Relevant patient characteristics for guiding tailored integrated diabetes primary care: a systematic review

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Aim: To identify which patient-related effect modifiers influence the outcomes of integrated care programs for type 2 diabetes in primary care. Background: Integrated care is a widespread management strategy for the treatment of type 2 diabetes. However, most integrated care programs are not tailored to patients’ needs, preferences and abilities. There is increasing consensus that such a patient-centered approach could improve the management of type 2 diabetes. Thus far, it remains unclear which patient-related effect modifiers should guide such an approach. Methods: PubMed, CINAHL and EMBASE were searched for empirical studies published after 1998. A systematic literature review was conducted according to the PRISMA guidelines. Findings: In total, 23 out of 1015 studies were included. A total of 21 studies measured the effects of integrated diabetes care programs on hemoglobin A1c (HbA1c) and three on low-density lipoprotein cholesterol, systolic blood pressure and health-care utilization. In total, 49 patient characteristics were assessed as potential effect modifiers with HbA1c as an outcome, of which 46 were person or health-related and only three were context-related. Younger age, insulin therapy and longer disease duration were associated with higher HbA1c levels in cross-sectional and longitudinal studies. Higher baseline HbA1c was associated with higher HbA1c at follow-up in longitudinal studies. Information on context- and person-related characteristics was limited, but is necessary to help identify the care needs of individual patients and implement an effective integrated type 2 diabetes tailored care program.

Key words: integrated health-care systems; patient-centered care; primary care; review; type 2 diabetes mellitus

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Introduction

Diabetes is one of the most prevalent chronic conditions worldwide and a public health priority in many countries (Tamayo et al., 2014; International Diabetes Federation, 2015). In Europe, an estimated 9.8 million people suffer from diabetes; type 2 diabetes is responsible for 90% of cases. People with type 2 diabetes are at high risk for developing complications, such as cardiovascular disease and kidney failure, which in turn lead to increased health-care costs (Tamayo et al., 2014;...
international Diabetes Federation, 2015). To prevent diabetes-related co-morbidities and complications, and lower medical care expenditure for patients with type 2 diabetes, it is important to implement effective and efficient management strategies. An example of such a strategy is the implementation of integrated care. It aims to improve patient care and experience through improved coordination (Shaw et al., 2011).

The implementation of integrated care programs is widespread in North America, Europe, and other parts of the world (Kodner, 2009; Shaw et al., 2011). However, most integrated care programs are not tailored to patients’ needs and preferences, but rather highly standardized according to evidence-based guidelines for specific diseases, such as diabetes. Findings from recent studies suggest that not all patients benefit equally from such a standardized approach (Rothe et al., 2008; Pimouguet et al., 2011; Elissen et al., 2012). These studies report that patients with poorly controlled diabetes benefit mostly from intensive, provider-driven disease management, whereas patients with adequate glucose levels might maintain these levels independent of the type of care they receive.

In 2012, the European Association for the Study of Diabetes and the American Diabetes Association recommended a more patient-centered approach for the management of type 2 diabetes (Inzucchi et al., 2012). In a patient-centered approach, care is tailored according to individual patient needs and preferences (Committee on Quality of Health Care in America; Institute of Medicine, 2001; Inzucchi et al., 2012; American geriatrics society expert panel on person-centered care, 2016; Coulourides Kogan et al., 2016). It draws on the concept of ‘mass customization’, where goods and services are delivered with enough variety and customization that nearly everyone finds exactly what they want (Tseng and Hu, 2014). Dividing the population based on health-care needs creates groups that are more homogenous than the population as a whole. Hence, care offered to these groups will be more tailored to the patients’ needs, while acknowledging that a certain amount of heterogeneity within the subgroups will remain.

There is increasing consensus that a patient-centered approach could improve the management of type 2 diabetes (Inzucchi et al., 2012). However, to date, it is unclear what the best method is for establishing patient-centered care (Epstein and Street, 2011). Since intensive, provider-driven disease management is not beneficial to every type 2 diabetes patient, several studies have pointed toward patient characteristics – for example, number of co-morbidities, disease duration or attitude – as possible effect modifiers of treatment (Hasnain-Wynia and Baker, 2006; Inzucchi et al., 2012; Riddle and Karl, 2012; Scheen, 2016). These effect modifiers could be used to identify patients with different care needs and preferences, and subsequently serve as input to tailor treatment (Goldberger and Buxton, 2013; Constand et al., 2014). However, it is unclear which effect modifiers should guide a more patient-centered approach. Therefore, the aim of this systematic review was to identify which patient effect modifiers influence the outcomes of integrated care programs for type 2 diabetes in primary care. These effect modifiers can help to segment the chronically ill population into subgroups with similar health-care needs for whom, based on insight into their needs and preferences, a range of matching care and support options can be developed.

This review is the first part of the research project entitled ‘PROFiling patients’ healthcare needs to support Integrated, person-centered models for Long-term disease management (PROFIlE)’ (Elissen et al., 2016). The aim of this four-year Dutch project is explicitly not to develop another disease-specific approach, but we use type 2 diabetes as starting point to develop, validate and test so-called ‘patient profiles’ as an instrument to support more patient-centered chronic care management in practice.

Methods

Data sources and searches

A systematic literature search according to PRISMA guidelines (Moher et al., 2009) was performed on PubMed, CINAHL and EMBASE databases in January 2015. Included were English- or Dutch-language randomized controlled trials (RCT), prospective and retrospective cohort- and cross-sectional studies which: (1) focused on integrated care (defined below); (2) included adult patients (\(\geq 18\) years) with type 2 diabetes; (3) were
set in primary care; (4) measured effects on 1 or more measures of diabetes management [hemoglobin A1c (HbA1c), low-density lipoprotein cholesterol (LDL-c) and systolic blood pressure (SBP)], and/or health-care utilization as outcome variables; and (5) included sub-analyses with patient characteristics as independent variables. In line with previous research, integrated care was defined as interventions combining two or more components of the well-known Chronic Care Model (CCM) (Busetto et al., 2016). The CCM stresses the need for a more proactive health-care system by focusing on four components: self-management support (eg, patient education), decision support (eg, evidence-based guidelines), delivery system design (eg, care process) and clinical information systems (eg, electronic registries) (McCulloch et al., 1998; Coulter et al., 2015). Since the CCM was developed in 1998, only studies published in or after 1998 were included (Austin et al., 2000). The search strategy included targeted terms related to diabetes, integrated care, CCM components, care outcomes and subgroup analyses based on patient characteristics. The complete search terms and search string can be found in Table 1. The snowball method was used to search for other relevant studies.

