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Keypoints

- There is generally low adherence of both people with type 2 diabetes (T2DM) and care providers to recommended treatment guidelines.
- Current opinion advocates a multidisciplinary approach to the treatment of T2DM. This includes system support to encourage use of evidence-based guidelines, reorganization of practice systems and team functions, support for patient self-management, improved access to expertise, and enhanced availability of clinical information to facilitate monitoring and feedback on physicians' performance.
- The key elements of quality diabetes care delivered by a multidisciplinary team include periodic risk stratification, protocol-driven care with regular review, patient empowerment, treatment-to-target, and good record keeping to monitor clinical progress and outcomes.

Introduction

According to the World Health Organization (WHO), four chronic non-communicable diseases – diabetes, cancer, respiratory and cardiovascular diseases (CVD) – account for 60% of global deaths (i.e. 35 million deaths per year) [1]. In Europe and China, 30–40% of patients with acute myocardial infarction have a known history of diabetes. In the remaining subjects, 70% of patients have either diabetes or intermediate hyperglycemia on formal 75-g oral glucose tolerance testing [2,3]. In addition, diabetes and hypertension frequently coexist. Both are important considerations in the majority of cardiovascular deaths worldwide, which are estimated to be 18 million annually. The number of people with diabetes is projected to increase from 285 million in 2010 to 435 million by 2030 [4]. The resulting increase will lead to considerable losses in productivity as well as greatly increasing the burden on health care systems.

Treatment of diabetes and associated complications is costly. In 2006, the WHO estimated that in both developing and developed areas, 2.5–15% of health care budgets were spent on diabetes-related illnesses. The International Diabetes Federation (IDF) also estimated that 7–13% of annual health care expenditure was spent on treatment of diabetic complications [5]. The total direct annual costs of diabetes in eight European countries were estimated at €29 billion, with an estimated yearly cost of €2834 per patient [6]. In the USA, diabetes is associated with an annual direct medical expenditure of \$91.8 billion. The per capita cost was estimated to be \$13 243 for individuals with diabetes com-

pared to \$2560 for those without [7]. In China, one of the countries with the most rapid increase in diabetes prevalence, \$558 billion in national income is expected to be lost over the next 10 years as a result of premature deaths caused by non-communicable diseases including heart disease, stroke and diabetes [8].

Early diagnosis and aggressive control of risk factors can prevent complications in both type 1 (T1DM) and type 2 diabetes mellitus (T2DM) [9–11]. International organizations such as the IDF, as well as many national organizations, have published clinical recommendations and set standards to guide clinical practice, in order to optimize metabolic control and prevent complications [12].

Evidence for optimization of diabetes control

To date, most evidence supporting the beneficial effects of optimal diabetes care on clinical outcomes [10,13,14] were collected under closely supervised clinical trial conditions. In the Diabetes and Complications Clinical Trial (DCCT), which lasted for 6.5 years, patients with T1DM treated intensively had an HbA_{1c} level 2% (22 mmol/mol) lower than those who were conventionally treated (7.2% vs 9.1%, 55 vs 76 mmol/mol). After the study was completed, the authors continued to follow these patients in the Epidemiology of Diabetes Interventions and Complications (EDIC) study. There was progressive deterioration in glycemic control once these intensively treated patients returned to their usual care setting; however, patients previously treated conventionally also improved, and both groups converged to achieve HbA_{1c} levels of 8% (64 mmol/mol) [15]. Despite this convergence, patients previously treated intensively maintained over 50% risk reduction in all diabetes-associated complications, including cardiovascular events [16].

Similar findings have also been reported following the post-UK Prospective Diabetes Study (UKPDS). People with T2DM who were previously treated with an intensive regimen continued to have lower rates of complications and all-cause mortality than patients treated conventionally, 10 years after discontinuation of the trial [17]. In the Steno-2 Study, individuals were treated intensively in an attempt to attain control for all major risk factors (HbA_{1c}, blood pressure [BP] and low density lipoprotein [LDL] cholesterol), and had 50–60% risk reduction in microvascular and macrovascular complications compared with those conventionally treated [18]. As in the DCCT and UKPDS, in the post-Steno Study period, people who had been treated intensively in the main trial maintained more than 60% risk reduction in all-cause death compared with those conventionally treated for 13.3 years [19]. Findings from these landmark studies clearly demonstrate the beneficial effects of achieving risk factor control during the early course of disease to achieve long-term benefits.

Diabetes care – the reality

Despite the evidence, national and international surveys have indicated that diabetes management remains suboptimal, regardless of the studied populations and health care settings. It should also be remembered that most of these recommendations, guidelines, surveys and studies emanate from settings, countries and areas that are relatively well-resourced.

According to the National Health and Nutritional Examination Surveys (NHANES), conducted between 1988–1994 and 1999–2002 in the USA, amongst patients with diabetes aged 18–75, although there was a non-significant reduction in the proportion of patients with HbA_{1c} >9% (>75 mmol/mol), since the numbers of patients with HbA_{1c} 6–8% (64–86 mmol/mol) increased, there was no significant change in mean HbA_{1c} between these intervals [20]. In the 1999–2002 survey, there was increased use of multiple antidiabetic agents for control [21], yet nearly half continued to have HbA_{1c} levels greater than the American Diabetes Association (ADA) recommendation, of 7% and 20% had HbA_{1c} >9% (>75 mmol/mol).

There was also no significant change in the distribution of blood pressure, 33% having BP >140/90 mmHg. In the 1999–2002 survey, 60% achieved LDL cholesterol concentrations of <3.4 mmol/L and received annual screening for eye and foot complications. The levels of care were noted to be suboptimal, especially in females and in those under the age of 45 years [22,23]. Thus, between these surveys, some improvements were documented but many problems remained.

Tables 57.1–57.3 summarize the adequacy of glycaemic, blood pressure and lipid control in various settings during the last two decades. Despite much data, there has been little change in average values attained or percentage of patients reaching treatment goals.

Table 57.1 summarizes adequacy of glycaemic control from the 1988–1994 NHANES, up to the latest International Diabetes Management Practice Study (IDMPS) conducted in 2005 [24].

