BMJ Open

Association between full monitoring of physiological and lifestyle target indicators and HbA1c level in primary type 2 diabetes care: an observational cohort study (ELZHA-cohort 1)

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-027208
Article Type:	Research
Date Submitted by the Author:	10-Oct-2018
Complete List of Authors:	van Bruggen, Sytske; Leiden University Medical Center, Public Health and Primary Care; Eerstelijns Zorggroep Haaglanden, Rauh, Simone Kasteleyn, Marise; LUMC Bonten, Tobias N.; Leids Universitair Medisch Centrum, Public Health and primary Care Chavannes, Niels; Leiden University Medical Center, Public Health and Primary Care Numans, Mattijs; Leiden University Medical Centre, 4Department of Public Health and Primary Care
Keywords:	General diabetes < DIABETES & ENDOCRINOLOGY, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, PRIMARY CARE

Association between full monitoring of physiological and lifestyle target indicators and HbA1c level in primary type 2 diabetes care: an observational cohort study (ELZHA-cohort 1)

Sytske van Bruggen [1,2], Simone P Rauh [3], Marise J Kasteleyn [1],Tobias N Bonten, [1], Niels H Chavannes, [1], Mattijs E Numans, [1]

1) Department of Public Health and Primary Care, Leiden University Medical Centre, Leiden, The Netherlands
2) Eerstelijns Zorggroep Haaglanden (ELZHA), The Hague, The Netherlands
3) Department of Epidemiology and Biostatistics, Amsterdam Public Health Research Institute, VU University Medical Centre, Amsterdam, The Netherlands

Corresponding author: Sytske van Bruggen, s.van_bruggen@lumc.nl

Leiden University Medical Centre

Afdeling Public Health en Eerstelijnsgeneeskunde (PHEG), kamer V6.26

Postbus 9600

2300 RC Leiden

Tel. +31 (0) 71 – 526 84 34

Manuscript: 2.460 words

Abstract

Objective

Management of type 2 diabetes mellitus (T2DM) requires frequent patient monitoring. Within a collective care group setting, doubts on the clinical effects of registration are a barrier for full adoption of T2DM registration in general practice. We explored whether full monitoring of physiological and lifestyle-related target indicators within a care group approach is associated with lower HbA_{1c} levels.

Design Observational, real-life cohort study

Setting Primary care data registry from the EerstelijnsZorggroepHaaglanden care group.

Exposure The care group provides general practitioners collectively with organisational support to facilitate structured T2DM primary care. Patients are offered quarterly medical and lifestyle-related consultation.

Main outcome measure Full monitoring of each target indicator in patients with T2DM. which includes minimally one measure of HbA_{1c} level, systolic blood pressure, LDL, BMI, smoking behaviour and physical exercise between January and December 2014; otherwise, patients were defined as ´incompletely monitored´. HbA_{1c} levels of 8,137 fully-monitored and 3,958 incompletely-monitored patients were compared, adjusted for the confounders diabetes duration, age and gender. Since recommended HbA_{1c} values depend on age, medication use and diabetes duration, analyses were stratified into three HbA_{1c} profile groups. Linear multilevel analyses enabled adjustment for general practice.

Results Compared to incompletely-monitored patients, fully-monitored patients had significantly lower HbA_{1c} levels [95%CI] in the first (-2.03 [-2.53;-1.52]mmol/mol) (-0.19% [-0.23%;-0.14%]), second (-3.36 [-5.28;-1.43]mmol/mol) (-0.31% [-0.48%;-0.13%]) and third HbA1c profile group (-1.89 [-3.76;-0.01]mmol/mol) (-0.17% [-0.34%;0.00%]).

Conclusions/interpretation This study shows that in a care group setting, fully-monitored patients had significantly lower HbA_{1c} levels compared with incompletely-monitored patients. Since this difference might have considerable clinical impact in terms of T2DM-related risks, this might help general practices in care group settings to overcome barriers on adequate registration and thus improve structured T2DM primary care. From population health management perspective, we recommend a systematic approach to adjust the structured care protocol for incompletely-monitored subgroups.

Strenghts and limitations of this study

- The observational real-life design of this study prevented any interference with daily routines of GP practices, thus contributing to good reliability and representativeness of our findings
- Because the availability of patient data on age, medication use and diabetes duration allowed to conduct our analyses - in correspondence with professional GP guidelines - for specific HbA1c threshold groups, the findings are relevant and useful for clinical practice
- Taking into consideration that a missing registration does not necessarily reflect a lack of care, but might be caused by technical or practical problems instead, the associations found in this study might be underestimated.

1. Introduction

Type 2 diabetes is a typical lifestyle-related disease [1]. The course of type 2 diabetes and potential complications are influenced by smoking behavior [2, 3], BMI [4] and physical exercise [5]. Adopting a healthier lifestyle, e.g. by smoking cessation or weight loss, is known to be very demanding for individual patients [6, 7]. It has been established that attention for non-conscious motivational factors affecting an individual's behavior is important to realise sustained behavioral change [8]. In addition, to avoid relapse [9, 10] and maintain long-term behavioral change, follow-up support for lifestyle-related themes is recommended [11, 12]. Accordingly, guidelines for general practitioners (GPs) emphasize to monitor not only HbA_{1c} levels, but also the physiological target indicators systolic blood pressure and LDL, as well as lifestyle-related indicators [13, 14].

However, for an average GP, providing structured primary diabetes care with sufficient attention for both physiological monitoring and lifestyle adaptation [15] is known to be challenging [16]. Therefore, in many Western countries, varying from the US and Europe [17, 18] to New-Zealand [19], an increasing number of GPs has delegated the regular structured primary diabetes care to nurse practitioners.

It is known that implementing structured primary diabetes care and delegation of tasks to a nurse practitioner has considerable impact on the organization of the GP practice [20, 21]. For example, in the USA, an evaluation of the recent Comprehensive Primary Care (CPC) program revealed a need to refine practice workflows, to incorporate new staff roles, and to overcome incompatibility of health technology systems [22]. In the Netherlands, most GPs have joined together in local 'care groups' [23] that provide logistic and quality support to individual GP practices. In addition, collective structured diabetes care protocols are negotiated with local health insurance companies. The agreements between care groups and health insurance companies on structured diabetes care protocols enable GPs to offer high-quality intensive primary diabetes care. To illustrate, on an annual basis, four

consultations at the GP practice with an explicit focus on lifestyle support are facilitated, as well as paramedical diabetes care (e.g. annual screening of fundus and feet); participation is free of charge for patients. It is known that providing a structured diabetes care protocol is associated with better monitoring of patients [24]. In addition, adequate registration of the diabetes-related patient health indicators is associated with improvement of the care process [25].

According to a recent study, care group participation is associated with improvement of the proportion patients with full monitoring of physiological and life style related target indicators [26]. However, a review on chronical care programs in primary care reported that doubts among care providers on the clinical effects of an intervention are a barrier for adoption [27]. To our knowledge little is known about the relationship between full monitoring of physiological as well as lifestyle related target diabetes indicators in a care group setting and clinical health outcomes. The Hba_{1c} level is established as a key diabetes health indicator [28]. Therefore, this study aims to investigate the association between full monitoring of physiological and lifestyle-related diabetes target indicators and HbA_{1c} level, in patients with type 2 diabetes who receive a TYPE structured diabetes care protocol, facilitated by a care group.

2. Research design and methods

2.1 Study design and population

Data were used of type 2 diabetes patients from the observational Eerstelijns Zorggroep Haaglanden (ELZHA) cohort, which is based on primary care registry data from a care group collective in the western part of the Netherlands. In January 2015, the care group numbered 168 GP practices (n=24,459 patients with type 2 diabetes). On a periodic basis, GP members share an overview of their patient monitoring data with the care group. In February 2017, all GP practices were informed in writing and, based on an opt-out procedure, were invited to participate in this cohort. For the present study, pseudonymized data on monitoring of diabetes target indicators and HbA_{1c} levels from patients were used from the calendar year 2014. Patients receiving continuously structured primary diabetes care from January 2014 through December 2014 were included. At least one registration of HbA_{1c} in 2014 was necessary for inclusion. Since systolic blood pressure and LDL guidelines are specified for patients aged ≤80 years, patients aged ≥80 years were excluded. Patients were also excluded in case of missing data on age, gender or disease duration. Finally, because missing data on medication use were partly caused by technical problems, patients without registration of medication prescription were also excluded.

2.2 Exposure

Details of the ELZHA cohort study have been described previously (Van Bruggen et al., submitted). In short, within a care group setting, the structured primary care protocol includes a quarterly diabetes consultation, in which diabetes-related target indicators are checked and lifestyle education is provided, combined with 'paramedical' care such as an annual foot check, fundus screening and dietician´s counseling. To facilitate the organization and quality control of this protocol, GP practices receive practical and logistic support,

including a computerized system to improve the care process and outcomes. Measurement of the diabetes target indicators (HbA_{1c} level, systolic blood pressure, LDL level, BMI, smoking behaviour and physical exercise) took place in 2014 at the end of each quarter. In the present study, patients were regarded as 'fully monitored' when at least one measure of each of the target indicators was registered between January and December 2014. If one or more target indicators were not registered, patients were defined as ´incompletely monitored´.

2.3 Outcomes

The outcome of this study was HbA_{1c} level; this was computed in two steps. First, for each quarter, a mean HbA_{1c} value was calculated based on all available HbA_{1c} measures in that quarter. Based on the mean HbA_{1c} levels of all quarters, a mean was computed for the whole calendar year. HbA_{1c} level is presented in % and mmol/mol.

