence of patients with type 2 diabetes to their treatment regimens.[23] Poorer adherence in these patients has also been associated with an increase in the number of tablets, multiple daily dosing schedules and the concurrent use of several types of oral hypoglycaemic agents.[12,21-23] Furthermore, compliance with fixed dosed combination therapy is found to be higher than adherence to dual therapy.[19,20] In general, simple anti-hyperglycaemic regimens are associated with better adherence than complex multi-drug regimens. A recent study, however, was unable to demonstrate such a relationship; despite the complexity of medical regimens, patients reported very high 7-day medication adherence rates. Moreover, a higher number of prescribed medications was not associated with poorer per-medicine adherence.[18] Our finding that the number of drug prescriptions was not related with adherence to oral blood glucose or lipid-lowering medications is in line with these findings. During the intervention the mean number of drug prescriptions increased in both study groups. This, however, did not result in a lower adherence to blood glucose, blood pressure and cholesterol lowering medications. Despite the wide spread of polypharmacy, approximately 80% of the participating patients demonstrated an adherence index ≥ 0.8 for oral blood glucose, blood pressure and cholesterol lowering drugs at completion of the study. Therefore, physicians should not feel deterred from prescribing multiple agents in order to reduce the cardiovascular risks of patients diagnosed with diabetes.

Multiple studies demonstrated an association between non-adherence to prescribed medications and both glycaemic and lipid control but failed to show a significant relationship between adherence and blood pressure elevations.[14-16,38,39] This may be due to the fact that many factors in addition to adherence (e.g., heredity, environment) can influence the outcome of blood pressure lowering treatment[38,40] Because many control visits are being scheduled in a fasting state and some participating patients may not have taken their medications prior to the assessment, blood pressure levels could be inconsistent with usual medication adherence. On the other hand, blood pressure could erroneously appear well controlled if a patient who is in general non-adherent has taken his anti-hypertensive medications prior to the assessment. As HbA1c percentages are related with glucose control over a 90-day period, they are likely to be more consistent with patients' usual adherence despite delayed medication intake on the day of assessment. The same applies for the relationship between adherence and cholesterol levels. As it is highly unlikely that skipping a single morning dose will influence lipid control, cholesterol levels on the day of assessment are probably consistent with usual medication adherence.

This study had a number of strengths. Firstly, ascertainment of drug coverage was good as all pharmacies in the greater Apeldoorn region and three general practitioners having their own pharmacy participated. Secondly, our study was conducted among patients who had no financial barriers to care. This design helps to isolate the relationship between local guidelines, polypharmacy and patients' adherence but may limit generalisability to other populations. Thirdly, we were well informed about patients' characteristics including age, gender, macrovascular and microvascular co morbidity, level of education and quality of life. This enabled us to adjust our models for potential confounding. Our study may be limited by the use of pharmacy data to quantify patients' adherence to prescribed medications. Although the adherence index is an objective method for measuring adherence, filling of a prescription does not necessarily mean that the medication has been taken. On the other hand, the possession of medications is a prerequisite for actually consuming drugs. Furthermore, other established methods like the use of Medication Event Monitoring Systems may be interventions in their own right. Consequently these methods may enhance patients' compliance and give rise to an over optimistic estimate of drug adherence in the general population. In addition, some bias may have resulted from the fact that all patients took part voluntarily and may have been more motivated than the average patient and may therefore have demonstrated a greater adherence to different medication regimens. Finally, the use

of a single imputation procedure may have resulted in an underestimation of the standard errors or too small p-values.[41] However, this potential problem was countered by the use of a significance level of 0.01.

To conclude, we found a substantial increase of multiple drug use in both study groups and a significant association between adherence, HbA1c and total cholesterol levels. We also demonstrated a significant relationship between the number of medications that had been prescribed during the last six months of the study and patients' adherence to blood pressure lowering drugs. Adherence over the year of the intervention to oral blood glucose, blood pressure and cholesterol lowering drugs did not differ between the intervention and the control group. Therefore, it is unlikely that the lack of cardiovascular risk reduction in the trial was caused by a reduced treatment adherence of the participating patients. Given the relationship between the number of drug prescriptions and patients' adherence to blood pressure lowering medications, it may be wise to discuss adherence before prescribing multiple drug regimens.

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7

Towards an effective and relevant measurement of the quality of diabetes care.

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Clinical guidelines and quality indicators have been developed to improve the quality of diabetes care. Notwithstanding great efforts, diabetes guidelines are still inadequately followed and patients suffer from poorly controlled cardiovascular risk factors, such as hyperglycemia, high blood pressure and high cholesterol levels.[1-8] Apparently, new strategies are needed to further improve patients' cardiovascular risks.

More and more, healthcare systems are moving towards reward based programmes and health care providers are called upon to demonstrate the quality of their work. Pay for performance is expected to bring additional improvements to the quality of diabetes care.[6] This demand for quality and transparency raises the question what constitutes the quality of diabetes care. Often, quality is interpreted in terms of HbA1c, blood pressure and cholesterol levels. In our opinion this approach is an oversimplification that might harm both, physicians and patients.

Quality of care

Defining quality is difficult. It is not tangible and its definition depends on the point of view of the definer.[9] The American Institute of Medicine defines quality as "doing the right thing, at the right time, in the right way, for the right person - and having the best possible results".[10] From this definition four major aspects of quality are inferred namely: effectiveness, safety, timeliness and demand orientation. Generally, these aspects are considered to be the core aspects of quality. When exploring these core aspects it is useful to distinguish the well-known Donabedian triad: structure, process and outcome of care.[11] More recently this triad has been supplemented with two other classes of quality indicators: access of care and patient experience measures.[12] In light of these five quality indicators, we will discuss different aspects of the quality of diabetes care and formulate recommendations for future assessment systems.

Structure as quality indicator

The three-part approach to quality assessment, i.e. structure, process and outcome, is possible only because good structure improves the likelihood of good process and good process increases the likelihood of a good outcome.[11] Therefore, it is necessary to have established a relationship between structure, process and outcome before structure can be a valid indicator of the quality of diabetes care. Knowledge about the link between structure, process and outcome may proceed from studies involving well known organizational concepts, like shared care, case management,

disease management and the chronic care model. In the following we will discuss these different concepts and their relation to the outcome of diabetes care.

Shared care

Shared care involves the joint participation of hospital consultants and general practitioners in the planned delivery of care informed by an enhanced information exchange over and above routine discharge and referral notices.[13] In general, diabetes shared care can be equally as effective as conventional hospital care.[14] The introduction of this concept, however, does not lead to improvements in the process or the biomedical outcomes of diabetes care.[15] Recently, a Cochrane review indicated that there is no evidence to support the widespread introduction of shared care services at present.[16]

Case management

Case management usually involves the assignment of authority to a professional (the case manager) who is not the provider of direct health care but who oversees and is responsible for coordinating and implementing care.[17] In interventions involving diabetes, the case manager is generally a non-physician, most commonly a nurse. Case management has five essential features: identification of eligible patients, assessment, development of an individual care plan, implementation of the care plan, and monitoring of outcomes. Case management significantly improves the process of diabetes care and glycaemic control, especially when case managers are authorized to adjust medications without awaiting physician approval.[17-21] There is, however, only little evidence in support of significant improvements in blood pressure, lipid concentrations, weight or quality of life.