The latter is a 5-year survey documenting changes in diabetes treatment practice in developing regions including Asia, Eastern Europe and Latin America. It shows that only 37% of people with T2DM achieved HbA_{1c} ≤7% (53 mmol/mol). The results were similar in both developed and low and middle income countries [14,21,24–26], different health care settings, primary care [27–32] and specialist centers [33–36].

Table 57.2 summarizes adequacy of blood pressure control in the same period. The blood pressure target in earlier years was 140/90 mmHg, when approximately 40–60% of people with T2DM achieved target [14,29,37]. There was a tendency to improvement in the study conducted by the Department of Veteran Affairs in the USA. In this study, conducted between 1996 and 2000, the proportion of people with T2DM achieving the target blood pressure increased from 40% to 52% [30]. The DiabCare studies in Asia demonstrated that over 70% and 90% of people with T2DM were able to achieve the target of systolic and diastolic blood pressure of ≤140 and ≤90 mmHg, respectively [34]. Emerging evidence of the importance of blood pressure control led to the target blood pressure being revised to <130/80 mmHg. This is not accompanied by further improvement in terms of rate of achievement of targets. Recent studies in different countries and settings showed that only half of people with T2DM were able to achieve the target of 130/80 mmHg [24,26,31,33].

With regard to lipid control (Table 57.3), there was a slow but gradual improvement, probably because of the availability of effective treatment of LDL cholesterol with 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase inhibitors. In the 1980s and early 1990s, the rate of achievement of target LDL cholesterol <2.6 mmol/L was around 10–15% [14,37]. This had increased to approximately 25–30% subsequently [24,27,29,31,33]. For those on HMG-CoA reductase inhibitors, as illustrated from a study in Sweden, nearly half of patients were able to achieve the target [26].

There are obvious limitations in these studies including heterogeneity of populations in different studies, retrospective reviews, incomplete documentation for medical record review and inaccuracy for claims data. Despite the limitations and lack of comparability of the many studies, the results summarized in Tables 57.1–57.3 indicate the same trend. It should also be noted that, most of these surveys come from well-resourced settings and developed countries, where laboratory assessment for HbA_{1c} is readily available.

The Institute of Medicine has defined quality of care as “the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge” [38,39]. There is ongoing controversy as to the degree to which outcomes can be directly related to processes of care, yet both are considered as important measures of quality. Thus, the degree of adherence to recommended guidelines, based on available clinical evidence, provides guidance to the degree of quality of care. Table 57.4 summarizes attempts to address this issue specifically and includes surveys that assess quality of care as measured by frequency of measurement for HbA_{1c}. In early years, less than one-third of patients received HbA_{1c} monitoring [14,40,41]. Since the early

Table 57.1 Adequacy of glycemic control in various health care settings in patients with type 1 (T1DM) and type 2 diabetes mellitus (T2DM).

Health care setting	Number of patients	Survey year	Method	Findings	Reference
Population-based (US NHANES III and BRFSS)*	4085	1988–1995	Patient survey, clinical examination	42.9% had HbA _{1c} <7% (53 mmol/mol) 18.0% had HbA _{1c} >9.5% (80 mmol/mol)	[14]
Primary care (Netherlands) and managed care organization (USA)	2498 (379 patients from the Netherlands and 2119 patients from USA)	1992–1997	Medical record review and administrative data	In 1996, 43.1% vs. 16.8% of patients had HbA _{1c} <7% (53 mmol/mol); and 85.6% vs 56.7% had HbA _{1c} ≤8.5% (69 mmol/mol) in Netherlands and USA, respectively	[27]
Population survey (USA)	1480	1995	Patient survey, clinical examination	Mean HbA _{1c} 7.6% (60 mmol/mol); 44.6% had HbA _{1c} <7% (53 mmol/mol), 37.1% >8% (64 mmol/mol)	[25]
Community health center (USA)	2865	1995	Medical record review	Mean HbA _{1c} 8.6% (70 mmol/mol) 39% of patients had HbA _{1c} ≤8.0% (64 mmol/mol)	[28]
Primary care (USA)	9557–9985	1995–1997	Medical record review	34–42% with HbA _{1c} >9.5% (80 mmol/mol)	[29]
Veterans' Affairs (USA)	9578 (in 1995) to 25 764 (in 2000)	1995–2000	Medical record review and administrative data	72%, 82% and 87% had HbA _{1c} <10% (86 mmol/mol) from 1995–1998, 59% and 62% had HbA _{1c} <8% (64 mmol/mol) in 1999 and 2000	[30]
Diabetes clinic, general medical (resident) clinic and university (faculty) clinic (USA)	6386	1995–2005	Clinical examination	43.7% of type 2 diabetes had HbA _{1c} <7% (53 mmol/mol)	[33]
Primary care and hospital outpatient clinics (Sweden)	17 547 T2DM in 1996 and 57 119 in 2003	1996 and 2003	Medical record review and administrative data	Mean HbA _{1c} was 7.8% (62 mmol/mol) in 1996 and 7.2% (55 mmol/mol) in 2003. 16% of patients had HbA _{1c} <6.5% (48 mmol/mol) in 2003	[31]
Primary care (UK)	18 642	1997	Questionnaire survey and audit data	42.9% with HbA _{1c} within normal range of local laboratory	[32]
National Diabetes Registry (Sweden)	9424 T1DM in 1997 and 13 612 T2DM in 2004	1997 and 2004	Medical record review	Mean HbA _{1c} was 8.3% (67 mmol/mol) in 1997 and 8% (64 mmol/mol) in 2004 17.4% and 21.1% had HbA _{1c} <7% (53 mmol/mol) respectively in 1997 and 2004	[26]
Primary care and hospital outpatient clinics (Asia)	24 317 T2DM in 230 centers	1998	Medical record review and patient interview	Mean HbA _{1c} was 8.6% (70 mmol/mol) in 18 211 patients, 21% had HbA _{1c} <7% (53 mmol/mol)	[34]
Primary care and hospital outpatient clinic (China)	2246 T2DM in 1998 and 2702 in 2006	1998 and 2006	Medical record review	Mean HbA _{1c} was 8.7% (72 mmol/mol) in 1998 and 7.6% (60 mmol/mol) in 2006	[35]
Population-based survey (US NHANES)	15 332 participants, 16.8% diabetes	1999–2004	Patient interview and administration data	52.2% had HbA _{1c} <7% (53 mmol/mol)	[21]
Specialist pediatric center in Western Pacific Region	2312 T1DM	2001–2002	Medical record review	Mean HbA _{1c} was 8.3% (67 mmol/mol)	[36]
Primary care and specialist center (Asia, Eastern Europe and Latin America)	11 799	2005–2010	Medical record review	Mean HbA _{1c} was 8.3% (67 mmol/mol) in 1898 patients with T1DM, 25.3% had HbA _{1c} ≤7% (53 mmol/mol); Mean HbA _{1c} was 7.8% (62 mmol/mol) in 9901 patients with T2DM, 36.4% had HbA _{1c} ≤7% (53 mmol/mol); % of patients achieved HbA _{1c} ≤7% (53 mmol/mol) by ethnic group (Asia, Eastern Europe, Latin America) was 21.0 vs 31.3 vs 21.1 in T1DM and 37.3 vs 36.0 vs 36.0 in T2DM	[24]

