BMJ open

Diabetes care in a shared care prospective observational study: trends and age differences in the period 1998-2008 (ZODIAC-19)

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2012-001387
Article Type:	Research
Date Submitted by the Author:	26-Apr-2012
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Primary Subject Heading:	Diabetes and endocrinology
Secondary Subject Heading:	Diabetes and endocrinology, Epidemiology
Keywords:	General diabetes < DIABETES & ENDOCRINOLOGY, GERIATRIC MEDICINE, PRIMARY CARE, Vascular medicine < INTERNAL MEDICINE

Title: Diabetes care in a shared care prospective observational study: trends and age differences in the period 1998-2008 (ZODIAC-19)

Short title: Trends in diabetes care in the period 1998-2008

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Word count: main text 2707; abstract 300.

Number of tables: 2; number of figures: 2.

Abstract

Objective: The Zwolle Outpatient Diabetes project Integrating Available Care (ZODIAC) study was initiated in 1998 to investigate the effects of shared care for patients with type 2 diabetes mellitus (T2DM) in the Netherlands, and to reduce the number of diabetes-related complications. Benchmarking the performance of diabetes care was and is an important aspect of this study. We aimed to investigate trends in diabetes care, within the ZODIAC study for a wide variety of quality indicators during a long follow-up period (1998-2008), with special interest for different age groups.

Design: Prospective observational cohort study.

Setting: Primary care, Zwolle, The Netherlands.

Participants: Patients with T2DM.

Methods: A dataset of quality measures was collected annually during the patient's visit to the practice nurse or general practitioner. Linear time trends from 1998-2008 were estimated using linear mixed models in which we adjusted for age and gender. Age was included in the model as a categorical variable: for each follow-up year all participants were categorised into the categories <60, 60-75 and >75 years. Differences in trends between the age categories were investigated by adding an interaction term to the model.

Results: The number of patients who were reported to participate increased in the period 1998-2008 from 1622 to 27.438. All quality indicators improved in this study, except for body mass index. The prevalence albuminuria decreased in an eleven-year-period from 42% to 21%. No relevant differences between the trends for the 3 age categories were observed. During all years of follow-up, mean blood pressure and body mass index were the lowest and highest, respectively, in the group of patients <60 years (data not shown).

Conclusion: Quality of diabetes care within the Dutch ZODIAC study, a shared care project, has considerably improved in the period 1998-2008. There were no relevant differences between trends across various age categories.

Keywords: Diabetes mellitus type 2; Observational studies.

Article focus

- Shared care, defined as care for patients with a chronic condition provided in cooperation between primary and secondary health care, has been promoted and developed in order to reduce the number of diabetes-related complications.
- There is limited data whether improvements in diabetes care in the past decades are comparable across different age categories.
- We aimed to investigate trends in diabetes care, within a shared care project, during a long follow-up period (1998-2008), with a special focus on different age groups.

Key messages

- Quality of diabetes care within the Dutch ZODIAC study, a shared care project, has considerably improved in the period 1998-2008.
- Large improvements were observed for all quality indicators studied in this study, except for BMI.
- No relevant differences between the trends for the 3 age categories were observed.

Strengths and limitations

- Strengths of our study are the long follow-up period and the high number of participants.
- A causal relationship between shared care and the observed improvements can not be proved due to the observational design of our study.

- **Introduction**

Ever since it was established that type 2 diabetes mellitus (T2DM) leads to significant morbidity and mortality [1,2], prevention and (early) treatment of both microvascular and macrovascular complications of T2DM have become important goals in diabetes care. Efforts to improve the quality of diabetes care are necessary in order to reduce morbidity and mortality associated with T2DM [3,4]. Since adequate treatment of patients with T2DM often needs the involvement of more than one caregiver, shared care, defined as care for patients with a chronic condition provided in cooperation between primary and secondary health care, has been promoted and developed [5].

The *Zwolle Outpatient Diabetes project Integrating Available Care* (ZODIAC) study was initiated in 1998 to investigate the effects of shared care for patients with T2DM in the Netherlands [6]. Benchmarking the performance of diabetes care was and is an important aspect of this initiative. Previous reports from the ZODIAC study showed that structured shared care with task delegation to nurses leads to improvements in quality of diabetes care and life expectancy [6-8]. However, effectiveness of shared care in general was not demonstrated in a 2007 Cochrane review [5]. Inadequate length of follow-up was mentioned by the authors as a possible explanation for the lack of evidence.

Although diabetes care has improved considerably during the past decades in patients with diabetes, there is limited data whether these improvements are comparable across different age categories [9,10]. A cross-sectional study from France showed that quality of care had considerably improved for patients ≥65 years with T2DM in the period 2001-2007 [11]. Unfortunately, trends for patients >75 years were not described separately in this study. Although the number of patients with T2DM >75 years is increasing, the evidence for cardiovascular risk interventions in this age category is low [12]. Data from observational studies show that classic cardiovascular risk factors may even have different consequences in elderly patients [13-17].

In the present study, we aimed to investigate trends in diabetes care, within a shared care project, for a wide variety of quality indicators during a long follow-up period (1998-

2008). Because of limited evidence for cardiovascular risk interventions in old age, we had specific interest whether the same trends were observed for different age groups (<60, 60-75 and >75 years).

Methods and Patients

Study population and ZODIAC

The ZODIAC study started in 1998 as a prospective observational study for patients with T2DM [6]. Participating practices were allocated to one of the two intervention groups or to the standard care group. The interventions involved extensive or limited task delegation from general practitioners to practice nurses and/or diabetes specialist nurses. Moreover, it included a diabetes register, structured recall, facilitated generalist-specialist communication, audit and feedback, patient-specific reminders, and it emphasized patients' education [6]. The patients participating in the ZODIAC study are known with T2DM and exclusively treated in primary care. Patients who were already treated in secondary care for their diabetes, patients with a very short life expectancy (including patients with active cancer) and patients with insufficient cognitive abilities were excluded from participation. In the first years of ZODIAC, only patients in the surrounding area of the city of Zwolle participated in the study. Because of the improvements in the quality of diabetes care in the two intervention groups, the shared care project has expanded gradually in the past decade. Firstly, the shared care project became the standard for diabetes care in the entire Zwolle region (2002-2003), and in 2005-2006 the project expanded to the northeast region of the Netherlands. The number of participating general practitioners (GPs) has increased from 53 in 1998 to 459 in 2008. Patient numbers increased from 1622 to 27.438 in this time frame, and nowadays even more than 60.000 patients are participating. A benchmark of annually gathered quality measures of this cohort, based on the guidelines of the Dutch College of General Practitioners and the Dutch Diabetes Federation, has been developed [18].

Data collection

The dataset of quality measures is collected annually during the patient's visit to the practice nurse and/or GP. At baseline, additional data were collected including a full medical history. The dataset contains many quality measures, including data on cardiovascular risk control, treatment and complications. Distinction is made between process and outcome measures.

Process measures indicate whether tests or assessments have been performed, e.g. the number of patients whose HbA1c level has been determined. Outcome measures reflect the results of the assessments, such as the mean systolic blood pressure or the proportion of patients with a systolic blood pressure <140 mm Hg. Table 1 shows an overview of the measures we investigated in this study for each year of follow-up.

Statistical analyses

Continuous variables are represented as means and 95% confidence intervals (95% CI) for the normally distributed values. Normality was evaluated using Q-Q plots and histograms. Nominal variables are represented as the proportion of patients together with 95% CIs. Linear time trends from 1998-2008 were estimated using linear mixed models (SAS PROC MIXED for continuous variables and PROC GLIMMIX for binary variables) in which we adjusted for age and gender. Age was included in the model as a categorical variable: for each follow-up year all participants were categorised into the categories <60, 60-75 and >75 years. All trends were visually inspected and quadratic trend analysis was only performed when such a trend was likely based on the plot. Differences in trends between the age categories were investigated by adding an interaction term to the model. A significant trend for interaction with age means that differences exist between the trends of the 3 age categories. All analyses were performed with SPSS version 18.0.0 software (SPSS inc., Chicago, Illinois, USA) and with SAS 9.2 software (SAS Institute Inc., Cary, NC, USA).

The manuscript was written based on the 'Strengthening the reporting of observational studies in epidemiology' (STROBE) statement [19].

Ethics statement

The ZODIAC study and the informed consent procedure were approved by the local medical ethics committee of the Isala Clinics, Zwolle, the Netherlands. In the first years of ZODIAC, verbal informed consent was obtained from all patients and the consent was documented in

the patient's records. According to Dutch law, written informed consent was not necessary for this type of study in 1998. Nowadays, written informed consent is obtained. All data were analysed anonymously.

Results

The number of patients who were reported to participate in this shared care project increased in the period 1998-2008 from 1622 to 27.438. Mean age decreased with time from 68.9 to 67.4 years (p for trend <0.0001). A gradual increase was observed for the proportion of male patients participating in the project. Median diabetes duration remained rather constant at 5 years throughout the whole study period. The proportion of patients aged older than 75 years was 31.0% in 1998 and declined to 26.3% in 2008. The number of patients who did not participate in the study due to short life expectancy of insufficient cognitive abilities is unknown after 1999. The results for all process and outcome measures of each year for the overall study group are presented in table 2.

Process measures

All process measures show a similar trend (table 2): a gradual increase in the first years of the project followed by a decrease in the years 2002 and 2003, an increase in the upcoming two years, followed by a decrease in 2006 again and a rising trend in the process measures in the last two years. Body mass index (BMI), the lipid profile and the ACR were less often measured in patients aged >75 years compared to the younger patients (p for interaction with age for all variables <0.0001). Figure 1 illustrates the trends for the process measure of ACR, BMI and blood pressure in the total study population.

Outcome measures

Figure 2 presents the trends for outcome measures over time for the overall study group and also stratified according to the 3 age categories.

Glycemic control and diabetes treatment

The decline in mean HbA1c over time is reflected in the proportion of patients achieving the target value of <7%; 35.8% in 1998 compared to 67.0% in 2008. The differences between the 3 age categories seem to be small, although the proportion of patients with an HbA1c

≥8.5% tended to be the highest for patients aged <60 years in all years (p for interaction with age 0.0773). The proportion of patients treated with only a diet increased over time from 16.6% to 23.8%. A total of 15.5% used insulin in 1998 and this proportion declined to 12.8% in 2008.

Blood pressure and treatment

Mean blood pressure has decreased over time in all age groups, with the lowest values in the youngest patient category (p for interaction with age <0.0001). In 1998 about one fifth (22.0%) had a systolic blood pressure <140 mmHg, compared to 47.7% in 2008. The number of patients with antihypertensive medication increased in all age groups. With advancing age the number of patients using these agents also increased (p for interaction with age <0.0001). A remarkable decrease in 2003 was directly followed by a large increase in 2004.

Lipids and treatment

Mean total cholesterol-HDL ratio has decreased in the period 1998-2006, followed by a small increase in the last two years (p for quadratic trend <0.0001). Patients aged <60 years performed worse with regard to the mean cholesterol-HDL ratio compared to the older patients categories (p for interaction with age <0.0001). Approximately one quarter (23.0%) of the patients participating in 1998 had a ratio <4. This proportion increased to 61.1% in 2008, which is also reflected in the number of patients receiving lipid-lowering drugs: 10.2% in 1998 and 62.8% in 2008. As was the case with the number of patients using antihypertensives, a remarkable decrease was also observed for the number of patients using lipid-lowering drugs in 2003.

Renal function

Mean values of serum creatinine have remained rather constant throughout the whole study period. The prevalence of micro- and macroalbuminuria in 1998 was 33.6% and 8.3%,

respectively. These proportions declined over time to 18.5% and 2.4%, respectively. The highest prevalence of microalbuminuria was observed for the group >75 years (p for interaction with age <0.0001).

Body mass index

After an increase in the first five years, mean BMI remained rather constant afterwards. In the highest age category, the highest proportion of patients with a BMI <25 kg/m^2 was observed and vice versa (p for interaction with age <0.0001).

Discussion

Quality of diabetes care within the Dutch ZODIAC study, a shared care project, has considerably improved in the period 1998-2008. Large improvements were observed for all quality indicators studied in this study, except for BMI. Each time that large groups of general practices joined the shared care initiative (2002 and 2006), there was a short relapse in the process measures, which was mostly redressed within one year. No relevant differences between the trends for the 3 age categories were observed. During all years of follow-up, mean blood pressure and BMI were the lowest and highest, respectively, in the group of patients <60 years. Patients in this age category also had the highest cholesterol-HDL ratio values and the lowest albumin-creatinine ratio values throughout the whole study period.

Striking changes were the increase in the use of blood pressure and lipid lowering drugs. This increased use was also reflected in the improvements in blood pressure and lipid levels. Remarkably, the decrease in HbA1c was not accompanied by an increase in the proportional use of oral blood glucose lowering drugs or insulin. Instead, an increase in the proportion of patients on a diet was observed for all age categories. One could hypothesize that more patients with early diagnosed T2DM were included in the last years of the study. However, median diabetes duration did not relevantly change throughout the study. Patient education and better adherence to lifestyle advices could be another possible explanations.

The results of our study confirm previous reports on the improvements in risk factor control during the past decades [9-11]. However, this is the first study presenting the results of a large shared care project with a follow-up period of more than 10 years. Although strictly speaking causality can not be proved in our study, this study does demonstrate the impressive results that can be achieved in a shared care setting. The two decreases in the process measures, that were observed after the expansion of the ZODIAC project in 2002 and 2006, and the quick rebound afterwards, suggest positive effects of participating in the project (figure 1). Other factors, that may also explain the improvements in quality of care, should be considered when interpreting the results. Firstly, national and international guidelines advocating more strict treatment in patients with T2DM have been published in

the period 1998-2008. For example, in 1999 and in 2006 revisions of the guideline T2DM of the Royal Dutch College of General Practitioners were published [18,20]. Secondly, financial incentives from health insurance companies for general practitioners that provide care of a high quality have been introduced in the past decade. Although a recent Cochrane review concluded that there is insufficient evidence to support the use of such financial incentives, positive effects on quality of care can also not be excluded [21].

To our knowledge, our study is the first study that also specifically investigated the trends in diabetes care for patients aged older than 75 years. This population is of special interest for two reasons. Firstly, more than one quarter of the type 2 diabetic population in primary care in the Netherlands is >75 years. Secondly, clinical trials in old age investigating cardiovascular risk interventions, such as hypertension treatment, are either lacking or subject to selection bias [22-24]. Since the evidence for strict cardiovascular risk control in old age is low, and old age is characterized by a high prevalence of complications and comorbidities [25,26], the question arises whether the target values should be the same for elderly patients. Although this study observed the same improvements in the various quality measures across all age categories, it remains unsure whether these improvements will have the same beneficial effects on cardiovascular comorbidity and mortality in the oldest elderly as in younger patients with T2DM.

The main limitation of our study is that the data in our study have been provided by practice nurses and GPs as part of the yearly benchmark. As a consequence, the quality and reliability of the data is dependent on the accuracy of the data providers. For example, the number of patients using lipid lowering treatment in 2003 is an extreme outlier compared to the other years and is probably not representative for the actual number of patients. This difference suggests a fault in providing or collecting the data. When a patient is registered as not using a statin, this could either mean that he or she is actually not using a statin or that it is incorrectly registered. However, with respect to the process parameters this may have led at the most to an underestimation of the actual measures. Also, our study only comprises patients whom data have been reported by the GPs. It is not unlikely that GPs have opted

not to provide data of patients who never show up at their diabetes check-ups. Furthermore, the number of patients who did not participate in the study due to short life expectancy of insufficient cognitive abilities is unknown after 1999.

Strengths of our study are the long follow-up period and the high number of participants, especially in the last years of the ZODIAC study. Because of the size of our database, it is important to realize that small differences may easily lead to statistical significant differences while some can hardly be called relevant. For example, the mean serum creatinine level fluctuates around 95 µmol/L throughout the whole study period, but there is a slight positive (i.e. upward) linear trend for males above 75 years, while for women there is a slight negative linear trend for all age categories and as consequence the overall linear trend is highly significant ($p<0.0001$).

In conclusion, our study shows that quality of diabetes care within the Dutch ZODIAC study has considerably improved in the period 1998-2008, irrespective of age. Future studies are needed to establish whether the improvements in old age also lead to reductions in morbidity and mortality.

Data sharing: no additional data available.

Competing interest declaration

All authors declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

Funding source

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Contributors

KJJH (guarantor), ID, NK and HJGB designed the study; KJJH and HJGB acquired the data used in this study; KJJH and KHG analysed the data; KJJH and KHG performed the statistical analyses; and all authors participated in interpretation of the data. All authors had full access to all of the data. KJJH drafted the manuscript and all authors participated in revision of the manuscript. NK, STH, KM and HJGB supervised the study.

Tables

Table 1. *Overview of the process and outcome measures studied*

Parameter	Process measure	Outcome measure
HbA1c	% of patients measured	mean HbA1c (%)
		% HbA1c < 7.0%
		% HbA1c ≥ 8.5%
Glucose lowering treatment	N.A.	% diet only
		% oral medication only
		% insulin with or without oral medication
Blood pressure	% of patients measured	mean SBP (mm Hg)
		% SBP < 140 mm Hg
Antihypertensive treatment	N.A.	% patients using antihypertensive drugs
Cholesterol-HDL ratio	% of patients measured	mean total cholesterol-HDL ratio
		% total cholesterol-HDL ratio <4
Lipid-lowering drugs	N.A.	% patients using lipid-lowering drugs
Renal function	% of patients with creatinine measurements	mean creatinine (µmol/L)
	% of patients with ACR measurements	% micro-albuminuria
		% macro-albuminuria
BMI	% of patients measured	mean BMI (kg/m^2)
		% BMI < 25 kg/m^2

Abbreviations: N.A.: not applicable; SBP: systolic blood pressure; ACR: albumin-creatinine ratio; BMI: body mass index.