Disease management

Disease management can be described as: 'the programmatic and systematic approach of specific diseases and health problems using management instruments to improve the quality and efficiency of care'.[22] This care approach is businesslike with strong emphasis on working with protocols, not targeted at the individual patient but at the population at risk and focused on education and self-management instead of on treatment itself. Clearly, these disease management programs improve screening for retinopathy, foot complications, neuropathy and proteinuria. They also have modest, but clinically and statistically significant effects on glycaemic control.[17,18,23] There is, however, insufficient evidence of a positive effect on patients' blood pressure, weight, lipid concentrations and costs.[17,18,23-25]

Chronic care model

The chronic care model contains six elements that are considered to be essential for providing high quality care to patients with chronic illnesses: delivery system design, self management support, decision support, clinical information systems, community resources and healthcare organization.[26] Each of these components has been studied rigorously, but evidence regarding the effects of the model as a whole is limited. A recent review and a meta-analysis found that programmes based on one or more elements of the chronic care model could improve process or outcome measures for patients with diabetes.[27,28] Both studies, however, were unable to demonstrate a synergistic effect of the different elements of the chronic care model. Single interventions were just as successful as interventions containing more than one element of the model.

Apparently, the concepts mentioned above can improve the process of diabetes care and patients' glycaemic control, but there is little evidence in support of a relationship between these concepts and improvements in other important patient related outcomes. Therefore assessment of the structure of care should only be used as a quality indicator in combination with other indicators, like process and outcome measures.

Process as quality indicator

The process of care is possibly best described as what is actually done in giving and receiving care. It includes not only practitioner's activities in making a diagnosis and recommending or implementing treatment but also patient's activities in seeking care and following up on the practitioners' advise.[29] Process measures, like other quality measures, are subject to potential bias due to the fact that sicker patients need more care, which gives greater opportunity for errors. It has, therefore, been advocated to express process errors as a function of opportunity for those errors, as this approach may adjust (at least in part) for potential case mix bias.[30] Furthermore, better adherence to process measures does not automatically mean better quality of care: not adhering to a guideline by healthcare professionals after thorough discussion with a patient may well be an example of high quality care.[31,32] Nevertheless, process measures have two fundamental advantages over outcome measures. Firstly, process measures are more sensitive than outcome measures to differences in the quality of care.[9,33] It has become apparent that even under ideal conditions death rates are insensitive to quite wide variations in the quality of care. A study on the sensitivity of measures of process and outcome in treating acute

myocardial infarction, for example, made clear that process measures based on the results of randomized controlled trials were able to detect relevant differences between hospitals that could not be identified by comparing hospital specific mortality.[34] Secondly, process measures are direct measures of quality and therefore easy to interpret: the more patients receiving a proven therapy without a contra indication, the better.[9,33]

To be suitable as a quality indicator, process measures have to be relevant. That is to say, improved adherence of health care providers to these measures must lead to better patient outcomes.[9] Most large-scale quality improvement initiatives, however, show only modest improvements in some process measures, but fail to demonstrate better outcomes.[35] One may wonder why there is such a discrepancy between process and outcome of diabetes care. It has been suggested that the selection of quality indicators and measurements is driven by what can be measured and provides simplicity at the expense of meaning.[36] Besides, little information is usually collected at the individual patient or case level, which makes the validity of these measurements even more doubtful.[31] There is, therefore, a need for process measures that are both closely associated with the outcome of care and collected at an individual level.

It has become apparent that variance in patient's glycaemic control is strongly influenced by physician related factors such as intensification of medications.[37] Healthcare providers' failure to initiate or intensify therapy when indicated has been called clinical inertia.[38] Several studies demonstrated the high prevalence of clinical inertia but failed to show a relationship between physicians' failure to intensify therapy and different outcomes of diabetes care.[39-41] A recent study demonstrated that on average a 15% higher frequency of treatment intensification was associated with a 0.15% lower level of HbA1c.[42] Not only clinical inertia but also patients' adherence to prescribed medications is considered an important part of the process of diabetes care. The World Health Organization made clear that only fifty percent of the patients diagnosed with type 2 diabetes were fully compliant with their treatment regimen.[43] In accordance with these findings, a systematic review involving patients' adherence to taking diabetes medications found adherence rates to vary between 36 and 93%.[44] Although multiple studies demonstrated an association between patients' adherence to prescribed medications and poor glycaemic or lipid control, they frequently failed to show a significant relationship between compliance with anti-hypertensive regimens and blood pressure levels.[45-49]

Recently, we performed a study on clinical inertia among general practitioners and another study on adherence to prescribed medications by the patients with type 2 diabetes of these practitioners.[50,51] In these studies, the files of local pharmacies were used to calculate adherence indices for blood glucose lowering, anti-hypertensive and cholesterol lowering drugs. The files were also used to establish whether healthcare professionals timely intensified treatment for patients with poor glycaemic control. It became apparent that non-adherence and lack of treatment intensification occurred frequently and were associated with different outcomes of diabetes care, like glycaemic and lipid control. In light of these results and those of other studies.[5,41,46,47,49,52,53] We strongly believe that practical measures of clinical inertia and patients' adherence would represent a useful addition to future measure sets.

Outcome as quality indicator

The outcome of care can be described as the effects of care on the health status of patients and populations. Health status can itself be viewed rather narrowly as physical or physiological function or, more broadly, to include psychological function and social performance.[11] Outcome measures are especially useful where technical skills are essential. In cardio surgery, for example, it does not only matter that the procedure has been performed on the appropriate patients, but also how well that procedure was carried out. Furthermore, outcome measures can be used as a form of process control, in the sense that deviating outcomes of diabetes care may give rise to further investigation[30] However, outcome measures have a number of disadvantages. Firstly, these measures can be affected not only by medical interventions, but also by patient factors like severity of disease, socio-economic status, age gender, co-morbidity and non-adherence to treatment regimens.[9,30,33] In other words, the outcome of diabetes care strongly depends on the case-mix. Therefore, case-mix differences have to be taken into account when comparing the quality of care in different settings.[54,55] In this respect it should be kept in mind that risk adjustment cannot allow for case mix variables that are unknown. Nor can it allow for differences in definitions or in how the same definitions are applied. For these reasons, residual differences in the outcome of care can not be attributed unambiguously to differences in the quality of care.[30,56] Secondly, as outcomes result from all processes received by the patient, they reflect the activities of many clinicians and support services.[52] Finally, outcome measures provide only little information about how improvements should be made.[33] Because blame is attributed without specification what the problem is and where its solution lies,

performance judgment based on outcome measures tends to stigmatize. Such a stigma can induce distrust and dysfunctional behavior, which in turn may hamper quality improvement.[30,56]

Patient experience as quality indicator

There is a growing recognition that patients' opinions about care are important indicators of the quality of care, because dissatisfaction with medical care is associated with non-adherence and discontinuation of treatment.[57,58] In patients with diabetes, non-adherence and treatment discontinuation are associated with higher HbA1c and LDL cholesterol levels and an increased risk of complications.[46,47,49,52] Evidently, patient experience measures can only be valid indicators of quality if a direct relationship has been established between these measures and other outcomes of care. A study on satisfaction with services provided in primary care and outcomes in type 2 diabetes demonstrated that overall satisfaction was correlated with the outcome of care as measured by HbA1c.[59] These findings are in accordance with the results of a large population study on health related quality of life and treatment satisfaction. In this study, patients with higher HbA1c levels were less satisfied with the treatment they received than other patients.[60]

Given the relationship demonstrated above, patient satisfaction may be considered an essential element of quality assessment. It is the patient's judgment on the quality of care in all its aspects, taking also the interpersonal process into account.[29] However, patient experience measures are like other outcome measures subject to potential confounding due to the fact that they vary by many features such as age, wealth and ethnic background. Therefore robust adjustment systems have to be in place before these measures can be used to evaluate the quality of care in different settings.