**Table 1** Search terms and search string

| #  | Category                        | Search terms                                                                                                                                 |
|----|---------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|
| 1  | Diabetes                        | Diabetes OR diabetes mellitus OR diabetic patient OR type 2 diabetes OR type 2 diabetes mellitus OR T2DM OR NIDDM                              |
| 2  | Integrated care                 | Integrated care OR disease management OR disease state management OR comprehensive healthcare OR comprehensive health care OR shared care OR coordinated care OR case management OR chronic care model OR primary care OR primary health care OR outpatient clinic OR outpatient services OR primary health care OR primary healthcare OR primary health clinics OR general practice OR family practice OR community care |
| 3  | CCM – self-management support   | Self-management OR self-management support OR self-care OR patient-centeredness OR patient-centered care OR behavioral support OR motivational support OR self-management education OR patient education |
| 4  | CCM – delivery system design    | Delivery system design OR care pathway OR critical pathway OR individualized care OR clinical case management OR medicines management OR medication management OR comorbidities management OR health literacy OR cultural sensitivity OR practice nurse OR care team OR health care team OR healthcare team OR patient care team OR personalized care OR personalized management OR individualized management OR multidisciplinary care team OR tailored care OR tailored support OR multidisciplinary care |
| 5  | CCM – decision support          | Decision support, clinical reminders, clinician reminders, patient reminders, provider education, reminder systems, individualized care plans, individual care plans |
| 6  | CCM – clinical information system | Clinical information system, clinical information systems, clinical registry, health information system, health information systems, health information technology, electronic registry, clinical reminders, clinician reminders, patients reminders, provider feedback, performance monitoring, ICT device, patient portal, patient registry, diabetes registry, telemonitoring, telehealth, teleassistance, telehomecare, videconferencing, mobile phone |
| 7  | Outcome measures                | Glycemic control, glycaemic control, diabetic control, diabetes control, diabetes status, Charlson Comorbidity Index, resource use, health care use, health care utility, service use, resource utility, service utility |
| 8  | Subgroup analysis               | Factor, predictor, predictive factor, determinant, patient characteristic, patient characteristics, patient feature, patient features, patient dynamics, subgroup, subgroups, segment, strata, classes |
| 9  | Complete search string          | #1 AND (#2 OR (#3 AND #4) OR (#3 AND #5) OR (#3 AND #6) OR (#4 AND #5) OR (#4 AND #6) OR (#5 AND #6)) AND #7 AND #8 |

CCM = Chronic Care Model.
reviewers (D.H. and A.E.). More than 90% agreement was reached. Therefore, the remainder of the titles and abstracts were screened by 1 reviewer (D.H.). Second, the first 20 full texts were screened independently by two reviewers (D.H. and A.E.). Again, more than 90% agreement was reached and therefore, each reviewer independently screened half of the full texts. Third, the reference lists of the included studies were screened to obtain additional studies. Steps 1 and 2 of the study selection process were then repeated.

Data extraction and quality assessment

Descriptive data on studies were extracted by 1 reviewer (D.H.) between August and October 2015. Studies were coded for author names, year of publication, country, study design, length of follow-up, population size, age, percentage of males and CCM components. In case of uncertainties, a group discussion was held with two other authors (A.E. and M.B.).

The Effective Public Health Practice Project Quality Assessment Tool (EPHPP) was used to assess the quality of the included studies (Armijo-Olivo et al., 2012). This tool was chosen because it allows the assessment of different study designs. The studies were rated based on six domains: (1) selection bias; (2) study design; (3) confounders; (4) blinding; (5) data collection; and (6) withdrawals and dropouts. Each domain was rated as ‘strong,’ ‘moderate’ or ‘weak’. A global rating was given based on the number of weak components.

Two reviewers (D.H. and M.B.) independently performed the quality assessment for each study. Disagreements were resolved via discussion conform EPHPP guidelines.

Data synthesis and analysis

The included studies were categorized according to: (1) the reported outcome(s) of interest (HbA1c, LDL-c, SBP and/or health-care utilization); and (2) the type of patient characteristic(s) investigated in subgroup analyses. Characteristics were classified as person-related (predisposing), context-related (enabling) or health-related (illness level) characteristics according to Andersen and Newman’s (1973) Behavioral Model of Health Service Use. The model provides a theoretical framework for viewing health services utilization, taking into account both societal and individual characteristics. The model was chosen, because the individual characteristics can inform tailored care by, for example, helping determine the best intensity of care for the individual patient. Relationships between outcomes and characteristics were depicted as ‘+’ for significant positive relationships, as ‘−’ for significant negative relationships and as ‘0’ for non-significant relationships.

Results

Search results

In total, 1374 studies were identified through electronic databases and by checking the references of the included studies. Figure 1 shows the flow diagram of the study selection. Most studies were excluded because none relevant outcomes were reported (n = 453), and/or type of care was not integrated (n = 257). After the title, abstract and full text screening, 27 studies were included (Groeneveld et al., 2001; Ostgren et al., 2002; El-Kebbi et al., 2003; Rothman et al., 2003; Rothman et al., 2004; Uitewaal et al., 2004; Benoit et al., 2005; Sperl-Hillen and O’Connor, 2005; Uitewaal et al., 2005; De Alba Garcia et al., 2006; Nielsen et al., 2006; Taweeapolcharoen et al., 2006; Trief et al., 2006; Wahba and Chang, 2007; Mold et al., 2008; Al Omari et al., 2009; De Fine Olvarius et al., 2009; Robinson et al., 2009; Kellow et al., 2011; Cardenas-Valladolid et al., 2012; Elissen et al., 2012; Liu et al., 2013; Quah et al., 2013; LeBlanc et al., 2015; Luijks et al., 2015; Moreira et al., 2015; Quinn et al., 2016).

Quality assessment

The methodological quality of the included studies can be found in Supplementary Table 1. The domains with the most ‘weak’ ratings were confounders (n = 10), blinding (n = 9) and selection bias (n = 9). Almost all studies (n = 25) scored high on the domain data collection. The overall study quality was strong for four studies, moderate for 11 studies and low for 12 studies. Most studies with low quality had a cross-sectional study design and did not report on or adjust for possible confounders.

Study and sample characteristics

Of the included studies, nine (33.3%) were retrospective cohort studies, seven (25.9%)
Figure 1 Flow diagram of the study selection. *Qualitative, or mixed-method studies; †any outcome other than hemoglobin A1c, low-density lipoprotein cholesterol, blood pressure or health-care utilization; ‡independent variable is not a person-, context- or health-related patient characteristic (eg, health-care provider characteristics); §setting is not a primary care setting (eg, hospital). CCM=Chronic Care Model; DM=diabetes mellitus.
cross-sectional studies, seven (25.9%) (randomized) controlled studies and four (14.8%) prospective cohort studies. Table 2 shows that the median follow-up duration for retrospective cohort, prospective cohort and randomized controlled studies \((n=20)\) was 15 months (range 6–112). The median sample size consisted of 376 individuals (range 80–105 056) with an average age of 60.0 years (range 50.5–70.9); the percentage of male subjects ranged from 31.3 to 68.0.

Table 2 also provides an overview of the CCM components implemented in each study. Eight studies included all four components of the CCM model. The CCM component delivery system design was included in most studies \((n=25)\), followed by self-management support \((n=20)\). Of the studies that included the components delivery system design, most introduced a care team \((n=13)\), followed by regular follow-up visits \((n=8).\) Self-management support was mostly realized through individual educational sessions on diabetes, health and nutrition \((n=14).\)

### Outcome variables

**HbA1c**

In total, 18 uncontrolled studies – including prospective, retrospective and cross-sectional cohort designs – measured the effects of integrated care programs on HbA1c. In addition, seven studies compared the influence of patient characteristics on the effectiveness of integrated diabetes care programs between intervention and control groups. In total, 51 patient characteristics were assessed as potential effect modifiers of the relationship between integrated care and HbA1c. The results will be presented according to study design. For RCTs all characteristics assessed by this study design will be discussed. Due to the high number of characteristics assessed by the cross-sectional, retrospective and prospective cohort studies, only characteristics assessed by three or more studies will be presented.

(Randomized) controlled trials: Five RCTs and two controlled trials (CTs) compared the influence of patient characteristics on the effectiveness of integrated diabetes care programs on the HbA1c level between intervention and control groups (Table 3). In total, eight patient characteristics were evaluated as potential modifiers.