Table 2. *Characteristics of all participants in the ZODIAC study for the period 1998-2008*

		1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	*P for*
		n=1622	n=1767	n=1462	n=1615	n=1761	n=4029	n=4729	n=4508	n=18469	n=24940	n=27438	*trend**
Age		68.9 (68.4;69.5)	68.9 (68.3;69.4)	67.8 (67.2;68.4)	67.8 (67.2;68.3)	67.0 (66.5;67.6)	67.6 (67.2;67.9)	67.5 (67.2;67.9)	67.5 (67.2;67.8)	67.4 (67.2;67.6)	67.0 (66.9;67.2)	67.4 (67.2;67.5)	<0.0001
Sex (female)		58.0 (55.6;60.4)	58.2 (55.9;60.5)	56.2 (53.7;58.8)	56.9 (54.5;59.3)	55.4 (53.1;57.7)	54.7 (53.2;56.2)	53.8 (52.4;55.2)	53.5 (52.1;55.0)	52.6 (51.9;53.3)	52.6 (51.9;53.2)	51.9 (51.3;52.5)	<0.0001
DM duration		5.2 [2.5;9.8]	5.7 [3.0;10.5]	5.6 [2.8;10.4]	5.0 [2.1;9.9]	4.5 [2.1;9.0]	4.5 [2.3;8.5]	4.9 [2.3;8.5]	5.0 [2.6;8.7]	4.7 [2.4;8.1]	4.8 [2.4;8.1]	5.3 [2.9;8.8]	<0.0001
HbA1c	process	88.6 (87.0;90.1)	86.4 (84.8;88.0)	97.4 (96.6;98.2)	91.1 (89.7;92.5)	91.6 (90.3;92.9)	83.6 (82.5;84.8)	85.9 (84.9;86.8)	96.1 (95.5;96.6)	87.8 (87.3;88.3)	85.8 (85.4;86.2)	95.5 (95.3;95.8)	<0.0001
	mean	7.5 (7.4;7.5)	7.5 (7.4;7.5)	7.3 (7.2;7.3)	7.0 (7.0;7.1)	7.1 (7.0;7.1)	7.0 (6.9;7.0)	7.0 (7.0;7.0)	6.8 (6.8;6.9)	6.7 (6.7;6.8)	6.7 (6.7;6.7)	6.7 (6.7;6.7)	<0.0001
	% <7	40.4 (37.9;43.0)	40.6 (38.1;43.1)	46.6 (44.0;49.2)	56.7 (54.2;59.2)	53.3 (50.9;55.8)	57.2 (55.5;58.8)	57.0 (55.5;58.5)	61.9 (60.5;63.4)	67.5 (66.8;68.2)	69.8 (69.2;70.5)	70.1 (69.6;70.7)	<0.0001
	% ≥8.5	13.2 (11.5;15.0)	12.9 (11.2;14.6)	9.7 (8.2;11.2)	7.8 (6.5;9.2)	7.4 (6.2;8.7)	5.7 (4.9;6.5)	5.6 (4.9;6.3)	3.4 (2.8;3.9)	3.0 (2.8;3.3)	2.6 (2.4;2.8)	2.3 (2.1;2.5)	<0.0001
DM treatment	Diet only	16.6 (14.9;18.5)	18.5 (16.8;20.4)	18.5 (16.6;20.6)	18.2 (16.4;20.2)	23.1 (21.2;25.1)	21.9 (20.7;23.2)	21.3 (20.1;22.5)	20.1 (18.9;21.3)	24.1 (23.5;24.7)	24.9 (24.3;25.4)	23.8 (23.3;24.3)	<0.0001
	% OBLD only	67.9 (65.6;70.2)	65.9 (63.6;68.0)	65.7 (63.3;68.1)	65.0 (62.6;67.2)	61.5 (59.2;63.8)	64.5 (63.0;66.0)	62.1 (60.7;63.5)	63.0 (61.6;64.4)	63.8 (63.1;64.4)	62.8 (62.2;63.4)	63.4 (62.9;64.0)	<0.0001
	% insulin	15.5 (13.8;17.3)	15.6 (14.0;17.4)	15.7 (14.0;17.7)	16.8 (15.1;18.7)	15.4 (13.8;17.2)	13.6 (12.5;14.6)	16.6 (15.6;17.7)	16.9 (15.9;18.1)	12.2 (11.7;12.6)	12.3 (11.9;12.7)	12.8 (12.4;13.2)	<0.0001

SBP	process	88.7 (87.2;90.3)	88.5 (87.0;90.0)	97.3 (96.4;98.1)	97.0 (96.1;97.8)	96.4 (95.5;97.2)	77.2 (75.9;78.5)	92.8 (92.1;93.5)	95.7 (95.1;96.3)	93.4 (93.0;93.8)	96.7 (96.5;96.9)	98.5 (98.4;98.7)	<0.0001
	mean	154.5 (153.3;155.8)	150.3 (149.1;151.4)	149.4 (148.2;150.6)	145.9 (144.9;146.9)	144.4 (143.4;145.4)	146.7 (146.0;147.4)	145.9 (145.3;146.5)	144.6 (144.0;145.2)	141.9 (141.7;142.2)	141.2 (140.9;141.4)	140.0 (139.8;140.2)	<0.0001
	% <140	22.0 (19.9-24.2)	26.4 (24.2;28.6)	29.4 (27.0;31.8)	33.0 (30.7;35.3)	34.6 (32.4;36.9)	33.2 (31.5;34.8)	37.9 (36.4;39.3)	40.8 (39.3;42.2)	43.0 (42.2;43.7)	44.6 (43.9;45.2)	47.7 (47.1;48.3)	0.0003
SBP treatment	% drugs	41.1 (38.8;43.5)	49.6 (47.3;52.0)	55.0 (52.4;57.5)	61.1 (58.7;63.5)	65.7 (63.4;67.9)	46.7 (45.1;48.2)	69.7 (68.4;71.0)	72.7 (71.4;74.0)	73.5 (72.8;74.1)	73.7 (73.2;74.3)	74.6 (74.1;75.1)	<0.0001
Chol-HDL Ratio	process	73.3 (71.2;75.5)	74.9 (72.9;77.0)	96.4 (95.4;97.3)	91.9 (90.6;93.2)	92.3 (91.0;93.5)	77.2 (75.9;78.5)	79.5 (78.4;80.7)	87.8 (86.9;88.8)	83.1 (82.6;83.7)	84.2 (83.7;84.6)	94.2 (94.0;94.5)	<0.0001
	mean	5.2 (5.1;5.3)	4.8 (4.7;4.9)	4.5 (4.5;4.6)	4.4 (4.3;4.5)	4.1 (4.0;4.1)	4.0 (3.9;4.0)	3.8 (3.8;3.9)	3.8 (3.7;3.8)	3.6 (3.6;3.7)	3.7 (3.7;3.7)	3.8 (3.8;3.8)	<0.0001
	% <4	23.0 (20.7;25.4)	30.7 (28.2;33.1)	35.6 (33.1;38.1)	42.3 (39.8;44.8)	49.8 (47.4;52.3)	55.0 (53.2;56.7)	59.2 (57.7;60.8)	61.7 (60.2;63.2)	67.1 (66.3;67.8)	64.5 (63.8;65.1)	61.1 (60.5;61.7)	<0.0001
LLD	% drugs	10.2 (8.9;11.8)	13.5 (12.0;15.2)	20.8 (18.8;23.0)	26.2 (24.1;28.4)	29.9 (27.8;32.1)	21.7 (20.4;23.0)	35.8 (34.5;37.2)	40.1 (38.7;41.5)	54.3 (53.6;55.1)	59.7 (59.1;60.4)	62.8 (62.2;63.3)	<0.0001
Creatinine	process	89.1 (87.6;90.7)	87.3 (85.8;88.9)	97.5 (96.7;98.3)	91.9 (90.6;93.2)	91.8 (90.5;93.1)	84.7 (83.6;85.8)	85.7 (84.7;86.7)	93.1 (92.4;93.9)	87.8 (87.3;88.3)	85.5 (85.1;86.0)	95.4 (95.1;95.6)	<0.0001
	mean	96.5 (51.7;141.2)	95.0 (48.9;141.1)	93.8 (50.2;137.4)	96.8 (52.9;140.7)	98.2 (54.4;142.0)	95.4 (52.9;137.8)	96.5 (53.9;139.1)	97.7 (55.6;139.7)	92.9 (47.0;138.7)	98.9 (52.9;144.8)	98.7 (51.9;145.5)	<0.0001
ACR	process	65.8 (63.5;68.2)	68.0 (65.9;70.2)	93.5 (92.2;94.8)	85.4 (83.7;87.1)	84.8 (83.2;86.5)	57.4 (55.9;58.9)	62.0 (60.6;63.4)	69.9 (68.5;71.2)	59.0 (58.3;59.7)	66.8 (66.2;67.4)	82.3 (81.9;82.8)	<0.0001
	% micro	33.6 (30.8;36.4)	32.6 (30.0;35.3)	31.4 (28.9;33.8)	29.4 (27.0;31.8)	25.1 (22.9;27.3)	22.1 (20.4;23.8)	24.4 (22.9;26.0)	23.2 (21.8;24.7)	19.2 (18.5;20.0)	19.8 (19.2;20.4)	18.5 (18.0;19.0)	<0.0001

	% macro	8.3 (6.7;10.0)	7.7 (6.2;9.2)	6.7 (5.3;8.0)	4.7 (3.6;5.8)	4.8 (3.7;5.9)	3.7 (2.9;4.4)	3.9 (3.2;4.6)	4.2 (3.5;4.9)	2.9 (2.6;3.2)	2.5 (2.2;2.7)	2.4 (2.2;2.6)	<0.0001
BMI	process	69.0 (66.7;71.2)	69.5 (67.3;71.6)	96.9 (96.0;97.7)	96.7 (95.8;97.5)	95.7 (94.8;96.7)	62.3 (60.8;63.8)	83.0 (82.0;84.1)	88.4 (87.5;89.4)	78.1 (77.5;78.7)	88.1 (87.7;88.5)	93.1 (92.8;93.4)	<0.0001
	mean	29.0 (28.7;29.2)	28.9 (28.6;29.1)	29.3 (29.0;29.5)	29.4 (29.2;29.7)	29.5 (29.3;29.7)	29.6 (29.4;29.7)	29.6 (29.5;29.8)	29.5 (29.4;29.7)	29.5 (29.5;29.6)	29.5 (29.5;29.6)	29.5 (29.5;29.6)	0.1399
	% <25	20.4 (18.0;22.7)	20.4 (18.1;22.6)	17.4 (15.5;19.4)	16.7 (14.8;18.5)	15.8 (14.0;17.5)	16.2 (14.8;17.7)	16.1 (14.9;17.2)	16.3 (15.1;17.4)	16.8 (16.2;17.4)	17.1 (16.6;17.6)	17.1 (16.6;17.6)	0.6638

All data are mean values or proportions together with their 95% confidence intervals, or median values together with the interquartile range. * P for trend is based on age- and gender-adjusted analyses. Abbreviations: DM: diabetes mellitus, OBLD: oral blood glucose lowering drugs, SBP: systolic blood pressure, LLD: lipid lowering drugs, MDRD: modification of diet in renal disease, ACR: albumin-creatinine ratio, BMI: body mass index.

Figures

Figure 1. Process measures for albumin-creatinine ratio (ACR), body mass index (BMI) and blood pressure.

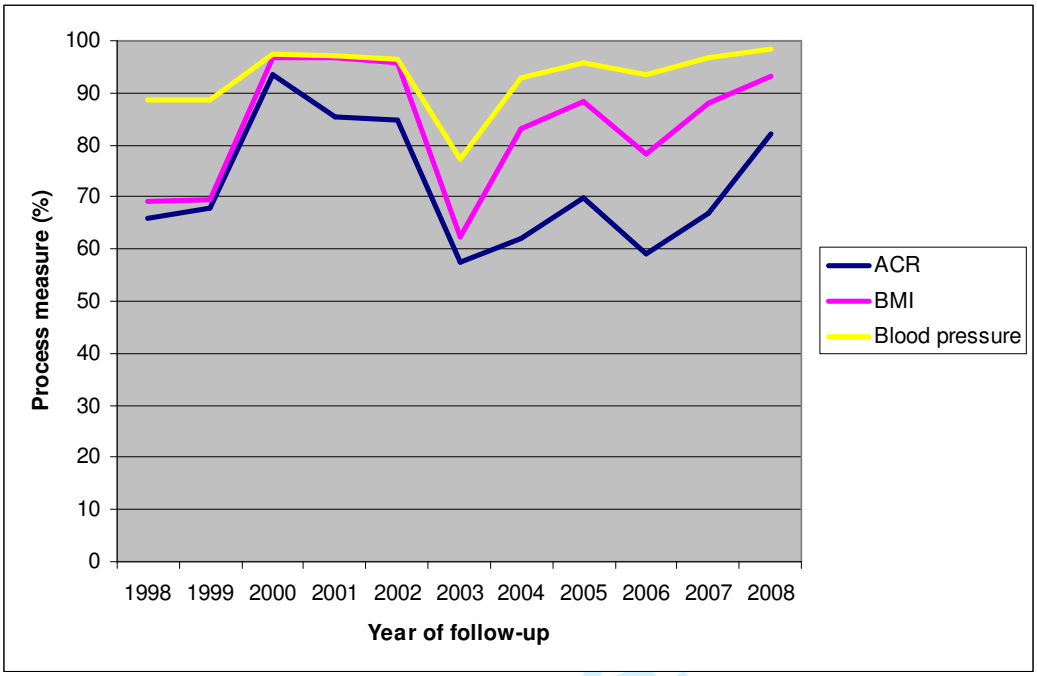
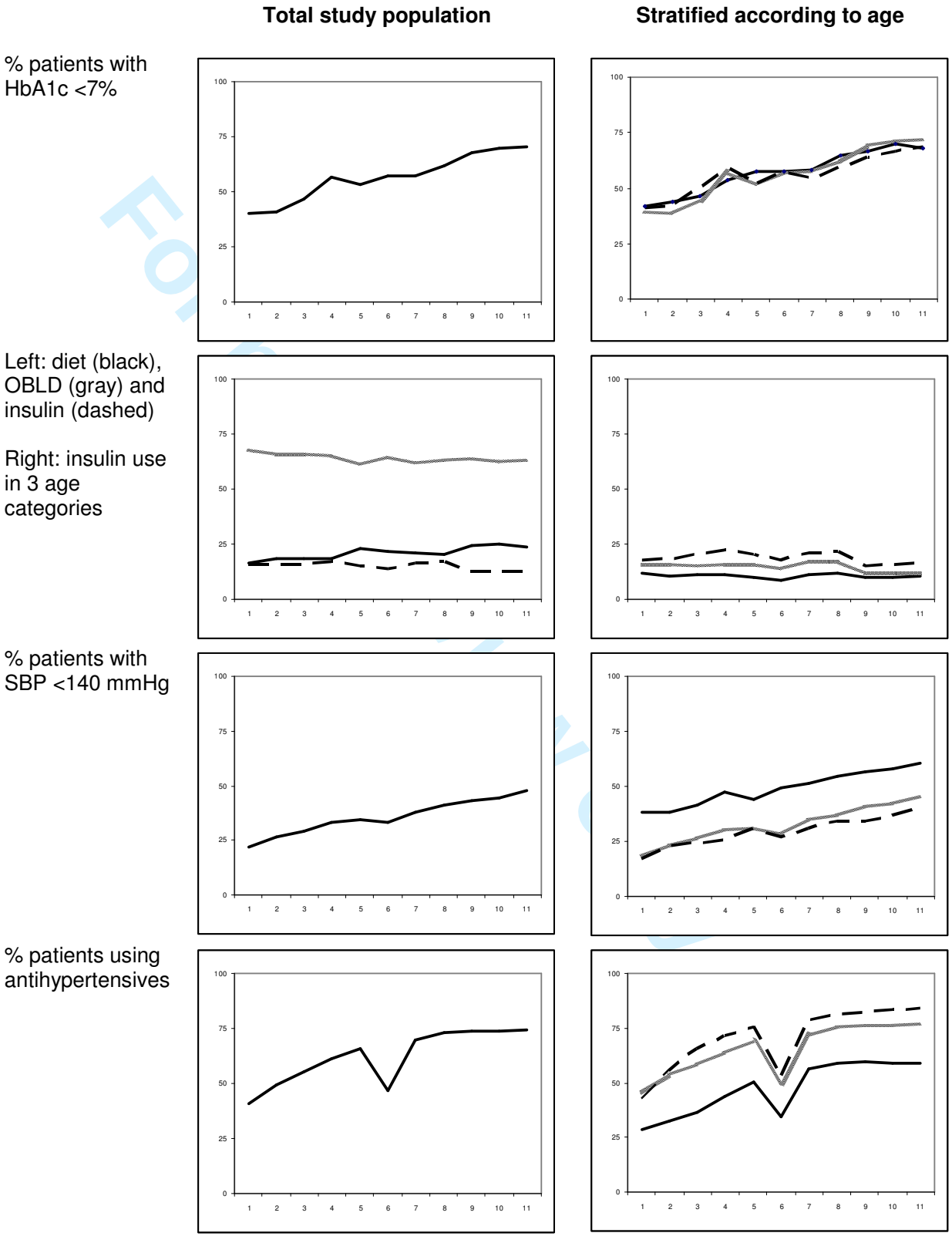
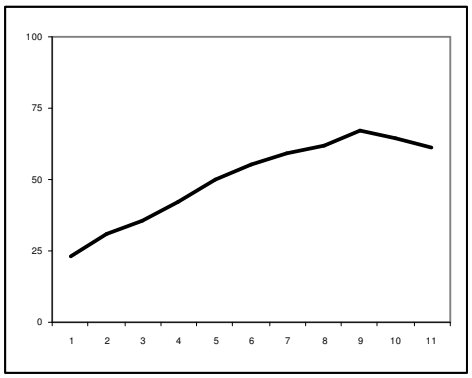
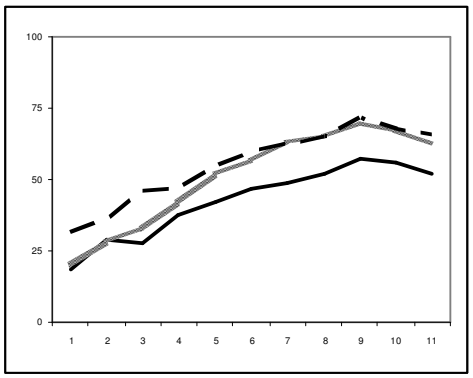


Figure 2. Outcome measures for the total study population and stratified according to age (<60 (black line), 60-75 (grey line) and >75 (black dashed line) years).