Access to care as quality indicator

Access to care is considered one of the five principal indicators of the quality of care. Limited access may account for some of the racial disparities in health status found in the United States. Population based studies suggest that ethnic minorities and people with a lower socioeconomic position have significantly higher rates of diabetes-related complications and experience worse long-term outcomes.[61-65] As ethnic minorities and poorer people with diabetes tend to be less adequately insured than those with a higher socioeconomic position, differential access to care may contribute to these findings.[66] Multiple studies suggest that offering a more uniform

access to care may reduce ethnic disparities in both process and outcome of diabetes care. Recently, a study on ethnicity, socioeconomic position and quality of care for adults with diabetes found that in managed care settings minority was not consistently associated with worse processes or outcomes of care.[67] These findings may be the result of fewer barriers to diabetes care and the presence of incentives within managed care organizations to deliver adequate care. Another example of the consequences of limited access to care is given by a study on the unintended effects of limits on prescription- drug benefits for Medicare beneficiaries.[68] In this study, a cap on drug benefits was associated with poorer adherence to drug therapy and poorer control of blood pressure, lipid levels and glucose levels. Furthermore, the savings in drug costs were offset by increases in costs of hospitalization and emergency care. These results demonstrate the negative effects of a limited access to pharmaceutical care. This is of particular concern in diabetes care where there is strong evidence that drugs are cost effective. Therefore, equal access to care is an important aspect of the quality of diabetes care. In this respect it should be kept in mind that improving access to care is mainly a political issue that goes far beyond the scope of individual physicians.

Combining process and outcome measures to evaluate the quality of care

In light of the advantages and disadvantages mentioned above, it is possibly best to include in any system of quality assessment, a combination of different indicators. This allows complementation of weaknesses in one approach by strengths in another and helps to interpret the findings.[29] An example of such a combination of indicators may well be the set of performance measures developed by the Diabetes Quality Improvement Project (DQIP) in the United States. In an effort to standardize quality measurement, the DQIP developed a set of nine accountability measures that contained six indicators for care processes and three for outcomes of care (table 1).[69] Required criteria for these measures included a firm evidence base, feasibility, reliability, suitability for uniform application across health care systems and variability across populations so that improvements could be monitored.[69] The introduction of the DQIP set was highly successful; the set has been adopted in several programs in the United States and in other countries[70-72] and its use is expected to play an important role in translating clinical interventions into practice that will improve quality of life and clinical outcomes for patients with diabetes. However, until recently there was only limited evidence in support of a relationship between these measures and long-term outcomes of diabetes care.

Table 1 DQIP Accountability Measure Set

Process measures
Percentage of patients receiving at least one HbA1c test/year
Percentage of patients receiving a lipid profile once in 2 years
Percentage of patients assessed for nephropathy
Percentage of patients receiving a periodic dilated eye exam
Annual foot exam
Smoking cessation counseling
Outcome measures
Percentage of patients with the highest risk glucose level (i.e., HbA1c >9.5%)
Percentage of patients with a low-density lipoprotein cholesterol level <3.4 mmol/l
Percentage of patients with blood pressure <140/90 mm Hg

In an effort to predict the long-terms outcomes of diabetes care, the Quality of Care and Outcomes in Type 2 Diabetes (QuED) study group developed a quality of care summary score based on readily available process and intermediate outcome measures (table 2). Only indicators with a strong link with vascular complications were used. In contrast with the accountability measures developed by the DQIOP,

Table 2 Scoring System

Quality of care indicator	**Score**
HbA1c ≥8.0%	0
HbA1c <8.0% but measurement less than 1/year	5
HbA1c <8.0% and measurement at least 1/year	10
Blood pressure ≥140/90	0
Blood pressure values <140/90 mmHg but measurement less than 1/year	5
Blood pressure values <140/90 mmHg and measurement at least 1/year	10
LDL cholesterol ≥3.4 mmol/l	0
LDL cholesterol <3.4 mmol/l but measurement less than 1/year	5
LDL cholesterol <3.4 mmol/l and measurement at least 1/year	10
Not treated with ACE-inhibitors despite the presence of microalbuminuria	0
Treated with ACE-inhibitors in the presence of microalbuminuria or microalbuminuria absent but measurement less than 1/year	5
Treated with ACE-inhibitors in the presence of microalbuminuria or microalbuminuria absent and measurement at least 1/year	10
Score range	**0-40**

the QuED summary score also takes the appropriate prescription of ACE-inhibitors into account. After adjusting for case-mix and clustering, a linear relationship between this quality score and the incidence of cardiovascular events was found.[73] Recently, the QuED summary score and a slightly adapted version of this score were used to evaluate the quality of diabetes care across different health care settings.[54] It appeared that both the summary score and the adapted version were applicable to different healthcare settings and could be easily interpreted.

As already mentioned, measures of clinical inertia and patients' adherence may represent a very useful addition to future measure sets. Therefore, multiple measures of clinical inertia and adherence have been proposed. Measuring these parameters, however, goes far beyond the use of relatively simple process measures like the frequency of blood pressure control or the percentage of patients that have been screened for diabetes related eye or foot diseases. The common denominator of most indicators of clinical inertgia is their emphasis on glucose control. However, to be a useful tool for quality measurement and improvement, indicators for clinical inertia must also focus on blood pressure and LDL-cholesterol.[74] Preferably, such measures evaluate care over an extended period of time, are based on widely accepted clinical practice recommendations, sensitive to differences in practice and linked to outcomes of diabetes care.[39] Like indicators for clinical inertia, indicators for adherence must have a firm evidence base. Furthermore, these measures need to take patients' adherence to oral blood glucose lowering drugs as well as anti-hypertensive and lipid lowering medications into account. Except for indicators for inertia and patients' adherence, future measure sets should contain a combination of process and intermediate outcome measures that are closely linked to the long-term outcomes of diabetes care. For this purpose the QuED measure set is possibly best equipped. Not only measures that are related to cardiovascular complications should be included, but also DQIP like process measures have to be taken into account. Finally, future sets preferably contain patient experience measures, as these reflect the interaction between healthcare providers and patients and judge the quality of care in all its aspects. A 14-item measure set based on these observations is presented in table 3.

Beyond quality assessment

Quality assessment is not a goal in itself. Above all, it is a tool for health care improvement. The results of quality assessments can be used to provide health care professionals with performance feedback. Audit and feedback are common tools for

Table 3 Future measure set

Process measures
From medical records or electronic data
1. Percentage of patients receiving at least one HbA1c test/year
2. Percentage of patients receiving at least one blood pressure measurement/year
3. Percentage of patients receiving at least one lipid profile/year
4. Percentage of patients receiving at least one assessment for nephropathy/year
5. Percentage of patients receiving an eye exam (high-risk annually, low-risk biennially)
6. Percentage of patients receiving at least one foot exam/year
From medical records or electronic data combined with prescription refill data
7. Percentage of patients receiving treatment intensification when indicated (separate percentages for patients with hyperglycemia, high blood pressure and cholesterol levels above target)
From prescription refill data
8. Percentage of adherent patients (separate percentages for patients with hyperglycemia, high blood pressure and cholesterol levels above target)
From medical records or electronic data or patient survey
9. Percentage of patients receiving at least one smoking cessation counseling/year
Outcome measures
From medical records or electronic data
10. Percentage of patients with HbA1c < 8.0%
11. Percentage of patients with blood pressure <140/90 mm Hg
12. Percentage of patients with a low-density lipoprotein cholesterol level <3.4 mmol/l
13. Percentage of patients treated with ACE-inhibitors in the presence of microalbuminuria
Patient satisfaction
From patient survey
14. Measurement of patients' satisfaction using a validated questionnaire (for example the diabetes treatment satisfaction questionnaire)

health care improvement that have been studied extensively. However, only few of these studies have been randomized controlled trials.[75,76] Several recent reviews showed small to moderate improvements to the quality of care as a result of audit and feedback.[75-78] A Cochrane review confirmed the positive effects of audit and feedback, but with varying effectiveness.[79] Of the 85 studies included in this review, only four involved diabetes care. Of these four studies, two comparisons showed that audit and feedback were more effective than providing care as usual.[80] The

results of the review did not support the mandatory or unevaluated use of audit and feedback as an intervention to change practice.
Besides audit and feedback additional incentives may be needed. In 2004, the UK government introduced a new contract for general practitioners that gave financial incentives for the achievement of quality standards of process and outcome in diabetes care across 18 clinical indicator domains. Recently the results have been published of a study involving a comparison of published quality of care reports with the results of the quality and outcomes frame work for diabetes.[6] The study made clear that the quality framework's financial incentives led to substantial improvements in many process indicators and in all major outcomes including blood pressure, HbA1c and lipid levels. These results confirm the positive effects of combining a quality assessment with modest financial incentives. Apparently, pay for performance can enhance the quality of diabetes care.