2.4 Analysis

For patient characteristics, categorical variables were reported as numbers and percentages. Continuous variables were reported as means with standard deviation (SD) or, when non-normally distributed, as medians with interquartile ranges (IQR). Linear multilevel analyses were conducted to compare HbA_{1c} levels of fully-monitored and incompletely-monitored patients. Multilevel analyses allowed to adjust the individual observations (level 1) for GP practice (level 2). In addition, the analyses were adjusted for patient age, duration of diabetes and gender, which are relevant possible confounders with regard to HbA_{1c} outcomes.

Tailored on specific key patient characteristics (age, intensity of medication treatment, and disease duration) professional GP guidelines distinguish three patient profile groups for

HbA_{1c} targets [13]: **1)** for patients aged <70 years, and for older patients with a mild treatment regime (only metformin monotherapy prescription or lifestyle coaching), a target HbA_{1c} value of 7.0% (53 mmol/mol) is recommended. In the present study, since missing data on medication might reflect administrative omissions rather than absence of medication treatment, patients without data on medication were excluded; **2)** for patients aged ≥70 years who need more intensive treatment and were diagnosed with diabetes <10 years previously, a target HbA_{1c} value of 7.5% (58 mmol/mol) is recommended; **3)** for patients aged ≥70 years who need more intensive treatment and were diagnosed with diabetes ≥10 years previously, a target HbA_{1c} value of 8.0% (64 mmol/mol) is recommended.

In view of the relevance for clinical practice, separate analyses were conducted and reported for each of these HbA_{1c} profile groups. In addition, we tested for a significant interaction effect between monitoring completeness and HbA_{1c} profile group. A p-value <0.05 was considered statistically significant; for interaction, a p-value <0.1 was considered statistically significant.

Descriptive statistics were analysed using SPSS, version 24.0. Multilevel analyses were performed using ML WiN (Version 2.28).

2.5 Patient and public involvement

Since this study was targeted on a GP supporting approach of structured primary diabetes care, patients were not actively involved.

2.6 Ethical considerations

Since the pseudonymized patient data contained only age and gender, the data could be aggregated without enabling investigators to identify individual patients. Due to the high number of patients, informed consent of individual patients was not required.

The study protocol was approved by the Medical Ethical Committee of the Leiden University Medical Center (code G16.102/SH/sh).

3. Results

This study included 167 GP practices (99%) with a total of 24,198 patients with type 2 diabetes ; of these, 12,095 patients met the inclusion criteria (for a detailed flowchart of inclusion see Figure 1). By definition, in this population HbA_{1c} was always monitored, as not having an HbA_{1c} measure available was an exclusion criterion for the present study. Of patients who were incompletely monitored, information on physical exercise was most often missing, followed by smoking, BMI, LDL, and systolic blood pressure (Figure 2).

Characteristics of our study population, classified by HbA_{1c} profile and monitoring completeness, are presented in Table 1. Compared to incompletely-monitored patients, fully-monitored patients had lower mean HbA_{1c} levels in all three HbA_{1c} profiles. In addition, fully-monitored patients had a longer duration of diabetes than incompletely-monitored patients.

The crude analysis showed that, compared with incompletely-monitored patients, the mean HbA_{1c} of fully-monitored patients was significantly lower in the first profile (-1.95 [95% CI -2.41; -1.49] mmol/mol) (-0.18% [-0.22%; -0.14%]), second profile (-2.03 [95 % CI -3.41;-0.66] mmol/mol) (-0.19% [-0.31%; -0.06%]) and third profile (-1.53 [95 % CI -2.96;-0.10] mmol/mol) (-0.14% [-0.27%; -0.01%]) (Table 2). Multilevel analyses with adjustment for diabetes duration, age and gender revealed similar significant associations in the first (-2.03 [95 % CI -2.53; -1.52] mmol/mol) (-0.19% (-0.23%; -0.14%]), second (-3.36 [95 % CI -5.28; -1.43] mmol/mol) (-0.31% [-0.48%; -0.13%]) and third profile (-1.89 [95 % CI -3.76; -0.01] mmol/mol) (-0.17% [-0.34%; 0.00%]). The magnitude of these associations did not significantly differ between the HbA_{1c} profile groups (p=0.44 and p=0.35 for the second and third profile, respectively, compared with the first profile).

4. Discussion

This study explored whether monitoring completeness of physiological and lifestyle-related diabetes target indicators in a care group setting is associated with HbA_{1c} level. In all HbA_{1c} profile groups – defined based on patient age, intensity of medication treatment and disease duration – we found that fully-monitored patients had lower HbA_{1c} levels than incompletely-monitored patients; the differences ranged from 0.17% (1.89 mmol/mol) to 0.31% (3.36 mmol/mol), indicating that adequate diabetes monitoring of physiological and lifestyle indicators in primary care is associated with better HbA_{1c} levels. To our knowledge, this is the first study to analyse the association between systematic diabetes monitoring in primary care and HbA_{1c} levels. Apart from one longitudinal Dutch study on structured primary diabetes care in a care group setting which reported a sharp decrease in the proportion of patients with a HbA_{1c} level ≥53 mmol/mol [24], research on absolute HbA_{1c} differences is scarce and findings appear to be somewhat inconsistent [29-32]. Therefore, caution is required when comparing our findings with any earlier studies. However, for each 1% (10.9 mmol/mol) reduction in mean HbA_{1c}, a significant decrease in health risk has been reported, ranging from 21% for any endpoint related to diabetes including deaths, to 14% for myocardial infarction, and 37% for microvascular complications [33]. Further, our finding that registration of physical exercise was most often lacking, is in line with an earlier small-size study in which only 19% of patients with type 2 diabetes reported 'being guided properly' with regard to physical exercise [34].

Our finding that, compared with incomplete monitoring, full monitoring of patients is associated with a lower HbA_{1c} level might be explained by continuity of care in several ways. First, if patients are monitored at least once a year, an increasing HbA_{1c} level might be noticed at an early stage, resulting in fast and adequate treatment. Second, periodic monitoring and coaching of patients with regard to weight loss, smoking cessation and physical exercise contributes to enduring lifestyle adaptation [11, 12], which may lead to lower HbA_{1c} levels [35].

Since fully-monitored patients with type 2 diabetes have significantly lower HbA_{1c} levels, their risk for any diabetes-related health complication is lower compared to incompletely-monitored patients. Thus, in general, incomplete monitoring of a patient should be interpreted as an important sign of diabetes-related health risks. As reported by others [36], a tailored approach based on data registry and adjusted to patient characteristics (e.g. monitoring completeness), is recommended. This might help GP's to overcome barriers on full adoption of the care group monitoring approach. In addition, the present findings might be relevant for other structured diabetes primary care settings which focus on frequent monitoring and adequate registration of diabetes-related health outcomes, such as the Comprehensive Primary Care Plus program in the USA [37].

The present study is characterised by several strengths. First, in our view, an important strength of this study is the design: although randomized clinical trials might help to eliminate bias, adequate powering and generalizability are familiar problems [38], whereas observational studies allow to include large study populations. For example, in this study, all patients participating in a structured primary diabetes care program were enrolled, thereby contributing to high representativeness of our study population. Second, generally, since our study design did not interfere with the daily routine of GP practices, we assume adequate reliability of our findings. Thus, the observational real-life setting in our study reflects the reality of diabetes monitoring and HbA_{1c} levels in primary care. Our design is in line with other studies that also used a pragmatic approach to conduct diabetes related studies in primary care [39-41]. Third, patients were included if they participated for at least one year, which contributes to the stability and, thus, the validity of our findings. Finally, conducting separate analyses for each HbA_{1c} profile group allowed adjustment for the variety in the recommended HbA_{1c} target values.

Nevertheless, this study is also subject to some limitations that need to be mentioned. First, since no control group was included, no causal relation between monitoring completeness and HbA_{1c} level can be proven. Second, a missing registration does not necessarily mean

that the care has not been provided. For example, missings might be caused by technical problems, or lack of time for registration. Patients being considered erroneously as 'incompletely monitored' might have underestimated the associations found, although we did correct our analyses for age, diabetes duration, gender and GP practice.

For future research, it might be useful to analyse the context of diabetes target monitoring and explore whether the association that we found reflects a causal relationship between monitoring completeness and HbA_{1c} level. In addition, from the GP perspective, examining potential barriers to complete monitoring might provide keys to improvement of the monitoring process. To ameliorate the primary diabetes care of incompletely-monitored patients, exploration of their preferences and needs is suggested. In addition, an evaluation of financial costs and benefits of this care approach is recommended.

To summarize, in patients with type 2 diabetes within a care group setting, full monitoring of physiological and lifestyle target indicators is associated with lower HbA_{1c} levels compared with incomplete monitoring. These differences might be expected to have a considerable clinical impact in terms of diabetes-related risks. We recommend a systematic approach to analyzing the needs of incompletely-monitored patient groups, and to adjust the structured care protocol for these subgroups in terms of population health management.

Article Information

Acknowledgments. The authors thank the family physicians and patients of the ELZHA care group for the use of their data for this study.

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

Duality of Interest. No potential conflicts of interest relevant to this article were reported. All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and 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 three years; no other relationships or activities that could appear to have influenced the submitted work."

Transparency Declaration

The lead author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Author Contributions. SvB analysed data and wrote the manuscript. SR analysed data and reviewed the manuscript. MK reviewed and edited the manuscript. TB reviewed the manuscript. NC reviewed the manuscript and contributed to the discussion. MN is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Data sharing statement. The data that support the findings of this study are available from the corresponding author on request.