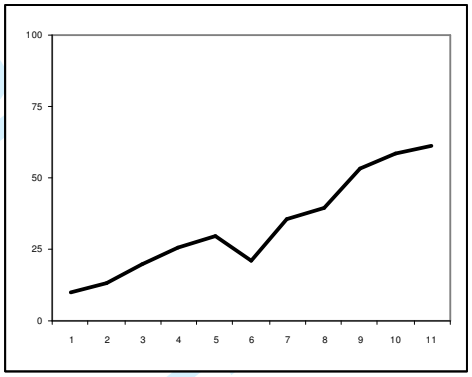


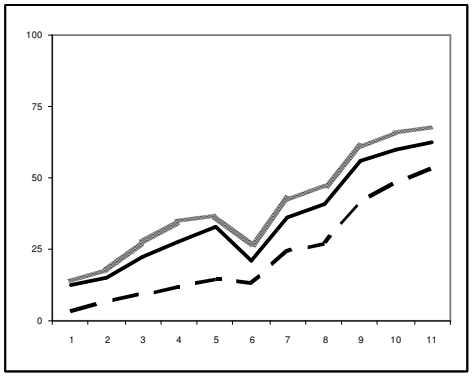
% patients with ratio <4



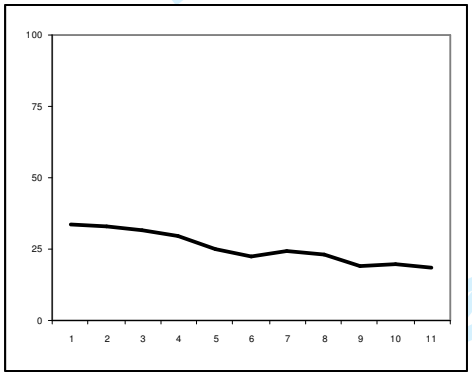


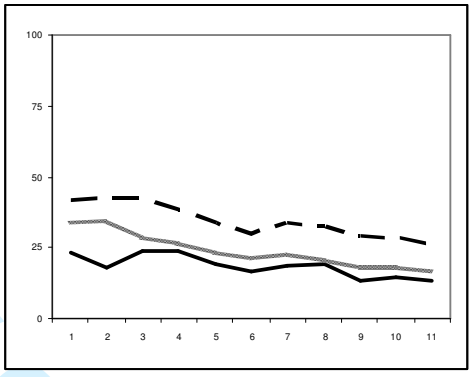
% patients using lipid lowering drugs



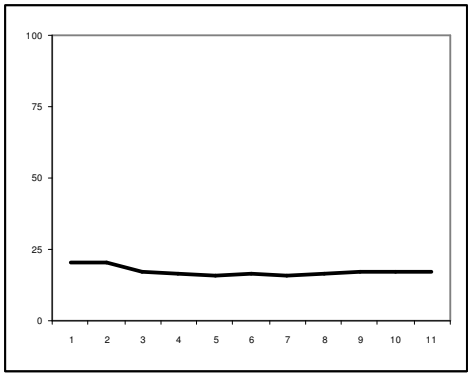


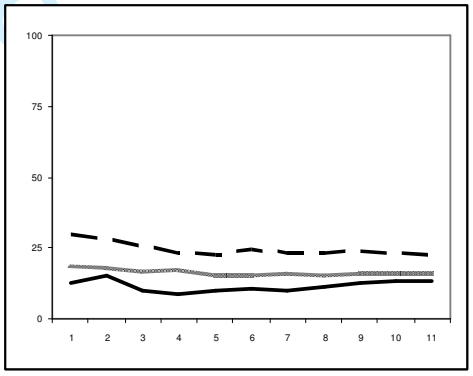
% patients with microalbuminuria





% patients with BMI <25 kg/m^2





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STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract *See page 1, the title page: 'Diabetes care in a shared care prospective observational study: trends and age differences in the period 1998-2008 (ZODIAC-19)'.*
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found *See page 2 for the structured abstract.*
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported *On pages 3 and 4 you will find a short introduction which explains the reasons why we performed the current study.*
Objectives	3	State specific objectives, including any prespecified hypotheses *Our primary objective was to investigate trends in diabetes care, within a shared care project, for a wide variety of quality indicators during a long follow-up period. Because of the limited evidence in old age, we had specific interest whether the same trends were observed for different age groups. Our objectives are mentioned in the last paragraph of the introduction (pages 3 and 4).*
Methods		
Study design	4	Present key elements of study design early in the paper *See first lines of the first paragraph of the methods section (page 5).*
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection *See first paragraph (study population) of the methods section (page 5) for setting, locations, relevant dates. In the second paragraph information about data collection is given (page 5 and 6).*
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *See first paragraph (study population) and the second paragraph (data collection) of the methods section (page 5).*
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed *Not applicable.*
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable *All relevant variables are mentioned in the paragraph 'Data collection' (page 5 and 6), and in table 1 (page 16).*
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group *See page 5 and 6 for the paragraph 'Data collection' where the methods of measurements are described.*
Bias	9	Describe any efforts to address potential sources of bias *The main bias in observational studies is selection bias. We have tried to avoid this to ask all eligible patients to participate in our study. However, patients who were already treated in secondary care, patients with a very short life expectancy and patients with insufficient cognitive abilities were excluded from participation. This selection method is described on page 5.Unfortunately, the number of patients who did not participate in the study because of the aforementioned reasons is not known*

		after 1999. Our study only comprises patients whom data have been reported by the GPs. It is not unlikely that GPs have opted not to provide data of patients who never show up at their diabetes check-ups. These limitations are discussed in the discussion section of our manuscript.
Study size	10	Explain how the study size was arrived at *See the first paragraph on page 5. All patients with T2DM who visit the GP or practice nurse for his/her diabetes are asked to participate in the study. Therefore, no sample size calculations were performed.*
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why *We mentioned in the paragraph 'statistical analyses' how we used the various variables in our analyses. See page 6 of our manuscript for the statistical analyses.*
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding *See page 6 of our manuscript.*
		(*b*) Describe any methods used to examine subgroups and interactions *We stratified our analyses according to different age groups. Differences in trends between age categories were investigated by adding an interaction term to the model. See page 6 of our manuscript for the statistical analyses.*
		(*c*) Explain how missing data were addressed *Not all data were known for all patients. However, the proportion of missing data is given for all variables of interest: process measures. See page 5 and 6 for the paragraph 'Data collection' in which we explain the terms process and outcome measures.*
		(*d*) If applicable, explain how loss to follow-up was addressed *Not applicable.*
		(*e*) Describe any sensitivity analyses *We did not perform any sensitivity analyses.*
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed *In the first paragraph of the results section we describe the total number of patients which participated in our study. Patients who were already treated in secondary care, patients with a very short life expectancy and patients with insufficient cognitive abilities were excluded from participation. Unfortunately, the number of patients who did not participate in the study because of the aforementioned reasons is not known after 1999. Therefore, we are not able to exactly present the requested numbers.*
		(b) Give reasons for non-participation at each stage *Not applicable.*
		(c) Consider use of a flow diagram *Not applicable.*
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders *See table 2.*
		(b) Indicate number of participants with missing data for each variable of interest *See table 2. Process measures are presented for all variables of interest.*
		(c) Summarise follow-up time (eg, average and total amount) *Not applicable due to the design of the study.*
Outcome data	15*	Report numbers of outcome events or summary measures over time

		See table 2, figures 1 and 2, and the data mentioned in the results sections on pages 8 to 10.
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included *See table 2, figures 1 and 2, and the data mentioned in the results sections on pages 8 to 10.*
		(*b*) Report category boundaries when continuous variables were categorized *We stratified our analyses according to different age group; see the paragraph 'statistical analyses' on page 6.*
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period *Not applicable.*
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses *We have performed analyses stratified according to age categories. This was a pre-specified aim of the study.*
Discussion		
Key results	18	Summarise key results with reference to study objectives *See the first paragraph of the discussion section, page 11.*
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias *See the last paragraph on page 12.*
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence *See last paragraph of the discussion on page 13.*
Generalisability	21	Discuss the generalisability (external validity) of the study results *The most important bias of our study is selection bias, since our study only comprises patients whom data have been reported by the GPs. This limitation is discussed in the last paragraph on page 12.*
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based *We had no external funding source.*

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

A prospective observational study of quality of diabetes care in a shared care setting: trends and age differences (ZODIAC-19)

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2012-001387.R1
Article Type:	Research
Date Submitted by the Author:	15-Jul-2012
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Primary Subject Heading:	Diabetes and endocrinology
Secondary Subject Heading:	Diabetes and endocrinology, Epidemiology
Keywords:	General diabetes < DIABETES & ENDOCRINOLOGY, GERIATRIC MEDICINE, PRIMARY CARE, Vascular medicine < INTERNAL MEDICINE

Title: ~~Diabetes care in a shared care~~ A prospective observational study of quality of diabetes care in a shared care setting: trends and age differences ~~in the period 1998-2008~~ (ZODIAC-19)

Short title: Trends in diabetes care in the period 1998-2008

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Word count: main text ~~2707~~3366; abstract 300.

Number of tables: 2; number of figures: 2.

Abstract

Objective: The Zwolle Outpatient Diabetes project Integrating Available Care (ZODIAC) study was initiated in 1998 to investigate the effects of shared care for patients with type 2 diabetes mellitus (T2DM) in the Netherlands, and to reduce the number of diabetes-related complications. Benchmarking the performance of diabetes care was and is an important aspect of this study. We aimed to investigate trends in diabetes care, within the ZODIAC study for a wide variety of quality indicators during a long follow-up period (1998-2008), with special interest for different age groups.

Design: Prospective observational cohort study.

Setting: Primary care, Zwolle, The Netherlands.

Participants: Patients with T2DM.

Methods: A dataset of quality measures was collected annually during the patient's visit to the practice nurse or general practitioner. Linear time trends from 1998-2008 were estimated using linear mixed models in which we adjusted for age and gender. Age was included in the model as a categorical variable: for each follow-up year all participants were categorised into the categories <60, 60-75 and >75 years. Differences in trends between the age categories were investigated by adding an interaction term to the model.

Results: The number of patients who were reported to participate increased in the period 1998-2008 from 1622 to 27.438. All quality indicators improved in this study, except for body mass index. The prevalence albuminuria decreased in an eleven-year-period from 42% to 21%. No relevant differences between the trends for the 3 age categories were observed. During all years of follow-up, mean blood pressure and body mass index were the lowest and highest, respectively, in the group of patients <60 years (data not shown).

Conclusion: Quality of diabetes care within the Dutch ZODIAC study, a shared care project, has considerably improved in the period 1998-2008. There were no relevant differences between trends across various age categories.

Keywords: Diabetes mellitus type 2; Observational studies.

Article focus

- Shared care, defined as care for patients with a chronic condition provided in cooperation between primary and secondary health care, has been promoted and developed in order to reduce the number of diabetes-related complications.
- There is limited data whether improvements in diabetes care in the past decades are comparable across different age categories.
- We aimed to investigate trends in diabetes care, within a shared care project, during a long follow-up period (1998-2008), with a special focus on different age groups.

Key messages

- Quality of diabetes care within the Dutch ZODIAC study, a shared care project, has considerably improved in the period 1998-2008.
- Large improvements were observed for all quality indicators studied in this study, except for BMI.
- No relevant differences between the trends for ~~the 3~~different age categories were observed.

Strengths and limitations

- Strengths of our study are the long follow-up period and the high number of participants.
- A causal relationship between shared care and the observed improvements can~~-~~not be proved due to the observational design of our study.

Introduction

Ever since it was established that type 2 diabetes mellitus (T2DM) leads to significant morbidity and mortality [1,2], prevention and (early) treatment of both microvascular and macrovascular complications of T2DM have become important goals in diabetes care. Efforts to improve the quality of diabetes care are necessary in order to reduce morbidity and mortality associated with T2DM [3,4]. Since adequate treatment of patients with T2DM often needs the involvement of more than one caregiver, shared care, defined as care for patients with a chronic condition provided in cooperation between primary and secondary health care, has been promoted and developed [5].

The *Zwolle Outpatient Diabetes project Integrating Available Care* (ZODIAC) study was initiated in 1998 to investigate the effects of shared care for patients with T2DM in the Netherlands [6]. Benchmarking the performance of diabetes care was and is an important aspect of this initiative. Previous reports from the ZODIAC study showed that structured shared care with task delegation to nurses leads to improvements in quality of diabetes care and life expectancy [6-8]. However, effectiveness of shared care in general was not demonstrated in a 2007 Cochrane review [5]. Inadequate length of follow-up was mentioned by the authors as a possible explanation for the lack of evidence.

Although diabetes care has improved considerably during the past decades in patients with diabetes, there is limited data whether these improvements are comparable across different age categories [9,10]. A cross-sectional study from France showed that quality of care had considerably improved for patients ≥65 years with T2DM in the period 2001-2007 [11]. Unfortunately, trends for patients >75 years were not described separately in this study. Although the number of patients with T2DM >75 years is increasing, the evidence for cardiovascular risk interventions in this age category is low [12]. Data from observational studies show that classic cardiovascular risk factors may even have different consequences in elderly patients [13-17].

In the present study, we aimed to investigate trends in diabetes care, within a shared care project, for a wide variety of quality indicators during a long follow-up period (1998-

2008). Because of limited evidence for cardiovascular risk interventions in old age, we had specific interest whether the same trends were observed for different age groups (<60, 60-75 and >75 years).

Methods and Patients

Study population and ZODIAC

The ZODIAC study started in 1998 as a prospective observational study for patients with T2DM [6]. Participating practices were allocated to one of the two intervention groups or to the standard care group. The interventions involved extensive or limited task delegation from general practitioners to practice nurses and/or diabetes specialist nurses. Moreover, it included a diabetes register, structured recall, facilitated generalist-specialist communication, audit and feedback, patient-specific reminders, and it emphasized patients' education [6]. The patients participating in the ZODIAC study are known with T2DM and exclusively treated in primary care. Patients who were already treated in secondary care for their diabetes, patients with a very short life expectancy (including patients with active cancer) and patients with insufficient cognitive abilities were excluded from participation. In the first years of ZODIAC, only patients in the surrounding area of the city of Zwolle participated in the study. Because of the improvements in the quality of diabetes care in the two intervention groups, the shared care project has expanded gradually in the past decade. Firstly, the shared care project became the standard for diabetes care in the entire Zwolle region (2002-2003), and in 2005-2006 the project expanded to the northeast region of the Netherlands. Patients who were received standard care in the beginning of the project, switched to shared care in 2002-2003 when the shared care project became the standard for the entire Zwolle region. These patients were included in the current analyses from the moment they switched to shared care. The number of participating general practitioners (GPs) has increased from 53 in 1998 to 459 in 2008. Patient numbers increased from 1622 to 27.438 in this time frame, and nowadays even more than 60.000 patients are participating. A benchmark of annually gathered quality measures of this cohort, based on the guidelines of the Dutch College of General Practitioners and the Dutch Diabetes Federation, has been developed [18].

Data collection

The dataset of quality measures is collected annually during the patient's visit to the practice nurse and/or GP. These quality measures are collected in the general practitioners' patients information systems, and each year the relevant data are uploaded and sent to our diabetes centre for benchmarking and research purposes. At baseline, additional data were collected including a full medical history. The dataset contains many quality measures, including data on cardiovascular risk control, treatment and complications. Distinction is made between process and outcome measures. Process measures indicate whether tests or assessments have been performed, e.g. the number of patients whose HbA1c level has been determined. Outcome measures reflect the results of the assessments, such as the mean systolic blood pressure or the proportion of patients with a systolic blood pressure <140 mm Hg. Table 1 shows an overview of the measures we investigated in this study for each year of follow-up.

Participating practices were instructed to perform blood pressure measurements in supine position after at least 5 min of rest, and to calculate the mean blood pressure of two recording for each visit. Laboratory data (HbA1c, serum creatinine and lipid profile) were determined using standard hospital procedures. Until 2005, all procedures were performed in the clinical chemistry laboratory of the Isala Clinics (Zwolle region). Because of the expansion of the project in 2005-2006 to the northeast region of the Netherlands, laboratories of other regions started participating. HbA1c was measured using affinity chromatography *high-performance liquid chromatography* (HPLC, Ultra 2, Trinity Biotech, Kansas City, MO) in the Zwolle region (coefficient of variation approximately 1.5%) [19]. There are differences in the methods used in the various laboratories in the northeast region of the Netherlands. Generally speaking, the variation coefficient has decreased in the study period due to the worldwide standardization of HbA1c measurements and improved techniques. Because of the high number of patients in the last years of the project, it is not likely that differences in the coefficient of variation coefficient have influenced the results.

Statistical analyses

Continuous variables are represented as means and 95% confidence intervals (95% CI) for the normally distributed values. Normality was evaluated using Q-Q plots and histograms. Nominal variables are represented as the proportion of patients together with 95% CIs. ~~Linear time trends from 1998-2008 were estimated using linear mixed models (SAS PROC MIXED for continuous variables and PROC GLIMMIX for binary variables) in which we adjusted for age and gender. Age was included in the model as a categorical variable: for each follow-up year all participants were categorised into the categories <60, 60-75 and >75 years. All trends were visually inspected and quadratic trend analysis was only performed when such a trend was likely based on the plot. Differences in trends between the age categories were investigated by adding an interaction term to the model. A significant trend for interaction with age means that differences exist between the trends of the 3 age categories.~~The database contained 37.320 unique patients and data of 92.340 unique yearly diabetic check-ups. For 9.279 patients, we only had data of one diabetic check-up. The descriptive statistics were strictly cross-sectional and included observations of all visits (n=92.340). Since cross-sectional outcomes are influenced by changes in population (in- and outmigration), besides changes in quality of care, cross-sectional outcomes tend to overestimate time trends when compared to longitudinal analyses [20]. Therefore, we estimated linear time trends from 1998-2008 using a linear mixed model for continuous variables (SAS PROC MIXED) and a generalized linear mixed model for binary variables (PROC GLIMMIX, using the logit link function) in which we adjusted for age and gender. In all analyses time, age and sex were modelled as fixed effects. Since the estimated linear time trends are based on individual changes over time, data of at least 2 visits were necessary. As a consequence, these longitudinal analyses were based on 83.061 visits of 28.041 patients. Age was included in the model as a categorical variable: for each follow-up year all participants were categorised into the categories <60, 60-75 and >75 years. All time trends were visually inspected and a quadratic time trend was only introduced when such a trend was likely based on the plot. Differences in trends between men and women and the age categories were investigated by adding interaction terms for age and time and sex and

time to the model. A significant interaction for age and time means that differences exist between the time trends for the 3 age categories. The same applies for the interaction between sex and time. All analyses were performed with SPSS version 18.0.0 software (SPSS inc., Chicago, Illinois, USA) and with SAS 9.2 software (SAS Institute Inc., Cary, NC, USA).

The manuscript was written based on the 'Strengthening the reporting of observational studies in epidemiology' (STROBE) statement [~~19~~21].

Ethics statement

The ZODIAC study and the informed consent procedure were approved by the local medical ethics committee of the Isala Clinics, Zwolle, the Netherlands. In the first years of ZODIAC, verbal informed consent was obtained from all patients and the consent was documented in the patient's records. According to Dutch law, written informed consent was not necessary for this type of study in 1998. Nowadays, written informed consent is obtained. All data were analysed anonymously.

Results

The number of patients who were reported to participate in this shared care project increased in the period 1998-2008 from 1622 to 27.438. Mean age decreased with time from 68.9 to 67.4 years (p for trend <0.0001). A gradual increase was observed for the proportion of male patients participating in the project. Median diabetes duration remained rather constant at 5 years throughout the whole study period. The proportion of patients aged older than 75 years was 31.0% in 1998 and declined to 26.3% in 2008. The number of patients who did not participate in the study due to short life expectancy of insufficient cognitive abilities is unknown after 1999. The results for all process and outcome measures of each year for the overall study group are presented in table 2.

Process measures

All process measures show a similar trend (table 2): a gradual increase in the first years of the project followed by a decrease in the years 2002 and 2003, an increase in the upcoming two years, followed by a decrease in 2006 again and a rising trend in the process measures in the last two years. Body mass index (BMI), the lipid profile and the ACR were less often measured in patients aged >75 years compared to the younger patients (p for interaction with age for all variables <0.0001). Figure 1 illustrates the trends for the process measure of ACR, BMI and blood pressure in the total study population.

Outcome measures

Figure 2 presents the trends for outcome measures over time for the overall study group and also stratified according to the 3 age categories.

Glycemic control and diabetes treatment

The decline in mean HbA1c over time is reflected in the proportion of patients achieving the target value of <7%; 35.8% in 1998 compared to 67.0% in 2008. The differences between the 3 age categories seem to be small, although the proportion of patients with an HbA1c

≥8.5% tended to be the highest for patients aged <60 years in all years (p for interaction with age 0.0773). The proportion of patients treated with only a diet increased over time from 16.6% to 23.8%. A total of 15.5% used insulin in 1998 and this proportion declined to 12.8% in 2008.

Blood pressure and treatment

Mean blood pressure has decreased over time in all age groups, with the lowest values in the youngest patient category (p for interaction with age <0.0001). In 1998 about one fifth (22.0%) had a systolic blood pressure <140 mmHg, compared to 47.7% in 2008. The number of patients with antihypertensive medication increased in all age groups. With advancing age the number of patients using these agents also increased (p for interaction with age <0.0001). A remarkable decrease in 2003 was directly followed by a large increase in 2004.