Conclusion

Clearly, a relationship exists between structure and process of diabetes care. The association between structure and outcome, on the other hand, is less clear. Therefore, assessment of care structure should only be used as a quality measure in combination with other indicators. Given the limited evidence of an association between process and outcome of diabetes care, process measures should be interpreted carefully. However, when a relationship between a certain process and outcome has been demonstrated, process measures should be used in preference over outcome measures as they are easier to interpret and more sensitive to differences in the quality of care. Especially, in interpreting outcome measures, case-mix differences must be accounted for and robust adjustment systems have to be developed to ensure that these measures can be interpreted reliably. However, if these systems are in place and data collection has been standardized, outcome measures can provide information about the essence of the quality of care: the patient's health status.

Given the strengths and weaknesses of structure, process and outcome indicators, a combination of measures must be included in any system of quality assessment. Preferably, such a combination contains indicators that are closely linked to the long-term outcomes of diabetes care. As there is growing evidence of a link between treatment intensification, patients' adherence to their treatment regimens and the outcomes of care, measures of clinical inertia and non-adherence in patients

with diabetes should be incorporated in future assessment systems. Finally, access to care should not be limited by personal financial constraints because adequate control of glucose, blood pressure and lipid levels is essential to prevent cardiovascular complications and an increase in the associated communal costs.

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Summary

Evidently, tight control of glucose, blood pressure, and cholesterol levels decreases the risk of developing diabetes related macro- and microvascular complications and cardiovascular death. Knowledge on the importance of stringent diabetes control is reflected in current diabetes guidelines recommending ambitious treatment goals for HbA1c, cholesterol and blood pressure levels. Unfortunately, these guidelines are inadequately translated into daily practice and treatment remains substandard in many patients with diabetes.

The aim of this thesis is to evaluate different methods to bridge the gap between daily practice and best care. Furthermore, it encompasses different aspects of quality measurement. In the Netherlands, a quality incentive is expected to ensue particularly from improved collaboration between healthcare professionals and arguments in favour of sharing and delegating care tasks are being made. Whether this view is supported by sufficient evidence is, however, questionable. Therefore, the first study included in this thesis is a systematic review of studies on the effects of sharing and delegating diabetes care tasks. The results of this review are presented in the second chapter of this thesis. In the third chapter, we present the results of a study on the quality of diabetes management in general practice and at the outpatient clinic of a regional hospital. In this study a summary score has been used to evaluate the quality of diabetes care in these different settings. Subsequently, we performed a study on the effects of a multifaceted intervention to implement a locally adapted guideline on the shared care for patients with type 2 diabetes. The results of this study are discussed in the fourth chapter. In the chapters five and six, we present the results of our studies on the effects of clinical inertia and patients' adherence on the outcomes of diabetes care. Finally, in chapter seven, we discuss different aspects of the quality of diabetes care and formulate recommendations for future quality assessment systems.

Chapter 1

General introduction

In the first chapter a general introduction on the subject of this thesis is given. After a short comment on the implementation of clinical guidelines and the multiple strategies that have been developed to improve guideline adherence, the different research questions that are at the base of this thesis have been formulated. These questions are:

- Does the sharing and delegation of care tasks improve the quality of diabetes care and reduce cardiovascular risks in patients with type 2 diabetes?

- What is the quality of diabetes care in the primary and secondary care setting when this quality is measured with a summary score based on both process and outcome measures and case mix and clustering are taken into account?

- Does the multifaceted implementation of a locally adapted national guideline improve the outcomes of primary diabetes care?

- How often occurs clinical inertia in general practice, what is the association between clinical inertia and the outcomes of diabetes care and what are the determinants of clinical inertia in general practice?

- How often occurs polypharmacy in general practice, how adherent are patients with type 2 diabetes to their treatment regimens, what is the relationship between polypharmacy and patients´ adherence and what is the association between adherence and the outcome of diabetes care?

Chapter 2

Shared and delegated systems are not quick remedies for improving diabetes care: a systematic review

Background: type 2 diabetes is an important, chronic condition notorious for its costly and disabling complications. Nowadays, enhanced cooperation is expected to improve the quality of diabetes care and reduce cardiovascular risks in patients with diabetes. It is, however, questionable whether this assumption is evidence based.
Methods: using a structured literature search, we selected systematic reviews, randomised controlled trials (RCT's), and other effect evaluations regarding the sharing and delegation of diabetes care tasks.
Results: finally, 22 studies were included in this review. The process of care improved in all studies that investigated this quality aspect. HbA1c improved in seven reviews and in five other studies. All included reviews and four RCT's were unable to demonstrate a positive effect on the height of patients' blood pressure levels. Total cholesterol level improved in two reviews and five other studies.
Conclusion: the sharing and delegation of diabetes care tasks leads to a significant improvement of the process of care and a reduction in HbA1c percentage. This

improvement, however, has so far not led to better cardiovascular risk management. For a number of reasons, a truly accurate estimation of the effects of shared and delegated diabetes care within the Dutch healthcare system is not possible yet.

Chapter 3

Overall quality of diabetes care in a defined geographic region: different sides of the same story

Objective: to evaluate the quality of diabetes management in primary and secondary care in a defined geographic region in the Netherlands using a quality score.
Methods: a cross-sectional study was carried out in 30 general practices among 2042 patients with type 2 diabetes, (1640 primary and 402 secondary care). Quality of diabetes management was assessed by a score comprising process and outcome indicators (range 0 to 40). Clustering at practice level and differences in patient characteristics (case-mix) were taken into account.
Results: at the outpatient clinic, patients were younger (mean 64.1 years, SD 12.5 versus mean 67.1 years, SD 11.7, $p<0.001$), had more diabetes related complications (macrovascular: 39.7% versus 24.3%, $p<0.001$ and microvascular: 25.9% versus 7.3%, $p<0.001$) and lower quality of life scores (EuroQol-5D: mean 0.60, SD 0.29 versus mean 0.80, SD 0.21, $p<0.001$). After adjusting for case-mix and clustering, there was a weak association between the setting of treatment and HbA1c (primary care: mean 7.1%, SD 1.1 versus secondary care: mean 7.6%, SD 1.2, $p<0.016$) and between setting and systolic blood pressure (primary care: mean 145.7mmHg, SD 19.2 versus secondary care: 147.77mmHg, SD 21.0, $p<0. 035$). The quality of care sum scores in primary and secondary care differed significantly with a higher score in primary care (mean 19.6, SD 8.5 versus mean 18.1, SD 8.7, $p<0.01$). However, after adjusting for case-mix and clustering, this difference lost significance.
Conclusion: general practitioners and internists are treating different categories of type 2 diabetes patients. But, the overall quality of diabetes management in primary and secondary care is equal. There is much room for improvement. Future guidelines may differentiate between different categories of patients.

Chapter 4

Implementation of locally adapted guidelines on type 2 diabetes

Objective: to assess the effects of a facilitator enhanced multifaceted intervention to implement a locally adapted guideline on the shared care for people with type 2 diabetes.

Methods: during 1 year a cluster-randomized trial was performed in 30 general practices. In the intervention group, nurse facilitators enhanced guideline implementation by analysing barriers to change, introducing structured care, training practice staff and giving performance feedback. Targets for HbA1c%, systolic blood pressure as well as indications for the prescription of angiotensin converting enzyme and angiotensin receptor blocking agents differed from the national guidelines. In the control group, GPs were asked to continue the care for people with diabetes as usually. Generalized estimating equations were used to control for the clustered design of the study.