Licence

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd ("BMJ"), and its Licencees to permit this article (if accepted) to be published in The BMJ's editions and any other BMJ products and to exploit all subsidiary rights, as set out in *our licence*." "

References

[1] Howells L, Musaddaq B, McKay AJ, Majeed A (2016) Clinical impact of lifestyle interventions for the prevention of diabetes: an overview of systematic reviews. BMJ Open 6: e013806

[2] Fagard RH (2009) Smoking amplifies cardiovascular risk in patients with hypertension and diabetes. Diabetes Care 32 Suppl 2: S429-431

[3] Qin R, Chen T, Lou Q, Yu D (2013) Excess risk of mortality and cardiovascular events associated with smoking among patients with diabetes: meta-analysis of observational prospective studies. Int J Cardiol 167: 342-350

[4] Gray N, Picone G, Sloan F, Yashkin A (2015) Relation between BMI and diabetes mellitus and its complications among US older adults. South Med J 108: 29-36

[5] Dempsey PC, Blankenship JM, Larsen RN, et al. (2017) Interrupting prolonged sitting in type 2 diabetes: nocturnal persistence of improved glycaemic control. Diabetologia 60: 499-507

[6] Babb S, Malarcher A, Schauer G, Asman K, Jamal A (2017) Quitting Smoking Among Adults - United States, 2000-2015. MMWR Morb Mortal Wkly Rep 65: 1457-1464

[7] Twyman L, Bonevski B, Paul C, Bryant J (2014) Perceived barriers to smoking cessation in selected vulnerable groups: a systematic review of the qualitative and quantitative literature. BMJ Open 4: e006414

[8] Papies EK (2016) Health goal priming as a situated intervention tool: how to benefit from nonconscious motivational routes to health behaviour. Health Psychol Rev 10: 408-424

[9] Arterburn DE, Bogart A, Sherwood NE, et al. (2013) A multisite study of long-term remission and relapse of type 2 diabetes mellitus following gastric bypass. Obes Surg 23: 93-102

[10] Hawkins J, Hollingworth W, Campbell R (2010) Long-term smoking relapse: a study using the british household panel survey. Nicotine Tob Res 12: 1228-1235

[11] Pjanic, Muller R, Laimer M, Hagenbuch N, Laederach K, Stanga Z (2017) Evaluation of a multiprofessional, nonsurgical obesity treatment program: which parameters indicated life style changes and weight loss? J Eat Disord 5: 14

[12] Venditti EM, Wylie-Rosett J, Delahanty LM, et al. (2014) Short and long-term lifestyle coaching approaches used to address diverse participant barriers to weight loss and physical activity adherence. Int J Behav Nutr Phys Act 11: 16

[13] Rutten GEHM DGW, Nijpels G, Houweling ST, Van de Laar FA, Bilo HJ, Holleman F,Burgers JS, Wiersma Tj, Janssen PGH (2013) NHG-Standaard Diabetes mellitus type 2 (derde herziening). Huisarts en Wetenschap 56: 512-525

[14] (NICE guideline 2015) Type 2 diabetes in adults: management. In. National Institute for Health and Care Excellence, United Kingdom

[15] Ekong G, Kavookjian J (2016) Motivational interviewing and outcomes in adults with type 2 diabetes: A systematic review. Patient Educ Couns 99: 944-952

[16] Rushforth B, McCrorie C, Glidewell L, Midgley E, Foy R (2016) Barriers to effective management of type 2 diabetes in primary care: qualitative systematic review. Br J Gen Pract 66: e114-127

[17] Maier C, Aiken L., and Busse R. (2017) Nurses in advanced roles in primary care: Policy levers for implementation. In: OECD Health Working Papers, Paris

[18] Mergenthal K, Beyer M, Gerlach FM, Guethlin C (2016) Sharing Responsibilities within the General Practice Team - A Cross-Sectional Study of Task Delegation in Germany. PLoS One 11: e0157248

[19] Hefford M, Love T, Cumming J, Finlayson M, Raymont A (2011) The financial impact of clinical task substitution between practice nurses and GPs in New Zealand primary care centres. N Z Med J 124: 59-65

[20] Ferrante JM, Shaw EK, Bayly JE, et al. (2018) Barriers and Facilitators to Expanding Roles of Medical Assistants in Patient-Centered Medical Homes (PCMHs). J Am Board Fam Med 31: 226-235

[21] McInnes S, Peters K, Bonney A, Halcomb E (2015) An integrative review of facilitators and barriers influencing collaboration and teamwork between general practitioners and nurses working in general practice. J Adv Nurs 71: 1973-1985
[22] Dale SB, Ghosh A, Peikes DN, et al. (2016) Two-Year Costs and Quality in the Comprehensive Primary Care Initiative. N Engl J Med 374: 2345-2356
[23] Struijs JN, Van Til JT, Baan CA (2009) Experimenteren met de keten-dbc diabetes: de eerste zichtbare effecten. RIVM, Bilthoven, pp 19-62
[24] Hendriks SH, van Hateren KJ, Groenier KH, et al. (2015) Sex Differences in the Quality of Diabetes Care in the Netherlands (ZODIAC-45). PLoS One 10: e0145907
[25] Hoque DME, Kumari V, Hoque M, Ruseckaite R, Romero L, Evans SM (2017) Impact of clinical registries on quality of patient care and clinical outcomes: A systematic review. PLoS One 12: e0183667
[26] Van Bruggen S, Kasteleyn MJ, Rauh SP, Bonten TN, Chavannes NH, Numans ME (2018) A multidisciplinary Type 2 Diabetes care protocol within a primary care group leads to a higher proportion of fully-monitored patients (ELZHA cohort-1). In: Annual Meeting. North American Primary Care Research Group, Chicago (Illinois), United States
[27] Kadu MK, Stolee P (2015) Facilitators and barriers of implementing the chronic care model in primary care: a systematic review. BMC Fam Pract 16: 12
[28] Lacey RE, Sacker A, Bell S, et al. (2017) Work-family life courses and BMI trajectories in three British birth cohorts. Int J Obes (Lond) 41: 332-339
[29] Fuchs S, Henschke C, Blumel M, Busse R (2014) Disease management programs for type 2 diabetes in Germany: a systematic literature review evaluating effectiveness. Dtsch Arztebl Int 111: 453-463
[30] Gabbay RA, Lendel I, Saleem TM, et al. (2006) Nurse case management improves blood pressure, emotional distress and diabetes complication screening. Diabetes Res Clin Pract 71: 28-35
[31] Kostev K, Rockel T, Jacob L (2017) Impact of Disease Management Programs on HbA1c Values in Type 2 Diabetes Patients in Germany. J Diabetes Sci Technol 11: 117-122
[32] Wiefarn S, Kostev K, Heumann C, Rettelbach A (2017) [Effect of the Disease Management Program on HbA1c Value in Type 2 Diabetes Mellitus Patients: A Retrospective Comparison between Disease Management Programs and Standard Care]. Dtsch Med Wochenschr 142: e148-e155
[33] Stratton IM, Adler AI, Neil HA, et al. (2000) Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ 321: 405-412
[34] Stuij M, Elling A, Abma TA (2017) Conflict between diabetes guidelines and experienced counselling in sports and physical activity. An exploratory study. Eur J Public Health 27: 157-159
[35] Umpierre D, Ribeiro PA, Kramer CK, et al. (2011) Physical activity advice only or structured exercise training and association with HbA1c levels in type 2 diabetes: a systematic review and meta-analysis. JAMA 305: 1790-1799
[36] Aronson R, Orzech N, Ye C, Brown RE, Goldenberg R, Brown V (2016) Specialist-Led Diabetes Registries and Prevalence of Poor Glycemic Control in Type 2 Diabetes: The Diabetes Registry Outcomes Project for A1C Reduction (DROP A1C). Diabetes Care 39: 1711-1717
[37] Sessums LL, McHugh SJ, Rajkumar R (2016) Medicare's Vision for Advanced Primary Care: New Directions for Care Delivery and Payment. JAMA 315: 2665-2666
[38] Frakt AB (2015) An observational study goes where randomized clinical trials have not. JAMA 313: 1091-1092
[39] Hippisley-Cox J, Coupland C (2016) Diabetes treatments and risk of heart failure, cardiovascular disease, and all cause mortality: cohort study in primary care. BMJ 354: i3477
[40] Price DB, Russell R, Mares R, et al. (2016) Metabolic Effects Associated with ICS in Patients with COPD and Comorbid Type 2 Diabetes: A Historical Matched Cohort Study. PLoS One 11: e0162903

[41] Smits KPJ, Sidorenkov G, Navis G, et al. (2017) Prescribing Quality and Prediction of Clinical Outcomes in Patients With Type 2 Diabetes: A Prospective Cohort Study. Diabetes Care 40: e83-e84