Lipids and treatment

Mean total cholesterol-HDL ratio has decreased in the period 1998-2006, followed by a small increase in the last two years (p for quadratic trend <0.0001). Patients aged <60 years performed worse with regard to the mean cholesterol-HDL ratio compared to the older patients categories (p for interaction with age <0.0001). Approximately one quarter (23.0%) of the patients participating in 1998 had a ratio <4. This proportion increased to 61.1% in 2008, which is also reflected in the number of patients receiving lipid-lowering drugs: 10.2% in 1998 and 62.8% in 2008. As was the case with the number of patients using antihypertensives, a remarkable decrease was also observed for the number of patients using lipid-lowering drugs in 2003.

Renal function

Mean values of serum creatinine have remained rather constant throughout the whole study period. The prevalence of micro- and macroalbuminuria in 1998 was 33.6% and 8.3%,

respectively. These proportions declined over time to 18.5% and 2.4%, respectively. The highest prevalence of microalbuminuria was observed for the group >75 years (p for interaction with age <0.0001).

Body mass index

After an increase in the first five years, mean BMI remained rather constant afterwards. In the highest age category, the highest proportion of patients with a BMI <25 kg/m^2 was observed and vice versa (p for interaction with age <0.0001).

Discussion

Quality of diabetes care within the Dutch ZODIAC study, a shared care project, has considerably improved in the period 1998-2008. Large improvements were observed for all quality indicators studied in this study, except for BMI. Each time that large groups of general practices joined the shared care initiative (2002 and 2006), there was a short relapse in the process measures, which was mostly redressed within one year. No relevant differences between the trends for the 3 age categories were observed. During all years of follow-up, mean blood pressure and BMI were the lowest and highest, respectively, in the group of patients <60 years. Patients in this age category also had the highest cholesterol-HDL ratio values and the lowest albumin-creatinine ratio values throughout the whole study period.

Striking changes were the increase in the use of blood pressure and lipid lowering drugs. This increased use was also reflected in the improvements in blood pressure and lipid levels. Remarkably, the decrease in HbA1c was not accompanied by an increase in the proportional use of oral blood glucose lowering drugs or insulin. Instead, an increase in the proportion of patients on a diet was observed for all age categories. One could hypothesize that more patients with early diagnosed T2DM were included in the last years of the study. However, median diabetes duration did not relevantly change throughout the study. Patient education and better adherence to lifestyle advices could be ~~an~~other possible explanations.

The results of our study confirm previous reports ~~on the~~ that also observed improvements in risk factor control during the past decades [9-11,22]. However, this is the first study presenting the results of a large shared care project with a follow-up period of more than 10 years. Although ~~strictly speaking causality can not be proved in our study,~~ this study ~~does demonstrate~~demonstrates the impressive results that ~~can be~~ have been achieved in a shared care setting~~.~~, it should be emphasized that causality cannot be proved by our study. The two decreases in the process measures, that were observed after the expansion of the ZODIAC project in 2002 and 2006, and the quick rebound afterwards, suggest positive effects of participating in the project (figure 1). ~~Other~~However, there are many other factors~~,~~ that may also explain the improvements in quality of care~~, should be~~

~~considered when interpreting the results.~~. Firstly, national and international guidelines advocating ~~more strict~~stricter treatment in patients with T2DM have been published in the period 1998-2008. For example, in 1999 and in 2006 revisions of the guideline T2DM of the Royal Dutch College of General Practitioners were published [18,~~20].~~23]. It could be that adherence to these guidelines, irrespective of participating in shared care projects, is the most important factor explaining the general tendency to improved diabetes care. Secondly, financial incentives from health insurance companies for general practitioners that provide care of a high quality have been introduced in the past decade. Although a recent Cochrane review concluded that there is insufficient evidence to support the use of such financial incentives, positive effects on quality of care can also not be excluded [~~21~~24].

To our knowledge, our study is the first study that also specifically investigated the trends in diabetes care for patients aged older than 75 years. This population is of special interest for two reasons. Firstly, more than one quarter of the type 2 diabetic population in primary care in the Netherlands is >75 years. Secondly, clinical trials in old age investigating cardiovascular risk interventions, such as hypertension treatment, are either lacking or subject to selection bias [~~22-24~~25-27]. Since the evidence for strict cardiovascular risk control in old age is low, ~~and~~ old age is characterized by a high prevalence of complications and comorbidities ~~[25,26], the question arises whether the target values should be the same for~~ , and elderly patients~~. Although~~ are at increased risk for possible adverse events, less strict treatment targets for elderly patients with T2DM have been advocated in literature [28-30]. Generally speaking, individualizing target values is more and more advocated in literature nowadays [30]. Take for example hypertension treatment in old age. Whereas a systolic blood pressure target value of 140 mmHg should be used for patients >75 years without many comorbidities who are not using insulin, it is unknown whether this target value is also appropriate for the overall elderly population [27]. In conclusion, although the current study observed the same improvements in the various quality measures across all age categories, it remains unsure whether these improvements will have the same beneficial

effects on cardiovascular comorbidity and mortality in the oldest elderly as in younger patients with T2DM.

~~The main limitation of our study is that~~Our study has several important limitations that need to be addressed. Firstly, it is important to realise that the cross-sectional data presented in table 2 and figure 2 are influenced by changes in population (in- and outmigration), besides possible changes in quality of care. Since the estimated linear time trends were based on individual changes over time, it is possible to conclude that there is an improvement over time. However, these improvements are probably smaller than the cross-sectional data suggest, since cross-sectional outcomes on HbA1c overestimate improvements over time when compared to longitudinal outcomes [20]. Secondly, because of its observational design a causal relationship between shared care and the observed improvements cannot be proven. Unfortunately, we were not able to include a control group of patients with diabetes receiving standard care. Thirdly, the data in our study have been provided by practice nurses and GPs as part of the yearly benchmark. As a consequence, the quality and reliability of the data is dependent on the accuracy of the data providers. For example, the number of patients using lipid lowering treatment in 2003 is an extreme outlier compared to the other years and is probably not representative for the actual number of patients. This difference suggests a fault in providing or collecting the data. When a patient is registered as not using a statin, this could either mean that he or she is actually not using a statin or that it is incorrectly registered. However, with respect to the process parameters this may have led at the most to an underestimation of the actual measures. Also, our study only comprises patients whom data have been reported by the GPs. It is not unlikely that GPs have opted not to provide data of patients who never show up at their diabetes check-ups. Furthermore, the number of patients who did not participate in the study due to short life expectancy of insufficient cognitive abilities is unknown after 1999.

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Strengths of our study are the long follow-up period and the high number of participants, especially in the last years of the ZODIAC study. Because of the size of our database, it is important to realize that small differences may easily lead to statistical

significant differences while some can hardly be called relevant. For example, the mean serum creatinine level fluctuates around 95 µmol/L throughout the whole study period, but there is a slight positive (i.e. upward) linear trend for males above 75 years, while for women there is a slight negative linear trend for all age categories ~~and as consequence the overall linear~~while the overall linear (very slightly positive) trend is nevertheless highly significant ($p<0.0001$).

In conclusion, our study shows that quality of diabetes care within the Dutch ZODIAC study has ~~considerably~~ improved in the period 1998-2008, irrespective of age. Future studies are needed to ~~establish~~elucidate whether there is a causal relationship between shared care and the improvements. Whether the large improvements observed in old age ~~also~~ will lead to reductions in morbidity and mortality~~.~~, remains also to be determined.

Data sharing: no additional data available.

Competing interest declaration

All authors declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

Funding source

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Contributors

KJJH (guarantor), ID, NK and HJGB designed the study; KJJH and HJGB acquired the data used in this study; KJJH and KHG analysed the data; KJJH and KHG performed the statistical analyses; and all authors participated in interpretation of the data. All authors had full access to all of the data. KJJH drafted the manuscript and all authors participated in revision of the manuscript. NK, STH, KM and HJGB supervised the study.

Tables

Table 1. *Overview of the process and outcome measures studied*

Parameter	Process measure	Outcome measure
HbA1c	% of patients measured	mean HbA1c (%)
		% HbA1c < 7.0%
		% HbA1c ≥ 8.5%
Glucose lowering treatment	N.A.	% diet only
		% oral medication only
		% insulin with or without oral medication
Blood pressure	% of patients measured	mean SBP (mm Hg)
		% SBP < 140 mm Hg
Antihypertensive treatment	N.A.	% patients using antihypertensive drugs
Cholesterol-HDL ratio	% of patients measured	mean total cholesterol-HDL ratio
		% total cholesterol-HDL ratio <4
Lipid-lowering drugs	N.A.	% patients using lipid-lowering drugs
Renal function	% of patients with creatinine measurements	mean creatinine (µmol/L)
	% of patients with ACR measurements	% micro-albuminuria
		% macro-albuminuria
BMI	% of patients measured	mean BMI (kg/m^2)
		% BMI < 25 kg/m^2

Abbreviations: N.A.: not applicable; SBP: systolic blood pressure; ACR: albumin-creatinine ratio; BMI: body mass index.

Table 2. *Characteristics of all participants in the ZODIAC study for the period 1998-2008*

		1998 n=1622	1999 n=1767	2000 n=1462	2001 n=1615	2002 n=1761	2003 n=4029	2004 n=4729	2005 n=4508	2006 n=18469	2007 n=24940	2008 n=27438	*P for trend**
Age		68.9 (68.4;69.5)	68.9 (68.3;69.4)	67.8 (67.2;68.4)	67.8 (67.2;68.3)	67.0 (66.5;67.6)	67.6 (67.2;67.9)	67.5 (67.2;67.9)	67.5 (67.2;67.8)	67.4 (67.2;67.6)	67.0 (66.9;67.2)	67.4 (67.2;67.5)	<0.0001
Sex (female)		58.0 (55.6;60.4)	58.2 (55.9;60.5)	56.2 (53.7;58.8)	56.9 (54.5;59.3)	55.4 (53.1;57.7)	54.7 (53.2;56.2)	53.8 (52.4;55.2)	53.5 (52.1;55.0)	52.6 (51.9;53.3)	52.6 (51.9;53.2)	51.9 (51.3;52.5)	<0.0001
DM duration		5.2 [2.5;9.8]	5.7 [3.0;10.5]	5.6 [2.8;10.4]	5.0 [2.1;9.9]	4.5 [2.1;9.0]	4.5 [2.3;8.5]	4.9 [2.3;8.5]	5.0 [2.6;8.7]	4.7 [2.4;8.1]	4.8 [2.4;8.1]	5.3 [2.9;8.8]	<0.0001
HbA1c	process	88.6 (87.0;90.1)	86.4 (84.8;88.0)	97.4 (96.6;98.2)	91.1 (89.7;92.5)	91.6 (90.3;92.9)	83.6 (82.5;84.8)	85.9 (84.9;86.8)	96.1 (95.5;96.6)	87.8 (87.3;88.3)	85.8 (85.4;86.2)	95.5 (95.3;95.8)	<0.0001
	mean	7.5 (7.4;7.5)	7.5 (7.4;7.5)	7.3 (7.2;7.3)	7.0 (7.0;7.1)	7.1 (7.0;7.1)	7.0 (6.9;7.0)	7.0 (7.0;7.0)	6.8 (6.8;6.9)	6.7 (6.7;6.8)	6.7 (6.7;6.7)	6.7 (6.7;6.7)	<0.0001
	% <7	40.4 (37.9;43.0)	40.6 (38.1;43.1)	46.6 (44.0;49.2)	56.7 (54.2;59.2)	53.3 (50.9;55.8)	57.2 (55.5;58.8)	57.0 (55.5;58.5)	61.9 (60.5;63.4)	67.5 (66.8;68.2)	69.8 (69.2;70.5)	70.1 (69.6;70.7)	<0.0001
	% ≥8.5	13.2 (11.5;15.0)	12.9 (11.2;14.6)	9.7 (8.2;11.2)	7.8 (6.5;9.2)	7.4 (6.2;8.7)	5.7 (4.9;6.5)	5.6 (4.9;6.3)	3.4 (2.8;3.9)	3.0 (2.8;3.3)	2.6 (2.4;2.8)	2.3 (2.1;2.5)	<0.0001
DM treatment	Diet only	16.6 (14.9;18.5)	18.5 (16.8;20.4)	18.5 (16.6;20.6)	18.2 (16.4;20.2)	23.1 (21.2;25.1)	21.9 (20.7;23.2)	21.3 (20.1;22.5)	20.1 (18.9;21.3)	24.1 (23.5;24.7)	24.9 (24.3;25.4)	23.8 (23.3;24.3)	<0.0001
	% OBLD only	67.9 (65.6;70.2)	65.9 (63.6;68.0)	65.7 (63.3;68.1)	65.0 (62.6;67.2)	61.5 (59.2;63.8)	64.5 (63.0;66.0)	62.1 (60.7;63.5)	63.0 (61.6;64.4)	63.8 (63.1;64.4)	62.8 (62.2;63.4)	63.4 (62.9;64.0)	<0.0001
	% insulin	15.5 (13.8;17.3)	15.6 (14.0;17.4)	15.7 (14.0;17.7)	16.8 (15.1;18.7)	15.4 (13.8;17.2)	13.6 (12.5;14.6)	16.6 (15.6;17.7)	16.9 (15.9;18.1)	12.2 (11.7;12.6)	12.3 (11.9;12.7)	12.8 (12.4;13.2)	<0.0001

SBP	process	88.7 (87.2;90.3)	88.5 (87.0;90.0)	97.3 (96.4;98.1)	97.0 (96.1;97.8)	96.4 (95.5;97.2)	77.2 (75.9;78.5)	92.8 (92.1;93.5)	95.7 (95.1;96.3)	93.4 (93.0;93.8)	96.7 (96.5;96.9)	98.5 (98.4;98.7)	<0.0001
	mean	154.5 (153.3;155.8)	150.3 (149.1;151.4)	149.4 (148.2;150.6)	145.9 (144.9;146.9)	144.4 (143.4;145.4)	146.7 (146.0;147.4)	145.9 (145.3;146.5)	144.6 (144.0;145.2)	141.9 (141.7;142.2)	141.2 (140.9;141.4)	140.0 (139.8;140.2)	<0.0001
	% <140	22.0 (19.9-24.2)	26.4 (24.2;28.6)	29.4 (27.0;31.8)	33.0 (30.7;35.3)	34.6 (32.4;36.9)	33.2 (31.5;34.8)	37.9 (36.4;39.3)	40.8 (39.3;42.2)	43.0 (42.2;43.7)	44.6 (43.9;45.2)	47.7 (47.1;48.3)	0.0003
SBP treatment	% drugs	41.1 (38.8;43.5)	49.6 (47.3;52.0)	55.0 (52.4;57.5)	61.1 (58.7;63.5)	65.7 (63.4;67.9)	46.7 (45.1;48.2)	69.7 (68.4;71.0)	72.7 (71.4;74.0)	73.5 (72.8;74.1)	73.7 (73.2;74.3)	74.6 (74.1;75.1)	<0.0001
Chol-HDL Ratio	process	73.3 (71.2;75.5)	74.9 (72.9;77.0)	96.4 (95.4;97.3)	91.9 (90.6;93.2)	92.3 (91.0;93.5)	77.2 (75.9;78.5)	79.5 (78.4;80.7)	87.8 (86.9;88.8)	83.1 (82.6;83.7)	84.2 (83.7;84.6)	94.2 (94.0;94.5)	<0.0001
	mean	5.2 (5.1;5.3)	4.8 (4.7;4.9)	4.5 (4.5;4.6)	4.4 (4.3;4.5)	4.1 (4.0;4.1)	4.0 (3.9;4.0)	3.8 (3.8;3.9)	3.8 (3.7;3.8)	3.6 (3.6;3.7)	3.7 (3.7;3.7)	3.8 (3.8;3.8)	<0.0001
	% <4	23.0 (20.7;25.4)	30.7 (28.2;33.1)	35.6 (33.1;38.1)	42.3 (39.8;44.8)	49.8 (47.4;52.3)	55.0 (53.2;56.7)	59.2 (57.7;60.8)	61.7 (60.2;63.2)	67.1 (66.3;67.8)	64.5 (63.8;65.1)	61.1 (60.5;61.7)	<0.0001
LLD	% drugs	10.2 (8.9;11.8)	13.5 (12.0;15.2)	20.8 (18.8;23.0)	26.2 (24.1;28.4)	29.9 (27.8;32.1)	21.7 (20.4;23.0)	35.8 (34.5;37.2)	40.1 (38.7;41.5)	54.3 (53.6;55.1)	59.7 (59.1;60.4)	62.8 (62.2;63.3)	<0.0001
Creatinine	process	89.1 (87.6;90.7)	87.3 (85.8;88.9)	97.5 (96.7;98.3)	91.9 (90.6;93.2)	91.8 (90.5;93.1)	84.7 (83.6;85.8)	85.7 (84.7;86.7)	93.1 (92.4;93.9)	87.8 (87.3;88.3)	85.5 (85.1;86.0)	95.4 (95.1;95.6)	<0.0001
	mean	96.5 (51.7;141.2)	95.0 (48.9;141.1)	93.8 (50.2;137.4)	96.8 (52.9;140.7)	98.2 (54.4;142.0)	95.4 (52.9;137.8)	96.5 (53.9;139.1)	97.7 (55.6;139.7)	92.9 (47.0;138.7)	98.9 (52.9;144.8)	98.7 (51.9;145.5)	<0.0001
ACR	process	65.8 (63.5;68.2)	68.0 (65.9;70.2)	93.5 (92.2;94.8)	85.4 (83.7;87.1)	84.8 (83.2;86.5)	57.4 (55.9;58.9)	62.0 (60.6;63.4)	69.9 (68.5;71.2)	59.0 (58.3;59.7)	66.8 (66.2;67.4)	82.3 (81.9;82.8)	<0.0001
	% micro	33.6 (30.8;36.4)	32.6 (30.0;35.3)	31.4 (28.9;33.8)	29.4 (27.0;31.8)	25.1 (22.9;27.3)	22.1 (20.4;23.8)	24.4 (22.9;26.0)	23.2 (21.8;24.7)	19.2 (18.5;20.0)	19.8 (19.2;20.4)	18.5 (18.0;19.0)	<0.0001

	% macro	8.3 (6.7;10.0)	7.7 (6.2;9.2)	6.7 (5.3;8.0)	4.7 (3.6;5.8)	4.8 (3.7;5.9)	3.7 (2.9;4.4)	3.9 (3.2;4.6)	4.2 (3.5;4.9)	2.9 (2.6;3.2)	2.5 (2.2;2.7)	2.4 (2.2;2.6)	<0.0001
BMI	process	69.0 (66.7;71.2)	69.5 (67.3;71.6)	96.9 (96.0;97.7)	96.7 (95.8;97.5)	95.7 (94.8;96.7)	62.3 (60.8;63.8)	83.0 (82.0;84.1)	88.4 (87.5;89.4)	78.1 (77.5;78.7)	88.1 (87.7;88.5)	93.1 (92.8;93.4)	<0.0001
	mean	29.0 (28.7;29.2)	28.9 (28.6;29.1)	29.3 (29.0;29.5)	29.4 (29.2;29.7)	29.5 (29.3;29.7)	29.6 (29.4;29.7)	29.6 (29.5;29.8)	29.5 (29.4;29.7)	29.5 (29.5;29.6)	29.5 (29.5;29.6)	29.5 (29.5;29.6)	0.1399
	% <25	20.4 (18.0;22.7)	20.4 (18.1;22.6)	17.4 (15.5;19.4)	16.7 (14.8;18.5)	15.8 (14.0;17.5)	16.2 (14.8;17.7)	16.1 (14.9;17.2)	16.3 (15.1;17.4)	16.8 (16.2;17.4)	17.1 (16.6;17.6)	17.1 (16.6;17.6)	0.6638

All data are mean values or proportions together with their 95% confidence intervals, or median values together with the interquartile range. * P for trend is based on age- and gender-adjusted analyses. Abbreviations: DM: diabetes mellitus, OBLD: oral blood glucose lowering drugs, SBP: systolic blood pressure, LLD: lipid lowering drugs, MDRD: modification of diet in renal disease, ACR: albumin-creatinine ratio, BMI: body mass index.