BRFSS, Behavioral Risk Factor Surveillance System; NHANES III, Third National Health and Nutrition Examination Survey.

Interpretation of the adequacy of glycemic control is affected by the laboratory methods used and the corresponding reference range, which might vary across studies. For simplicity, the table only describes the absolute values cited in the original papers, and direct comparisons between studies may not be valid.

Table 57.2 Adequacy of blood pressure control in various health care setting in type 1 (T1DM) and type 2 diabetes (T2DM).

Health care setting	Number of patients	Survey period	Method	Findings	Reference
Population-based (US NHANES III and BRFSS)	4085	1988–1995	Patient survey, clinical examination	65.7% had BP <140/90*	[14]
Population-based (US NHANES III)	733	1991–1994	Patient survey, clinical examination	59% of the hypertensive patients had BP >140/90	[37]
Primary care (USA)	9557–9985	1995–1997	Medical record review	64–66% had BP <140/90	[29]
Veterans Affairs (USA)	9578 (in 1995) to 25 764 (in 2000)	1995–2000	Medical record review and administrative data	40%, 44%, 45% and 52% has BP <140/90 (if hypertensive) from 1996–2000	[30]
Diabetes clinic, general medical (resident) clinic and university (faculty) clinic (USA)	6386	1995–2005	Clinical examination	36.7% of T2DM had BP ≤130/80	[33]
Primary care and hospital outpatient clinics (Swedish)	17 547 T2DM in 1996 and 57 119 in 2003	1996 and 2003	Medical record review and administrative data	Mean BP was 150/82 in 1996 and 143/78 in 2003. 13% of patients had BP <130/80 in 2003	[31]
National Diabetes Registry (Swedish)	9424 T1DM in 1997 and 13 612 T1DM in 2004	1997 and 2004	Medical record review	61.3% had BP ≤130/80 in 2004	[26]
Primary care and hospital outpatient clinics (Asia)	24 317 T2DM in 230 centers in Asia	1998	Medical record review and patient interview	Mean BP was 135/81; with 27% had systolic BP >140 and 10% had diastolic BP >90	[34]
Primary care and specialist center (Asia, Eastern Europe and Latin America)	11 799	2005–2010	Medical record review	44.9% T1DM and 19.2% T2DM patients had BP ≤130/80. By ethnic group (Asia, Eastern Europe and Latin America) was 47.4 vs 43.8 vs 44.1 in T1DM and 21.8 vs 20.1 vs 22.1 in T2DM	[24]

BRFSS, Behavioral Risk Factor Surveillance System; BP, blood pressure; NHANES III, Third National Health and Nutrition Examination Survey.

* BP is expressed in mmHg.

1990s, with the availability of results from the DCCT and UKPDS, the frequency of monitoring has gradually improved [27–29,42–44]. Recently, more than 90% of patients have HbA_{1c} regularly monitored in specialist clinics such as the Steno Diabetes Center [45] and in some primary care settings [30,46]. Elsewhere, monitoring is available in 70–80% of patients [24,32,47].

It is important to note that there is often a discrepancy between doctors' claims of frequency of monitoring and that occurring in practice. Although there appears to have been some improvements in the care processes over time, this has not been matched by improvement in rates of achieving treatment targets (Tables 57.1–57.3).

Discrepancy between evidence-based care and reality

The efficacy of optimization of diabetes control has been confirmed in randomized controlled trials conducted with stringent clinical trial protocols; however, despite improvements in some processes of care such as monitoring of HbA_{1c}, this has not been matched by improvement in rates of achieving treatment targets.

In addition, the level of care received by many patients does not meet recommended standards. In a previous survey in USA, only 25% of patients were aware of the term “glycated hemoglobin” or “HbA_{1c}” [43]. Only 72% of the subjects visited a health care provider for diabetes care at least once a year, and approximately 60% received complication screening. Furthermore, despite the proven benefits of many therapeutic agents, many people with diabetes were not prescribed insulin, angiotensin-converting enzyme (ACE) inhibitors or lipid-lowering drugs despite the presence of indications [48–53].

The factors that compromise quality of care have been examined in various studies, but have not been well understood. Nevertheless, some components are obvious.

Patients

Drug compliance by patients receiving chronic medications is consistently reported to be less than 50%, often because of insufficient education and reinforcement [54–56]. Moreover, there is considerable heterogeneity in the patterns and rates of non-adherence to individual components (e.g. diet, exercise, drugs) of a diabetes treatment regimen. Thus, the extent to which people with diabetes adhere to one aspect of the regimen might not cor-

Table 57.3 Adequacy of lipid control in various health care setting in type 1 (T1DM) and type 2 diabetes (T2DM).