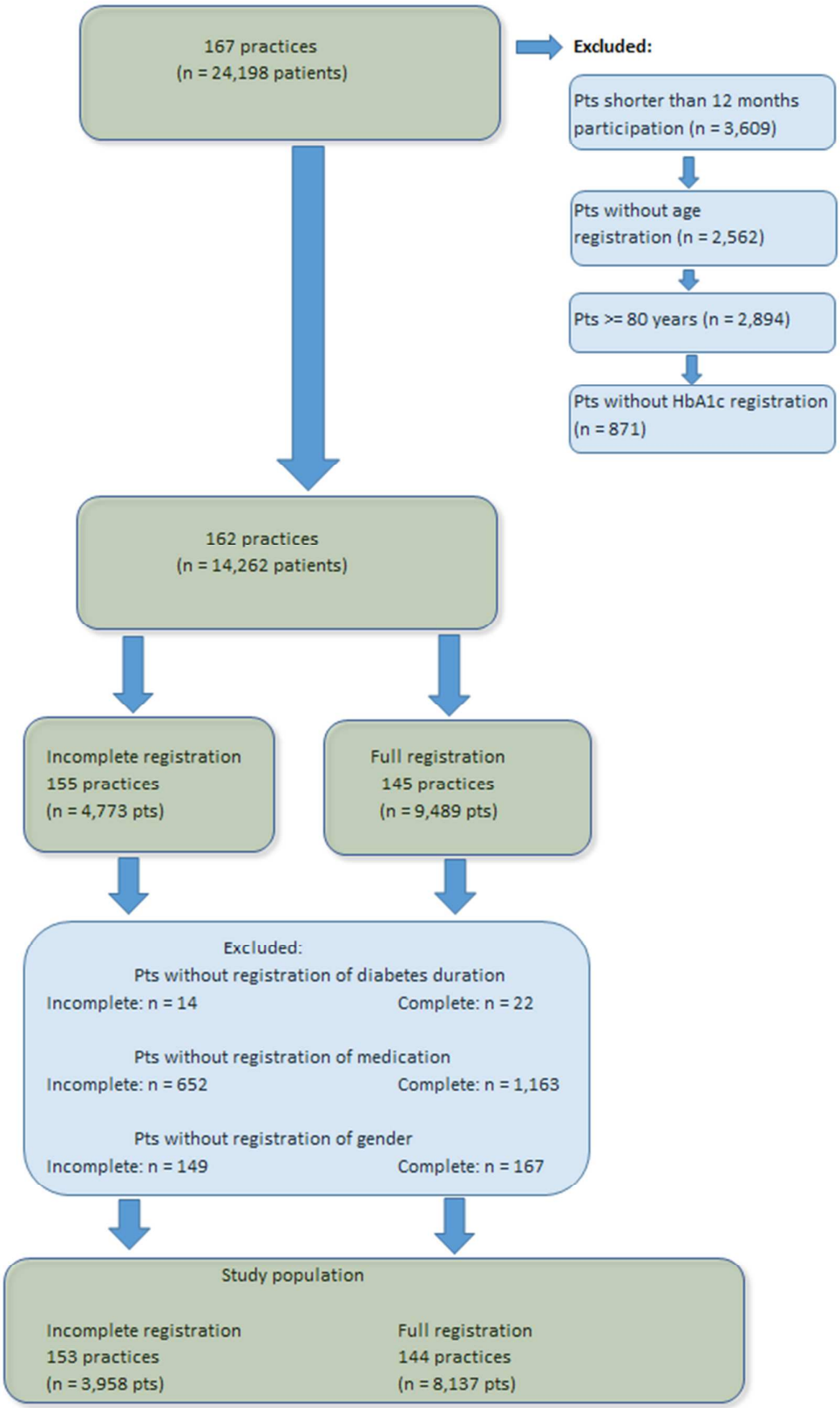


Figure 1. Flowchart of patient inclusion.
Pts = patients

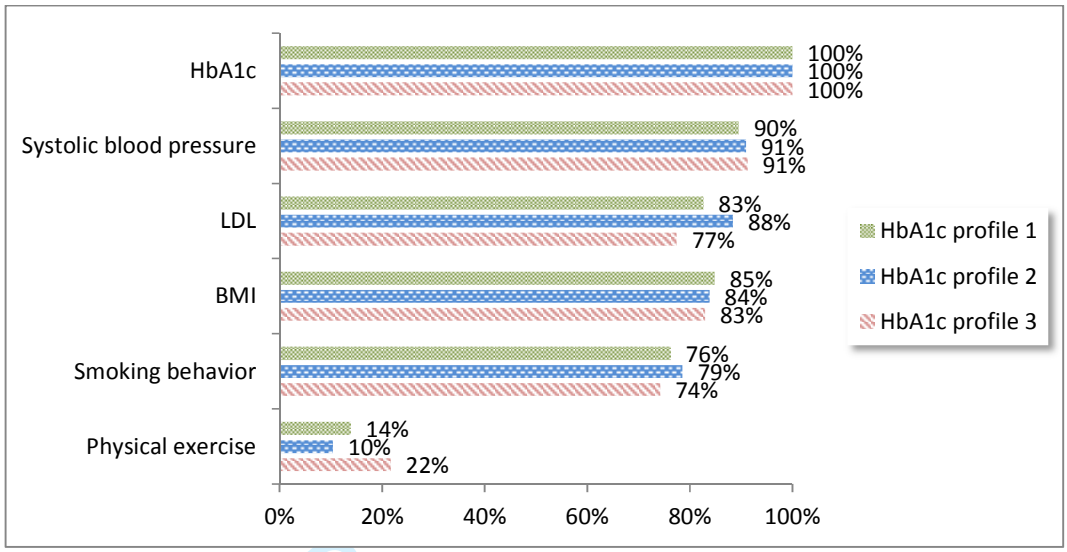


Figure 2. Overview of registered indicators in incompletely monitored patients within Hba1c profile
HbA1c: Hemoglobin A1c

Table 1. Characteristics of the study population: classified by HbA_{1c} profile and monitoring completeness.

		HbA_{1c} profile 1[1] *Target HbA_{1c}: 53 mmol/mol (7.0%)*		**HbA_{1c} profile 2**[2] *Target HbA_{1c}: 58 mmol/mol (7.5%)*		**HbA_{1c} profile 3**[3] *HbA_{1c}: 64 mmol/mol (8.0%)*	
		Incomplete n =3,345	**Complete** n =6,794	**Incomplete** n = 396	**Complete** n = 656	**Incomplete** n = 217	**Complete** n = 687
HbA_{1c} level: mean [SD]	mmol/ mol	53.51 (12.31)	51.56 (10.51)	55.91 (11.66)	53.87 (10.60)	55.12 (10.57)	53.60 (8.98)
	%	7.05 (1.13)	6.87 (0.96)	7.27 (1.07)	7.08 (0.97)	7.19 (0.97)	7.06 (0.82)
Diabetes duration, years: median [IQR][1]		3 [3 – 8]	7 [4 – 10]	3 [3 – 7]	7 [4 – 8]	13 [11 – 16]	13 [11 – 15]
Age (years): median [IQR] [2]		61 [54 – 67]	62 [55 – 68]	74 [72 – 76]	74 [71 – 76]	74 [72 – 77]	74 [72 – 76]
Gender: % female (n)		44 (1,465)	46 (3,106)	46 (183)	45 (297)	51(110)	46 (316)

1) Profile 1: patients aged <70 years, and older patients with a mild treatment regime (only metformin monotherapy prescription)

2) Profile 2: patients aged ≥70 years who need more intensive treatment and diagnosed with diabetes <10 years ago

3) Profile 3: patients aged ≥70 years who need more intensive treatment and diagnosed with diabetes ≥10 years ago

Table 2. Multilevel analyses evaluating the HbA_{1c} difference of fully-monitored patients compared to incompletely monitored patients.

		Profile 1			**Profile 2**			**Profile 3**		
		B	**95% CI**	**p-value**	**B**	**95% CI**	**p-value**	**B**	**95% CI**	**p-value**
Model 1[a)]	mmol / mol	-1.95	-2.41,-1.49	<0.001	-2.03	-3.41, -0.66	0.004	-1.53	-2,96, -0.10	0.037
	%	-0.18	-0.22; -0.14		-0.19	-0.31; -0.06		-0.14	-0.27; -0.01	
Model 2[b)]	mmol / mol	-2.03	-2.53, -1.52	<0.001	-3.36	-5.28, -1.43	0.001	-1.89	-3.76, -0.01	0.049
	%	-0.19	-0.23; -0.14		-0.31	-0.48; -0.13		-0.17	-0.34; 0.00	

a) Crude analysis

b) Multilevel analysis adjusted for age, diabetes duration and gender

BMJ Open

Association between full monitoring of biomedical and lifestyle target indicators and HbA1c level in primary type 2 diabetes care: an observational cohort study (ELZHA-cohort 1)

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-027208.R1
Article Type:	Research
Date Submitted by the Author:	04-Jan-2019
Complete List of Authors:	van Bruggen, Sytske; Leiden University Medical Center, Public Health and Primary Care; Eerstelijns Zorggroep Haaglanden, Rauh, Simone Kasteleyn, Marise; Leiden University Medical Center, Public Health and Primary Care Bonten, Tobias N.; Leids Universitair Medisch Centrum, Public Health and primary Care Chavannes, Niels; Leiden University Medical Center, Public Health and Primary Care Numans, Mattijs; Leiden University Medical Centre, Public Health and Primary Care
Primary Subject Heading:	Diabetes and endocrinology
Secondary Subject Heading:	Epidemiology, General practice / Family practice, Health services research, Public health
Keywords:	General diabetes < DIABETES & ENDOCRINOLOGY, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, PRIMARY CARE

Association between full monitoring of biomedical and lifestyle target indicators and HbA1c level in primary type 2 diabetes care: an observational cohort study (ELZHA-cohort 1)

Sytske van Bruggen[1,2], Simone P Rauh[3], Marise J Kasteleyn[1],Tobias N Bonten[1], Niels H Chavannes[1], Mattijs E Numans[1]

1) Department of Public Health and Primary Care, Leiden University Medical Centre, Leiden, The Netherlands
2) Eerstelijns Zorggroep Haaglanden (ELZHA), The Hague, The Netherlands
3) Department of Epidemiology and Biostatistics, Amsterdam Public Health Research Institute, VU University Medical Centre, Amsterdam, The Netherlands

Corresponding author: Sytske van Bruggen, s.van_bruggen@lumc.nl

Leiden University Medical Centre

Afdeling Public Health en Eerstelijnsgeneeskunde (PHEG), kamer V6.26

Postbus 9600

2300 RC Leiden

Tel. +31 (0) 71 – 526 84 34

Manuscript: 2,925 words

Abstract

Objective

Management of type 2 diabetes mellitus (T2DM) requires frequent patient monitoring. Within a collective care group setting, doubts on the clinical effects of registration are a barrier for full adoption of T2DM registration in general practice. We explored whether full monitoring of biomedical and lifestyle-related target indicators within a care group approach is associated with lower HbA_{1c} levels.