Results: in the intervention group, more people were seen on a 3-monthly basis (88% versus 69%, $P < 0.001$) and more blood pressure and bodyweight measurements were performed every 3 months (blood pressure 83% versus 66%, $P < 0.001$ and bodyweight 78.9% versus 48.5%, $P < 0.001$). Apart from a marginal difference in mean cholesterol, differences in HbA1c%, blood pressure, body mass index and treatment satisfaction were not significant.

Conclusion: multifaceted implementation of locally adapted shared care guidelines did improve the process of diabetes care but hardly changed intermediate outcomes. In the short term, local adaptation of shared care guidelines does not improve the cardiovascular risks of people with type 2 diabetes

Chapter 5

Clinical Inertia in General Practice: widespread and related to the outcome of diabetes care

Objective: clinical inertia is considered a major barrier to better diabetes care. We assessed its prevalence, predictors and associations with achieved levels of HbA1c, blood pressure and cholesterol.

Materials and Methods: we used the baseline and follow-up data of a RCT that compared usual care with care in line with a locally adapted national guideline. Duration of this study was one year. It took place in the Netherlands and involved 30 general practices and 1283 patients. Randomisation was at practice level.

Treatment targets differed between study groups (intervention group: HbA1c ≤ 8.0% and blood pressure <140/85 and controls: HbA1c ≤ 8.5% and blood pressure < 150/85). Clinical inertia was defined as the failure to intensify therapy when indicated. A complete medication profile of all participating patients was obtained. Clustering at practice level was controlled for.
Results: in the intervention and control group, the percentages of patients with poor diabetes or lipid control that did not receive treatment intensification were 45 and 90 percent approximately. More control group patients with blood pressure levels above target did not receive treatment intensification (72.7% versus 63.3%, p<0.05). In poorly controlled hypertensive patients, inertia was associated with the height of systolic blood pressure at baseline (adjusted OR 0.98, 95% CI 0.98-0.99) and the frequency of blood pressure control (adjusted OR 0.89, 95% CI 0.81-0.99). If a practice nurse managed these patients, clinical inertia was less common (adjusted OR 0.12, 95% CI 0.02-0.91). In both study groups, cholesterol decreased significantly more in patients who received proper treatment intensification.
Conclusion: general practitioners were more inclined to control blood glucose levels than blood pressure or cholesterol levels. Inertia in response to poorly controlled high blood pressure was less common if nurses assisted general practitioners.

Chapter 6

High refill adherence in general practice among patients with type 2 diabetes despite extensive polypharmacy

Objective: non-adherence with diabetes treatment has been associated with higher HbA1c and LDL cholesterol levels and is considered a major barrier to better outcomes of care. In addition, an inverse relationship has been established between multiple drug use and patients' adherence. The aim of this study is to investigate the occurrence of polypharmacy and patients' non-adherence in general practice, their mutual relationship and the association between adherence and the intermediate outcomes of diabetes care.
Materials and Methods: we used the baseline and follow-up data of an RCT that compared usual care with care in accordance with a locally adapted national guideline. This study took place in the Netherlands and involved 30 general practices and 1283 patients. We obtained a complete medication profile of all participants and calculated the number of prescribed drugs and the adherence indices for oral blood glucose, blood pressure and cholesterol lowering drugs.

Patients with an adherence index < 0.8 were considered non-adherent. Clustering at practice level and case-mix were taken into account.
Results: approximately 80% of the participating patients demonstrated an adherence index ≥ 0.8 for oral blood glucose, blood pressure and cholesterol lowering drugs. In the intervention group, increase of drug prescriptions exceeded that of controls (1.1 ± 2.0 versus 0.6 ± 1.5, p<0.001, adjusted p<0.05). There was evidence of a inverse relationship between the number of drugs that had been prescribed during the last six months of the study and patients' adherence to blood pressure lowering medications (adjusted OR 0.84, 95% CI 0.78 to 0.91). After one year, HbA1c and total cholesterol levels were significantly lower in adherent patients.
Conclusion: during the intervention the mean number of drug prescriptions increased in both study groups. This did not result in a lower adherence to blood glucose, blood pressure and cholesterol lowering medications. Given the relationship between the number of medications and patients' adherence to blood pressure lowering drugs, it may be wise to discuss adherence before prescribing multiple drug regimens.

Chapter 7

General discussion

In this chapter, the main findings of the studies presented in this thesis as well as different aspects of the quality of diabetes care are discussed. In the greater Apledoorn region, the quality of diabetes management in general practice and secondary care is equal. However, as mean quality scores are rather low (approximately 20 out of 40 points), there is much room for improvement. Local adaptation and implementation of shared care guidelines are considered important tools to enforce such a quality improvement. Both the results of our review and the results of the randomized controlled trial presented in this thesis demonstrate the limited effects of local adaptation and shared care on the outcomes of diabetes management. Therefore, adaptation and implementation of shared care guidelines should not be considered a wonder drug. Our studies on clinical inertia and patients' adherence made clear that especially clinical inertia is widespread. Both inertia and non-adherence to treatment regimens are related to the outcomes of diabetes care and represent important targets for quality improvement initiatives.

When exploring the quality of diabetes care it is useful to distinguish the classic Donobedian traid structure, process and outcome. More and more patients' opinions

and access to care have been recognized to be important indicators of the quality of care also. In light of the advantages and disadvantages of each of these measures, it is advisable to include in any system of quality assessment, a combination of different indicators. This allows complementation of weaknesses in one approach by strengths in another. Preferably, such a combination contains indicators that are both readily available and closely linked to the hard endpoints of diabtes care. Recently, the Quality of Care and Outcomes in Type 2 Diabetes (QuED) study group developed such a combination of process and outcome measures. As there is growing evidence of a link between treatment intensification, patients' adherence to their treatment regimens and the outcomes of care, measures of clinical inertia and non-adherence should be incorporated in future assessment systems. Based on these observations, a 14-item measure set has been proposed.

Samenvatting

Diabetes mellitus type 2 is een frequent voorkomende aandoening die mede door het optreden van complicaties tot hoge kosten kan leiden. De afgelopen vijftien jaar is het duidelijk geworden dat door het streven naar een normaal bloedglucosegehalte, een zo laag mogelijke bloeddruk en een zo normaal mogelijk vetspectrum het risico op complicaties wordt verkleind. Op basis van deze resultaten is een groot aantal richtlijnen gepubliceerd die een strikte regulatie van het bloedglucosegehalte, de bloeddruk en het cholesterolgehalte aanbevelen. Helaas worden deze richtlijnen onvoldoende opgevolgd en schiet de behandeling van patiënten met diabetes nog vaak tekort.

Het doel van dit proefschrift is meer inzicht te krijgen in methoden die een bijdrage kunnen leveren aan het verbeteren van de kwaliteit van de diabeteszorg. Bovendien wordt stil gestaan bij de problemen die zich voordoen bij het meten van de kwaliteit van die zorg. In eerste instantie hebben wij een systematisch literatuuronderzoek verricht naar de effecten van het delen en delegeren van de zorg voor patiënten met diabetes. De resultaten van dit onderzoek zijn beschreven in het tweede hoofdstuk van dit proefschrift. Vervolgens gaan wij in het derde hoofdstuk nader in op de vraag hoe de kwaliteit van de diabeteszorg in de huisartsenpraktijk zich verhoud tot die in de polikliniek van een regionaal ziekenhuis. In hoofdstuk vier beschrijven we de resultaten van ons onderzoek naar de gevolgen van het invoeren van een locale werkafspraak voor de kwaliteit van de diabeteszorg. In het vijfde en zesde hoofdstuk bespreken wij achtereenvolgens in welke mate het niet tijdig bijsturen van de behandeling en het onvoldoende opvolgen van de behandelingsadviezen bepalend zijn voor de uitkomst van de diabeteszorg. In het laatste hoofdstuk wordt, deels aan de hand van de resultaten van het eigen onderzoek, dieper ingegaan op diverse aspecten van het meten en het verbeteren van de kwaliteit van de zorg voor patiënten met diabetes.