Health care setting	Number of patients	Survey period	Method	Findings	Reference
Population-based (US NHANES III and BRFSS)	4085	1988–1995	Patient survey, clinical examination	11.0% had LDL <2.6, 42.0% had LDL <3.4	[14]
Population-based (US NHANES III)	733	1991–1994	Patient survey, clinical examination	15.4% had LDL <2.6, 49.3% had LDL <3.4, 58.4% had TG <2.3. 41% of those known to have dyslipidemia had LDL <3.4	[37]
Primary care (Netherlands) and managed care organization (USA)	2498 (379 patients from Netherlands and 2119 patients from USA)	1992–1997	Medical record review and administrative data	In 1996, 23.1% vs. 40.4% of patients had total cholesterol <5.2 in Netherlands and USA, respectively	[27]
Primary care (USA)	9557–9985	1995–1997	Medical record review	48–52% had TC <5.2, with median TG 2.2	[29]
Veterans Affairs (USA)	9578 (in 1995) to 25 764 (in 2000)	1995–2000	Medical record review and administrative data	62%, 68%, 72% and 76% has LDL <3.4 from 1996–2000	[30]
Diabetes clinic, general medical (resident) clinic and university (faculty) clinic	6386	1995–2005	Clinical examination	28.6% of T2DM had LDL <2.6	[33]
Primary care and hospital outpatient clinics (Swedish)	17 547 T2DM in 1996 and 57 119 in 2003	1996 and 2003	Medical record review and administrative data	28% of patients in 2003 had TC <4.5 mmol/L	[31]
National Diabetes Registry (Swedish)	9424 T1DM in 1997 and 13 612 T1DM in 2004	1997 and 2004	Medical record review	Among those on LLD, 48% had LDL <2.5 mmol/L	[26]
Primary care and specialist center (Asia, Eastern Europe and Latin America)	11 799	2005–2010	Medical record review	39.5% T1DM and 33.2% T2DM had LDL <100 mg/dL; 73.1% T1DM and 49.0% T2DM had TG <150 mg/dL	[24]

BRFSS, Behavioral Risk Factor Surveillance System; LDL, low density lipoprotein cholesterol; LLD, lipid lowering drugs; NHANES III, Third National Health and Nutrition Examination Survey; TC, total cholesterol; TG, triglycerides.

All lipid values in mmol/L unless otherwise stated.

Interpretation of the adequacy of dyslipidemia treatment is affected by the laboratory methods used and thus the corresponding reference range might vary across studies. For simplicity, the table only describes the absolute values cited in the original papers, and direct comparisons between studies may not be valid.

relate with their adherence to other components. Previous studies have shown that only 69% of people with diabetes follow a diet and less than half engage in regular exercise [57]. The reported adherence to self-monitoring of blood glucose ranges from 53% to 70% [58]. Earlier studies have indicated that only 7% of patients with diabetes adhere to all aspects of the treatment regimen [59], while over half made errors with insulin dosage and three-quarters of patients were judged to be in an “unacceptable” category regarding the quality, quantity and timing of meals [60].

In attempts to extrapolate results from clinical trials to daily practice, it is important to individualize interventions taking into account all potential factors. For example, in the elderly, side effects of interventions must be balanced against long-term benefits, limited life expectancy and co-morbidities. Other factors such as education level, access to care, compliance and motivation may also contribute to patient adherence, in addition to treatment-related factors such as adverse effects, polypharmacy and cost [42,43,49]. It is recommended that people with diabetes should be educated about the nature of the disease with particular focus on chronicity and long-term complications, as well as preventability.

Physicians

The key role of health care providers is to equip people with diabetes with knowledge and skills related to self-management, to individualize medical and behavioral regimens, to assist with informed decisions, and provide social and emotional support via a collaborative relationship [61,62]. An important factor is the inertia of physicians in failing to modify the management of patients in response to an abnormal clinical result [63,64]. In a previous study by Kaiser Permanente, one of the major health management organizations in USA, there was on average 15 months and 21 months lapse before escalation of treatment in patients with HbA_{1c} of >8% (64 mmol/mol) on metformin and sulfonylurea monotherapy, respectively [65]. Despite the complexity and rapid advances in diabetes management, generalists often did not perceive the need for further training in the field of diabetes [66–69]. Involvement of other non-medical health care professionals may also not be welcomed in some traditional settings.

Health care system

Traditional medical practice is organized to respond quickly to acute problems, but does not adequately serve the needs of

Table 57.4 Frequency of HbA_{1c} monitoring in various health care settings in type 1 (T1DM) and type 2 diabetes (T2DM).

Health care setting	Number of patients	Survey period	Method	Performance index (frequency of HbA _{1c} measurements in last year or % of patients with at least 1 HbA _{1c} measured in last year)	Reference
Primary care (USA)	1429 doctors	1989	Mail and telephone questionnaire survey	16–18% of physicians measured every 2–3 months	[40]
Population-based (US NHANES III and BRFSS)	4085	1988–1995	Patient survey, clinical examination	28.8% with monitoring available	[14]
Primary care (USA)	97 388	1990–1991	"Claims-based" profile	16% with monitoring ever	[41]
Primary care (Netherlands) and managed care organization (USA)	2498 (379 patients from Netherlands and 2119 patients from USA)	1992–1997	Medical record review and administrative data	Frequency of measurement improved from 1992 to 1996, with 1.89 in Netherlands and 1.10 tests/year in USA. 80.7% (Netherlands) and 57.4% (USA) had more than 1 measurement over last 12 months	[27]
Primary care (USA)	1376	1993	Reimbursement profile	26% had HbA _{1c} in last 1 year; 19% in African Americans and 27% in Caucasians	[104]
General practitioners or specialist care centers (Hungary)	4824	1993	Administrative database	12% had >1 measurement	[42]
Population-based (USA)	2118	1994	Patient survey	61.8% had HbA _{1c} in last 1 year	[43]
Community private practices (USA)	30 589	1994	Administrative database	69.4% had HbA _{1c} in last 1 year	[44]
Community health center (USA)	2865	1995	Medical record review	54.6% had HbA _{1c} in last 1 year	[28]
Primary care (USA)	9557–9985	1995–1997	Medical record review	70% had HbA _{1c} in last 1 year	[29]
Steno Diabetes Center (Denmark)	2011 (T1DM)	1995–1997	Patient survey	55, 65 and 80% had HbA _{1c} in last 1 year from 1995–1997	[45]
Veterans Affairs (USA)	9578 (in 1995) to 25 764 (in 2000)	1995–2000	Medical record review and administrative data	>99.5%, had HbA _{1c} in last 1 year mean frequency 3 tests/yr	[30]
Health Management Organization (USA)	3612	1997	Patient survey, administrative database	59%, 85%, 91%, 93% and 94% had HbA _{1c} in last 1 year from 1995–2000	[46]
Primary care (UK)	18 642	1997	Questionnaire survey and audit data	89.0% had HbA _{1c} in last 1 year	[32]
Primary care (Germany)	5057	2001	Medical record review	83.0% had HbA _{1c} in last 1 year	[47]
Primary care and specialist center (Asia, Eastern Europe and Latin America)	11 799	2005–2010	Medical record review	69.5% of the insulin-treated patients, 64.3% of patients on single oral antidiabetic agent and 41.1% for those on diet had HbA _{1c} in last 1 year	[24]
				77.6% T1DM and 64.2% T2DM had HbA _{1c} ever monitored. By countries (Asia, Eastern Europe and Latin America) was 81.1 vs 73.1 vs 81.4 for T1DM and 64.0 vs 55.8 vs 75.5 for T2DM	