Figures

Figure 1. Process measures for albumin-creatinine ratio (ACR), body mass index (BMI) and blood pressure.

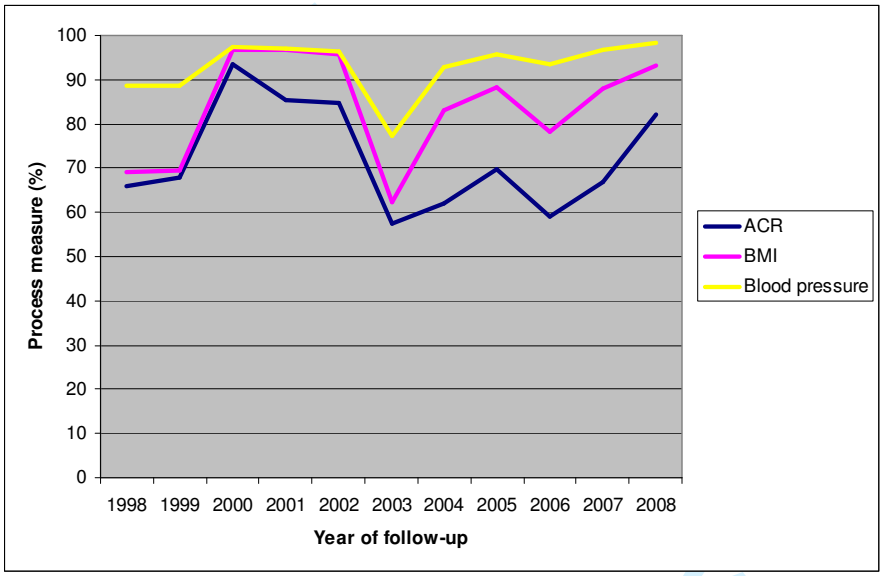
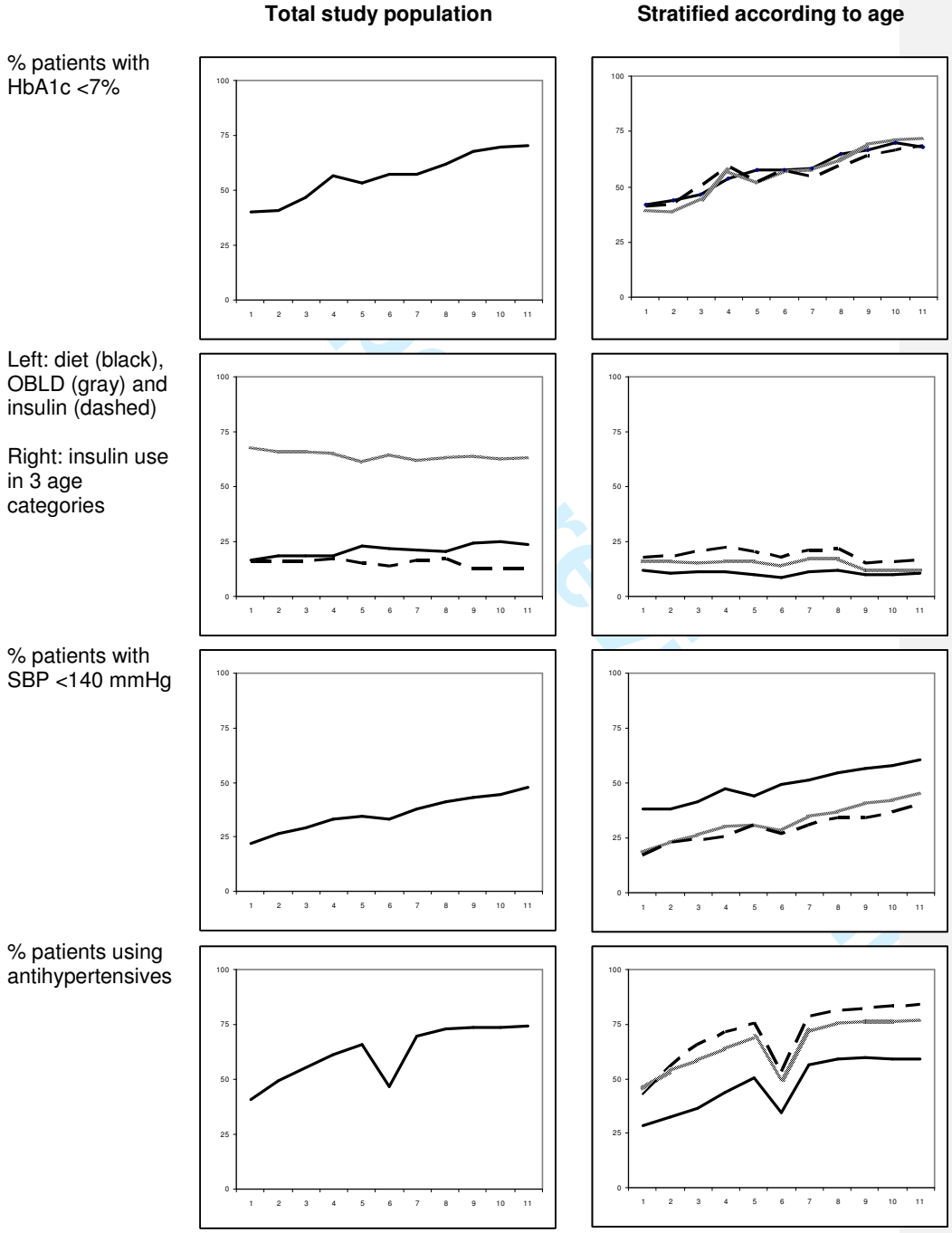
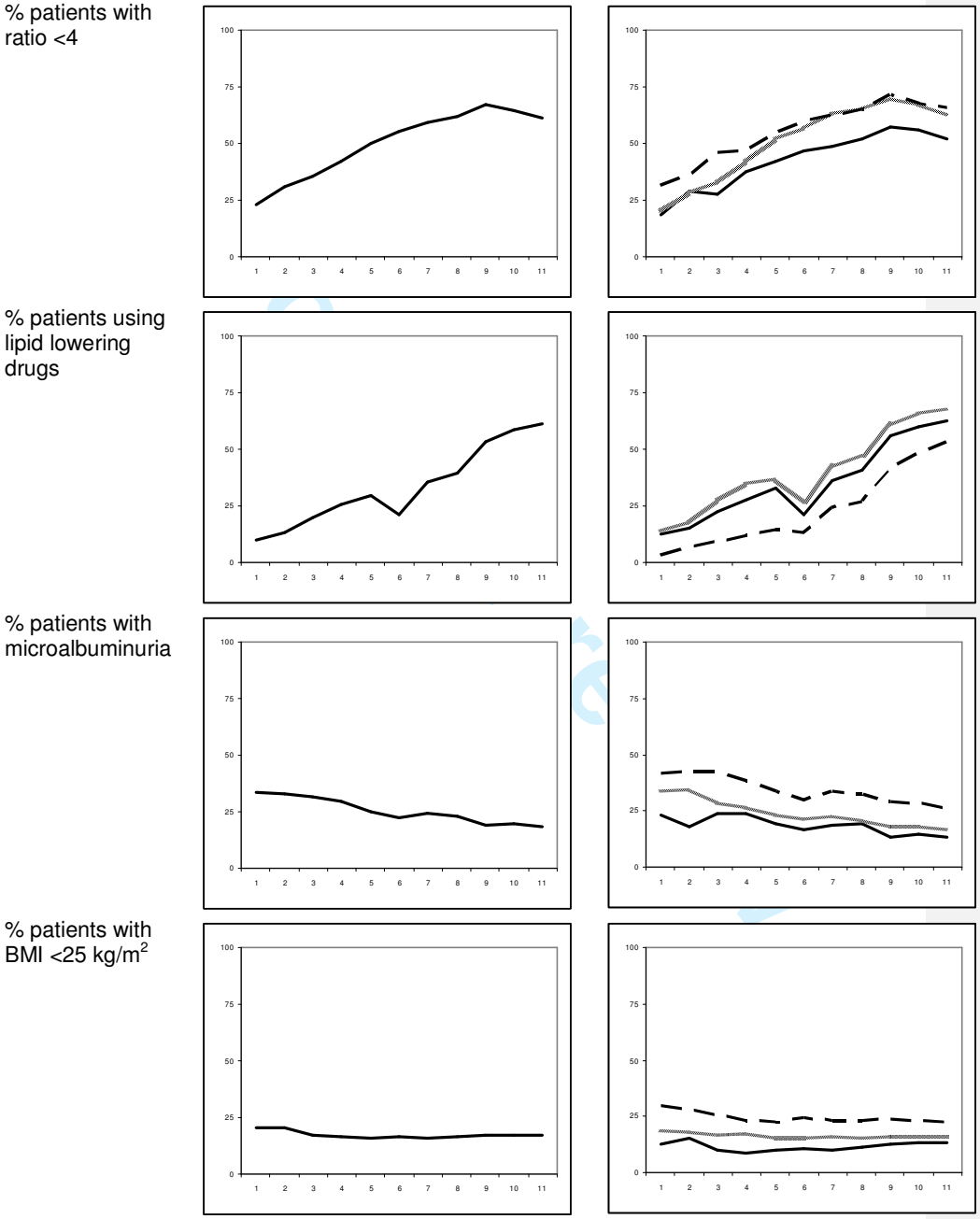


Figure 2. Outcome measures for the total study population and stratified according to age (<60 (black line), 60-75 (grey line) and >75 (black dashed line) years).





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Title: A prospective observational study of quality of diabetes care in a shared care setting: trends and age differences (ZODIAC-19)

Short title: Trends in diabetes care in the period 1998-2008

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Word count: main text 3366; abstract 300.

Number of tables: 2; number of figures: 2.

Abstract

Objective: The Zwolle Outpatient Diabetes project Integrating Available Care (ZODIAC) study was initiated in 1998 to investigate the effects of shared care for patients with type 2 diabetes mellitus (T2DM) in the Netherlands, and to reduce the number of diabetes-related complications. Benchmarking the performance of diabetes care was and is an important aspect of this study. We aimed to investigate trends in diabetes care, within the ZODIAC study for a wide variety of quality indicators during a long follow-up period (1998-2008), with special interest for different age groups.

Design: Prospective observational cohort study.

Setting: Primary care, Zwolle, The Netherlands.

Participants: Patients with T2DM.

Methods: A dataset of quality measures was collected annually during the patient's visit to the practice nurse or general practitioner. Linear time trends from 1998-2008 were estimated using linear mixed models in which we adjusted for age and gender. Age was included in the model as a categorical variable: for each follow-up year all participants were categorised into the categories <60, 60-75 and >75 years. Differences in trends between the age categories were investigated by adding an interaction term to the model.

Results: The number of patients who were reported to participate increased in the period 1998-2008 from 1622 to 27.438. All quality indicators improved in this study, except for body mass index. The prevalence albuminuria decreased in an eleven-year-period from 42% to 21%. No relevant differences between the trends for the 3 age categories were observed. During all years of follow-up, mean blood pressure and body mass index were the lowest and highest, respectively, in the group of patients <60 years (data not shown).

Conclusion: Quality of diabetes care within the Dutch ZODIAC study, a shared care project, has considerably improved in the period 1998-2008. There were no relevant differences between trends across various age categories.

Keywords: Diabetes mellitus type 2; Observational studies.

Article focus

- Shared care, defined as care for patients with a chronic condition provided in cooperation between primary and secondary health care, has been promoted and developed in order to reduce the number of diabetes-related complications.
- There is limited data whether improvements in diabetes care in the past decades are comparable across different age categories.
- We aimed to investigate trends in diabetes care, within a shared care project, during a long follow-up period (1998-2008), with a special focus on different age groups.

Key messages

- Quality of diabetes care within the Dutch ZODIAC study, a shared care project, has considerably improved in the period 1998-2008.
- Large improvements were observed for all quality indicators studied in this study, except for BMI.
- No relevant differences between the trends for different age categories were observed.

Strengths and limitations

- Strengths of our study are the long follow-up period and the high number of participants.
- A causal relationship between shared care and the observed improvements cannot be proved due to the observational design of our study.

Introduction

Ever since it was established that type 2 diabetes mellitus (T2DM) leads to significant morbidity and mortality [1,2], prevention and (early) treatment of both microvascular and macrovascular complications of T2DM have become important goals in diabetes care. Efforts to improve the quality of diabetes care are necessary in order to reduce morbidity and mortality associated with T2DM [3,4]. Since adequate treatment of patients with T2DM often needs the involvement of more than one caregiver, shared care, defined as care for patients with a chronic condition provided in cooperation between primary and secondary health care, has been promoted and developed [5].

The *Zwolle Outpatient Diabetes project Integrating Available Care* (ZODIAC) study was initiated in 1998 to investigate the effects of shared care for patients with T2DM in the Netherlands [6]. Benchmarking the performance of diabetes care was and is an important aspect of this initiative. Previous reports from the ZODIAC study showed that structured shared care with task delegation to nurses leads to improvements in quality of diabetes care and life expectancy [6-8]. However, effectiveness of shared care in general was not demonstrated in a 2007 Cochrane review [5]. Inadequate length of follow-up was mentioned by the authors as a possible explanation for the lack of evidence.

Although diabetes care has improved considerably during the past decades in patients with diabetes, there is limited data whether these improvements are comparable across different age categories [9,10]. A cross-sectional study from France showed that quality of care had considerably improved for patients ≥65 years with T2DM in the period 2001-2007 [11]. Unfortunately, trends for patients >75 years were not described separately in this study. Although the number of patients with T2DM >75 years is increasing, the evidence for cardiovascular risk interventions in this age category is low [12]. Data from observational studies show that classic cardiovascular risk factors may even have different consequences in elderly patients [13-17].

In the present study, we aimed to investigate trends in diabetes care, within a shared care project, for a wide variety of quality indicators during a long follow-up period (1998-

2008). Because of limited evidence for cardiovascular risk interventions in old age, we had specific interest whether the same trends were observed for different age groups (<60, 60-75 and >75 years).

Methods and Patients

Study population and ZODIAC

The ZODIAC study started in 1998 as a prospective observational study for patients with T2DM [6]. Participating practices were allocated to one of the two intervention groups or to the standard care group. The interventions involved extensive or limited task delegation from general practitioners to practice nurses and/or diabetes specialist nurses. Moreover, it included a diabetes register, structured recall, facilitated generalist-specialist communication, audit and feedback, patient-specific reminders, and it emphasized patients' education [6]. The patients participating in the ZODIAC study are known with T2DM and exclusively treated in primary care. Patients who were already treated in secondary care for their diabetes, patients with a very short life expectancy (including patients with active cancer) and patients with insufficient cognitive abilities were excluded from participation. In the first years of ZODIAC, only patients in the surrounding area of the city of Zwolle participated in the study. Because of the improvements in the quality of diabetes care in the two intervention groups, the shared care project has expanded gradually in the past decade. Firstly, the shared care project became the standard for diabetes care in the entire Zwolle region (2002-2003), and in 2005-2006 the project expanded to the northeast region of the Netherlands. Patients who were received standard care in the beginning of the project, switched to shared care in 2002-2003 when the shared care project became the standard for the entire Zwolle region. These patients were included in the current analyses from the moment they switched to shared care. The number of participating general practitioners (GPs) has increased from 53 in 1998 to 459 in 2008. Patient numbers increased from 1622 to 27.438 in this time frame, and nowadays even more than 60.000 patients are participating. A benchmark of annually gathered quality measures of this cohort, based on the guidelines of the Dutch College of General Practitioners and the Dutch Diabetes Federation, has been developed [18].

Data collection

The dataset of quality measures is collected annually during the patient's visit to the practice nurse and/or GP. These quality measures are collected in the general practitioners' patients information systems, and each year the relevant data are uploaded and sent to our diabetes centre for benchmarking and research purposes. At baseline, additional data were collected including a full medical history. The dataset contains many quality measures, including data on cardiovascular risk control, treatment and complications. Distinction is made between process and outcome measures. Process measures indicate whether tests or assessments have been performed, e.g. the number of patients whose HbA1c level has been determined. Outcome measures reflect the results of the assessments, such as the mean systolic blood pressure or the proportion of patients with a systolic blood pressure <140 mm Hg. Table 1 shows an overview of the measures we investigated in this study for each year of follow-up.

Participating practices were instructed to perform blood pressure measurements in supine position after at least 5 min of rest, and to calculate the mean blood pressure of two recording for each visit. Laboratory data (HbA1c, serum creatinine and lipid profile) were determined using standard hospital procedures. Until 2005, all procedures were performed in the clinical chemistry laboratory of the Isala Clinics (Zwolle region). Because of the expansion of the project in 2005-2006 to the northeast region of the Netherlands, laboratories of other regions started participating. HbA1c was measured using affinity chromatography *high-performance liquid chromatography* (HPLC, Ultra 2, Trinity Biotech, Kansas City, MO) in the Zwolle region (coefficient of variation approximately 1.5%) [19]. There are differences in the methods used in the various laboratories in the northeast region of the Netherlands. Generally speaking, the variation coefficient has decreased in the study period due to the worldwide standardization of HbA1c measurements and improved techniques. Because of the high number of patients in the last years of the project, it is not likely that differences in the coefficient of variation coefficient have influenced the results.

Statistical analyses

Continuous variables are represented as means and 95% confidence intervals (95% CI) for the normally distributed values. Normality was evaluated using Q-Q plots and histograms. Nominal variables are represented as the proportion of patients together with 95% CIs. The database contained 37.320 unique patients and data of 92.340 unique yearly diabetic check-ups. For 9.279 patients, we only had data of one diabetic check-up. The descriptive statistics were strictly cross-sectional and included observations of all visits (n=92.340). Since cross-sectional outcomes are influenced by changes in population (in- and outmigration), besides changes in quality of care, cross-sectional outcomes tend to overestimate time trends when compared to longitudinal analyses [20]. Therefore, we estimated linear time trends from 1998-2008 using a linear mixed model for continuous variables (SAS PROC MIXED) and a generalized linear mixed model for binary variables (PROC GLIMMIX, using the logit link function) in which we adjusted for age and gender. In all analyses time, age and sex were modelled as fixed effects. Since the estimated linear time trends are based on individual changes over time, data of at least 2 visits were necessary. As a consequence, these longitudinal analyses were based on 83.061 visits of 28.041 patients. Age was included in the model as a categorical variable: for each follow-up year all participants were categorised into the categories <60, 60-75 and >75 years. All time trends were visually inspected and a quadratic time trend was only introduced when such a trend was likely based on the plot. Differences in trends between men and women and the age categories were investigated by adding interaction terms for age and time and sex and time to the model. A significant interaction for age and time means that differences exist between the time trends for the 3 age categories. The same applies for the interaction between sex and time. All analyses were performed with SPSS version 18.0.0 software (SPSS inc., Chicago, Illinois, USA) and with SAS 9.2 software (SAS Institute Inc., Cary, NC, USA).