Sex and age were the person-related characteristics evaluated as potential effect modifiers. Three studies assessed sex as a potential modifier, of which two found that women in the intervention group had statistically significant lower HbA1c values at follow-up compared to women in the control group (Uitewaal et al., 2005; Nielsen et al., 2006). For men, no statistically significant difference was found. The third study did not find a statistically significant relationship (Moreira et al., 2015). Age was assessed by two studies. Both found that younger patients receiving integrated diabetes care had statistically significantly lower HbA1c values at follow-up compared to patients receiving usual care (Moreira et al., 2015; Quinn et al., 2016).

Three health-related characteristics were evaluated as potential effect modifiers of the relationship between integrated diabetes care programs and HbA1c: literacy status, income and number schooling years. Literacy status was assessed by one study (Rothman et al., 2004), which found that patients in the intervention group with low literacy status \((<6th\) grade\) had statistically significant lower HbA1c values at follow-up compared to patients with low literacy status receiving usual care. Monthly income and number of schooling years were also each assessed by one study. Patients with lower monthly income \((<\$118.26)\) and \(\leq\) four years of schooling at baseline receiving integrated diabetes care had significantly lower HbA1c values at follow-up compared to patient receiving usual care (Moreira et al., 2015).

Three health-related characteristics were evaluated as potential effect modifiers of the relationship between integrated diabetes care programs and HbA1c: fasting blood glucose (FBG), depression and diabetes mellitus (DM) duration. Each characteristic was assessed by one study. Patients with high FBG \((>10\) mmol/L\) at baseline receiving integrated diabetes care had significantly lower HbA1c levels at follow-up compared to patients receiving usual care (Groeneveld et al., 2001). For patients with a FBG \(\leq 10\) mmol/L no significant difference was found in HbA1c levels at follow-up between the intervention and control groups. Depression was not an effect modifier of the association between integrated diabetes care programs and HbA1c (Trief et al., 2006). Patients with a DM duration \(<5\) years receiving integrated diabetes care had significantly lower HbA1c levels...
### Table 2  Study and sample characteristics

| Study characteristics | Sample characteristics | CCM |
|-----------------------|------------------------|-----|
| Study                 | Country     | Study design | Follow-up (months) | n  | Age (SD or range) | Sex (% male) | Description of components |
| Al Omari et al. (2009)| JOR CS      | N/A          | 337                 | 54.1 (11.3) | 52.1 | Regular group counseling with the presence of family physicians, nurses, pharmacists and dieticians. |
| Benoit et al. (2005) | USA RC     | 24           | 573                 | 55.4 (10.1) | 31.3 | Leaflets related to diabetes. |
| Cardenas-Valladolid et al. (2012) | ES PC | 24 | 23488 | 69.7 (14.5) | 48.4 | Interventions focused on drug therapy compliance, change in lifestyle, health education and self-management. |
| De Fine Olivarius et al. (2009) | DK PC | 66 | 581 | 64.7 (55.7–73.2) | 51.9 | Individualized goal setting. |
| Elissen et al. (2012) | NL RC      | 20–24        | 105056              | 65.7 (11.9) | Unknown | National Diabetes Care Standard includes general modules on information, education and self-management support, smoking, cessation, physical activity, nutrition and diet. |
| El-Kebbi et al. (2003) | USA RC    | 5–12         | 2539                | 55.0 (12.0) | 44.0 | Education program emphasizing lifestyle modifications and self-management skills offered to all patients at their initial visit and projects 8 to 8 return visits within the first year. |
| Study characteristics | Sample characteristics | CCM |
|-----------------------|-----------------------|-----|
| Study                 | Country | Study design | Follow-up (months) | n | Age (SD or range) | Sex (% male) | Description of components | Self-management support | Delivery system design | Clinical information systems | Decision support |
| De Alba Garcia et al. (2006) | Mex | CS | N/A | 796 | 60.5 (10.8) | 38.6 | Diabetes and nutrition education Diabetes and exercise support groups | Care team (physicians, nutritionist and psychologist) |
| Groeneveld et al. (2001) | NL | RCT | 12 | I: 91 C: 155 | I: 62.7 (11) C: 62.3 (10) | I: 34.1 C: 46.4 | Counseling by a diabetes educator (nurse) and dietician at the 'Diabetes Service', a monitoring and advisory service | Care team consisting of diabetes educator (nurse), dietician and GP. Patients were called up and reviewed every three months. If insulin was started contacts were more frequent |
| Kellow, Savige and Khalil (2011) | AUS | RC | 60 | 272 | 62.1 (11.6) | 49.0 | Diabetes education at the health service diabetes education department | |
| LeBlanc et al. (2015) | USA | RC | 12 | 14430 | 63 (55.0–76.0) | 52.5 | | Health management Follow-up every three months |
| Liu et al. (2013) | CH | CS | N/A | 960 | 68.3 (10.4) | 39.6 | | Evidence-based treatment guidelines Community diabetes prevention and treatment guidelines provide glycemic control targets |
| Luijks et al. (2015) | NL | PC | 60 | 610 | 63 (12.5) | 48.2 | | Routine three-monthly check-up visits Electronic medical record system |
| Mold et al. (2008) | UK | RC | 11 | 646 | < 50: 16.4% 50–59: 18.3% 60–69: 31.1% ≥ 70: 34.2% | 54.3 | Dietary advice is offered at each consultation | | Electronic medical record system |
| Moreira et al. (2015) | Brazil | RCT | 12 | I: 40 C: 40 | I: 50.0 (6.5) C: 50.3 (7.3) | I: 40 C: 30 | Educational activities focused on providing orientation about physical activities, healthy diet, monitoring capillary glycemia, and acute and chronic complications | Quarterly nursing consultations, bimonthly educational group activities. When necessary referral for a consultation with a primary health-care physician, nurse, nephrologist, pharmacist and nutritionist. Home visits and phone contacts on a monthly basis with the case manager |
| Study characteristics | Sample characteristics | CCM |
|-----------------------|------------------------|-----|
|                       |                        | Description of components |
|                       |                        | Self-management support |
|                       |                        | Delivery system design |
|                       |                        | Clinical information systems |
|                       |                        | Decision support |
| Study | Country | Study design | Follow-up (months) | n | Age (SD or range) | Sex (% male) |
|-------|---------|-------------|--------------------|----|------------------|------------|
| Nielsen et al. (2006) | DK | RCT | 72 | I: 459 C: 415 | Median I: 63.0 (53.8–71.4) C: 63.7 (65.6–71.6) | I: 48.8 C: 52.3 |
| Östgren et al. (2002) | SWE | CS | N/A | 376 | HbA1c < 6.5: 69.6 (10.4) HbA1c ≥ 6.5: 70.9 (9.8) | 50.5 |
| Quah et al. (2013) | SG | CS | N/A | 688 | 62.2 (11.1) | 44.0 |
| Quinn et al. (2016) | USA | RCT | 12 | 118 | Age <55 years: I: 47.3 (6.8) C: 47.5 (7.5) Age ≥ 55 years: I: 59.0 (2.9) C: 59.5 (2.8) | Mobile diabetes management software application, which allowed patient to enter diabetes self-care data on a phone and receive automated, real-time messages that were educational, behavioral, motivational and specific to the entered data |
| Robinson et al. (2009) | USA | PC | 18 | 315 | 64.4 (15.8) | 41.9 |

individualized goal setting
Follow-up every three months
Annual screening for diabetic complications
Annual descriptive feedback reports on individual patients
Clinical guidelines supported by annual half day seminar
Structured education program
Specially trained nurses, supervised by the physician. Team also included a dietician and a podiatrist
Structured treatment program, including annual check-up at hypertension and diabetes outpatient clinic including examinations concerning vision, peripheral sensibility of vibration and peripheral pulsation and laboratory tests
Routine three-monthly visit to polyclinics
Patients could communicate with ‘virtual’ case managers on the phone or electronically
Quarterly online reports that summarized patients’ glycemic and metabolic control, etc.
Clinical guidelines