Design Observational, real-life cohort study

Setting Primary care data registry from the EerstelijnsZorggroepHaaglanden care group.

Exposure The care group provides general practitioners collectively with organisational support to facilitate structured T2DM primary care. Patients are offered quarterly medical and lifestyle-related consultation.

Main outcome measure Full monitoring of each target indicator in patients with T2DM. which includes minimally one measure of HbA_{1c} level, systolic blood pressure, LDL, BMI, smoking behaviour and physical exercise between January and December 2014; otherwise, patients were defined as ´incompletely monitored´. HbA_{1c} levels of 8,137 fully-monitored and 3,958 incompletely-monitored patients were compared, adjusted for the confounders diabetes duration, age and gender. Since recommended HbA_{1c} values depend on age, medication use and diabetes duration, analyses were stratified into three HbA_{1c} profile groups. Linear multilevel analyses enabled adjustment for general practice.

Results Compared to incompletely-monitored patients, fully-monitored patients had significantly lower HbA_{1c} levels [95%CI] in the first (-2.03 [-2.53;-1.52]mmol/mol) (-0.19% [-0.23%;-0.14%]), second (-3.36 [-5.28;-1.43]mmol/mol) (-0.31% [-0.48%;-0.13%]) and third HbA1c profile group (-1.89 [-3.76;-0.01]mmol/mol) (-0.17% [-0.34%;0.00%]).

Conclusions/interpretation This study shows that in a care group setting, fully-monitored patients had significantly lower HbA_{1c} levels compared with incompletely-monitored patients. Since this difference might have considerable clinical impact in terms of T2DM-related risks, this might help general practices in care group settings to overcome barriers on adequate registration and thus improve structured T2DM primary care. From population health management perspective, we recommend a systematic approach to adjust the structured care protocol for incompletely-monitored subgroups.

Strenghts and limitations of this study

- The observational real-life design of this study prevented any interference with daily routines of GP practices, thus contributing to good reliability and representativeness of our findings
- Because the availability of patient data on age, medication use and diabetes duration allowed to conduct our analyses - in correspondence with professional GP guidelines - for specific HbA1c threshold groups, the findings are relevant and useful for clinical practice
- Taking into consideration that a missing registration does not necessarily reflect a lack of care, but might be caused by technical or practical problems instead, the associations found in this study might be underestimated.

1. Introduction

Type 2 diabetes is a typical lifestyle-related disease (1). The course of type 2 diabetes and potential complications are influenced by smoking behaviour (2, 3), BMI (4) and physical exercise (5). Adopting a healthier lifestyle, e.g. by smoking cessation or weight loss, is known to be very demanding for individual patients (6, 7). It has been established that attention for non-conscious motivational factors affecting an individual's behaviour is important to realise sustained behavioural change (8). In addition, to avoid relapse (9, 10) and maintain long-term behavioural change, follow-up support for lifestyle-related themes is recommended (11, 12). Accordingly, in the Netherlands, a nationally acknowledged scientific council of general practitioners (GPs) has determined professional guidelines for diabetes primary care (13).). In correspondence with the NICE guidelines (14), it is recommended to monitor at least once a year not only HbA_{1c} levels, but also the biomedical target indicators systolic blood pressure and LDL, as well as lifestyle-related indicators.

However, for an average GP, providing structured primary diabetes care with sufficient attention for both biomedical monitoring and lifestyle adaptation (15) is reported to be challenging (16). Therefore, in many Western countries, varying from the US and Europe (17, 18) to New-Zealand (19), an increasing number of GPs has delegated the regular structured primary diabetes care to nurse practitioners.

It is known that implementing structured primary diabetes care and delegation of tasks to a nurse practitioner has considerable impact on the organization of the GP practice (20, 21). For example, in the USA, an evaluation of the recent Comprehensive Primary Care (CPC) program revealed a need to refine practice workflows, to incorporate new staff roles, and to overcome incompatibility of health technology systems (22). To improve the delivery of structured primary diabetes care in the Netherlands, most GPs have joined together in local 'care groups' (23). Care groups negotiate collective structured diabetes care protocols with the funding institutions of Dutch primary care, namely, local health insurance companies –.

For GPs, participation in a care group is voluntary. However, the logistic and quality support to individual GP practices which is part of the care group approach, might be seen as an incentive for care group participation. That is, the agreements between care groups and health insurance companies on structured diabetes care protocols enable GPs to offer high-quality intensive primary diabetes care. To illustrate, on an annual basis, four consultations at the GP practice with an explicit focus on lifestyle support are facilitated, as well as complementary allied health (e.g. annual screening of fundus and feet). All patients who receive diabetes care in GP practice are eligible for participation in the structured care protocol. It is known that providing a structured diabetes care protocol is associated with better monitoring of patients (24). In addition, adequate registration of the diabetes-related patient health indicators is associated with improvement of the care process (25). The costs of this protocol are fully covered by health insurance companies. For patients, participation is free of charge.

According to a recent study, care group participation is associated with improvement of the proportion patients with full monitoring of biomedical and life style related target indicators (26). However, a review on chronic care programs in primary care reported that doubts among care providers on the clinical effects of an intervention are a barrier for adoption (27). To our knowledge little is known about the relationship between full monitoring of biomedical as well as lifestyle related target diabetes indicators in a care group setting and clinical health outcomes. The Hba_{1c} level is established as a key diabetes health indicator (28). Therefore, this study aims to investigate the association between full monitoring of biomedical and lifestyle-related diabetes target indicators and HbA_{1c} level, in patients with type 2 diabetes who receive a structured diabetes care protocol, facilitated by a care group.

2. Research design and methods

2.1 Study design and population

Data were used of type 2 diabetes patients from the observational Eerstelijns Zorggroep Haaglanden (ELZHA) cohort, which is based on primary care registry data from a care group in the western part of the Netherlands. In January 2015, the care group numbered 168 GP practices (n=24,459 patients with type 2 diabetes). On a periodic basis, GP members share an overview of their patient monitoring data with the care group. In February 2017, all GP practices were informed in writing and, based on an opt-out procedure, were invited to participate in this cohort. For the present study, pseudonymized data on monitoring of diabetes target indicators and HbA_{1c} levels from patients were used from the calendar year 2014. Patients receiving continuously structured primary diabetes care from January 2014 through December 2014 at the same GP practice were included. At least one registration of HbA_{1c} in 2014 was necessary for inclusion. Since systolic blood pressure and LDL guidelines are specified for patients aged ≤80 years, patients aged ≥80 years were excluded. Patients were also excluded in case of missing data on age, gender or disease duration. Finally, because missing data on medication use were partly caused by technical problems, patients without registration of medication prescription were also excluded.

2.2 Exposure

Details of the ELZHA cohort study have been described previously (Van Bruggen et al., submitted). In short, within a care group setting, GPs are able to invite all their T2DM patients with primary care treatment for this structured care protocol. During a standard diabetes consultation or at time of diagnosis, patients are informed about this care protocol. Patients who provide consent to be enrolled, can join the structured primary care protocol. The protocol includes a quarterly diabetes consultation, in which diabetes-related target indicators are checked and lifestyle education is provided, combined with complementary allied health such as an annual foot check, fundus screening and dietician´s counselling. To facilitate the organization and quality control of this protocol, GP practices receive practical and logistic support, including a computerized system to improve the care process and

outcomes. Measurement of the diabetes target indicators (HbA_{1c} level, systolic blood pressure, LDL level, BMI, smoking behaviour and physical exercise) took place in 2014 at the end of each quarter. In the present study, patients were regarded as 'fully monitored' when each target indicator was registered at least once between January and December 2014. If one or more target indicators were not registered minimally one time in calendar year 2014, patients were defined as ´incompletely monitored´.

2.3 Outcomes

The outcome of this study was HbA_{1c} level; this was computed in two steps. First, for each quarter, a mean HbA_{1c} value was calculated based on all available HbA_{1c} measures in that quarter. Based on the mean HbA_{1c} levels of all quarters, a mean was computed for the whole calendar year. HbA_{1c} level is presented in % and mmol/mol.

2.4 Analysis

For patient characteristics, categorical variables were reported as numbers and percentages. Continuous variables were reported as means with standard deviation (SD) or, when non-normally distributed, as medians with interquartile ranges (IQR). Baseline characteristics of excluded patients were, if available, compared to the study population. Linear multilevel analyses were conducted to compare HbA_{1c} levels of fully-monitored and incompletely-monitored patients. Multilevel analyses allowed to adjust the individual observations (level 1) for GP practice (level 2). In addition, the analyses were adjusted for patient age, duration of diabetes and gender, which are relevant possible confounders with regard to HbA_{1c} outcomes.