The manuscript was written based on the 'Strengthening the reporting of observational studies in epidemiology' (STROBE) statement [21].

Ethics statement

The ZODIAC study and the informed consent procedure were approved by the local medical ethics committee of the Isala Clinics, Zwolle, the Netherlands. In the first years of ZODIAC, verbal informed consent was obtained from all patients and the consent was documented in the patient's records. According to Dutch law, written informed consent was not necessary for this type of study in 1998. Nowadays, written informed consent is obtained. All data were analysed anonymously.

Results

The number of patients who were reported to participate in this shared care project increased in the period 1998-2008 from 1622 to 27.438. Mean age decreased with time from 68.9 to 67.4 years (p for trend <0.0001). A gradual increase was observed for the proportion of male patients participating in the project. Median diabetes duration remained rather constant at 5 years throughout the whole study period. The proportion of patients aged older than 75 years was 31.0% in 1998 and declined to 26.3% in 2008. The number of patients who did not participate in the study due to short life expectancy of insufficient cognitive abilities is unknown after 1999. The results for all process and outcome measures of each year for the overall study group are presented in table 2.

Process measures

All process measures show a similar trend (table 2): a gradual increase in the first years of the project followed by a decrease in the years 2002 and 2003, an increase in the upcoming two years, followed by a decrease in 2006 again and a rising trend in the process measures in the last two years. Body mass index (BMI), the lipid profile and the ACR were less often measured in patients aged >75 years compared to the younger patients (p for interaction with age for all variables <0.0001). Figure 1 illustrates the trends for the process measure of ACR, BMI and blood pressure in the total study population.

Outcome measures

Figure 2 presents the trends for outcome measures over time for the overall study group and also stratified according to the 3 age categories.

Glycemic control and diabetes treatment

The decline in mean HbA1c over time is reflected in the proportion of patients achieving the target value of <7%; 35.8% in 1998 compared to 67.0% in 2008. The differences between the 3 age categories seem to be small, although the proportion of patients with an HbA1c

≥8.5% tended to be the highest for patients aged <60 years in all years (p for interaction with age 0.0773). The proportion of patients treated with only a diet increased over time from 16.6% to 23.8%. A total of 15.5% used insulin in 1998 and this proportion declined to 12.8% in 2008.

Blood pressure and treatment

Mean blood pressure has decreased over time in all age groups, with the lowest values in the youngest patient category (p for interaction with age <0.0001). In 1998 about one fifth (22.0%) had a systolic blood pressure <140 mmHg, compared to 47.7% in 2008. The number of patients with antihypertensive medication increased in all age groups. With advancing age the number of patients using these agents also increased (p for interaction with age <0.0001). A remarkable decrease in 2003 was directly followed by a large increase in 2004.

Lipids and treatment

Mean total cholesterol-HDL ratio has decreased in the period 1998-2006, followed by a small increase in the last two years (p for quadratic trend <0.0001). Patients aged <60 years performed worse with regard to the mean cholesterol-HDL ratio compared to the older patients categories (p for interaction with age <0.0001). Approximately one quarter (23.0%) of the patients participating in 1998 had a ratio <4. This proportion increased to 61.1% in 2008, which is also reflected in the number of patients receiving lipid-lowering drugs: 10.2% in 1998 and 62.8% in 2008. As was the case with the number of patients using antihypertensives, a remarkable decrease was also observed for the number of patients using lipid-lowering drugs in 2003.

Renal function

Mean values of serum creatinine have remained rather constant throughout the whole study period. The prevalence of micro- and macroalbuminuria in 1998 was 33.6% and 8.3%,

respectively. These proportions declined over time to 18.5% and 2.4%, respectively. The highest prevalence of microalbuminuria was observed for the group >75 years (p for interaction with age <0.0001).

Body mass index

After an increase in the first five years, mean BMI remained rather constant afterwards. In the highest age category, the highest proportion of patients with a BMI <25 kg/m^2 was observed and vice versa (p for interaction with age <0.0001).

Discussion

Quality of diabetes care within the Dutch ZODIAC study, a shared care project, has considerably improved in the period 1998-2008. Large improvements were observed for all quality indicators studied in this study, except for BMI. Each time that large groups of general practices joined the shared care initiative (2002 and 2006), there was a short relapse in the process measures, which was mostly redressed within one year. No relevant differences between the trends for the 3 age categories were observed. During all years of follow-up, mean blood pressure and BMI were the lowest and highest, respectively, in the group of patients <60 years. Patients in this age category also had the highest cholesterol-HDL ratio values and the lowest albumin-creatinine ratio values throughout the whole study period.

Striking changes were the increase in the use of blood pressure and lipid lowering drugs. This increased use was also reflected in the improvements in blood pressure and lipid levels. Remarkably, the decrease in HbA1c was not accompanied by an increase in the proportional use of oral blood glucose lowering drugs or insulin. Instead, an increase in the proportion of patients on a diet was observed for all age categories. One could hypothesize that more patients with early diagnosed T2DM were included in the last years of the study. However, median diabetes duration did not relevantly change throughout the study. Patient education and better adherence to lifestyle advices could be other possible explanations.

The results of our study confirm previous reports that also observed improvements in risk factor control during the past decades [9-11,22]. However, this is the first study presenting the results of a large shared care project with a follow-up period of more than 10 years. Although this study demonstrates the impressive results that have been achieved in a shared care setting, it should be emphasized that causality cannot be proved by our study. The two decreases in the process measures, that were observed after the expansion of the ZODIAC project in 2002 and 2006, and the quick rebound afterwards, suggest positive effects of participating in the project (figure 1). However, there are many other factors that may also explain the improvements in quality of care. Firstly, national and international guidelines advocating stricter treatment in patients with T2DM have been published in the

period 1998-2008. For example, in 1999 and in 2006 revisions of the guideline T2DM of the Royal Dutch College of General Practitioners were published [18,23]. It could be that adherence to these guidelines, irrespective of participating in shared care projects, is the most important factor explaining the general tendency to improved diabetes care. Secondly, financial incentives from health insurance companies for general practitioners that provide care of a high quality have been introduced in the past decade. Although a recent Cochrane review concluded that there is insufficient evidence to support the use of such financial incentives, positive effects on quality of care can also not be excluded [24].

To our knowledge, our study is the first study that also specifically investigated the trends in diabetes care for patients aged older than 75 years. This population is of special interest for two reasons. Firstly, more than one quarter of the type 2 diabetic population in primary care in the Netherlands is >75 years. Secondly, clinical trials in old age investigating cardiovascular risk interventions, such as hypertension treatment, are either lacking or subject to selection bias [25-27]. Since the evidence for strict cardiovascular risk control in old age is low, old age is characterized by a high prevalence of complications and comorbidities, and elderly patients are at increased risk for possible adverse events, less strict treatment targets for elderly patients with T2DM have been advocated in literature [28-30]. Generally speaking, individualizing target values is more and more advocated in literature nowadays [30]. Take for example hypertension treatment in old age. Whereas a systolic blood pressure target value of 140 mmHg should be used for patients >75 years without many comorbidities who are not using insulin, it is unknown whether this target value is also appropriate for the overall elderly population [27]. In conclusion, although the current study observed the same improvements in the various quality measures across all age categories, it remains unsure whether these improvements will have the same beneficial effects on cardiovascular comorbidity and mortality in the oldest elderly as in younger patients with T2DM.

Our study has several important limitations that need to be addressed. Firstly, it is important to realise that the cross-sectional data presented in table 2 and figure 2 are

influenced by changes in population (in- and outmigration), besides possible changes in quality of care. Since the estimated linear time trends were based on individual changes over time, it is possible to conclude that there is an improvement over time. However, these improvements are probably smaller than the cross-sectional data suggest, since cross-sectional outcomes on HbA1c overestimate improvements over time when compared to longitudinal outcomes [20]. Secondly, because of its observational design a causal relationship between shared care and the observed improvements cannot be proven. Unfortunately, we were not able to include a control group of patients with diabetes receiving standard care. Thirdly, the data in our study have been provided by practice nurses and GPs as part of the yearly benchmark. As a consequence, the quality and reliability of the data is dependent on the accuracy of the data providers. For example, the number of patients using lipid lowering treatment in 2003 is an extreme outlier compared to the other years and is probably not representative for the actual number of patients. This difference suggests a fault in providing or collecting the data. When a patient is registered as not using a statin, this could either mean that he or she is actually not using a statin or that it is incorrectly registered. However, with respect to the process parameters this may have led at the most to an underestimation of the actual measures. Also, our study only comprises patients whom data have been reported by the GPs. It is not unlikely that GPs have opted not to provide data of patients who never show up at their diabetes check-ups. Furthermore, the number of patients who did not participate in the study due to short life expectancy of insufficient cognitive abilities is unknown after 1999.

Strengths of our study are the long follow-up period and the high number of participants, especially in the last years of the ZODIAC study. Because of the size of our database, it is important to realize that small differences may easily lead to statistical significant differences while some can hardly be called relevant. For example, the mean serum creatinine level fluctuates around 95 µmol/L throughout the whole study period, but there is a slight positive (i.e. upward) linear trend for males above 75 years, while for women

there is a slight negative linear trend for all age categories while the overall linear (very slightly positive) trend is nevertheless highly significant ($p<0.0001$).

In conclusion, our study shows that quality of diabetes care within the Dutch ZODIAC study has improved in the period 1998-2008, irrespective of age. Future studies are needed to elucidate whether there is a causal relationship between shared care and the improvements. Whether the large improvements observed in old age will lead to reductions in morbidity and mortality, remains also to be determined.

Data sharing: no additional data available.

Competing interest declaration

All authors declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

Funding source

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Contributors

KJJH (guarantor), ID, NK and HJGB designed the study; KJJH and HJGB acquired the data used in this study; KJJH and KHG analysed the data; KJJH and KHG performed the statistical analyses; and all authors participated in interpretation of the data. All authors had full access to all of the data. KJJH drafted the manuscript and all authors participated in revision of the manuscript. NK, STH, KM and HJGB supervised the study.

Tables

Table 1. *Overview of the process and outcome measures studied*

Parameter	Process measure	Outcome measure
HbA1c	% of patients measured	mean HbA1c (%)
		% HbA1c < 7.0%
		% HbA1c ≥ 8.5%
Glucose lowering treatment	N.A.	% diet only
		% oral medication only
		% insulin with or without oral medication
Blood pressure	% of patients measured	mean SBP (mm Hg)
		% SBP < 140 mm Hg
Antihypertensive treatment	N.A.	% patients using antihypertensive drugs
Cholesterol-HDL ratio	% of patients measured	mean total cholesterol-HDL ratio
		% total cholesterol-HDL ratio <4
Lipid-lowering drugs	N.A.	% patients using lipid-lowering drugs
Renal function	% of patients with creatinine measurements	mean creatinine (µmol/L)
	% of patients with ACR measurements	% micro-albuminuria
		% macro-albuminuria
BMI	% of patients measured	mean BMI (kg/m^2)
		% BMI < 25 kg/m^2

Abbreviations: N.A.: not applicable; SBP: systolic blood pressure; ACR: albumin-creatinine ratio; BMI: body mass index.

Table 2. *Characteristics of all participants in the ZODIAC study for the period 1998-2008*

		1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	*P for*
		n=1622	n=1767	n=1462	n=1615	n=1761	n=4029	n=4729	n=4508	n=18469	n=24940	n=27438	*trend**
Age		68.9 (68.4;69.5)	68.9 (68.3;69.4)	67.8 (67.2;68.4)	67.8 (67.2;68.3)	67.0 (66.5;67.6)	67.6 (67.2;67.9)	67.5 (67.2;67.9)	67.5 (67.2;67.8)	67.4 (67.2;67.6)	67.0 (66.9;67.2)	67.4 (67.2;67.5)	<0.0001
Sex (female)		58.0 (55.6;60.4)	58.2 (55.9;60.5)	56.2 (53.7;58.8)	56.9 (54.5;59.3)	55.4 (53.1;57.7)	54.7 (53.2;56.2)	53.8 (52.4;55.2)	53.5 (52.1;55.0)	52.6 (51.9;53.3)	52.6 (51.9;53.2)	51.9 (51.3;52.5)	<0.0001
DM duration		5.2 [2.5;9.8]	5.7 [3.0;10.5]	5.6 [2.8;10.4]	5.0 [2.1;9.9]	4.5 [2.1;9.0]	4.5 [2.3;8.5]	4.9 [2.3;8.5]	5.0 [2.6;8.7]	4.7 [2.4;8.1]	4.8 [2.4;8.1]	5.3 [2.9;8.8]	<0.0001
HbA1c	process	88.6 (87.0;90.1)	86.4 (84.8;88.0)	97.4 (96.6;98.2)	91.1 (89.7;92.5)	91.6 (90.3;92.9)	83.6 (82.5;84.8)	85.9 (84.9;86.8)	96.1 (95.5;96.6)	87.8 (87.3;88.3)	85.8 (85.4;86.2)	95.5 (95.3;95.8)	<0.0001
	mean	7.5 (7.4;7.5)	7.5 (7.4;7.5)	7.3 (7.2;7.3)	7.0 (7.0;7.1)	7.1 (7.0;7.1)	7.0 (6.9;7.0)	7.0 (7.0;7.0)	6.8 (6.8;6.9)	6.7 (6.7;6.8)	6.7 (6.7;6.7)	6.7 (6.7;6.7)	<0.0001
	% <7	40.4 (37.9;43.0)	40.6 (38.1;43.1)	46.6 (44.0;49.2)	56.7 (54.2;59.2)	53.3 (50.9;55.8)	57.2 (55.5;58.8)	57.0 (55.5;58.5)	61.9 (60.5;63.4)	67.5 (66.8;68.2)	69.8 (69.2;70.5)	70.1 (69.6;70.7)	<0.0001
	% ≥8.5	13.2 (11.5;15.0)	12.9 (11.2;14.6)	9.7 (8.2;11.2)	7.8 (6.5;9.2)	7.4 (6.2;8.7)	5.7 (4.9;6.5)	5.6 (4.9;6.3)	3.4 (2.8;3.9)	3.0 (2.8;3.3)	2.6 (2.4;2.8)	2.3 (2.1;2.5)	<0.0001
DM treatment	Diet only	16.6 (14.9;18.5)	18.5 (16.8;20.4)	18.5 (16.6;20.6)	18.2 (16.4;20.2)	23.1 (21.2;25.1)	21.9 (20.7;23.2)	21.3 (20.1;22.5)	20.1 (18.9;21.3)	24.1 (23.5;24.7)	24.9 (24.3;25.4)	23.8 (23.3;24.3)	<0.0001
	% OBLD only	67.9 (65.6;70.2)	65.9 (63.6;68.0)	65.7 (63.3;68.1)	65.0 (62.6;67.2)	61.5 (59.2;63.8)	64.5 (63.0;66.0)	62.1 (60.7;63.5)	63.0 (61.6;64.4)	63.8 (63.1;64.4)	62.8 (62.2;63.4)	63.4 (62.9;64.0)	<0.0001
	% insulin	15.5 (13.8;17.3)	15.6 (14.0;17.4)	15.7 (14.0;17.7)	16.8 (15.1;18.7)	15.4 (13.8;17.2)	13.6 (12.5;14.6)	16.6 (15.6;17.7)	16.9 (15.9;18.1)	12.2 (11.7;12.6)	12.3 (11.9;12.7)	12.8 (12.4;13.2)	<0.0001

SBP	process	88.7 (87.2;90.3)	88.5 (87.0;90.0)	97.3 (96.4;98.1)	97.0 (96.1;97.8)	96.4 (95.5;97.2)	77.2 (75.9;78.5)	92.8 (92.1;93.5)	95.7 (95.1;96.3)	93.4 (93.0;93.8)	96.7 (96.5;96.9)	98.5 (98.4;98.7)	<0.0001
	mean	154.5 (153.3;155.8)	150.3 (149.1;151.4)	149.4 (148.2;150.6)	145.9 (144.9;146.9)	144.4 (143.4;145.4)	146.7 (146.0;147.4)	145.9 (145.3;146.5)	144.6 (144.0;145.2)	141.9 (141.7;142.2)	141.2 (140.9;141.4)	140.0 (139.8;140.2)	<0.0001
	% <140	22.0 (19.9-24.2)	26.4 (24.2;28.6)	29.4 (27.0;31.8)	33.0 (30.7;35.3)	34.6 (32.4;36.9)	33.2 (31.5;34.8)	37.9 (36.4;39.3)	40.8 (39.3;42.2)	43.0 (42.2;43.7)	44.6 (43.9;45.2)	47.7 (47.1;48.3)	0.0003
SBP treatment	% drugs	41.1 (38.8;43.5)	49.6 (47.3;52.0)	55.0 (52.4;57.5)	61.1 (58.7;63.5)	65.7 (63.4;67.9)	46.7 (45.1;48.2)	69.7 (68.4;71.0)	72.7 (71.4;74.0)	73.5 (72.8;74.1)	73.7 (73.2;74.3)	74.6 (74.1;75.1)	<0.0001
Chol-HDL Ratio	process	73.3 (71.2;75.5)	74.9 (72.9;77.0)	96.4 (95.4;97.3)	91.9 (90.6;93.2)	92.3 (91.0;93.5)	77.2 (75.9;78.5)	79.5 (78.4;80.7)	87.8 (86.9;88.8)	83.1 (82.6;83.7)	84.2 (83.7;84.6)	94.2 (94.0;94.5)	<0.0001
	mean	5.2 (5.1;5.3)	4.8 (4.7;4.9)	4.5 (4.5;4.6)	4.4 (4.3;4.5)	4.1 (4.0;4.1)	4.0 (3.9;4.0)	3.8 (3.8;3.9)	3.8 (3.7;3.8)	3.6 (3.6;3.7)	3.7 (3.7;3.7)	3.8 (3.8;3.8)	<0.0001
	% <4	23.0 (20.7;25.4)	30.7 (28.2;33.1)	35.6 (33.1;38.1)	42.3 (39.8;44.8)	49.8 (47.4;52.3)	55.0 (53.2;56.7)	59.2 (57.7;60.8)	61.7 (60.2;63.2)	67.1 (66.3;67.8)	64.5 (63.8;65.1)	61.1 (60.5;61.7)	<0.0001
LLD	% drugs	10.2 (8.9;11.8)	13.5 (12.0;15.2)	20.8 (18.8;23.0)	26.2 (24.1;28.4)	29.9 (27.8;32.1)	21.7 (20.4;23.0)	35.8 (34.5;37.2)	40.1 (38.7;41.5)	54.3 (53.6;55.1)	59.7 (59.1;60.4)	62.8 (62.2;63.3)	<0.0001
Creatinine	process	89.1 (87.6;90.7)	87.3 (85.8;88.9)	97.5 (96.7;98.3)	91.9 (90.6;93.2)	91.8 (90.5;93.1)	84.7 (83.6;85.8)	85.7 (84.7;86.7)	93.1 (92.4;93.9)	87.8 (87.3;88.3)	85.5 (85.1;86.0)	95.4 (95.1;95.6)	<0.0001
	mean	96.5 (51.7;141.2)	95.0 (48.9;141.1)	93.8 (50.2;137.4)	96.8 (52.9;140.7)	98.2 (54.4;142.0)	95.4 (52.9;137.8)	96.5 (53.9;139.1)	97.7 (55.6;139.7)	92.9 (47.0;138.7)	98.9 (52.9;144.8)	98.7 (51.9;145.5)	<0.0001
ACR	process	65.8 (63.5;68.2)	68.0 (65.9;70.2)	93.5 (92.2;94.8)	85.4 (83.7;87.1)	84.8 (83.2;86.5)	57.4 (55.9;58.9)	62.0 (60.6;63.4)	69.9 (68.5;71.2)	59.0 (58.3;59.7)	66.8 (66.2;67.4)	82.3 (81.9;82.8)	<0.0001
	% micro	33.6 (30.8;36.4)	32.6 (30.0;35.3)	31.4 (28.9;33.8)	29.4 (27.0;31.8)	25.1 (22.9;27.3)	22.1 (20.4;23.8)	24.4 (22.9;26.0)	23.2 (21.8;24.7)	19.2 (18.5;20.0)	19.8 (19.2;20.4)	18.5 (18.0;19.0)	<0.0001