Hoofdstuk 1

In het eerste hoofdstuk wordt een inleiding gegeven op het onderwerp van dit proefschrift. Na een korte uiteenzetting over de voorwaarden die aan een succesvolle strategie voor het implementeren van richtlijnen kunnen worden verbonden, volgt een nadere uitwerking van de vragen waar dit proefschrift een antwoord op tracht te geven. Deze vragen luiden als volgt:

- Verbetert het delen en delegeren van zorgtaken de kwaliteit van de diabeteszorg en leidt dit tot een verlaging van het cardiovasculaire risico van patiënten met diabetes mellitus type 2?

- Wat is de kwaliteit van de diabeteszorg in de eerste en tweede lijn indien deze gemeten wordt met een op zowel proces[1] als uitkomstmaten[2] gebaseerd meetinstrument?

- Leidt de implementatie van een locale werkafspraak over de zorg voor patiënten met diabetes mellitus type 2 tot een verbetering van de kwaliteit van de diabeteszorg?

- Hoe vaak komt klinische inertie[3] voor in de huisartspraktijk, wat is het verband tussen inertie en de uitkomst van de zorg voor patiënten met diabetes en wat zijn de mogelijke determinanten van het optreden van inertie in de eerste lijn?

- Hoe vaak krijgen patiënten meerdere medicijnen voorgeschreven en in welke mate halen zij de voorgeschreven middelen af bij de apotheek, wat is relatie tussen het aantal voorgeschreven middelen en het afhalen hiervan en wat is de relatie tussen het afhalen van medicatie en de uitkomst van de diabeteszorg?

Hoofdstuk 2

Op dit moment verwacht men, dat het verbeteren van de samenwerking tussen specialisten, huisartsen en paramedici een kwaliteitsimpuls geeft. Hierbij speelt het delen en delegeren van zorgtaken een belangrijke rol. Het is echter de vraag of deze verwachting op voldoende bewijs is gebaseerd. Om deze vraag te beantwoorden hebben wij de beschikbare literatuur over de effecten van het delen en delegeren van de diabeteszorg systematisch onderzocht. Onze zoekactie in medline (1990-20050) leverde 2406 treffers op. Uiteindelijk sloten wij 22 onderzoeken in: vijf over het delen, 13 over het delegeren en vier over het delen en delegeren van de zorg. Het zorgproces verbeterde in alle studies die het delen en/of delegeren van de

[1] De wijze waarop de zorg wordt geleverd

[2] De effecten van de geleverde zorg op middellange en lange termijn zoals de hoogte van het bloedsuikergehalte of het optreden van cardiovasculaire sterfte en ziekte

[3] Het achterwege laten van het aanpassen van de medicatie terwijl dat wel geindiceerd is

diabeteszorg onderzochten. Het HbA1c % nam in zeven reviews en in vier van de overige onderzoeken af. De bloeddruk daalde in vier niet gerandomiseerde onderzoeken en in drie van de zeven RCT's, maar in niet één van de ingesloten reviews. Het cholesterol nam in twee reviews, één RCT en vier niet gerandomiseerde onderzoeken af. Op grond van de resultaten van ons onderzoek is het aannemelijk dat het delen van zorgtaken tussen huisartsen en specialisten even effectief kan zijn als de traditionele ziekenhuiszorg. De introductie van transmurale[4] zorg verbetert de wijze waarop de patiënt in de eerste lijn wordt behandeld en bevordert de daling van het HbA1c percentage[5] maar die zorg heeft geen positief effect op de hoogte van de bloeddruk of op het cholesterolgehalte. Uit ons onderzoek blijkt bovendien dat de effecten van het delegeren van de diabeteszorg matig en wisselend zijn. De inzet van diabetesverpleegkundigen lijkt vooralsnog uitsluitend op de korte termijn tot een verlaging van het HbA1c percentage te leiden. Er is echter onvoldoende bewijs voor een gunstige invloed op het vetspectrum, de bloeddruk of de BMI. Het delen en delegeren van zorgtaken speelt een belangrijke rol bij een nieuw concept voor de zorg dat disease management[6] wordt genoemd. De conclusies over dit zorgconcept zijn eenduidig: de introductie van disease management verbetert de wijze waarop de zorg wordt geleverd en leidt tot een daling van het HbA1c percentage. Verder kan het een positieve invloed op de bloeddruk hebben. Er is echter nog onvoldoende bewijs voor een effect van disease management op het gewicht en het lipidengehalte.

De conclusies van dit literatuuronderzoek worden door een aantal zaken beperkt. In Nederland zijn slechts weinig gecontroleerde onderzoeken gedaan naar de gevolgen van het delen en delegeren voor de kwaliteit van de diabeteszorg. Een deel van het internationale onderzoek is door de patiëntenselectie, de setting, de financiering en de organisatie van de zorg niet generaliseerbaar en daardoor beperkt van toepassing

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[4] Zorg die is toegesneden op de behoefte van de patiënt en die wordt gegeven op basis van afspraken over samenwerking, afstemming en regie tussen generalistische en specialistische zorgverleners

[5] HbA1c is hemoglobine waaraan glucose is gehecht. Hemoglobine is een eiwit in de rode bloedcellen, dat er voor zorgt dat deze cellen zuurstof kunnen opnemen in de longen en afgeven in de weefsels. Een grotere hoeveelheid glucose in het bloed leidt tot een hoger percentage hemoglobine waaraan glucose is gehecht. Omdat rode bloedcellen ongeveer twee tot drie maanden leven, is het percentage van het normale hemoglobine dat uit HbA1c bestaat een goede maat voor de glucoseregulatie van de afgelopen twee tot drie maanden.

[6] De programmatische en systematische aanpak van specifieke zieketen en gezondheidsproblemen door het gebruik van managementinstrumenten, met als doel de kwaliteit en doelmatigheid te bevorderen. Kenmerkend zijn delen en delegeren, een bedrijfsmatige benadering van de zorg, een sterke mate van protocollering, een populatiegerichte aanpak en nadruk op educatie en zelfmanagement

op de Nederlandse situatie. Bovendien is in een aantal publicaties onvoldoende omschreven hoe de zorg gedeeld dan wel gedelegeerd werd en is de follow-up van de meeste onderzoeken beperkt waardoor effecten op de lange termijn niet duidelijk zijn. Ten slotte wordt het delen en/of delegeren van de zorg vaak gecombineerd met andere interventies, zoals het introduceren van richtlijnen of het geven van feedback aan behandelaars. Deze factoren maken het moeilijk een echt nauwkeurige inschatting van de gevolgen van het delen en delegeren voor de Nederlandse diabeteszorg te geven.

Voor de dagelijkse praktijk betekenen deze resultaten dat op dit moment niet is aangetoond dat het delen en delegeren van zorgtaken een belangrijke bijdrage levert aan het verlagen van het cardiovasculaire risico voor patiënten met diabetes. Het verdient dan ook aanbeveling de gevolgen van de nieuwe zorgmodellen voor de kwaliteit van de diabeteszorg de komende jaren nauwkeurig te volgen en waar nodig het proces van zorgvernieuwing bij te sturen.