Tailored on specific key patient characteristics (age, intensity of medication treatment, and disease duration) professional Dutch GP guidelines recommend differentiated HbA1c targets

for three different patient profile groups based on age and prescribed medication. Details on the scientific determination of these target values are presented in the guidelines (13). To summarize, 1) for patients aged <70 years, and for older patients with a mild treatment regime (only metformin monotherapy prescription or lifestyle coaching), a target HbA1c value of 7.0% (53 mmol/mol) is recommended. 2) for patients aged ≥70 years who need more intensive treatment and were diagnosed with diabetes <10 years previously, a target HbA1c value of 7.5% (58 mmol/mol) is recommended; 3) for patients aged ≥70 years who need more intensive treatment and were diagnosed with diabetes ≥10 years previously, a target HbA1c value of 8.0% (64 mmol/mol) is recommended. In the present study, since missing data on medication might reflect administrative omissions rather than absence of medication treatment, patients without data on medication were excluded.

In view of the relevance for clinical practice, separate multi-level analyses were conducted and reported for each of these HbA_{1c} profile groups. In addition, in a non-stratified multi-level analysis, we tested whether the magnitude of the effect found in HbA1c profile 2 and 3 differed significantly from Hba1c profile 1. A p-value <0.05 was considered statistically significant; for interaction, a p-value <0.1 was considered statistically significant.

Descriptive statistics were analysed using SPSS, version 24.0. Multilevel analyses were performed using ML WiN (Version 2.28).

2.5 Patient and public involvement

Since this study was targeted on a GP supporting approach of structured primary diabetes care, patients were not actively involved.

2.6 Ethical considerations

Since the pseudonymized patient data contained only age and gender, the data could be aggregated without enabling investigators to identify individual patients. Due to the high number of patients, informed consent of individual patients was not required.

The study protocol was approved by the Medical Ethical Committee of the Leiden University Medical Center (code G16.102/SH/sh).

3. Results

This study included 167 GP practices (99%) with a total of 24,198 patients with type 2 diabetes; of these, 12,095 patients met the inclusion criteria (for a detailed flowchart of inclusion see Figure 1). By definition, in this population HbA1c was always monitored, as not having an HbA1c measure available was an exclusion criterion for the present study. Comparing characteristics of the excluded patients (n = 12,103 patients) with the study population (n = 12,095 patients, see supplementary file, table 1), in excluded patients, mean HbA1c level (50.32 mmol/mol, SD = 12.8 mmol/mol; 6.76 % (SD = 3.32 %, 7.535 registrations missing) was slightly lower than in the study population (52.5 mmol/mol, SD=1.07 mmol/mol; 6.95 %, SD = 3.16%). Comparing the median diabetes duration of excluded patients (5 years, IQR: 3 – 9, 63 registrations missing) to the study population (6 years, IQR: 3 – 10), no substantial differences were found. Regarding median age, excluded patients (71 years, IQR: 60 – 82, 2,917 registrations missing) were older than included patients (median: 64 years, IQR: 56 – 71 years) and slightly more often female (50 % (n = 4,251; 3,530 registrations missing) versus 45 % (n = 5,477). More detailed characteristics of our study population, classified by HbA_{1c} profile and monitoring completeness, are presented in Table 1. Of patients who were incompletely monitored, information on physical exercise was most often missing, followed by smoking, BMI, LDL, and systolic blood pressure (Figure 2).

Compared to incompletely-monitored patients, fully-monitored patients had lower mean HbA1c levels in all three HbA1c profiles. In addition, fully-monitored patients had a longer duration of diabetes than incompletely-monitored patients.

The crude analysis showed that, compared with incompletely-monitored patients, the mean HbA_{1c} of fully-monitored patients was significantly lower in the first profile (-1.95 [95% CI -2.41; -1.49] mmol/mol) (-0.18% [-0.22%; -0.14%]), second profile (-2.03 [95 % CI -3.41;-0.66] mmol/mol) (-0.19% [-0.31%; -0.06%]) and third profile (-1.53 [95 % CI -2.96;-0.10] mmol/mol)

(-0.14% [-0.27%; -0.01%]) (Table 2). Multilevel analyses with adjustment for diabetes duration, age and gender revealed similar significant associations in the first (-2.03 [95 % CI -2.53; -1.52] mmol/mol) (-0.19% (-0.23%; -0.14%]), second (-3.36 [95 % CI -5.28; -1.43] mmol/mol) (-0.31% [-0.48%; -0.13%]) and third profile (-1.89 [95 % CI -3.76; -0.01] mmol/mol) (-0.17% [-0.34%; 0.00%]). The magnitude of these associations did not significantly differ between the HbA_{1c} profile groups (p=0.44 and p=0.35 for the second and third profile, respectively, compared with the first profile).

4. Discussion

This study explored whether monitoring completeness of biomedical and lifestyle-related diabetes target indicators in a care group setting is associated with HbA_{1c} level. In all HbA_{1c} profile groups – defined based on patient age, intensity of medication treatment and disease duration – we found that fully-monitored patients had lower HbA_{1c} levels than incompletely-monitored patients; the differences ranged from 0.17% (1.89 mmol/mol) to 0.31% (3.36 mmol/mol), indicating that adequate diabetes monitoring of biomedical and lifestyle indicators in primary care is associated with better HbA_{1c} levels. To our knowledge, this is the first study to analyse the association between systematic diabetes monitoring in primary care and HbA_{1c} levels. Apart from one longitudinal Dutch study on structured primary diabetes care in a care group setting which reported a sharp decrease in the proportion of patients with a HbA_{1c} level ≥53 mmol/mol (24), research on absolute HbA_{1c} differences is scarce and findings appear to be somewhat inconsistent (29-32). Therefore, caution is required when comparing our findings with any earlier studies. However, for each 1% (10.9 mmol/mol) reduction in mean HbA_{1c}, a significant decrease in health risk has been reported, ranging from 21% for any endpoint related to diabetes including deaths, to 14% for myocardial infarction, and 37% for microvascular complications (33). Further, our finding that registration of physical exercise was most often lacking, is in line with an earlier small-size

study in which only 19% of patients with type 2 diabetes reported 'being guided properly' with regard to physical exercise (34).

Our finding that, compared with incomplete monitoring, full monitoring of patients is associated with a lower HbA_{1c} level might be explained by continuity of care in several ways. First, if patients are monitored at least once a year, an increasing HbA_{1c} level might be noticed at an early stage, resulting in fast and adequate treatment. Second, periodic monitoring and coaching of patients with regard to weight loss, smoking cessation and physical exercise contributes to enduring lifestyle adaptation (11, 12), which may lead to lower HbA_{1c} levels (35).

Since fully-monitored patients with type 2 diabetes have significantly lower HbA_{1c} levels, their risk of any diabetes-related health complication is lower compared to incompletely-monitored patients. Thus, in general, incomplete monitoring of a patient should be interpreted as an important sign of diabetes-related health risks – especially since incomplete records might not only be caused by no-show, but also by low patient motivation, missing of prescribed lab tests and limited overall adherence to diabetes treatment. As reported by others (36), a tailored approach based on data registry and adjusted to patient characteristics (e.g. monitoring completeness), is recommended. This might encourage awareness in GP practice regarding adequate diabetes management and might help GP's to overcome barriers on full adoption of the care group monitoring approach. In addition, the present findings might be relevant for other structured diabetes primary care settings which focus on frequent monitoring and adequate registration of diabetes-related health outcomes, such as the Comprehensive Primary Care Plus program in the USA (37).

The present study is characterised by several strengths. First, in our view, an important strength of this study is the design: although randomized clinical trials might help to eliminate bias, adequate powering and generalizability are familiar problems (38), whereas observational studies allow to include large study populations. For example, in this study, all

patients participating in a structured primary diabetes care program were enrolled, thereby contributing to high representativeness of our study population. Second, generally, since our study design did not interfere with the daily routine of GP practices, we assume adequate reliability of our findings. Thus, the observational real-life setting in our study reflects the reality of diabetes monitoring and HbA_{1c} levels in primary care. Our design is in line with other studies that also used a pragmatic approach to conduct diabetes related studies in primary care (39-41). Third, since patients were included if they participated for at least one year at the same GP practice, bias caused by intermediate moving or referral to hospital diabetes care was avoided - which contributes to the stability and, thus, the validity of our findings. Finally, conducting separate analyses for each HbA_{1c} profile group allowed adjustment for the variety in the recommended HbA_{1c} target values.

Nevertheless, this study is also subject to some limitations that need to be mentioned. First, since no control group was included, no causal relation between monitoring completeness and HbA1c level can be proven. Second, a missing registration does not necessarily mean that the care has not been provided. For example, missings might be caused by technical problems, or lack of time for registration. Patients being considered erroneously as 'incompletely monitored' might have underestimated the associations found, although we did correct our analyses for age, diabetes duration, gender and GP practice.

For future research, it might be useful to analyse the context of diabetes target monitoring and explore whether the association that we found reflects a causal relationship between monitoring completeness and HbA_{1c} level. In addition, from the GP perspective, examining potential barriers to complete monitoring, including potential benefits such as an increase of the proportion patients with HbA1c levels within recommended values, might provide keys to improvement of the monitoring process. To ameliorate the primary diabetes care of incompletely-monitored patients, exploration of their preferences and needs is suggested. In addition, an evaluation of financial costs and benefits of this care approach is recommended.