Data are for patients unless otherwise stated.

BRFSS, Behavioral Risk Factor Surveillance System; NHANES III, Third National Health and Nutrition Examination Survey.

individuals with chronic illnesses, when emphases are to alter behavior and to deal with social and emotional impacts of symptoms as well as disabilities [70]. Health care systems need to ensure that the best possible treatment regimens are administered in order to control disease, alleviate symptoms, inform and support.

Thus, suboptimal quality of care is often caused by combinations of factors relating to the affected individual, to the medical care personnel and to the system of health care delivery. In the IDMPs [24], amongst patients in whom HbA_{1c}, BP and LDL cholesterol measurements were available, only 3.6% of patients attained target values for all three risk factors (BP <130/80 mmHg,

HbA_{1c} <7% (53 mmol/mol) and LDL cholesterol <2.6 mmol/L). In this survey, there was considerable heterogeneity between regions of patient-related factors (e.g. age, disease duration, presence of complications, body weight), health care systems (e.g. health insurance coverage, availability of specialist care, training by diabetes educator) and self-care (e.g. self-adjustment of insulin dosage) all being associated with the likelihood of reaching targets. The problem is particularly marked in low and middle income settings where it is exacerbated by multiple demands upon severely limited resources including those imposed by a continuing burden of infectious diseases and other issues such as accidents and injuries.

The evolving concept of disease management

It will be clear from the previous sections that although optimal care improves clinical outcomes in clinical trial settings, this is often not achieved in real clinical situations for the reasons discussed. This has led to attempts to develop models of care based on multidisciplinary approaches.

In recent years, there has been increasing emphasis on management via coordination and organization of individual components of care into a structured system. The latter is further supported by reinforcement through multiple contacts, including not only physician appointments, but also telephone reminders and visits to other health care professionals such as nurse practitioners, dietitians and pharmacists. According to Wagner *et al.* [70], there are five key elements to improve the outcomes of patients with chronic diseases:

- 1 A system to support the use of evidence-based guidelines;
- 2 Reorganization of practice systems and team functions;
- 3 Patient self-management support;
- 4 Improved access to expertise; and
- 5 Improved availability of clinical information to facilitate monitoring and feedback on physician's performance.

The Steno-2 study provides excellent evidence in support of the benefits of protocol-driven multifaceted care using a multidisciplinary approach in T2DM [13,18,19]. Patients randomized to the intensive treatment group were managed by a multidisciplinary team according to a protocol that specified a stepwise implementation of behavior modification, smoking cessation, aggressive control of glycemia, BP, lipids and microalbuminuria, and use of an ACE inhibitor and aspirin. The reductions in HbA_{1c}, BP, serum cholesterol and triglycerides levels and albuminuria were all significantly greater in the intensive care group than in the usual care group. These benefits in metabolic control were translated to risk reductions of cardiovascular morbidity and mortality by 53% (95% confidence interval [CI] 27–76%), nephropathy by 71% (95% CI 13–83%), retinopathy by 58% (95% CI 14–79%) and autonomic neuropathy by 63% (95% CI 21–82%). By the end of 13.3 years, patients previously treated intensively had lower all-cause mortality (hazard ratio [HR] 0.54; 95% CI 0.32–0.89), cardiovascular mortality (HR 0.43; 95% CI 0.19–0.94)

and cardiovascular events (HR 0.41; 95% CI 0.25–0.67) than the conventional care group.

In another multicenter randomized study comparing structured care delivered by a diabetologist–nurse team with conventional care, 60% of patients with T2DM with renal impairment receiving structured care attained three or more predefined treatment goals (HbA_{1c} <7% (53 mmol/mol); BP <130/80 mmHg; LDL cholesterol <2.6 mmol/L; triglycerides <2 mmol/L and use of ACE inhibitor or angiotensin receptor blocker) compared to 20% in the usual care group. After 2 years, patients who attained three or more treatment goals had 60% risk reduction in all-cause mortality and end-stage renal disease (HR 0.43; 95% CI 0.21–0.86) [71].

Implementation of quality structured care

This concept of disease management emphasizes an organized, proactive multidisciplinary approach to health care in complex and chronic diseases, of which diabetes is a prime example [72,73]. People with chronic diseases should be empowered to improve knowledge and self-management [74,75]. Preferences should be taken into account to individualize treatment plans. Evidence suggests that periodic attendance at a diabetes center [76] and frequent reminders by paramedical staff to reinforce self-management could improve metabolic control, clinical outcomes and survival [13,71,77–84]. Clinical information should be made easily available to provide support. Information technology can be used to monitor adherence to guidelines and provide feedback to the care providers (see Chapter 58) [70,72,85–87].

Provision of structured care to people with T2DM is best implemented through a series of interlinked processes based on these principles. These include risk stratification, protocol-driven care, regular review by a multidisciplinary team, patient empowerment and good record keeping to monitor progress (Figure 57.1).