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| Study characteristics | Sample characteristics | CCM |
|-----------------------|------------------------|-----|
| Study | Country | Study design | Follow-up (months) | n | Age (SD or range) | Sex (% male) | Description of components |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Rothman et al. (2003) | USA | RC | 6 | 138 | 57.0 (23–87) | 41.0 | Population-based quality improvement projects. All patients in the intervention group were targeted for individual coaching in self-management activities by the NP or pharmacy student. Diabetes education: 1-h educational session. Three pharmacists participated in the program. Referrals for ophthalmology, nutrition and podiatry also were suggested to the patient and provided when appropriate. All recommendations discussed with primary care provider. Intensive diabetes management from three clinical pharmacist practitioners and a diabetes care coordinator (DCC). Patients contacted every two to four weeks by telephone or in person by pharmacist or DCC. Application of evidence-based treatment algorithms to help manage glucose and cardiovascular risk. |
| Rothman et al. (2004) | USA | RCT | 12 | I: 98 C: 95 | I low literacy: 57 (10.5) I high literacy: 51 (13.1) C low literacy: 59 (10.4) C high literacy: 56 (10.9) | | One-to-one educational sessions including counseling and medication management. Communication individualized depending on patients literacy status. Nurses provided diabetes education and self-management training. Diabetes education nurses work closely with primary care physicians. Patient registry. Nurses use the registries to guide ‘active outreach’ to high-risk patients not in metabolic control or missing recommended tests. Drug formulary facilitated use of sulfonylureas, metformin, insulin, fibrates and 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors. |
| Sperl-Hillen and O’Connor (2005) | USA | RC | 112 | 5610–7650 | 59–61 | 52–54 | |
| Taweepolcharoen et al. (2006) | TH | CS | N/A | 1510 | 58.8 (10.9) | 34.6 | Group diabetes education supervised by registered nurses and dieticians. Clinic is served by three groups of working physicians, consisting of faculty members, family medicine residents and service GPs. There are also registered nurses and dieticians. |
| Study | Country | Study design | Follow-up (months) | n     | Age (SD or range) | Sex (% male) | CCM |
|-------|---------|--------------|-------------------|-------|------------------|--------------|-----|
| Trief et al. (2006) | USA     | CT           | 12                | 1665  | 70.8 (6.6)       | 37.2         | Self-management support: Nurse case manager provided diabetes education |
|       |         |              |                   |       |                  |              | Delivery system design: Nurse case manager provides, under the supervision of an endocrinologist, treatment planning and consultation to PCPs who maintained decision authority for their patients |
|       |         |              |                   |       |                  |              | Clinical information systems: Intervention subjects received a home telemedicine unit, ie, a web-enabled computer used to upload blood pressure and blood glucose measurements, to videoconference with a nurse case manager and dietician, and to access individualized graphic data displays and educational materials |
|       |         |              |                   |       |                  |              | Decision support: Four visits to the GP per year |
| Uitewaal et al. (2004) | NL      | RC           | 24                | T: 106 D: 90 | T: 50.5 (7.5) D: 55.3 (8.2) T: 43.3 D: 51.1 |
|       |         |              |                   |       |                  |              | Self-management support: Four visits to the GP per year |
|       |         |              |                   |       |                  |              | Delivery system design: Blood glucose and weight are measured at every visit. Other blood measures and feet and eye inspection every year |
|       |         |              |                   |       |                  |              | Clinical information systems: Computer-based patient records |
|       |         |              |                   |       |                  |              | Decision support: Guideline recommending four visits to the GP per year |
| Uitewaal et al. (2005) | NL      | CT           | 12                | I: 53 C: 51 | I: 50.6 (9.3) C: 53.5 (6.2) I: 40 C: 38 |
|       |         |              |                   |       |                  |              | Self-management support: Culturally acceptable and ethnic specific diabetes program for Turkish diabetes patients, consisting of seven individual education sessions and three group sessions |
|       |         |              |                   |       |                  |              | Delivery system design: Individual sessions consisting of four sessions with the educator and patient together and three ‘triangle’ sessions with the GP, educator and patient present, to discuss three-monthly assessment of glycemic control and cardiovascular risk factors |
|       |         |              |                   |       |                  |              | Clinical information systems: Computer-based patient records |

**Table 2 (Continued)**

**Study characteristics**
- **Country**
- **Study design**
- **Follow-up (months)**

**Sample characteristics**
- **n**
- **Age (SD or range)**
- **Sex (% male)**

**CCM**
- **Description of components**

- **Self-management support**
- **Delivery system design**
- **Clinical information systems**
- **Decision support**
| Study | Country | Study design | Follow-up (months) | n   | Age (SD or range) | Sex (% male) | Self-management support | Delivery system design | Clinical information systems | Decision support |
|-------|---------|--------------|-------------------|-----|------------------|-------------|------------------------|------------------------|--------------------------|-------------------|
| Whaba and Chang (2007) | USA | CS | N/A | 136 | 59.7 (15.2) | 51.5 | Individual care plan | Care team (dietitian, DM nurse educator and physician) | Patient prescribed a glucose meter and advised to keep a diary of those readings to share with the physician at each office visit | Plan of care developed specifically for the patient's clinical condition |

CCM = chronic care model; Jor = Jordan; CS = cross-sectional; N/A = not applicable; RC = retrospective cohort; ES = Spain; PC = prospective cohort; DK = Denmark; NL = the Netherlands; Mex = Mexico; RCT = randomized controlled trials; AUS = Australia; CH = China; SWE = Sweden; HbA1c = hemoglobin A1c; SG = Singapore; TH = Thailand; CT = controlled trial; PCP = prospective cohort physician; T = Turkish; D = Dutch; DM = diabetes mellitus
Table 3  Subgroup intervention effects on hemoglobin A1c (HbA1c)