	% macro	8.3 (6.7;10.0)	7.7 (6.2;9.2)	6.7 (5.3;8.0)	4.7 (3.6;5.8)	4.8 (3.7;5.9)	3.7 (2.9;4.4)	3.9 (3.2;4.6)	4.2 (3.5;4.9)	2.9 (2.6;3.2)	2.5 (2.2;2.7)	2.4 (2.2;2.6)	<0.0001
BMI	process	69.0 (66.7;71.2)	69.5 (67.3;71.6)	96.9 (96.0;97.7)	96.7 (95.8;97.5)	95.7 (94.8;96.7)	62.3 (60.8;63.8)	83.0 (82.0;84.1)	88.4 (87.5;89.4)	78.1 (77.5;78.7)	88.1 (87.7;88.5)	93.1 (92.8;93.4)	<0.0001
	mean	29.0 (28.7;29.2)	28.9 (28.6;29.1)	29.3 (29.0;29.5)	29.4 (29.2;29.7)	29.5 (29.3;29.7)	29.6 (29.4;29.7)	29.6 (29.5;29.8)	29.5 (29.4;29.7)	29.5 (29.5;29.6)	29.5 (29.5;29.6)	29.5 (29.5;29.6)	0.1399
	% <25	20.4 (18.0;22.7)	20.4 (18.1;22.6)	17.4 (15.5;19.4)	16.7 (14.8;18.5)	15.8 (14.0;17.5)	16.2 (14.8;17.7)	16.1 (14.9;17.2)	16.3 (15.1;17.4)	16.8 (16.2;17.4)	17.1 (16.6;17.6)	17.1 (16.6;17.6)	0.6638

All data are mean values or proportions together with their 95% confidence intervals, or median values together with the interquartile range. * P for trend is based on age- and gender-adjusted analyses. Abbreviations: DM: diabetes mellitus, OBLD: oral blood glucose lowering drugs, SBP: systolic blood pressure, LLD: lipid lowering drugs, MDRD: modification of diet in renal disease, ACR: albumin-creatinine ratio, BMI: body mass index.

Figures

Figure 1. Process measures for albumin-creatinine ratio (ACR), body mass index (BMI) and blood pressure.

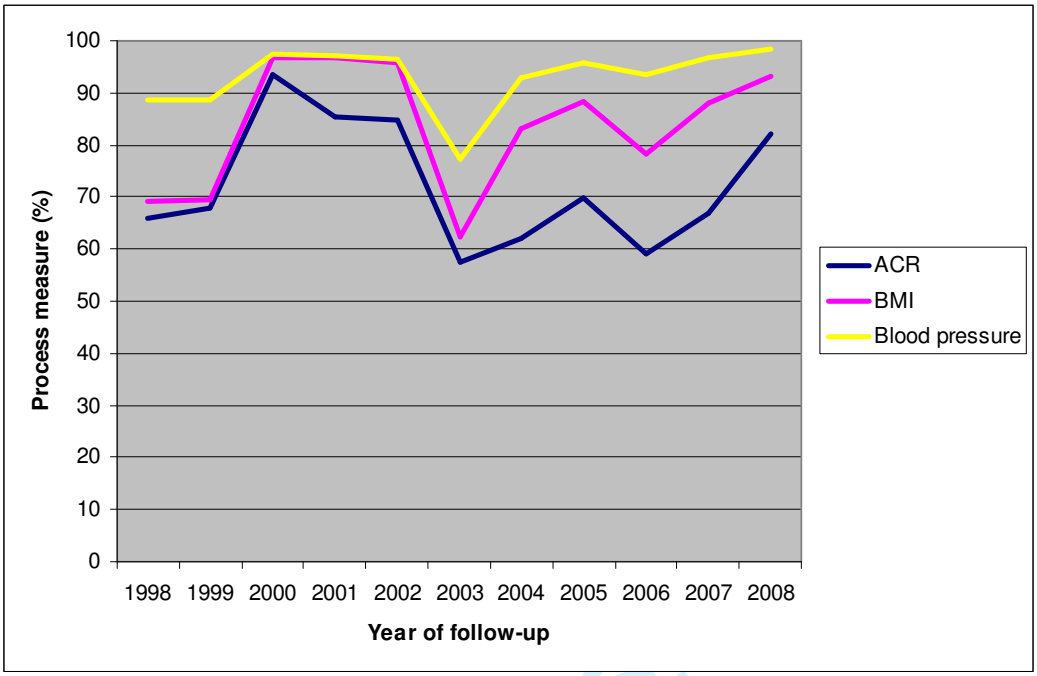
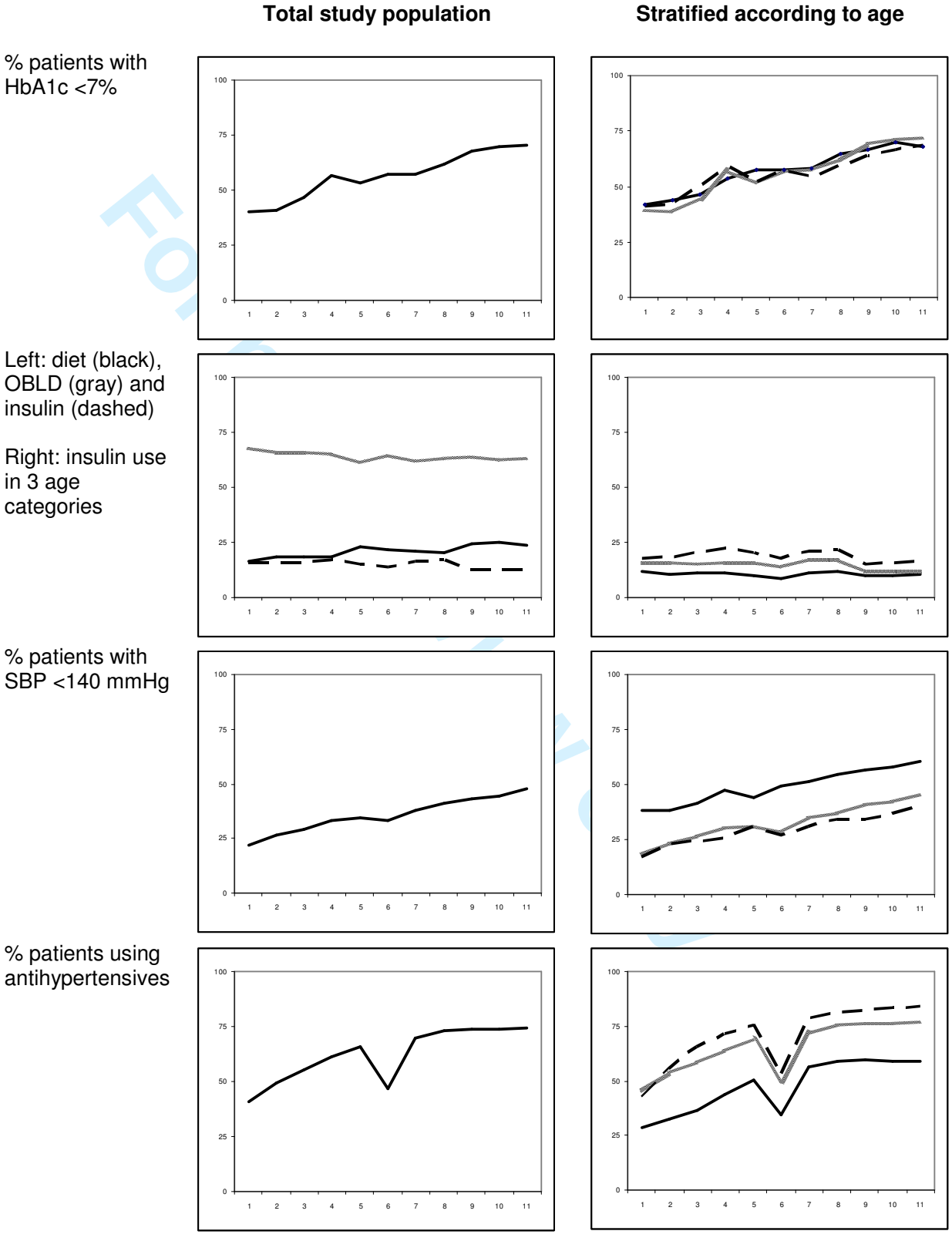
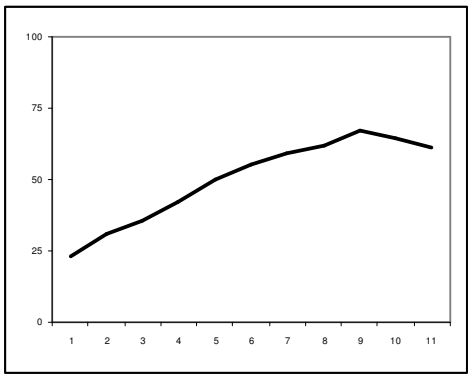
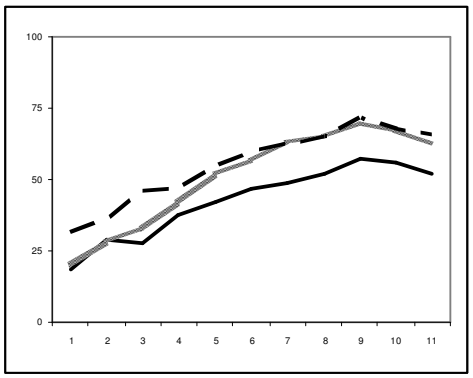


Figure 2. Outcome measures for the total study population and stratified according to age (<60 (black line), 60-75 (grey line) and >75 (black dashed line) years).

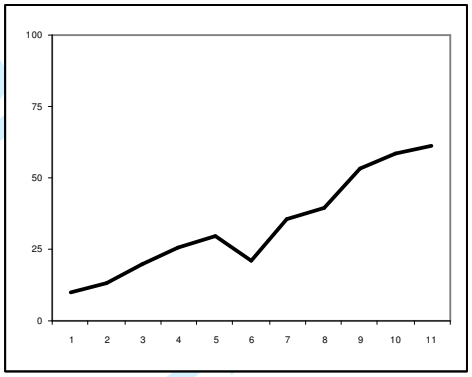


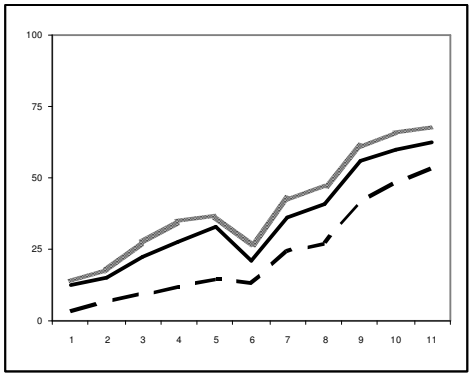
% patients with ratio <4



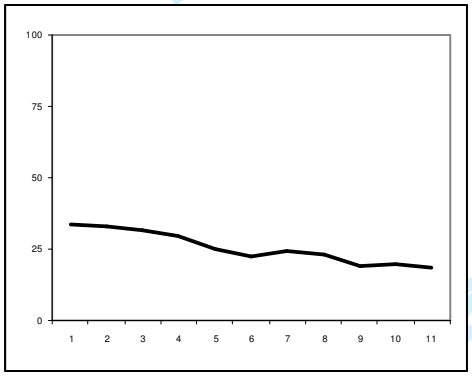


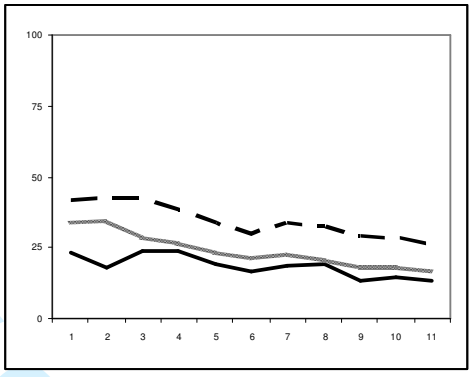
% patients using lipid lowering drugs



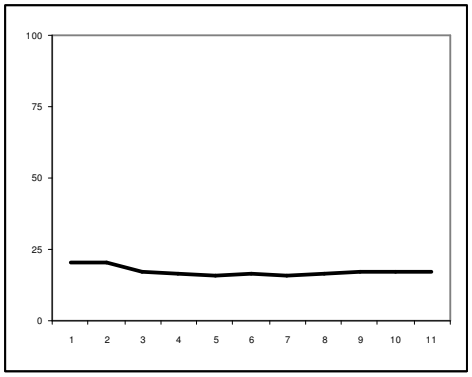


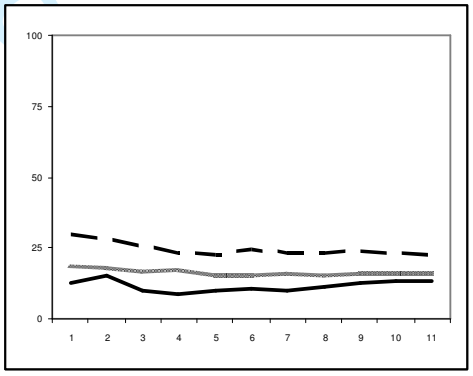
% patients with microalbuminuria





% patients with BMI <25 kg/m^2





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13 July 2012

Dear editor,

Electronically submitted, you will find the revision of our manuscript, entitled: “A prospective observational study of quality of diabetes care in a shared care setting: trends and age differences (ZODIAC-19)”.

Below you will find our response to the questions and suggestions of the two reviewers.

We are looking forward to hearing from you.

Yours faithfully,

Kornelis J.J. van Hateren

Reviewer: 1

Reviewer: Geert Goderis
competing interests: none to declare

The study is in general well performed with only few flaws in the description. There is a lack of clarity for some aspects;
- how were data collected, especially how happened the assessment of process parameters?
- in table 1: % of patients measured (eg HbA1c): is this at least once a year? What about 'optimal' follow-up (4 times a year)? It would be better to explain how process and outcomes were collected instead of giving the definition (p. 8, line 1-11 is superfluous)

Response of authors: The quality measures are collected in the general practitioners' patients information systems during the yearly diabetic check-ups, and each year the relevant data are uploaded and sent to our diabetes centre for benchmarking and research purposes. The participating practices were instructed to use the guidelines of the Royal College of General Practitioners for blood pressure measurement. Laboratory data were determined using standard hospital procedures. We included the following passage to the methods section:

Participating practices were instructed to perform blood pressure measurements in supine position after at least 5 min of rest, and to calculate the mean blood pressure of two recording for each visit. Laboratory data (HbA1c, serum creatinine and lipid profile) were determined using standard hospital procedures. Until 2005, all procedures were performed in the clinical chemistry laboratory of the Isala Clinics (Zwolle region). Because of the expansion of the project in 2005-2006 to the northeast region of the Netherlands, laboratories of other regions started participating. HbA1c was measured using affinity chromatography high-performance liquid chromatography (HPLC, Ultra 2, Trinity Biotech, Kansas City, MO) in the Zwolle region (coefficient of variation approximately 1.5%) [1]. There are differences in the methods used in the various laboratories in the northeast region of the Netherlands. Generally speaking, the variation coefficient has decreased in the study period due to the worldwide standardization of HbA1c measurements and improved techniques. Because of the high number of patients in the last years of the project, it is not likely that differences in the coefficient of variation coefficient have influenced the results.

In our opinion it is not superfluous to explain the definition of process and outcome measures, since many health care providers do not exactly know the differences between them.

It is correct that the % of patients measured indicates a measurement at least once a year. We opted not to investigate how many patients had their HbA1c measured 4 times a year since this follow-up is not advised in the Netherlands.

*Statistical methods: what was performed in SPSS and what in SAS? Statistical description of linear mixed models is very brief. What about assumption testing, outliers,...? Interaction term of which main effects? (time*age I suppose). A linear mixed model for binary outcomes is not possible PROC GLIMMIX is generalized linear mixed model with link function (and thus here a hierarchical logistic regression).*

Response of authors: We used SPSS for the descriptive statistics, and SAS was used for all other analyses. We inspected the residuals of the regression analyses for possible violations of the assumptions and outliers. Two interaction terms were added to the models: time* age and time*sex. We improved the statistical methods section on this issue.

We do not quite understand the reviewer's remark considering the use of PROC GLIMMIX in the case of binary responses. PROC GLIMMIX is a realization of the generalized linear model as was introduced by John Nelder and Robert Wedderburn in their 1972 article: "Generalized Linear Models" (Journal of the royal statistical society) [2]. An important difference between the general linear model and the generalized linear model is that in the former only continuous variables with normally distributed errors can be modeled, while in the latter also other types of responses and error distributions can be modeled (among others binary and count data). In the case of binary data the binomial distribution is used and the logit is the link function used in this case (the link function provides the relationship between the linear predictor and the mean of the distribution function. In the

case of normally distributed error the identity function is used). As a consequence, the general linear model is a special case of the generalized linear model (in the case of continuous variables PROC MIXED and PROC GLIMMIX give the same results).

Furthermore, in the literature the terms “multilevel models”, “hierarchical multilevel models”, “mixed models”, “nested models” are often used exchangeable. In our case the repeated measures are nested within the patients, so that is why we used the term “mixed models”. In our analyses we used the variables “time”, “age” and “sex” as fixed variables. We added this to the statistical methods section.

There is first a problem of internal validity of the results. I think it is not possible to make a comparison of 4508 patients in 2005 and 18469 patients in 2006. This 'sudden explosion' in patients is also not explained.

It is absolutely not clear to me how the "p for trend" (table 2) is related to the linear mixed models described in the method section. Time Trends in longitudinal analyses should analyse the timely evolution of individuals and thus take into account significance of the interaction term. This is important since the authors mention an improvement of diabetes care, which means a change (improvement) over time. The mere results do not allow this conclusion because they compare outcomes in different populations. (see remark above).

Response of authors: We thank the reviewer for his comments regarding the methods we used in our study. We acknowledge that the statistical design is rather complex and that our description in the methods section was too brief. Although the presented data for each year are cross-sectional data (table 2), the time trend analyses were longitudinal.