Risk stratification

Diabetes is characterized by clustering of multiple risk factors that interact in a complex manner to give rise to multiple complica-

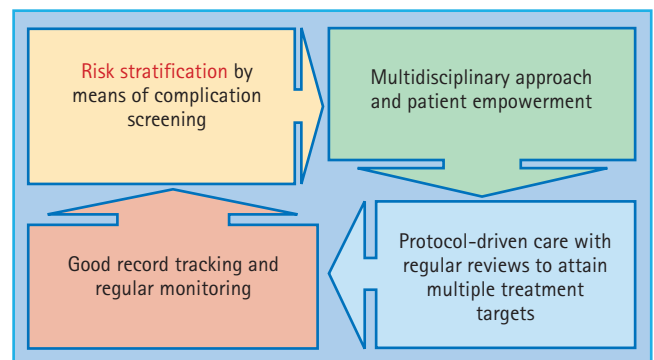


Figure 57.1 Components for quality structured care.

tions [88]. Both the IDF and American Diabetes Association (ADA) recommend that people with diabetes should undergo comprehensive assessment at presentation and annually thereafter to document personal, clinical and laboratory measurements. This enables stratification of risk and placement of patients within different care plans for targeted individualized treatment.

The UKPDS has provided longitudinal data which help to define the natural history of cardiovascular complications in T2DM. Using the UKPDS data, mathematical models have been developed to identify predictors (risk factors) for cardiovascular disease [89]. In addition, the Framingham Heart Study, started in 1948, has prospectively followed a large group of participants in the general population in order to identify factors contributing to development of CVD, and risk engines have also been developed to predict risk of CVD in this population [90]. Both the UKPDS and the Framingham risk equations show moderate effectiveness in risk stratification in UK and USA settings; however, external validation studies show that the performance varies considerably among different countries and ethnic groups [91]. In addition, there were only a few hundred people with diabetes in the original cohort of the Framingham Study, while the UKPDS recruited individuals in the early phase of diabetes. These pose definite limitations in applying the risk engines derived from these two studies to general diabetes populations in Europe, the USA and elsewhere.

Further modification and development of ethnic specific risk equations have now been carried out. For example, equations to predict diabetes complications such as coronary heart disease, stroke, end-stage renal failure, congestive heart failure as well as overall mortality have now been developed for Chinese populations, based on prospective follow-up of approximately 8000 patients, with median follow up of 6 years [89,92–95]. In this particular group of Chinese individuals with diabetes, the Framingham stroke risk engine underestimates, while the UKPDS risk engine overestimates, the risk of stroke. Both of these risk engines for CVD overestimate the risk of CVD in some populations such as Chinese. In addition, it was not possible to develop the UKPDS risk engine to assess risk of end-stage renal disease as an insufficient number of individuals developed this endpoint. Further development in this area is anticipated with expansion of studies into different settings and ethnic-specific areas.

Protocol driven care using a multidisciplinary approach

Diabetes management involves multiple contacts with different health care personnel, each specialized in a particular process or area of expertise. Non-medical personnel, notably nurse educators, nutritionists, pharmacists, physical trainers and podiatrists, are key members of a successful diabetes team. While the doctor adopts the leading and coordinating role in defining problems and needs, the professional knowledge and clinical skills of these non-medical staff are invaluable in providing counseling and holistic care to patients. These health care professionals can also assist physicians to provide follow-up, empower self-manage-

ment and support carers of patients with cognitive impairment and physical disabilities. This team approach allows physicians to spend more time in discussion of needs, setting of targets and options for management. In high risk individuals, such as those with co-morbidities or those receiving multiple medications, the pharmacist may have a unique role in providing education to patients in collaboration with physicians to improve the safe and effective use of pharmaceutical agents and reduce the risk of drug-related adverse effects and drug–drug interactions.

Given the large number of processes and personnel potentially involved in the delivery of such evidence-based and protocol-driven care, it is important to try to determine which aspects of care can be attributed to which components. In a meta-analysis of 66 publications examining 11 different strategies to improve diabetes care [96], two key strategies were associated with statistically significant incremental reductions in HbA_{1c} value. The first was team changes, which involved either the addition of a team member, shared care between primary care and specialist center, or multidisciplinary team care. This resulted in additional HbA_{1c} reduction by 0.33% (3.6 mmol/mol). The second was case management, which involved coordination in diagnosis, treatment or management by a person or multidisciplinary team in collaboration with or supplementary to the primary care clinician. This was associated with additional HbA_{1c} reduction of 0.22% (2.4 mmol/mol).

This has been replicated in various clinical settings. For example, the Chinese University of Hong Kong Diabetes Group has used different care prototypes since the 1990s to augment delivery of care using nurses and pharmacists. The latter were empowered to run clinics or provide telephone counseling to provide periodic assessments and reinforce treatment compliance. These prototypes consistently showed improved rates of treatment compliance and attainment of multiple treatment targets as well as reduced risk of death and cardiorenal complications by 50–70% in chronic diseases including diabetes with or without complications (Figure 57.2) [82–84]. These two strategies become key components and are applicable globally irrespective of the health care setting. In less resource-rich settings, some of these strategies can be met, at least partially, by appropriate training or relocation of existing staff in response to changing health needs.

Patient empowerment and self-care

In addition to team changes and case management, other processes that have been shown to improve disease control include patient education (effect sizes 0.24 [0.07–0.40]), reminders (0.27 [0.17–0.36]) and financial incentives (0.40 [0.26–0.54]) [86]. While adherence of physicians and care providers to care processes may improve health outcomes, patient adherence is a critical factor in realizing the benefits of these processes. Patients should be encouraged to participate actively in defining and achieving agreed treatment goals rather than conforming to medically defined regimens or instructions. In diabetes, behavioral changes, including adhering to a meal plan, engaging in regular