| Variables entered in multivariate regression model | Global quality rating | Person-related characteristics | Context-related characteristics | Health-related characteristics |
|---------------------------------------------------|-----------------------|-------------------------------|--------------------------------|-------------------------------|
| Study                                             |                       | Female | Male | Lower age$^a$ | Higher age$^b$ | Low literacy status | High literacy status | Monthly income $\leq$ $118,26$ | Monthly income $>118,26$ | $\leq$ Four years of schooling | $>$ Four years of schooling | FBG $>10$ mmol/ L | FBG $\leq10$ mmol/ L | Depression Yes | Depression No | DM duration $<5$ years | DM duration $>5$ years |
| Nielsen et al. (2006)                             | Clustering effect at the general practitioner level, interaction between age and baseline HbA1c, DM duration, BMI, number of DM-related consultations, interaction between the patients’ physical activity level, antidiabetic medication and dietary habits | Weak   | –    | o             |               | –                 | o                 | –                   | –                 | –                   | –                   | –                 | –                 | –                 | –                 | –                 |
| Uitewaal et al. (2005)c                           | Baseline HbA1c, sex, age, DM duration, DM medication, indicators of DM care | Weak   | –    | o             |               | –                 | –                 | –                   | –                 | –                   | –                   | –                 | –                 | –                 | –                 | –                 |
| Moreira et al. (2015)                             | Study group, time, age, all two-way interactions and three-way interaction | Weak   | –    | o             |               | –                 | –                 | –                   | –                 | –                   | –                   | –                 | –                 | –                 | –                 | –                 |
| Quinn et al. (2016)                               | N/A                   | Weak   | –    | o             |               | –                 | –                 | –                   | –                 | –                   | –                   | –                 | –                 | –                 | –                 | –                 |
| Rothman et al. (2004)                             | Baseline HbA1c, age, race, sex, income, DM medication, DM duration, income | Weak   | –    | o             |               | –                 | –                 | –                   | –                 | –                   | –                   | –                 | –                 | –                 | –                 | –                 |
| Moreira et al. (2015)                             | N/A                   | Weak   | –    | o             |               | –                 | –                 | –                   | –                 | –                   | –                   | –                 | –                 | –                 | –                 | –                 |
| Groeneveld et al. (2001)                          | N/A                   | Weak   | –    | o             |               | –                 | –                 | –                   | –                 | –                   | –                   | –                 | –                 | –                 | –                 | –                 |
| Trief et al. (2006)                               | Baseline HbA1c, ethnicity, age, sex, marital status, years of education, DM duration, insulin use, smoking, co-morbidity, clustering effect at the general practitioner level | Weak   | –    | o             |               | –                 | –                 | –                   | –                 | –                   | –                   | –                 | –                 | –                 | –                 | –                 |
| Moreira et al. (2015)                             | N/A                   | Weak   | –    | o             |               | –                 | –                 | –                   | –                 | –                   | –                   | –                 | –                 | –                 | –                 | –                 |

DM = diabetes mellitus; BMI = body mass index; N/A: not applicable; FBG = fasting blood glucose.

$a$ Lower age: $\leq 52$ years (Moreira et al., 2015), $<55$ years (Quinn et al., 2016).

$b$ Higher age: $>52$ years (Moreira et al., 2015), $\geq 55$ years (Quinn et al., 2016).

$c$ Intervention and control groups only consisted of patients with a baseline HbA1c $>7%$.

$O$: No significant relationship between the characteristic with HbA1c for people in the intervention group compared to usual care; $-$: significant negative relationship between the characteristic with HbA1c for patients in the intervention group compared to usual care.

DM = diabetes mellitus; BMI = body mass index; N/A: not applicable; FBG = fasting blood glucose. 

$a$ Lower age: $\leq 52$ years (Moreira et al., 2015), $<55$ years (Quinn et al., 2016).

$b$ Higher age: $>52$ years (Moreira et al., 2015), $\geq 55$ years (Quinn et al., 2016).

$c$ Intervention and control groups only consisted of patients with a baseline HbA1c $>7%$.

$O$: No significant relationship between the characteristic with HbA1c for people in the intervention group compared to usual care; $-$: significant negative relationship between the characteristic with HbA1c for patients in the intervention group compared to usual care.
at follow-up compared to patients receiving usual care (Moreira et al., 2015).

No RCTs assessed context-related characteristics as potential effect modifiers of the relationship between integrated diabetes care programs and HbA1c.

Prospective and retrospective cohort studies: In total, 11 prospective and retrospective cohort studies measured the effects of integrated diabetes care programs on HbA1c (Tables 4 and 5). Three studies compared the change in HbA1c between levels of patient characteristics (Rothman et al., 2003; Sperl-Hillen and O’Connor, 2005; Elissen et al., 2012). The other eight studies compared HbA1c levels at follow-up between levels of patient characteristics (El-Kebbi et al., 2003; Benoit et al., 2005; Mold et al., 2008; De Fine Olivarius et al., 2009; Robinson et al., 2009; Kellow et al., 2011; Cardenas-Valladolid et al., 2012; LeBlanc et al., 2015).

Most examined person-related characteristics were age (n = 11) and sex (n = 9). In seven studies the effect of integrated diabetes care programs on HbA1c differed significantly across ranges of age: younger patients had higher HbA1c levels at follow-up compared to older patients (n = 5) and experienced greater change from baseline in HbA1c (n = 2) (El-Kebbi et al., 2003; Benoit et al., 2005; Sperl-Hillen and O’Connor, 2005; Mold et al., 2008; Kellow et al., 2011; Elissen et al., 2012; LeBlanc et al., 2015). As to the latter, the direction of the measured change in HbA1c differed: one study found a significant improvement (Sperl-Hillen and O’Connor, 2005) and the other a significant increase (Elissen et al., 2012) in HbA1c. Age was not a significant effect modifier in the other four studies (Rothman et al., 2003; De Fine Olivarius et al., 2009; Robinson et al., 2009; Cardenas-Valladolid et al., 2012). The effect of integrated care on HbA1c did not differ between men and women in eight studies (El-Kebbi et al., 2003; Rothman et al., 2003; Benoit et al., 2005; Sperl-Hillen and O’Connor, 2005; De Fine Olivarius et al., 2009; Robinson et al., 2009; Kellow et al., 2011; LeBlanc et al., 2015). In one study females had significantly higher HbA1c levels at follow-up compared to males (Cardenas-Valladolid et al., 2012).

Most examined health-related characteristics were medication use (n = 8), baseline HbA1c (n = 7) and duration of type 2 diabetes (n = 6). The effect of integrated diabetes care programs on HbA1c was different for people on insulin therapy. These patients had higher HbA1c levels at follow-up compared with patients on diet and/or oral therapy in five studies (El-Kebbi et al., 2003; Benoit et al., 2005; Mold et al., 2008; De Fine Olivarius et al., 2009; LeBlanc et al., 2015) and less desirable changes in HbA1c from baseline (Sperl-Hillen and O’Connor, 2005). In two studies the relationship between integrated diabetes care programs and HbA1c did not differ between types of medication (Rothman et al., 2003; Kellow et al., 2011). In the studies assessing baseline HbA1c, patients with higher baseline HbA1c levels had higher HbA1c levels at follow-up (n = 3) (El-Kebbi et al., 2003; Benoit et al., 2005; LeBlanc et al., 2015), but did have greater improvements in HbA1c from baseline (n = 3) (Rothman et al., 2003; Sperl-Hillen and O’Connor, 2005; Elissen et al., 2012) compared to patients with lower baseline HbA1c levels. In one study baseline HbA1c was not a significant effect modifier (Kellow et al., 2011). The effect of integrated diabetes care programs on HbA1c differed significantly across ranges of diabetes duration in five studies. Patients with longer diabetes duration had significantly higher HbA1c levels at follow-up compared to patients with shorter diabetes duration (n = 5) (El-Kebbi et al., 2003; Benoit et al., 2005; Mold et al., 2008; Elissen et al., 2012; LeBlanc et al., 2015). In one study a significant opposite effect was found (Rothman et al., 2003).

Health insurance status was assessed by four studies. It did not seem to significantly modify the observed effect of integrated care on HbA1c in three studies (Rothman et al., 2003; Benoit et al., 2005; Robinson et al., 2009). Patients with no health insurance coverage had less desirable changes in HbA1c than those with health insurance coverage (Sperl-Hillen and O’Connor, 2005). No other context-related characteristics were examined by the included studies.

Cross-sectional studies: In total, six cross-sectional studies measured the modifying effect of patient characteristics on the relationship between integrated diabetes care programs and HbA1c (Tables 4 and 5).