To summarize, in patients with type 2 diabetes within a care group setting, full monitoring of biomedical and lifestyle target indicators is associated with lower HbA_{1c} levels compared with incomplete monitoring. These differences might be expected to have a considerable clinical impact in terms of diabetes-related risks. We recommend a systematic approach to analysing the needs of incompletely-monitored patient groups, and to adjust the structured care protocol for these subgroups in terms of population health management.

Article Information

Acknowledgments. The authors thank the GPs and patients of the ELZHA care group for the use of their data for this study.

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

Duality of Interest. No potential conflicts of interest relevant to this article were reported. All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and 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 three years; no other relationships or activities that could appear to have influenced the submitted work."

Transparency Declaration

The lead author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Author Contributions. SvB analysed data and wrote the manuscript. SR analysed data and reviewed the manuscript. MK reviewed and edited the manuscript. TB reviewed the manuscript. NC reviewed the manuscript and contributed to the discussion. MN is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Data sharing statement. The data that support the findings of this study are available from the corresponding author on request.

Licence

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd ("BMJ"), and its Licencees to permit this article (if accepted) to be published in The BMJ's editions and any other BMJ products and to exploit all subsidiary rights, as set out in *our licence*." "

References

1. Howells L, Musaddaq B, McKay AJ, Majeed A. Clinical impact of lifestyle interventions for the prevention of diabetes: an overview of systematic reviews. BMJ Open. 2016;6(12):e013806.
2. Fagard RH. Smoking amplifies cardiovascular risk in patients with hypertension and diabetes. Diabetes Care. 2009;32 Suppl 2:S429-31.
3. Qin R, Chen T, Lou Q, Yu D. Excess risk of mortality and cardiovascular events associated with smoking among patients with diabetes: meta-analysis of observational prospective studies. Int J Cardiol. 2013;167(2):342-50.
4. Gray N, Picone G, Sloan F, Yashkin A. Relation between BMI and diabetes mellitus and its complications among US older adults. South Med J. 2015;108(1):29-36.
5. Dempsey PC, Blankenship JM, Larsen RN, Sacre JW, Sethi P, Straznicky NE, et al. Interrupting prolonged sitting in type 2 diabetes: nocturnal persistence of improved glycaemic control. Diabetologia. 2017;60(3):499-507.
6. Babb S, Malarcher A, Schauer G, Asman K, Jamal A. Quitting Smoking Among Adults - United States, 2000-2015. MMWR Morb Mortal Wkly Rep. 2017;65(52):1457-64.
7. Twyman L, Bonevski B, Paul C, Bryant J. Perceived barriers to smoking cessation in selected vulnerable groups: a systematic review of the qualitative and quantitative literature. BMJ Open. 2014;4(12):e006414.
8. Papies EK. Health goal priming as a situated intervention tool: how to benefit from nonconscious motivational routes to health behaviour. Health Psychol Rev. 2016;10(4):408-24.
9. Arterburn DE, Bogart A, Sherwood NE, Sidney S, Coleman KJ, Haneuse S, et al. A multisite study of long-term remission and relapse of type 2 diabetes mellitus following gastric bypass. Obes Surg. 2013;23(1):93-102.
10. Hawkins J, Hollingworth W, Campbell R. Long-term smoking relapse: a study using the british household panel survey. Nicotine Tob Res. 2010;12(12):1228-35.
11. Pjanic, Muller R, Laimer M, Hagenbuch N, Laederach K, Stanga Z. Evaluation of a multiprofessional, nonsurgical obesity treatment program: which parameters indicated life style changes and weight loss? J Eat Disord. 2017;5:14.
12. Venditti EM, Wylie-Rosett J, Delahanty LM, Mele L, Hoskin MA, Edelstein SL, et al. Short and long-term lifestyle coaching approaches used to address diverse participant barriers to weight loss and physical activity adherence. Int J Behav Nutr Phys Act. 2014;11:16.
13. Rutten GEHM DGW, Nijpels G, Houweling ST, Van de Laar FA, Bilo HJ, Holleman F,Burgers JS, Wiersma Tj, Janssen PGH. NHG-Standaard Diabetes mellitus type 2 (derde herziening). Huisarts en Wetenschap 2013;56(10):512-25.
14. Type 2 diabetes in adults: management. United Kingdom: National Institute for Health and Care Excellence; NICE guideline 2015.
15. Ekong G, Kavookjian J. Motivational interviewing and outcomes in adults with type 2 diabetes: A systematic review. Patient Educ Couns. 2016;99(6):944-52.
16. Rushforth B, McCrorie C, Glidewell L, Midgley E, Foy R. Barriers to effective management of type 2 diabetes in primary care: qualitative systematic review. Br J Gen Pract. 2016;66(643):e114-27.
17. Maier C, Aiken L., and Busse R. Nurses in advanced roles in primary care: Policy levers for implementation. Paris; 2017. Report No.: 98.
18. Mergenthal K, Beyer M, Gerlach FM, Guethlin C. Sharing Responsibilities within the General Practice Team - A Cross-Sectional Study of Task Delegation in Germany. PLoS One. 2016;11(6):e0157248.
19. Hefford M, Love T, Cumming J, Finlayson M, Raymont A. The financial impact of clinical task substitution between practice nurses and GPs in New Zealand primary care centres. N Z Med J. 2011;124(1342):59-65.

20. Ferrante JM, Shaw EK, Bayly JE, Howard J, Quest MN, Clark EC, et al. Barriers and Facilitators to Expanding Roles of Medical Assistants in Patient-Centered Medical Homes (PCMHs). J Am Board Fam Med. 2018;31(2):226-35.
21. McInnes S, Peters K, Bonney A, Halcomb E. An integrative review of facilitators and barriers influencing collaboration and teamwork between general practitioners and nurses working in general practice. J Adv Nurs. 2015;71(9):1973-85.
22. Dale SB, Ghosh A, Peikes DN, Day TJ, Yoon FB, Taylor EF, et al. Two-Year Costs and Quality in the Comprehensive Primary Care Initiative. N Engl J Med. 2016;374(24):2345-56.
23. Struijs JN, Van Til JT, Baan CA. Experimenteren met de keten-dbc diabetes: de eerste zichtbare effecten. Bilthoven: RIVM; 2009. p. 19-62.
24. Hendriks SH, van Hateren KJ, Groenier KH, Houweling ST, Maas AH, Kleefstra N, et al. Sex Differences in the Quality of Diabetes Care in the Netherlands (ZODIAC-45). PLoS One. 2015;10(12):e0145907.
25. Hoque DME, Kumari V, Hoque M, Ruseckaite R, Romero L, Evans SM. Impact of clinical registries on quality of patient care and clinical outcomes: A systematic review. PLoS One. 2017;12(9):e0183667.
26. Van Bruggen S, Kasteleyn MJ, Rauh SP, Bonten TN, Chavannes NH, Numans ME. A multidisciplinary Type 2 Diabetes care protocol within a primary care group leads to a higher proportion of fully-monitored patients (ELZHA cohort-1). Annual Meeting; Chicago (Illinois), United States: North American Primary Care Research Group; 2018.
27. Kadu MK, Stolee P. Facilitators and barriers of implementing the chronic care model in primary care: a systematic review. BMC Fam Pract. 2015;16:12.
28. Lacey RE, Sacker A, Bell S, Kumari M, Worts D, McDonough P, et al. Work-family life courses and BMI trajectories in three British birth cohorts. Int J Obes (Lond). 2017;41(2):332-9.
29. Fuchs S, Henschke C, Blumel M, Busse R. Disease management programs for type 2 diabetes in Germany: a systematic literature review evaluating effectiveness. Dtsch Arztebl Int. 2014;111(26):453-63.
30. Gabbay RA, Lendel I, Saleem TM, Shaeffer G, Adelman AM, Mauger DT, et al. Nurse case management improves blood pressure, emotional distress and diabetes complication screening. Diabetes Res Clin Pract. 2006;71(1):28-35.
31. Kostev K, Rockel T, Jacob L. Impact of Disease Management Programs on HbA1c Values in Type 2 Diabetes Patients in Germany. J Diabetes Sci Technol. 2017;11(1):117-22.
32. Wiefarn S, Kostev K, Heumann C, Rettelbach A. [Effect of the Disease Management Program on HbA1c Value in Type 2 Diabetes Mellitus Patients: A Retrospective Comparison between Disease Management Programs and Standard Care]. Dtsch Med Wochenschr. 2017;142(21):e148-e55.
33. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ. 2000;321(7258):405-12.
34. Stuij M, Elling A, Abma TA. Conflict between diabetes guidelines and experienced counselling in sports and physical activity. An exploratory study. Eur J Public Health. 2017;27(1):157-9.
35. Umpierre D, Ribeiro PA, Kramer CK, Leitao CB, Zucatti AT, Azevedo MJ, et al. Physical activity advice only or structured exercise training and association with HbA1c levels in type 2 diabetes: a systematic review and meta-analysis. JAMA. 2011;305(17):1790-9.
36. Aronson R, Orzech N, Ye C, Brown RE, Goldenberg R, Brown V. Specialist-Led Diabetes Registries and Prevalence of Poor Glycemic Control in Type 2 Diabetes: The Diabetes Registry Outcomes Project for A1C Reduction (DROP A1C). Diabetes Care. 2016;39(10):1711-7.
37. Sessums LL, McHugh SJ, Rajkumar R. Medicare's Vision for Advanced Primary Care: New Directions for Care Delivery and Payment. JAMA. 2016;315(24):2665-6.
38. Frakt AB. An observational study goes where randomized clinical trials have not. JAMA. 2015;313(11):1091-2.