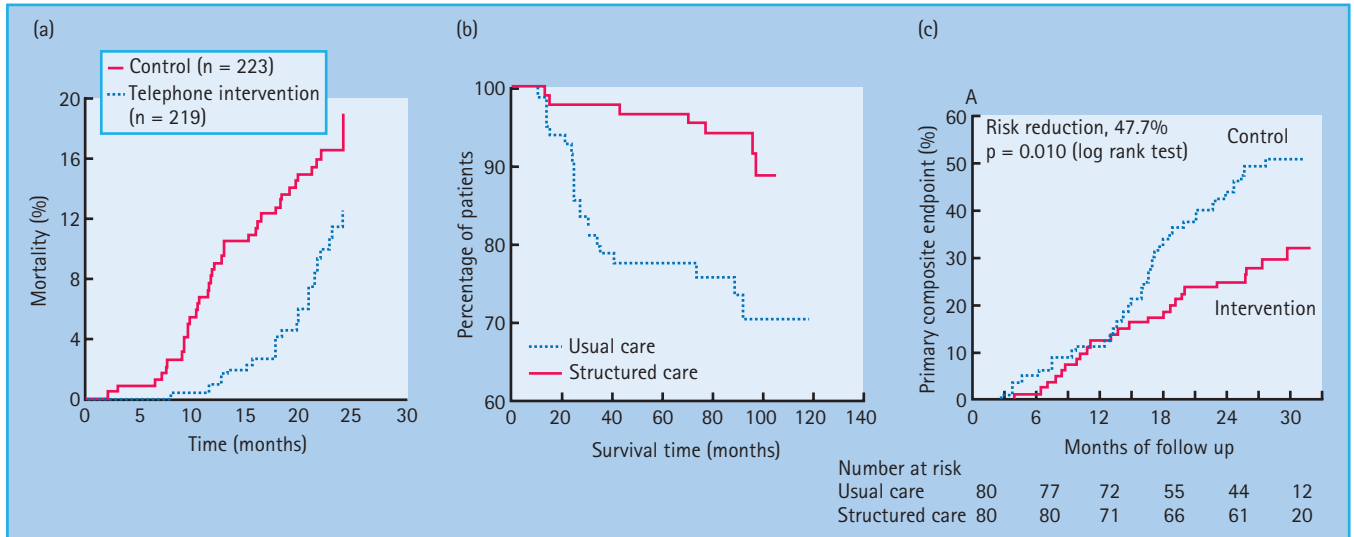
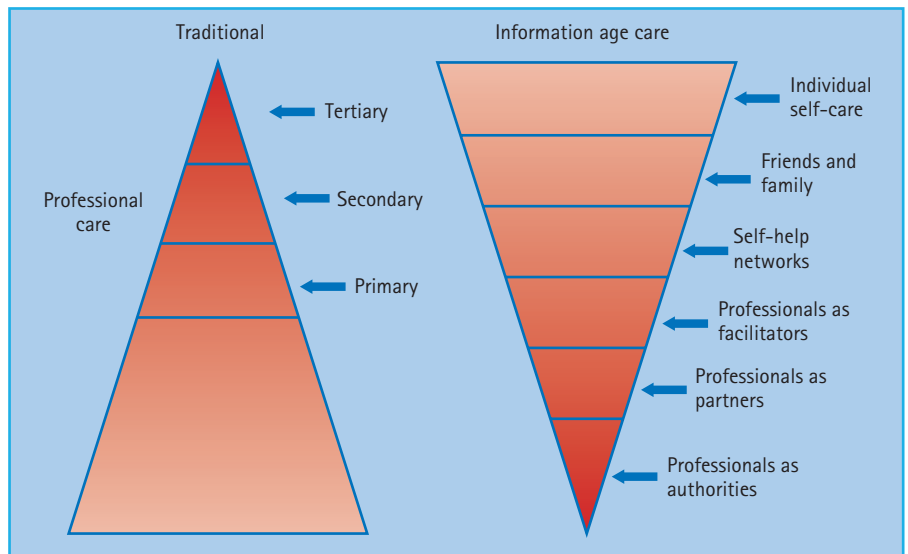


Figure 57.2 Effect of protocol-driven care using a multidisciplinary approach to reduce risk of complications in patients with chronic diseases including type 2 diabetes mellitus (T2DM) [82–84]. (a) Telephone counseling by a pharmacist between clinic visits reduced mortality rate by 50% in patients receiving five or more chronic medications. (b) Patients with T2DM without cardiorenal complications managed in a clinical trial setting was associated with a 70% risk

reduction in death rate compared with matched patients followed up in conventional care setting. (c) Patients with T2DM with chronic kidney disease managed by a pharmacist–doctor team had a 50% risk reduction in death and end-stage renal disease compared with patients managed in conventional care setting.

Figure 57.3 Change of paradigm using information technology to improve clinical and self-management. Adapted from Jennings *et al.* [109], with permission from Knowledge Exchange LLC.



physical exercise, taking medications regularly, monitoring blood glucose levels and other complications, and attending to foot care demand high levels of self-discipline and are important components of holistic care models [61].

Given the chronic nature of diabetes and large amount of data collected during contact with care providers, there is a need to develop a system to manage this information effectively and enable health care workers to make decisions, track clinical progress, monitor compliance and benchmark quality of care. The use of information technology can also empower people with

diabetes by making information more accessible and understandable. Such technology can also assist individuals with diabetes to keep their own health records, maintain control, and use them to manage their own care in an informed manner (Figure 57.3).

Importance of periodic monitoring and review

Depending on complications and control of risk factors, people with diabetes should be reviewed at intervals ranging from weekly to every few months; however, once stabilized, people with dia-

Table 57.5 Treatment targets, procedures and frequency of monitoring for individual target [12,105–108].

	Frequency	Procedures and targets
Glycemic control		
HbA _{1c}	NGSP of IFCC assay 2–6 monthly	6.5–7% (48–53 mmol/mol) Individualized target based on: <ul style="list-style-type: none"> • Duration of diabetes • Age/life expectancy • Co-morbid conditions • Known CVD or advanced microvascular complications • Hypoglycemic unawareness
Self-monitoring of blood glucose	≥3 daily for patients on intensive insulin regimen ≥1 daily with weekly profile for those on oral agents ± insulin ≥1 weekly profile for selected patients on diet Additional test with unstable or deteriorating condition	Preprandial BG 5–7 mmol/L Post-prandial <8–10 mmol/L
Blood pressure control	At every clinic visit	<130/80 mmHg
Lipid control	Yearly	LDL <2.6 mmol/L; or 30% reduction regardless of baseline LDL Triglycerides <2.3 mmol/L HDL >1.0 mmol/L in men, 1.3 mmol/L in women
Clinic visit	Every 3–6 months	Assess progress in achieving treatment goals: <ul style="list-style-type: none"> • Symptoms • Weight goals • Glycemic, blood pressure and lipid goals • Compliance and side effects of medications • Results of self-monitoring • Adherence to lifestyle including cessation of smoking and avoidance of excessive alcohol use Assess complications: <ul style="list-style-type: none"> • Events including admissions or procedures
Complication screening	Yearly May consider 2–3 yearly for retinopathy in patients with normal examination by experts	Self-care knowledge and beliefs Lifestyle adaptation Psychologic status Self-monitoring skills and equipment Body weight trend Glycemic, blood pressure and lipid control Cardiovascular risk Erectile dysfunction, neuropathy Foot condition Eye condition Kidneys Pre-pregnancy advice Medication review