Most examined person-related characteristics were age (n = 6), body mass index (BMI) (n = 6) and sex (n = 5). Four studies of integrated care programs found non-significant associations between age and HbA1c (Ostgren et al., 2002;
### Table 4  Relationship between hemoglobin A1c (HbA1c) and person-related and context-related characteristics

| Study                          | Variables entered in multivariate regression model                                                                 | Global quality rating | Socio-demographics | Lifestyle | Context-related characteristic |
|-------------------------------|---------------------------------------------------------------------------------------------------------------------|-----------------------|--------------------|-----------|-------------------------------|
|                               |                                                                                                                     |                       | Age                | Sex       | Ethnicity                    | Marital status | Education | BMI | Smoking | Health insurance |
| Cardenas-Valladolid et al. 2012 | Age, sex, DM medication                                                                                             | Moderate              | o                  | +         |                               |               |           |     |         |               |
| De Fine Olivarius et al. 2009 | Age, sex, BMI, HbA1c baseline, SBP, TC, urinary albumin                                                              | Moderate              | o                  | o         |                               |               |           |     |         |               |
| Benoit et al. 2005            | A1c, time, age, TC, DM duration, Medication                                                                       | Strong                | −                  | o         | o                | o             | d       | o   |         |               |
| Sperl-Hillen and O’Connor 2005 | Age, sex, baseline HbA1c, DM medication, depression, co-morbidities, PC physician variable (age, sex, specialty), diabetes educator visits, pharmacy coverage | Weak                  | +                  | o         |                               |               |           |     |         | f               |
| Elissen et al. 2012           | N/A                                                                   | Weak                  | −                  |           |                               |               |           |     |         | g               |
| El-Kebbi et al. 2003          | Year of presentation, age, sex, ethnicity, BMI, DM duration, baseline HbA1c, DM medication, no. of interval visits, follow-up duration | Strong                | −                  | o         | o     | o | d | n |         |               |
| LeBlanc et al. 2015           | Age, sex, DM duration, DM medication, Charlson co-morbidity index                                                  | Strong                | −                  |           |                               |               |           |     |         |               |
| Kellow, Savige and Khalil 2011 | Age, sex, OGTT, HbA1c, TC, HDL, TG, LDL/HDL ratio, weight change, body weight                                       | Moderate              | −                  |           |                               |               |           |     |         | i               |
| Mold et al. 2008              | N/A                                                                   | Moderate              | −                  | +         | o     | o | e | n |         |               |
| Robinson et al. 2009          | N/A                                                                   | Weak                  | o                  | o         | o     | o | o | o |         |               |
| Rothman et al. 2003           | Age, sex, ethnicity, education, insurance, BMI, HbA1c, DM medication, hypertension medication, hypercholesterolemia medication, recent diagnosis of DM, DM duration | Moderate              | o                  | o         | o     | o | n | o |         | o   |
| Al Omari et al. 2009          | DM medication, DM duration                                                                                          | Weak                  | o                  | o         |                               |               |           |     |         | p               |
| De Alba Garcia et al. 2006    | Age, sex, marital status, education, BMI, smoking, follow diet, glucose, family history of DM, DM duration, DM medication, SBP, DBP, TC, TG | Weak                  | o                  | o         | o | o | q | o | o | f |

**Notes:**
- a: Age
- b: Sex
- c: Ethnicity
- d: Marital status
- e: Education
- f: BMI
- g: Smoking
- h: Health insurance
Table 4 (Continued)

| Study                     | Variables entered in multivariate regression model                                                                 | Global quality rating | Person-related characteristics | Lifestyle | Context-related characteristic |
|---------------------------|-----------------------------------------------------------------------------------------------------------------------|-----------------------|--------------------------------|-----------|--------------------------------|
|                           |                                                                                                                       |                       | Socio-demographics             |           |                                |
|                           |                                                                                                                       |                       | Age                           | Sex<sup>a</sup> | Ethnicity | Marital status<sup>b</sup> | Education | BMI | Smoking | Health insurance |
| Ostgren et al. (2002)     | Age, sex, waist–hip ratio, TG, β-cell function                                                                      | Weak                  | o                             | o<sup>c</sup> | o<sup>d</sup> | o<sup>e</sup> | o<sup>f</sup> | o<sup>g</sup> |
| Quah et al. (2013)        | Age, sex, ethnicity, marital status, occupation, housing type, DM duration, DM medication, compliance to medication, self-monitoring, BMI | Moderate              | – o<sup>h</sup>               | o<sup>i</sup> | o<sup>j</sup> | o<sup>k</sup> | o<sup>l</sup> | o<sup>m</sup> |
| Taweepolcharoen et al. (2006) | Age, sex, DM duration, BMI, BP, fasting glucose, TG, HDL, LDL                                                        | Weak                  | o                             | +<sup>n</sup> | o<sup>o</sup> | o<sup>p</sup> |
| Whaba and Chang (2007)    | Age, DM duration, BMI, DM medication, hypertension, hyperlipidemia                                                   | Moderate              | – o<sup>q</sup>               | o<sup>r</sup> | o<sup>s</sup> | o<sup>t</sup> | o<sup>u</sup> |

BMI = body mass index; DM = diabetes mellitus; SBP = systolic blood pressure; TC = total cholesterol; PC = prospective cohort; N/A = not applicable; OGGT = oral glucose tolerance test; HDL = high-density lipoprotein; LDL = low-density lipoprotein; TG = triglycerides; BP = blood pressure.

<sup>a</sup> 0 = male, 1 = female.
<sup>b</sup> 0 = not married, 1 = married.
<sup>c</sup> 0 = Hispanic, black and white, 1 = Asian.
<sup>d</sup> 0 = current smoker, 1 = past smoker, 2 = never smoker.
<sup>e</sup> 0 = insured, 1 = County Medical Services, 3 = uninsured.
<sup>f</sup> 0 = pharmacy coverage, 1 = no pharmacy coverage.
<sup>g</sup> 0 = current smoker, 1 = none smoker/previous smoker.
<sup>h</sup> 0 = others, 1 = African American.
<sup>i</sup> 0 = non-smoker, 1 = current smoker.
<sup>j</sup> 0 = white, 1 = black Caribbean/African.
<sup>k</sup> 0 = white, 1 = Asian, 2 = black, 3 = other.
<sup>l</sup> 0 = insured, 1 = uninsured.
<sup>m</sup> 0 = black, 1 = others.
<sup>n</sup> 0 = less than high school, 1 = high school or higher.
<sup{o}</sup> 0 = Medicaid or pharmacy assistance programs, 1 = no Medicaid or pharmacy assistance program.
<sup>p</sup> 0 = current smoker, 1 = past and none smoker.
<sup>q</sup> 0 = none, 1 = incomplete primary, 2 = completed primary, 3 = primary.
<sup>r</sup> 0 = smoker, 1 = none smoker.
<sup>s</sup> 0 = Chinese, 1 = Malay, 2 = Indian, 3 = others.
<sup>t</sup> 0 = no formal education, 1 = formal education.
<sup>u</sup> 0 = none smoker, 1 = past smoker, 2 = current smoker.
<sup>v</sup> : positive significant relationship; o- non-significant relationship; –: significant negative relationship.
Table 5  Relationship between hemoglobin A1c (HbA1c) and health-related characteristics