It is not clear to us which interaction term the reviewer is referring to. Since the analyses were of a longitudinal nature the variable “time” is the within person effect of time. Introduced in the model as a continuous variable, this is the linear component (“linear time trend”). The interaction terms time*age and time*sex indicate to what extent this linear trend is different for the three age groups and/or different for men and women. When the graphs of the changes over time clearly showed a non-linear trend, a quadratic time*time term was incorporated in the model (or higher order polynomials).

We will use the HbA1c analyses as an example (please find the SAS output below). Our database consists of 37320 unique patients and 92340 unique yearly check-ups. For some patients we have 11 years of follow-up data: they started in the first year of the project and data were collected for all yearly check-ups. As a number of patients died or moved away during the course of the follow-up, not all patients starting in the first year of the project completed all 11 measurements. On the other hand, during the course of the project new patients were also included. The majority of patients that were included in our analyses, started to participate in 2006-2008. As a results, we only have data of a few yearly check-ups for the majority of patients. Obviously, we do not have follow-up data of patients that started to participate in 2008.

Our conclusions on timely improvements are not based on the cross-sectional data, but on the time trend analyses. We acknowledge that cross-sectional outcomes are influenced by changes in population (in- and outmigration) besides possible changes in the quality of care that the participants received [3]. Cross-sectional outcomes tend to overestimate time trends when compared to longitudinal analyses [3]. However, longitudinal analyses with complete data for all patients are also not possible because of the in- and outmigration of participants (death, moving away, new participants). We could present strictly longitudinal data for all patients that started in year 1 of the shared care project and completed 11 years of follow-up. However, trends based on these data will also be biased since many patients will have died before the end of the follow-up. Therefore, we have opted to present the cross-sectional data and perform longitudinal trend analysis in which we included all patients with at least two visits. Since our trend analyses are based on the individual changes, we do think it is possible to conclude that there is a timely improvement. However, it remains a point of debate whether the improvements are exactly of the same magnitude as the cross-sectional data (presented in table 2 and figure 2) suggest. Because of the overestimation that is associated with cross-sectional analyses, the true improvements are probably smaller. We made several changes to the methods section and included some comments in the discussion section with respect to the design of our study.

With respect to the question about the 'sudden explosion' of participants. This is explained in the first paragraph of the methods section: "In the first years of ZODIAC, only patients in the surrounding area of the city of Zwolle participated in the study. Because of the improvements in the quality of diabetes care in the two intervention groups, the shared care project has expanded gradually in the past decade. Firstly, the shared care project became the standard for diabetes care in the entire Zwolle region (2002-2003), and in 2005-2006 the project expanded to the northeast region of the Netherlands. The number of participating general practitioners (GPs) has increased from 53 in 1998 to 459 in 2008. Patient numbers increased from 1622 to 27.438 in this time frame, and nowadays even more than 60.000 patients are participating."

In the interpretation, the authors insinuate that improvement is due to shared care. However, there is a general tendency in almost all Western countries of improved diabetes care (e.g. Germany, Belgium, France,....) with several publications (e.g.Exp Clin Endocrinol Diabetes. 2009 Feb;117(2):88-94. Epub 2008 Aug 25). Improvement can be explained by organisational initiaves (CCM, shared care), but also by greater awareness since 2010 AND better medication (new OAD, antihypertensive drugs, widely use of statins,....) The authors should nuance their conclusions and place them in an international perspective referring to other articles describing time trends.
- In this perspective, the conclusions are somewhat trivial.

Response of authors: We fully agree with the reviewer that causality cannot be proven in our study. We acknowledge that we insinuate that the improvements in our study are caused by shared care. Several changes have been made to the discussion section. We included the reference about the time trends on diabetes care in Germany to the other references about improvements in diabetes care.

The authors emphasize the importance of the study for older people ('first study...', p.13,line15). But what are then the conclusions, the lessons learned of this study about older people? Older people follow the same trend? Yes, and so?

Response of authors: The lessons learned from this study is indeed that elderly patients follow the same trends as younger patients with diabetes. Since the evidence for strict cardiovascular risk control in old age is low, old age is characterized by a high prevalence of complications and comorbidities, and elderly patients are at increased risk for possible adverse events, less strict treatment targets for elderly patients with T2DM have been advocated in literature. Nevertheless, we observed large improvements in old age during the past decade. Although we cannot answer the question whether the improvements in old age are a 'good' or a 'bad' thing, it is important to become aware of these trends. We made a few changes to the paragraph in which we explain the importance of these findings in old age.

I do not agree that these results in this study (with a year by year change of included patients and a 'sudden explosion' of included patients in the year 2006 allow to conclude on a timely IMPROVEMENT. Outcomes are better, but this can be the result of other factors (eg. changing selection bias over the years).

Response of authors: Our conclusions on timely improvements are not based on the cross-sectional data, but on the time trend analyses. We acknowledge that cross-sectional outcomes are influenced by changes in population (in- and outmigration) besides possible changes in the quality of care that the participants received [3]. Cross-sectional outcomes tend to overestimate time trends when compared to longitudinal analyses [3]. However, in our opinion strictly longitudinal analyses are also not possible because of the same in- and outmigration of participants (death, moving away, new participants). We could present strictly longitudinal data for all patients that started in year 1 of the shared care project and completed 11 years of follow-up. However, trends based on these data will also be biased since many patients will have died before the end of the follow-up. Therefore, we have opted to present the cross-sectional data and perform longitudinal trend analysis in which we included all patients with at least two visits. Since our trend analyses are based on the individual changes, we do think it is possible to conclude that there is a timely improvement. However, it remains a point of debate whether the improvements are exactly of the same magnitude as the cross-sectional data (presented in table 2 and figure 2) suggest. Because of the overestimation that is associated with cross-sectional analyses, the true improvements are probably smaller. We made several changes to

the methods section and included some comments in the discussion section with respect to the design of our study.

The Title is somewhat confusing: "shared care prospective observational study": a study cannot be "shared care". Better would be: Prospective (observational) study of quality of diabetes care in a shared care setting: trends and age differences.

Response of authors: We thank the reviewer for his suggestion. We have changed the title.

There are two major methodological limitations in this study:
1. *No control group*
2. *no defined cohort*

Response of authors: We thank the reviewer for his interesting comments. It is correct that our study had no control group. Although are observational study is not able to prove a causal relationship between shared care and the observed improvements, a control group of patients with diabetes receiving standard care would have led to more insight.

The reviewer also mentions that there is no defined cohort. We interpreted this remark as that he is referring to the absence of many inclusion criteria. We respectfully disagree with his statement for two reasons. Firstly, we have described in the methods section how the study population was defined: "The patients participating in the ZODIAC study are known with T2DM and exclusively treated in primary care. Patients who were already treated in secondary care for their diabetes, patients with a very short life expectancy (including patients with active cancer) and patients with insufficient cognitive abilities were excluded from participation." Secondly, if the reviewer indeed refers to the absence of many inclusion criteria, this is not a methodological limitation in our opinion. We aimed to include a population that would be representative of the population in daily practice. Therefore, we see it as a strength that we have included as many patients as possible.

Every interpretation of the results should take into account these limitations and should compell to prudent, nuanced statements.

Response of authors: We made various changes throughout the manuscript. The methods have been described more elaborately and the limitations are discussed in more detail now.

Reviewer 2

Reviewer: David C. Aron, MD, MS
Associate Chief of Staff/Education
Louis Stokes Cleveland Dept. of Veterans Affairs Medical Center and Professor of Medicine and Epidemiology and Biostatistics, School of Medicine, and Professor of Organizational Behavior, Weatherhead School of Management, Case Western Reserve University

This is a very interesting paper that represents the best in linking research and practice.

There is some lack of clarity regarding patients initially including in the standard care group. Were they switched to shared care when that became the standard for the Zwolle region? Were they not included in the analysis?

Response of authors: We thank the reviewer for this comment. Patients who were received standard care in the beginning of the project, switched to shared care in 2002-2003 when the shared care project became the standard for the entire Zwolle region. These patients were included in the current analyses from the moment they switched to shared care. We have changed this in the methods section of the manuscript.

Another issue is A1c measurement. Were A1c measurements made using the same technology for the entire study. Did coefficients of variation for the assay vary among sites?

Response of authors: Laboratory data (HbA1c, serum creatinine and lipid profile) were determined using standard hospital procedures. Until 2005, all procedures were performed in the clinical chemistry laboratory of the Isala Clinics (Zwolle region). Because of the expansion of the project in 2005-2006 to the northeast region of the Netherlands, laboratories of other regions started participating. HbA1c was measured using affinity chromatography high-performance liquid chromatography (HPLC, Ultra 2, Trinity Biotech, Kansas City, MO) in the Zwolle region (coefficient of variation approximately 1.5%) [1]. There are differences in the methods (HPLCs and immune-assays) used in the various laboratories in the northeast region of the Netherlands. Unfortunately, we do not have the coefficients of variation for all laboratories. We have asked all clinical chemists to send us these data. If necessary, it is possible to include these data in the final manuscript. Generally speaking, the variation coefficient has decreased in the study period due to the worldwide standardization of HbA1c measurements and improved techniques. Because of the high number of patients in the last years of the project, it is not likely that differences in the coefficient of variation coefficient will influence the overall conclusion. Especially since the same method has been used for all patients until 2005.

I have inferred that the analytic approach is that of serial cross sections. This should be explicitly stated. Assuming this is the approach used, it is far from ideal and ignores the differences observed between serial cross sections and panel data. The latter approach has been reported but not cited: see Miller DR and Pogach. J Diabetes Sci Technol 2008;2:24-32 and Thompson W et al. HSR 2005;40:1818.

Response of authors: We thank the reviewer for his comments regarding the methods we used in our study. We acknowledge that the statistical design is rather complex and that our description in the methods section was too brief. Although the presented data for each year are cross-sectional data (table 2), the time trend analyses were longitudinal.

We will use the HbA1c analyses as an example (please find the SAS output below). Our database consists of 37320 unique patients and 92340 unique yearly check-ups. For some patients we have 11 years of follow-up data: they started in the first year of the project and data were collected for all yearly check-ups. The majority of patients that were included in our analyses, started to participate in 2006-2008. As a results, we only have data of a few yearly check-ups for the majority of patients. Obviously, we do not have follow-up data of patients that started to participate in 2008. The analysis presented below are the trend analyses for HbA1c as a continuous variable (SAS PROC MIXED for continuous variables). SAS used 83061 observations of 92340 observations in total. 9279 observations were not used, because this is the number of patients of which we have no follow-up data. The estimated linear time trends are based on individual changes over time; therefore, these analyses are longitudinal.

Our conclusions on timely improvements are not based on the cross-sectional data, but on the time trend analyses. We acknowledge that cross-sectional outcomes are influenced by changes in population (in- and outmigration) besides possible changes in the quality of care that the participants received [3]. Cross-sectional outcomes tend to overestimate time trends when compared to longitudinal analyses [3]. However, in our opinion strictly longitudinal analyses are also not possible because of the in- and outmigration of participants (death, moving away, new participants). We could present strictly longitudinal data for all patients that started in year 1 of the shared care project. However, trends based on these data will also be biased since many patients will have died after 10 years of follow-up. Therefore, we have opted to present the cross-sectional data and perform longitudinal trend analysis in which we included all patients with at least two visits. Since our trend analyses are based on the individual changes, we do think it is possible to conclude that there is a timely improvement. However, it remains a point of debate whether the improvements are exactly of the same magnitude as the cross-sectional data (presented in table 2 and figure 2) suggest. Because of the overestimation that is associated with cross-sectional analyses, the true improvements are probably smaller. We made several changes to the methods section and included some comments in the discussion section with respect to the design of our study.

Two major concerns:
1. One major concern relates to conclusions drawn from serial cross sections. This approach does not account for secular changes in the extent to which diabetes is screened for and for "admixture" of less seriously ill patients. Although the relatively constant median duration of disease is somewhat reassuring, the determination of duration is fraught with difficulties. This is also not much of an issue for process measures of care, but for outcomes, especially A1c which, as shown in UKPDS, deteriorate over time, it is important. Changes in the nature of the population are suggested by the decreasing proportion of patients on insulin. (See work by Pogach and Miller)

Response of authors: We would like refer to our previous answer. In short, since our conclusions are based on the longitudinal trend analyses, we are able to draw conclusions on timely improvements. However, the magnitude of these improvements is not exactly known. The cross-sectional outcomes probably overestimate the true longitudinal improvements.

2. Another concern is the issue of secular trends. That process measures of care improved is clear; that they resulted from shared care is not. This limitation is mentioned in the discussion. The temporary decreases in process measure adherence observed as large numbers of new sites were added could as easily be attributed to the effects of data reporting as to the mode of care delivery.

Response of authors: We fully agree with the reviewer that causality cannot be proved in our study. Although we mention that causality cannot be proved in our study, we acknowledge that we insinuate that the improvements in our study are caused by shared care. Several changes have been made to the discussion section.

It might be worth mentioning the arbitrary nature of the thresholds for intermendiate outcome measures, especially as the importance of individualizing care is gaining greater recognition.

Response of authors:
We thank the reviewer for this important comment. We underline that the importance of individualizing care is gaining greater recognition. Especially in old age, health status is very heterogeneous and therefore it is essential to individualise treatment strategies. Nevertheless, quality indicators are commonly used in daily practice and therefore this seems the most appropriate method to describe quality of diabetes care. We added a few sentences with respect to the importance of individualizing treatment targets in the discussion section.

References

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3. Miller DR, Pogach L. Longitudinal approaches to evaluate health care quality and outcomes: the veterans health administration diabetes epidemiology cohorts. J Diabetes Sci Technol 2008;2:24-32.

The Mixed Procedure

Model Information

Data Set	SYS.ZODIAC19_SEP2011
Dependent Variable	HBA1C
Covariance Structure	Compound Symmetry
Subject Effect	PATIENTID
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
SEX2	2	0 1
PATIENTID	37320	not printed
LFT_3CAT	3	1 2 3

Dimensions

Covariance Parameters	2
Columns in X	12
Columns in Z	0
Subjects	37320
Max Obs Per Subject	11

Number of Observations

Number of Observations Read	92340
Number of Observations Used	83061
Number of Observations Not Used	9279

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	233709.97027529	
1	2	213508.96028423	0.00000398
2	1	213508.83869140	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
CS	PATIENTID	0.5399
Residual		0.4523

The SAS System 13:55 Tuesday, December 6, 2011 2

The Mixed Procedure

Fit Statistics

-2 Res Log Likelihood	213508.8
AIC (smaller is better)	213512.8
AICC (smaller is better)	213512.8
BIC (smaller is better)	213529.9

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
1	20201.13	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
LFT_3CAT	2	3122	11.61	<.0001
SEX2	1	35E3	5.78	0.0162
JAAR2	1	48E3	789.74	<.0001
JAAR2*LFT_3CAT	2	48E3	13.83	<.0001

Definition of the variables used in our analysis:

jaar2: this variable defines the year of the check-up.
sex2: gender.
lft_cat: this variable defines to which age category the patient belongs.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract *See page 1, the title page: 'Diabetes care in a shared care prospective observational study: trends and age differences in the period 1998-2008 (ZODIAC-19)'.*
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found *See page 2 for the structured abstract.*
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported *On pages 3 and 4 you will find a short introduction which explains the reasons why we performed the current study.*
Objectives	3	State specific objectives, including any prespecified hypotheses *Our primary objective was to investigate trends in diabetes care, within a shared care project, for a wide variety of quality indicators during a long follow-up period. Because of the limited evidence in old age, we had specific interest whether the same trends were observed for different age groups. Our objectives are mentioned in the last paragraph of the introduction (pages 3 and 4).*
Methods		
Study design	4	Present key elements of study design early in the paper *See first lines of the first paragraph of the methods section (page 5).*
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection *See first paragraph (study population) of the methods section (page 5) for setting, locations, relevant dates. In the second paragraph information about data collection is given (page 5 and 6).*
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *See first paragraph (study population) and the second paragraph (data collection) of the methods section (page 5).*
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed *Not applicable.*
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable *All relevant variables are mentioned in the paragraph 'Data collection' (page 5 and 6), and in table 1 (page 16).*
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group *See page 5 and 6 for the paragraph 'Data collection' where the methods of measurements are described.*
Bias	9	Describe any efforts to address potential sources of bias *The main bias in observational studies is selection bias. We have tried to avoid this to ask all eligible patients to participate in our study. However, patients who were already treated in secondary care, patients with a very short life expectancy and patients with insufficient cognitive abilities were excluded from participation. This selection method is described on page 5.Unfortunately, the number of patients who did not participate in the study because of the aforementioned reasons is not known*

		after 1999. Our study only comprises patients whom data have been reported by the GPs. It is not unlikely that GPs have opted not to provide data of patients who never show up at their diabetes check-ups. These limitations are discussed in the discussion section of our manuscript.
Study size	10	Explain how the study size was arrived at *See the first paragraph on page 5. All patients with T2DM who visit the GP or practice nurse for his/her diabetes are asked to participate in the study. Therefore, no sample size calculations were performed.*
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why *We mentioned in the paragraph 'statistical analyses' how we used the various variables in our analyses. See page 6 of our manuscript for the statistical analyses.*
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding *See page 6 of our manuscript.*
		(*b*) Describe any methods used to examine subgroups and interactions *We stratified our analyses according to different age groups. Differences in trends between age categories were investigated by adding an interaction term to the model. See page 6 of our manuscript for the statistical analyses.*
		(*c*) Explain how missing data were addressed *Not all data were known for all patients. However, the proportion of missing data is given for all variables of interest: process measures. See page 5 and 6 for the paragraph 'Data collection' in which we explain the terms process and outcome measures.*
		(*d*) If applicable, explain how loss to follow-up was addressed *Not applicable.*
		(*e*) Describe any sensitivity analyses *We did not perform any sensitivity analyses.*
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed *In the first paragraph of the results section we describe the total number of patients which participated in our study. Patients who were already treated in secondary care, patients with a very short life expectancy and patients with insufficient cognitive abilities were excluded from participation. Unfortunately, the number of patients who did not participate in the study because of the aforementioned reasons is not known after 1999. Therefore, we are not able to exactly present the requested numbers.*
		(b) Give reasons for non-participation at each stage *Not applicable.*
		(c) Consider use of a flow diagram *Not applicable.*
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders *See table 2.*
		(b) Indicate number of participants with missing data for each variable of interest *See table 2. Process measures are presented for all variables of interest.*
		(c) Summarise follow-up time (eg, average and total amount) *Not applicable due to the design of the study.*
Outcome data	15*	Report numbers of outcome events or summary measures over time

		See table 2, figures 1 and 2, and the data mentioned in the results sections on pages 8 to 10.
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included *See table 2, figures 1 and 2, and the data mentioned in the results sections on pages 8 to 10.*
		(*b*) Report category boundaries when continuous variables were categorized *We stratified our analyses according to different age group; see the paragraph 'statistical analyses' on page 6.*
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period *Not applicable.*
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses *We have performed analyses stratified according to age categories. This was a pre-specified aim of the study.*
Discussion		
Key results	18	Summarise key results with reference to study objectives *See the first paragraph of the discussion section, page 11.*
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias *See the last paragraph on page 12.*
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence *See last paragraph of the discussion on page 13.*
Generalisability	21	Discuss the generalisability (external validity) of the study results *The most important bias of our study is selection bias, since our study only comprises patients whom data have been reported by the GPs. This limitation is discussed in the last paragraph on page 12.*
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based *We had no external funding source.*

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.