Hoofdstuk 3

Het is voor de kwaliteit van de diabeteszorg van belang de resultaten van die zorg op een objectieve wijze te meten en af te zetten tegen van te voren vastgestelde criteria. Daarom is het noodzakelijk te beschikken over een objectieve en betrouwbare manier om de kwaliteit van de zorg te meten. Recent werd door de “Quality of Care and Outcomes in Type 2 Diabetes study group” (QuED) een kwaliteitsscore ontwikkeld die aan deze criteria voldoet. De QuED score is zowel op proces als uitkomstmaten gebaseerd en vertoont een duidelijke relatie met het optreden van hart- en vaatziekten en de daardoor veroorzaakte sterfgevallen. Wij hebben een aan de plaatselijke omstandigheden aangepaste versie van deze score gebruikt om in Apeldoorn en omgeving de kwaliteit van de zorg in de eerste en de tweede lijn te meten. Aan dit onderzoek namen 2042 patiënten met diabetes mellitus type 2 deel. Van deze patiënten werden er 1640 in de eerste en 402 in de tweede lijn behandeld. In de eerste lijn vond een basismeting plaats waarbij de deelnemende patiënten werden onderzocht en diverse gegevens werden genoteerd. In de tweede lijn werd een uitvoerig statusonderzoek verricht. Zowel in de eerste als in de tweede lijn ontvingen patiënten een lijst die vragen bevatte over de kwaliteit van leven en de tevredenheid met de diabeteszorg. De bestanden van de plaatselijke apotheken en apotheekhoudende huisartsen werden gebruik om een compleet medicatieoverzicht van alle deelnemende patiënten te verkrijgen. Bij de analyse werd rekening

gehouden met bestaande verschillen tussen patiënten in leeftijd, geslacht, duur van de diabetes, micro-[7] en macrovasculaire[8] complicaties, opleiding, kwaliteit van leven en het gebruik van insuline (case-mix). Bovendien werd gecorrigeerd voor het verschijnsel dat patiënten met diabetes clusteren rondom behandelaars.

Patiënten die in de tweede lijn werden behandeld waren jonger, hadden al langer diabetes en meer micro- en macrovasculaire complicaties. Bovendien scoorden zij lager waar het de kwaliteit van hun leven betrof. Aanvankelijk bestond er een duidelijk verschil in de kwaliteit van de zorg tussen de eerste en de tweede lijn; de kwaliteitsscores van de huisartspraktijken waren hoger en ook de gemiddelde instelling van de diabetes en de tevredenheid met de zorg van de eerstelijns patiënten was beter. Tweedelijns patiënten scoorden beter waar het de behandeling met ACE-remmers of ATII receptor antagonisten betrof. Ook het totale cholesterolgehalte was bij deze patiënten beter. De meeste verschillen waren niet meer significant nadat met de bovenvermelde case-mix factoren en clustering rekening werd gehouden. Het gemiddelde HbA1c percentage en de systolische bloeddruk bleven in de eerste lijn echter significant lager dan in de tweede lijn. Bovendien hadden meer patiënten een HbA1c<8%.

De resultaten van dit onderzoek maken duidelijk dat de kwaliteit van de diabeteszorg in de eerste en tweede lijn vergelijkbaar is indien rekening wordt gehouden met case-mix en clustering. Gezien het feit dat de gemiddelde kwaliteitsscore zowel bij de huisartsen als de specialisten nog geen twintig punten bedraagt en het maximaal te behalen aantal punten veertig is, valt er nog veel winst te behalen.

Hoofdstuk 4

Het invoeren van standaarden wordt gezien als een goede manier om de kwaliteit van diabeteszorg te verbeteren. Het invoeren van dergelijke werkafspraken is echter niet eenvoudig. Succesvolle implementatiestrategieën zijn in de regel actief en gericht op verschillende aspecten van de zorg. Bovendien bestaat de verwachting dat het aanpassen aan locale omstandigheden leidt tot een betere acceptatie van richtlijnen. Daarom hebben wij onderzocht of het invoeren van een lokale

[7] Complicaties door schade aan de kleine bloedvaten zoals een verminderde nierfunctie of afwijkingen aan het netvlies

[8] Complicaties door schade aan de grote bloedvaten zoals hartvaatziekten en perifeer vaatlijden

werkafspraak voor de behandeling van patiënten met diabetes de kwaliteit van de zorg verbetert. Aan het onderzoek namen 1640 patiënten deel, die afkomstig waren uit 30 huisartspraktijken. De praktijken werden verdeeld in twee groepen: één groep voerde de nieuwe werkafspraak in (interventiegroep) en één groep behandelde de patiënten zoals gebruikelijk (controlegroep). De implementatie werd ondersteund door twee diabetesverpleegkundigen die de praktijken waar de werkafspraak werd ingevoerd, meerdere keren bezochten, behandelingsadviezen gaven, training en onderwijs verzorgden en feedback gaven aan de deelnemende huisartsen en praktijkmedewerkers. Na een jaar werden de resultaten in de beide groepen vergeleken. Bij het analyseren van de resultaten werd rekening gehouden met de eerder omschreven case-mix factoren en clustering.

Uit het onderzoek bleek, dat de wijze waarop de zorg werd geleverd in de interventiegroep duidelijk beter was dan in de controlegroep. Bovendien bereikten meer aanvankelijk slecht ingestelde patiënten een bevredigende instelling van hun diabetes. Aanvankelijk leek er tussen de beide groepen ook een verschil te bestaan in het gemiddelde HbA1c percentage maar na rekening gehouden te hebben met case-mix factoren en clustering was dit verschil niet langer significant. Wij konden geen verschillen aantonen in bloeddruk, BMI of tevredenheid met de zorg. Uiteindelijk vonden wij een klein verschil in het cholesterolgehalte tussen de patiënten uit de interventie- en die uit de controlegroep.

Op basis van ons onderzoek lijkt het niet waarschijnlijk dat het invoeren van locale werkafspraken een belangrijke bijdrage zal leveren aan het verbeteren van de kwaliteit van de diabeteszorg. Wij menen dan ook dat het beter is energie te spenderen aan het zo volledig mogelijk invoeren van landelijke richtlijnen dan aan het aanpassen van deze richtlijnen aan locale omstandigheden.

Hoofdstuk 5

In hoofdstuk 5 gaan wij nader in op de gevolgen van klinische inertie (het achterwege laten van het aanpassen van de medicatie terwijl dat wel geindiceerd is). Dit verschijnsel is waarschijnlijk wijdverspreid en wordt gezien als een belangrijke hindernis voor het verbeteren van de kwaliteit van de zorg. Klinische inertie wordt aan ten minste vier factoren toegeschreven, te weten: het overschatten van de geleverde zorg, het gebruik van “zachte” argumenten om het aanpassen van de therapie te vermijden, gebrek aan scholing en kennis en een gebrekkige organisatie

van de praktijk. Het is de vraag in hoeverre de teleurstellende resultaten van de eerder beschreven trial te wijten zijn aan het optreden van klinische inertie. Bovendien is het interessant te onderzoeken welke factoren met het optreden van inertie samenhangen.

Aan het onderzoek namen 1283 patiënten met diabetes mellitus type 2 deel. Van deze patiënten werd een compleet medicatieoverzicht verkregen. Dit overzicht was gebaseerd op de bestanden van de locale apothekers en de apotheekhoudende huisartsen. Wij bepaalden of de therapie bij patiënten werd gewijzigd, door het gebruik van bepaalde medicijnen bij aanvang van het onderzoek te vergelijken met dat wat zes maanden later werd voorgeschreven. Bij de analyse werd rekening gehouden met het clusteren van patiënten.

Zowel in de interventiegroep als in de controlegroep kwam klinische inertie frequent voor. Bij 40% van de patiënten met een slecht gereguleerde diabetes werd de therapie niet aangepast. Dit percentage bedroeg bij patiënten met een te hoge cholesterolwaarde zelfs 90%. In de controlegroep kwam klinische inertie bij patiënten met een te hoge bloeddruk duidelijk vaker voor dan in de interventiegroep (73% versus 64%, $p<0.05$). Bij diabetes patiënten met een te hoge bloeddruk hing het aanpassen van de medicatie samen met de hoogte van de systolische bloeddruk bij aanvang van het onderzoek en met het aantal controles. Klinische inertie trad minder vaak op als deze patiënten ook door een praktijkondersteuner werden behandeld. Bij patiënten met een te hoog cholesterolgehalte bleek dit gehalte in de beide onderzoeksgroepen significant meer af te nemen als de therapie tijdig werd aangepast. Een dergelijk verband kon niet worden vastgesteld bij patiënten met te hoog HbA1c percentage of een te hoge bloeddruk.