BG, blood glucose; CVD, cardiovascular disease; HDL, high density lipoprotein; LDL, low density lipoprotein; NGSP, National Glycohemoglobin Standardization Program.

betes should be reviewed by a health care professional at least once a year, no matter how mild the condition may appear. Based on various guidelines, the targets as well as procedures and frequency of monitoring for individual targets are summarized in Table 57.5.

This takes account of the possibility of silent deterioration of metabolic control and development of new risk factors or complications, as proper management cannot be initiated unless indexes of control are measured periodically [97]. In the study shown in Figure 57.2(a), which was conducted in the

early 1990s, the omission of the measurement of metabolic indices was associated with a 15-fold increased risk of death. The comparison group in this study had at least one measurement during a 7-year period of observation [82].

These findings are related to adjustment of regimens facilitated by periodic monitoring [97]. Patients receiving structured care have greater utilization of antihypertensive and lipid-lowering agents. Using ACE inhibitors as an example, despite the compelling evidence supporting their protective effects [98], clinicians in conventional care settings often withhold or discontinue these drugs for fear of side effects such as hyperkalemia and deterioration of renal function, especially in high risk patients who are those most likely to benefit [99,100]. This is further supported by the study shown in Figure 57.2(c), in T2DM with nephropathy, in which 60–70% of patients were treated with an ACE inhibitor or ARB at baseline. At the end of a 2-year study period, over 90% of subjects randomized to structured care delivered by a multidisciplinary team persisted with the treatment compared with less than 20% of subjects randomized to conventional care. Together with better risk factor control, increased usage of drugs, more clinical and laboratory assessments, this difference in usage of ACE inhibitor or ARB collectively contributed to the reduction in death and cardiorenal event rates between the structured and conventional care group [71,84].

Importance of attaining multiple targets

As shown in Table 57.5, multiple treatment targets, in addition to glycemic control, need to be taken into consideration when managing people with diabetes. In an observational study of 6386 patients with T2DM in Hong Kong, attainment of ≥ 2 treatment goals (HbA_{1c}, BP or LDL cholesterol) was associated with 30–50% risk reduction in new onset of CHD, demonstrating the importance of attaining multiple targets [33]. In the Steno-2 study in Denmark, which aimed to achieve multiple risk factor control, the overall relative risk reduction of 59% in composite cardiovascular events accords with the expected cumulative effects of control of individual risk factors in an additive manner [19]. This has been further replicated in another study, in individuals with diabetic nephropathy, in which more people receiving structured care attained ≥ 3 treatment goals (61%) compared with the conventional care group (28%). This difference translates to a 60–70% reduction in premature death and end-stage renal disease [71].

It has been estimated that use of HMG-CoA reductase inhibitors and blood pressure lowering drugs confers the largest benefit in reducing cardiovascular risk in the initial study period, with optimization of glycemic control and use of aspirin providing additional beneficial effects. The long-term glycemic beneficial effects of glucose lowering on diabetes-related endpoints are expected to occur later. Hence, the attainment of multiple treatment targets might explain the continuing divergence in cardiovascular endpoints, rather than a simple time–effect relationship. The importance of sustained benefits of long-term glycemic control is further supported by the legacy effect associated with

intensive blood glucose control, long after the cessation of the UKPDS [101] and the parallel findings of the DCCT/EDIC study [15,16].

Cost-effectiveness of multidisciplinary care

Cost-effectiveness analysis for intensive glycemic and blood pressure control has been performed based on results from the UKPDS [102]. The cost per quality-adjusted life year (QALY) for intensive blood glucose control with insulin or sulfonylureas was £6028 more than conventional treatment, while that with metformin in overweight patients was £1021 less than conventional treatment. These estimates suggest that intensive blood glucose therapy, particularly the use of metformin in obese patients with diabetes, was effective and cost-saving. The cost per QALY gained for tight blood pressure control was £369 based on the UKPDS. Similarly, according to the Centers for Disease Control (CDC) in the USA, the incremental cost:effectiveness ratio for intensive glycemic control was US\$41 384 per QALY. The respective costs for intensified blood pressure control and reduction of serum cholesterol were savings of US\$1959 and US\$51 889 per QALY [103]. Furthermore, these analyses suggested that these interventions were most cost-effective when instituted early during the course of disease.

Similar analysis has also been performed in the Steno-2 Study [19]. The incremental cost:effectiveness ratio for structured care versus conventional treatment was €3927 and €2538 per life year and per QALY gained, respectively. These incremental costs were mainly attributed to increased pharmacy and consultation costs. The author further pointed out that even assuming that patients in the structured care group continued to receive the most expensive treatment in a specialist setting in Denmark and that the treatment effects between the intensive and conventional groups might decline after completion of the 7.8-year intervention period, the incremental costs still represent good value for money. However, because of the multifaceted nature of the intervention, it was difficult to identify the contribution of individual factors to the improved outcome.

Conclusions

In conclusion, T2DM is a massive public health problem and is associated with reduced life expectancy by 10–12 years. It has major implications on quality of life, health care utilization and societal productivity. Diabetes management is complex and effective management requires creation of care models that take account of this complexity and facilitate care providers to attain multiple treatment targets and empower patients to adhere to self-management. Such models should include continuous quality improvement initiatives with measurement of key performance indices, validated outcome measures and risk–benefit analyses of interventions. Landmark trials such as Steno-2 study

have demonstrated the cost-effectiveness of the use of protocol-driven multidisciplinary care to manage and prevent diabetes complications. With appropriate organization of care, good clinical governance and patient empowerment, quality diabetes care should eventually become accessible, affordable and sustainable, irrespective of circumstances and resource setting.

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