| Study                      | Variables entered in multivariate regression model | Global quality rating | Health-related characteristics | Providers visits | DM duration | Medication\(^a\) | # Co-morbidities |
|----------------------------|---------------------------------------------------|-----------------------|-------------------------------|------------------|-------------|------------------|-----------------|
| **Prospective cohort studies** |                                                   |                       |                               |                  |             |                  |                 |
| Cardenas-Valladolid *et al.* (2012) | Age, sex, DM medication                           | Moderate              |                               |                  |             |                  |                 |
| De Fine Olivarius *et al.* (2009)       | Age, sex, BMI, HbA1c baseline, SBP, TC, urinary albumin | Moderate              |                               |                  |             |                  |                 |
| Benoit *et al.* (2005)                  | A1c, time, age, TC, DM duration, Medication        | Strong                | +                             | o                | o           | o                | +               |
| Sperl-Hillen and O'Connor (2005)        | Age, sex, baseline HbA1c, DM medication, depression, co-morbidities, PC physician variable (age, sex, specialty), diabetes educator visits, pharmacy coverage | Weak                  | +                             | o                | o           | o                | o               |
| Elissen *et al.* (2012)                 | N/A                                               | Weak                  | +                             |                  |             |                  | +               |
| El-Kebbi *et al.* (2003)                | Year of presentation, age, sex, ethnicity, BMI, DM duration, baseline HbA1c, DM medication, no. of interval visits, follow-up duration | Strong                | +                             |                  |             |                  | +               |
| Kellog, Savige and Khalil (2011)        | Age, sex, OGTT, HbA1c, TC, HDL, TG, LDL/HDL ratio, weight change, body weight | Moderate              | o                             | o                | o           | o                | o               |
| LeBlanc *et al.* (2015)                 | Age, sex, DM duration, DM medication, Charlson co-morbidity index | Strong                | +                             |                  |             |                  | +               |
| Mold *et al.* (2008)                    | N/A                                               | Moderate              | o                             |                  |             |                  | +               |
| Robinson *et al.* (2009)                | N/A                                               | Weak                  | o                             |                  |             |                  | +               |
| Rothman *et al.* (2003)                 | Age, sex, ethnicity, education, insurance, BMI, HbA1c, DM medication, hypertension medication, hypercholesterolemia medication, recent diagnosis of DM, DM duration | Moderate              | +                             |                  |             |                  | -               |

\(^a\) Medication includes HbA1c control, hypertension, cholesterol.
| Study                        | Variables entered in multivariate regression model                                      | Global quality rating | Health-related characteristics | Cross-sectional studies | DM duration | Medication\(^a\) | # Co-morbidities |
|-----------------------------|----------------------------------------------------------------------------------------|----------------------|-------------------------------|-------------------------|-------------|------------------|-----------------|
| Al Omari et al. (2009)      | DM medication, DM duration                                                             | Weak                | HbA1c | SBP | DBP | TC | HDL | LDL | TG | # Providers visits |                | +               | +               |
| De Alba Garcia et al. (2006) | Age, sex, marital status, education, BMI, smoking, follow diet, glucose, family history of DM, DM duration, DM medication, SBP, DBP, TC, TG | Weak                | o     | o   | o   | o   | o   | o   | o   | o       | +               | +               |
| Ostgren et al. (2002)       | Age, sex, waist–hip ratio, TG, \(\beta\)-cell function                                | Weak                | −     | −   | o   | +   |     |     |     | o       |                |                 |
| Quah et al. (2013)          | Age, sex, ethnicity, marital status, occupation, housing type, DM duration, DM medication, compliance to medication, self-monitoring, BMI | Moderate            | +     | +   | o   |     |     |     |     |               |                 |
| Taweepolcharoen et al. (2006) | Age, sex, DM duration, BMI, BP, fasting glucose, TG, HDL, LDL                           | Weak                | o     | o   | o   | o   |     |     |     | o       |                |                 |
| Whaba and Chang (2007)      | Age, DM duration, BMI, DM medication, hypertension, hyperlipidemia                     | Moderate            | o     | o   | o   | o   |     |     |     | o       |                |                 |

SBP = systolic blood pressure; DBP = diastolic blood pressure; TC = total cholesterol; HDL = high-density lipoprotein; LDL = low-density lipoprotein; TG = triglycerides; DM = diabetes mellitus; PC = primary care; OGTT = oral glucose tolerance test; N/A = not applicable; BMI = body mass index; BP = blood pressure.

+ : positive significant relationship; o: non-significant relationship; − : significant negative relationship.

\(^a\) 0 = no insulin, 1 = insulin.
De Alba Garcia et al., 2006; Taweepolcharoen et al., 2006; Al Omari et al., 2009). In two studies significant associations were found: in these studies, younger patients had higher HbA1c levels (Wahba and Chang, 2007; Quah et al., 2013). The effect of integrated diabetes care programs on HbA1c did not significantly differ between levels of BMI in all studies (Ostgren et al., 2002; De Alba Garcia et al., 2006; Taweepolcharoen et al., 2006; Wahba and Chang, 2007; Al Omari et al., 2009; Quah et al., 2013). The effect on HbA1c did also not differ between men and women in four studies (De Alba Garcia et al., 2006; Wahba and Chang, 2007; Al Omari et al., 2009; Quah et al., 2013). In one study females had significantly higher HbA1c levels compared to males (Taweepolcharoen et al., 2006).

Most examined health-related characteristics were duration of type 2 diabetes ($n = 6$) and medication use ($n = 4$). The effect of integrated care programs on HbA1c differed significantly across ranges of diabetes duration in four studies (De Alba Garcia et al., 2006; Taweepolcharoen et al., 2006; Al Omari et al., 2009; Quah et al., 2013). Patients with longer diabetes duration had higher HbA1c levels compared to patients with shorter diabetes duration in these studies. In two studies diabetes duration was not a significant effect modifier (Ostgren et al., 2002; Wahba and Chang, 2007). The effect of integrated care programs on HbA1c was also different for people on insulin therapy. These patients had higher HbA1c concentrations compared with patients on diet and/or oral therapy in three studies (De Alba Garcia et al., 2006; Al Omari et al., 2009; Quah et al., 2013). In one study type of medication was not a significant effect modifier (Wahba and Chang, 2007).

No context-related characteristics were assessed by three or more studies.

**LDL-c**

Three prospective and retrospective cohort studies measured the effect of integrated diabetes care programs on LDL-c. The RCTs and cross-sectional studies included in this review did not measure this effect. In total, 11 patient characteristics were assessed by the studies. Only those results that were assessed by at least two studies will be discussed.

Prospective and retrospective cohort studies: The person-related characteristic age was examined by three studies (Sperl-Hillen and O’Connor, 2005; Robinson et al., 2009; Elissen et al., 2012). The relationship between age and LDL-c was inconsistent: a negative and positive as well as a non-significant relationship were found.

The modifying effect of baseline LDL-c on the relationship between integrated diabetes care programs and changes in LDL-c over baseline was assessed by two studies (Sperl-Hillen and O’Connor, 2005; Elissen et al., 2012). Both found that patients with higher baseline LDL-c had greater LDL-c improvements.

No context-related characteristics were assessed by the included studies.

**SBP**

Four retrospective and prospective cohort studies measured the effect of integrated diabetes care programs on SBP. In total, nine patient characteristics were assessed by the studies. Only those results that were assessed by at least two studies will be discussed.