Op grond van de resultaten van dit onderzoek kan de conclusie worden getrokken dat klinische inertie bij de behandeling van patiënten met diabetes een belangrijke rol speelt. Dit onderzoek laat zien dat vooral bij patiënten met een slecht gereguleerde bloeddruk en een te hoog cholesterol gehalte inertie zeer frequent optreedt. Kennelijk is de behandeling vooral gericht op het verlagen van het bloedglucosegehalte en minder op het aanpakken van belangrijke cardiovasculaire risicofactoren als een te hoge bloeddruk of een verhoogd cholesterolgehalte.

Hoofdstuk 6

In tal van richtlijnen wordt gepleit voor het strikt reguleren van het bloedglucosegehalte, de bloeddruk en het cholesterolgehalte van patiënten met diabetes. Het is dan ook teleurstellend dat ondanks het op grote schaal invoeren van deze richtlijnen de uitkomsten van de diabeteszorg achter blijven. Het is zeker niet uitgesloten dat dit veroorzaakt wordt door het niet goed opvolgen van de richtlijnen. Het is echter ook goed mogelijk dat de soms tegenvallende uitkomsten van de zorg worden veroorzaakt door een gebrekkige compliance[9] van patiënten. Zo verklaarde de WHO recent dat slechts 50% van de patiënten met diabetes volledig trouw is aan de gegeven adviezen.

Bij de behandeling van diabetes is het vaak noodzakelijk patiënten meerdere geneesmiddelen tegelijkertijd voor te schrijven. Nu doet zich het probleem voor dat polyfarmacie[10] kan leiden tot een verminderde compliance. Het is dan ook goed voorstelbaar dat de teleurstellende resultaten van de in het vierde hoofdstuk beschreven interventie het gevolg zijn van het in verhoogde mate voorschrijven van geneesmiddelen met een verminderde geneesmiddelentrouw als gevolg. Om deze hypothese te toetsen hebben wij onderzocht hoe vaak polyfarmacie en een niet optimale geneesmiddelentrouw in de beide onderzoeksgroepen van de trial voorkwamen. Bovendien onderzochten wij de relatie tussen het gebrek aan compliance en de uitkomsten van de zorg.

Aan het onderzoek namen 1283 patiënten met diabetes mellitus type 2 deel. Van deze patiënten werd een compleet medicatieoverzicht verkregen. Dit overzicht was gebaseerd op de bestanden van de locale apothekers en de apotheekhoudende huisartsen. Bij alle deelnemende patiënten werd de dagelijkse dosis van alle chronisch gebruikte geneesmiddelen bepaald. Bovendien werd bij alle patiënten vastgesteld in welke mate zij de voorgeschreven medicatie bij de apotheek afnamen. Als uitkomstmaten werden het HbA1c percentage, de bloeddruk en het cholesterolgehalte na afloop van de interventie gebruikt. Bij de analyse van de gegevens werd met de eerder vermelde case-mix factoren en clustering rekening gehouden.

[9] Geneesmiddelentrouw

[10] Het gelijktijdig voorschrijven van verschillende geneesmiddelen

Het gebruik van geneesmiddelen steeg duidelijk gedurende de interventie. Ondanks de stijging van het geneesmiddelengebruik was de geneesmiddelentrouw van de deelnemende patiënten erg goed. Ruim 80% van hen gebruikte ten minste 80% van de voorgeschreven bloedglucose, bloeddruk of cholesterol verlagende medicijnen. Het het trouw innemen van de bloeddruk verlagende medicatie was gerelateerd aan aantal geneesmiddelen dat gedurende de laatste zes maanden van het onderzoek werd voorgeschreven. Een dergelijk verband werd niet gevonden tussen het aantal medicijnen en het correcte gebruik van bloedglucose of cholesterol verlagende geneesmiddelen. Er bestond een duidelijke relatie tussen het innemen van medicatie en de hoogte van het HbA1c percentage en het cholesterolgehalte. De relatie tussen het gebruik van bloedruk verlagende geneesmiddelen en de bloeddruk was minder duidelijk.

Op grond van deze resultaten lijkt het niet waarschijnlijk dat de teleurstellende resultaten van de trial het gevolg zijn van een verminderde geneesmiddelentrouw door het in verhoogde mate optreden van polyfarmacie. Wel is het gezien de relatie tussen het aantal voorgeschreven geneesmiddelen en het correct gebruiken van bloeddruk verlagende medicatie van belang eerst de geneesmiddelentrouw te bespreken voordat wordt overgegaan tot het intensiveren van de behandeling.

Hoofdstuk 7

In dit hoofdstuk worden de belangrijkste bevindingen van de bovenvermelde onderzoeken tegen het licht gehouden. Bovendien wordt dieper ingegaan op de diverse aspecten van het meten van de kwaliteit van de zorg. Uit de resultaten van ons onderzoek naar de kwaliteit van de diabeteszorg in de eerste en tweede lijn blijkt dat deze gelijk is. De gemiddelde score in zowel de huisartspraktijk als het ziekenhuis is echter laag (20 van de maximaal 40 te behalen punten). Er is dan ook ruimte voor verbetering. Hoewel het aanpassen van nationale richtlijnen aan locale omstandigheden en het invoeren van transmurale werkafspraken wordt gezien als een belangrijk middel om de kwaliteit van de zorg te verbeteren, blijkt uit de resultaten van zowel ons literatuuronderzoek als de in het vierde hoofdstuk gepresenteerde trial dat het aan locale omstandigheden aanpassen en implementeren van transmurale werkafspraken slechts een beperkt effect heeft op de uitkomst van de zorg. Onze onderzoeken naar klinische inertie en geneesmiddelentrouw laten zien dat vooral klinische inerte wijdverspreid is. Beide blijken geassocieerd met de

uitkomst van de diabeteszorg en kunnen, indien aanwezig, worden beschouwd als een belangrijke barrière voor de gewenste kwaliteitsverbetering.

Bij het bestuderen van de kwaliteit van de zorg spelen structuur, proces en uitkomstmaten een belangrijke rol. Meer en meer worden ook de mening van de patiënt en de toegankelijkheid van de zorg als kwaliteitsmaten gezien. Ieder van deze maten heeft zijn eigen voor en nadelen. Om die reden is het verstandig bij het meten van de kwaliteit van de zorg een combinatie van verschillende proces en uitkomst indicatoren toe te passen. Daar er bewijs is voor een associatie tussen klinische inertie, geneesmiddelentrouw en de uitkomst van de diabeteszorg is het wenselijk dat deze procesmaten worden toegevoegd aan bestaande indicatorsets. Op grond van deze overwegingen komen wij uiteindelijk tot een lijst van 14 indicatoren die in de toekomst gebruikt kunnen worden om de kwaliteit van de diabeteszorg te meten.

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Curriculum vitae

Rykel van Bruggen was born on June 19th, 1959, in Groningen, The Netherlands. After graduating from Hageveld College in Heemstede in 1978, he attended Delft University of Technology to become a naval architect. After one year he left Delft and started medical school at the University of Utrecht. He obtained his medical degree in 1986 and worked as an intern at the department of internal medicine at the Schieland Hospital (Schiedam). From 1987 until 1989 he was employed by the Leyenburg Hospital (the Hague) as an internal medicine resident. In 1989 he started vocational training at the University of Utrecht including training periods at the practices of Nico Zee (Gorkem) and Emile Boutens (Utrecht). In 1991 he started as a general practitioner in Apeldoorn, as the successor of J. Netel. Since 2003 he has been employed by the Julius Center for Health Sciences and Primary Care, University of Utrecht, where he completed this thesis. In 2008 he became a staff member of the department of Guideline Development and Research Policy at the Dutch College of General Practitioners.