39. Hippisley-Cox J, Coupland C. Diabetes treatments and risk of heart failure, cardiovascular disease, and all cause mortality: cohort study in primary care. BMJ. 2016;354:i3477.
40. Price DB, Russell R, Mares R, Burden A, Skinner D, Mikkelsen H, et al. Metabolic Effects Associated with ICS in Patients with COPD and Comorbid Type 2 Diabetes: A Historical Matched Cohort Study. PLoS One. 2016;11(9):e0162903.
41. Smits KPJ, Sidorenkov G, Navis G, Bouma M, Meulepas MA, Bilo HJG, et al. Prescribing Quality and Prediction of Clinical Outcomes in Patients With Type 2 Diabetes: A Prospective Cohort Study. Diabetes Care. 2017;40(7):e83-e4.

Figures and tables

Figure 1. Flowchart of patient inclusion.
Pts = patients

Figure 2. Overview of registered indicators in incompletely monitored patients within Hba1c profile
HbA1c: Hemoglobin A1c

Table 1. Characteristics of the study population: classified by HbA_{1c} profile and monitoring completeness.

		HbA_{1c} profile 1[1] *Target HbA_{1c}: 53 mmol/mol (7.0%)*		**HbA_{1c} profile 2**[2] *Target HbA_{1c}: 58 mmol/mol (7.5%)*		**HbA_{1c} profile 3**[3] *HbA_{1c}: 64 mmol/mol (8.0%)*	
		Incomplete	**Complete**	**Incomplete**	**Complete**	**Incomplete**	**Complete**
		n =3,345	n =6,794	n = 396	n = 656	n = 217	n = 687
HbA_{1c} level: mean [SD] [4]	mmol/mol	53.51 (12.31)	51.56 (10.51)	55.91 (11.66)	53.87 (10.60)	55.12 (10.57)	53.60 (8.98)
	%	7.05 (1.13)	6.87 (0.96)	7.27 (1.07)	7.08 (0.97)	7.19 (0.97)	7.06 (0.82)
Diabetes duration, years: median [IQR][5]		3 [3 – 8]	7 [4 – 10]	3 [3 – 7]	7 [4 – 8]	13 [11 – 16]	13 [11 – 15]
Age (years): median [IQR]		61 [54 – 67]	62 [55 – 68]	74 [72 – 76]	74 [71 – 76]	74 [72 – 77]	74 [72 – 76]
Gender: % female (n)		44 (1,465)	46 (3,106)	46 (183)	45 (297)	51(110)	46 (316)

1) Profile 1: patients aged <70 years, and older patients with a mild treatment regime (only metformin monotherapy prescription)

2) Profile 2: patients aged ≥70 years who need more intensive treatment and diagnosed with diabetes <10 years ago

3) Profile 3: patients aged ≥70 years who need more intensive treatment and diagnosed with diabetes ≥10 years ago

4) SD = standard deviation

5) IQR = interquartile range

Table 2. Multilevel analyses evaluating the HbA_{1c} difference of fully-monitored patients compared to incompletely monitored patients, stratified for HbA1c profile.

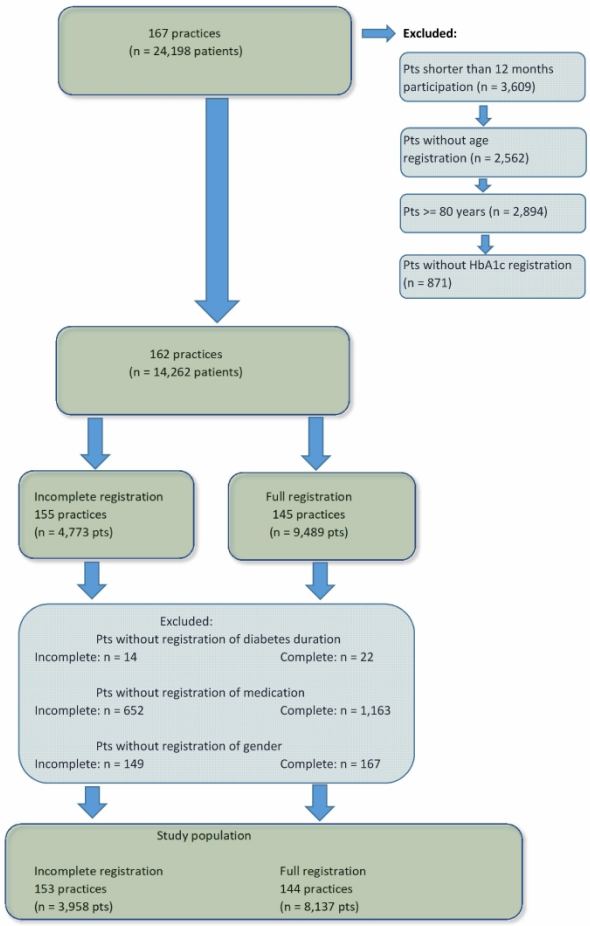
		Profile 1			**Profile 2**			**Profile 3**		
		B	**95% CI**	**p-value**	**B**	**95% CI**	**p-value**	**B**	**95% CI**	**p-value**
Model 1[a)]	mmol / mol	-1.95	-2.41,-1.49	<0.001	-2.03	-3.41, -0.66	0.004	-1.53	-2,96, -0.10	0.037
	%	-0.18	-0.22; -0.14		-0.19	-0.31; -0.06		-0.14	-0.27; -0.01	
Model 2[b)]	mmol / mol	-2.03	-2.53, -1.52	<0.001	-3.36	-5.28, -1.43	0.001	-1.89	-3.76, -0.01	0.049
	%	-0.19	-0.23; -0.14		-0.31	-0.48; -0.13		-0.17	-0.34; 0.00	

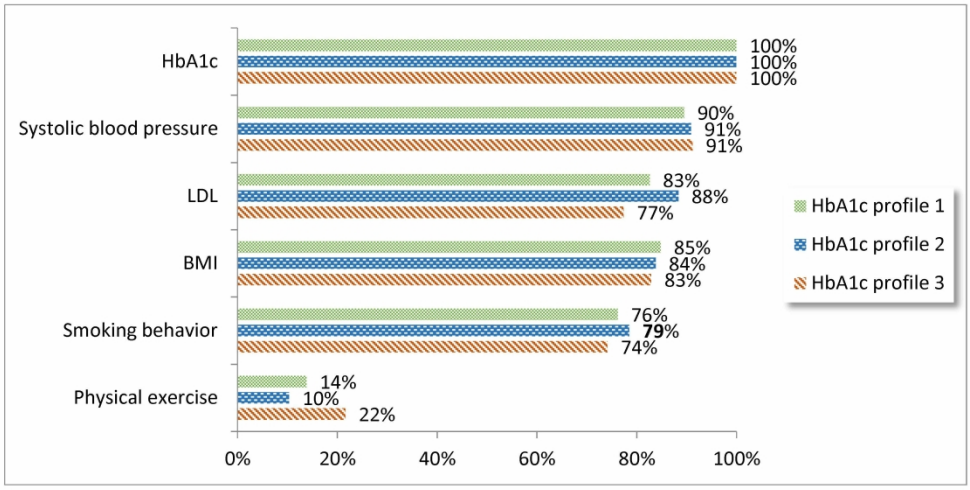
a) Crude analysis

b) Multilevel analysis adjusted for age, diabetes duration and gender

Flowchart inclusie

Figure 1. Flowchart of patient inclusion




HbA1c
Systolic blood pressure
LDL
BMI
Smoking behavior
Physical exercise
100%
100%
100%
90%
91%
91%
83%
88%
77%
85%
84%
83%
76%
79%
74%
14%
10%
22%
0%
20%
40%
60%
80%
100%
HbA1c profile 1
HbA1c profile 2
HbA1c profile 3

Association between full monitoring of biomedical and lifestyle target indicators and HbA1c level in primary type 2 diabetes care: an observational cohort study (ELZHA-cohort 1)

Supplementary file

Since missing data on medication prescription might reflect absence of medication treatment but also technical errors, all patients without medication registration were excluded. As a result, in the final analyses, T2DM patients with a lower HbA1c level and subsequently no medication prescription, were excluded.

Table 1. Characteristics of study population and excluded patients.

		Included patients	Excluded patients (n = 12,103)	
		n = 12,095	Outcomes	Missing registrations
HbA1c: mean (SD)	Mmol / mol	52.55 (11.07)	50.32 (12.8)	7,535
	%	6.95 (3.16)	6.76 (3.32)	
Diabetes duration, years: median [IQR][1]		6 [3 -10]	5 [3 – 9]	63
Age (years): median [IQR] [2]		64 [56 – 71]	71 [60 – 82]	2,917
Gender: % female (n)		45 (5.477)	50 (4.251)	3,530

1) SD = standard deviation

2) IQR = interquartile range

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page number
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2, 3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4, 5
Objectives	3	State specific objectives, including any prespecified hypotheses	5, 6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6, 7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6, 7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7, 8
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	*7, 8*
Bias	9	Describe any efforts to address potential sources of bias	7, 8
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7, 8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8 - 9
		(*b*) Describe any methods used to examine subgroups and interactions	8 – 9
		(*c*) Explain how missing data were addressed	6
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	

Continued on next page

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	10
		(b) Give reasons for non-participation at each stage	10
		(c) Consider use of a flow diagram	Present
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	10
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
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	10, 11
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11
Discussion			
Key results	18	Summarise key results with reference to study objectives	11, 12
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	13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
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	

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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 www.strobe-statement.org.