Retrospective cohort and prospective cohort studies: Age was measured by three studies (Mold et al., 2008; Robinson et al., 2009; Elissen et al., 2012). These studies found that higher age was associated with higher SBP at follow-up (Mold et al., 2008; Robinson et al., 2009) and greater improvement (Elissen et al., 2012). The modifying effect of ethnicity on integrated care programs and SBP was measured by two studies (Mold et al., 2008; Robinson et al., 2009). The effect was unclear, as results were inconsistent between these studies. Four other characteristics were assessed, one context-related and three health-related characteristics, by one study each.

**Health-care utilization**

Health-care utilization was assessed by three studies: one RCT (Nielsen et al., 2006), one retrospective cohort study (Uitewaal et al., 2004) and one cross-sectional study (Liu et al., 2013). Together they measured the modifying effect of integrated care programs and health-care utilization for five person-related characteristics, one context-related characteristic and one health-related characteristic. Most examined characteristic was sex, which was measured by two studies (Nielsen et al., 2006; Liu et al., 2013). Nielsen et al. (2006)
found that females in the intervention group had statistically significant more GP consultations per year compared to females in the control group (Nielsen et al., 2006). For males, no difference was found. Liu et al. found that the effect of integrated diabetes care programs on health-care utilization was different between males and females (Liu et al., 2013). Females had higher utilization of community health centers compared to male.

Discussion

This paper presents a literature review on relevant patient characteristics for guiding tailored integrated type 2 diabetes care in primary care. HbA1c was considered an outcome in 93% of the 27 studies identified. Many different patient characteristics were investigated by these studies. Findings indicate that the effect of integrated primary care programs on HbA1c differs significantly according to a number of person and health-related characteristics. Younger age, longer disease duration, higher baseline HbA1c and insulin therapy were associated with higher HbA1c levels. Health insurance status, living situation and income were the only context-related characteristics in the included studies and were not frequently assessed.

Compared to HbA1c, LDL-c, SBP and health-care utilization were included far less. It was found that higher baseline LDL-c lead to greater LDL-c improvement. Patients with higher age had higher SBP levels at follow-up as well as greater improvements in SBP compared to younger patients. The relationship between integrated care and health-care utilization seemed to be modified by sex: women had more consultations per year compared to men.

Several factors might explain the elevated HbA1c levels in a subset of patients with type 2 diabetes. Younger patients tend be more non-adherent to oral medication therapy and experience less profound diabetes-related health problems than older patients (Pyatak et al., 2014; Tunceli et al., 2015). The latter might cause them to believe that a proactive attitude toward their disease is less important. Moreover, younger patients and/or those with longer disease duration undergo a more rapid decline in β cell function and pancreatic insulin secretion, resulting in the need for a more complex and intensive drug therapy (Al Omari et al., 2009; Fonseca, 2009; Khattab et al., 2010; Kellow et al., 2011). Higher HbA1c levels for patients on insulin therapy compared to patients on diet and/or oral therapy could be due to a delayed start or low intensity of insulin therapy (Abraira et al., 1995; El-Kebbî et al., 2003; Mosenzon and Raz, 2013). Furthermore, maintaining glycemic control, while minimizing hypoglycemia and sticking to a diet might be difficult (Jin et al., 2008; Quah et al., 2013).

High HbA1c at baseline also seemed to be predictive of later HbA1c. First, type 2 diabetes is a heterogeneous disease in both pathogenesis and clinical manifestation (Inzucchi et al., 2012), thus a high HbA1c at baseline and at follow-up could be due to decreased insulin sensitivity, secretion and β-cell dysfunction (Heianza et al., 2012). Second, unhealthy lifestyle habits, such as low physical activity, and a diet rich in carbohydrates have been associated with less glycemic control (Mozaffarian et al., 2009; Inzucchi et al., 2012). Changing these lifestyle factors is easier said than done, making it difficult for patients to improve their glycemic control.

Several factors could explain the differences in levels of LDL-c, SBP and health-care utilization between levels of patient characteristics. Prescription of statins usually follows when LDL-c level is 2.5 mmol/L or higher, possibly leading to greater improvements in LDL-c for those patients with high baseline LDL-c levels (The Dutch college of general practitioners, 2011). The higher SBP levels at follow-up for older patients may be due to less stringent treatment targets (van Hateren et al., 2012; James et al., 2014). The greater health-care utilization by women compared to men might be explained by the difference in perception of illness between men and women. According to some studies, it is more culturally and socially accepted for women to be ill than it is for men (De Visser et al., 2009).

Overall, our results indicate the need to implement integrated diabetes care programs specifically tailored to the needs, values and preferences of younger patients and to those on insulin therapy, with longer disease duration and/or higher HbA1c levels and older patients with high SBP levels. These effect modifiers can help to provide the right care to the right person at the right time. At this moment, not every patient with
these characteristics receives such care. Current practice might therefore not be suitable for all patients. Lack of motivation, family support and feeling burned-out from managing diabetes are reported barriers to optimal self-management (Browne et al., 2013). To tackle these barriers, diabetes treatment programs should take them into account by, for example, providing shared decision making and simple and specific instructions and advice, involving family members and offering online consultations or evening primary care opening hours. In addition to patients who find it difficult to keep their diabetes under control, there is a large group of patients who does manage to control their diabetes (Rothe et al., 2008; Elissen et al., 2012). For these patients, fewer visits to primary care might have similar outcomes and thus should be taken into consideration by both the GP and the patient. Allowing care givers to provide care based on patient characteristics constitutes a promising approach for achieving the so-called ‘Triple Aim’ by: (1) improving patient experience, by including patients’ care needs, preferences, and abilities in treatment decisions; (2) improving population health and quality of life, by supporting tailored diabetes care; and (3) reducing the per capita cost of diabetes care, by reducing the over-, under- and misuse of health-care services (Berwick et al., 2008).

This review has several limitations that should be taken into account. First, given the scarceness of studies assessing the differences in the effect of integrated diabetes care programs on diabetes control measures by levels of patient characteristics, it was decided to include RCTs, prospective and retrospective cohort studies. However, this introduced significant heterogeneity and made it impossible to conduct a meta-analysis. Second, quality of the studies was weak for most studies. This was mainly due to the cross-sectional study design of more than one-third of the studies and the use of less robust statistical methods. Fortunately, it is unlikely that these studies altered the results, as their findings were similar to those of the other, more robust studies. Third, very few context- and person-related characteristics were analyzed. Studies performed in a non-integrated diabetes care setting, found that context-related characteristics, such as socio-economic status and social network, are associated with measures of diabetes control and are likely to be strong predictors of diabetes control (Jotkowitz et al., 2006; Nam et al., 2011). Person-related characteristics, such as low mastery and low self-efficacy, have been related to negative health outcomes (Bosma et al., 2014; Elissen et al., 2017). Traditionally, researchers and care providers have looked at diabetes from a mostly biomedical viewpoint, which might explain the relatively scarce collection of context- and person-related characteristics in routinely collected individual patient data (Hasnain-Wynia and Baker, 2006).

The current review provides a good understanding of which characteristics can help to identify patients with different health-care needs and preferences. However, to implement an effective integrated type 2 diabetes tailored care program, it is necessary to know which context- and person-related characteristics are important to identify patients. Furthermore, implementation of an effective tailored diabetes care program is only possible by taking into account the care preferences of patients and caregivers. In the next phase of the PROFILE project (Elissen et al., 2016), data rich in non-health-related characteristics will be analyzed to assess which of these are predictors of diabetes control measures and a discrete choice experiment will be conducted to gain knowledge on patients’ care preferences as a first step toward patient-centered diabetes care.

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Conflicts of interest
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