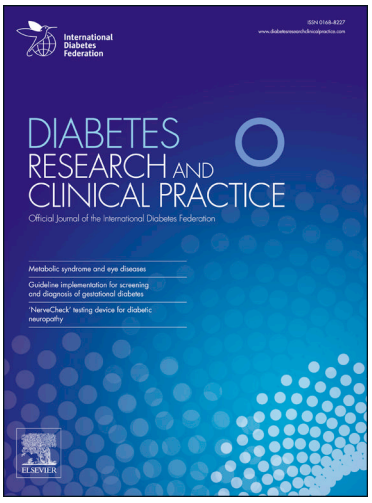
Achievement of guideline targets for blood pressure, lipid, and glycaemic control in type 2 diabetes : a meta-analysis



Review

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Achievement of guideline targets for blood pressure, lipid, and glycaemic control in type 2 diabetes: a meta-analysis

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Achievement of guideline targets for blood pressure, lipid, and glycaemic control in type 2 diabetes: a meta-analysis

Abstract

We assessed global achievement of targets recommended by the American Diabetes Association (ADA), European Association for the Study of Diabetes (EASD), and National Institute of Health and Care Excellence (NICE) for type 2 diabetes.

We searched Medline, Embase, and The Cochrane Library for observational studies reporting target attainment (2006 to 2017 inclusive) for HbA1c, blood pressure, or lipids (low density lipoprotein cholesterol [LDL-C], high density lipoprotein cholesterol [HDL-C], or triglycerides). Rates were pooled using a random-effects meta-analysis. Study quality and risk of small study of bias was assessed.

From 2,491 screened records, 24 studies were included reporting on 369,251 people from 20 countries. The pooled target achievement rates were; 42.8% (95% CI 38.1-47.5%) for glycaemic control, 29.0% (22.9-35.9%) for blood pressure, 49.2% (39.0-59.4%) for LDL-C, 58.2% (51.7-64.4%) for HDL-C, and 61.9% (55.2-68.2%) for triglyceride control. A higher proportion of people achieved HbA1c targets within Europe and North America than the rest of the world. A higher proportion of people achieved blood pressure targets in North America than Europe or the rest of the world. Meta regression showed no significant improvement in rates by year for any target.

The achievement of evidence-based targets is markedly suboptimal globally and not improving.

Word count: 199/200

Key words: Diabetes Mellitus, Type 2; Guideline Adherence; Blood Glucose; Blood Pressure; Cholesterol; Lipoproteins

Introduction

With the growing prevalence of type 2 diabetes (T2DM) worldwide there is an increasing burden of disease from complications, many of which are preventable.[1 2] Improvements in glycaemic control (HbA1c reduction) have been demonstrated to reduce both microvascular and macrovascular complications.[3] Blood pressure reduction in people with significant hypertension and diabetes reduces the risk of macrovascular disease when aiming for modest targets[4] although intensive blood pressure control (a target systolic blood pressure below 120 mmHg) has not been demonstrated to improve outcomes.[5] Similarly lipid control has also been demonstrated to reduce cardiovascular risk.[6-8] Many local, national, and international organisations have therefore developed guidelines which recommend evidence-based glycaemic, blood pressure, and lipid targets to improve outcomes in people with T2DM. Whilst there are a large number of guidelines available, previous analyses have demonstrated that they are broadly consistent.[9 10]

The European Association for the Study of Diabetes (EASD) and American Diabetes Association (ADA) joint position statement, first produced in 2006, provides evidence-based recommendations for glycaemic control in T2DM.[11] This position statement was updated in 2012[12], and again in 2015[13]. The ADA also separately produces annual guidelines (Standards of Medical Care in Diabetes) which additionally provide blood pressure and lipid targets.[14] The EASD in conjunction with the European Society of Cardiology (ESC) also provides recommendations for blood pressure and lipid control.[15] In the UK, the National Institute of Heath and Care Excellence (NICE) provides similar glycaemic control, blood pressure, and lipid recommendations.[16] A summary of glycaemic, blood pressure, and lipid targets from the most recent guidelines is provided in Supplementary Table S1.

Previous studies have suggested that achievement of glycaemic, blood pressure, and lipid targets in diabetes is markedly suboptimal.[17-19] A systematic assessment of the current levels of achievement of major diabetes guideline targets is important to provide a global overview of care quality in people with T2DM. We conducted a systematic review and meta-analysis to evaluate the achievement of targets set by the ADA, EASD and NICE guidelines for glycaemic, blood pressure, and lipid control in people with T2DM globally.

Methods

We performed a systematic review and meta-analysis to describe the proportion of people with T2DM achieving targets recommended by ADA, EASD, or NICE for glycaemic control, blood pressure, or lipid targets. Lipid targets comprised targets for low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), or triglycerides. This systematic review and meta-analysis was performed and reported in accordance with the review protocol registered with PROSPERO (Registration Number CRD42015027865) and in accordance with the PRISMA and MOOSE guidelines.[20 21]

Study selection

We identified observational studies that reported the proportion of people with T2DM achieving one or more of clinical targets of interest. As per our pre-specified inclusion criteria we included only those studies which provided a comparison against guidelines published by the ADA, EASD, or NICE in the last 10 years (2006 onwards). We excluded studies which provided a comparison against other guidelines, which assessed or involved an intervention, which included children, or which included

people with other types (type 1 diabetes, gestational diabetes, monogenic diabetes, or secondary diabetes) where outcomes for those with T2DM were not reported separately.

We searched the Medline, Embase, and Cochrane Library electronic databases from 1st January 2006 to 22nd February 2017. The search strategy incorporated both Medical subject headings (MeSH) and keywords for T2DM, guidelines, and adherence (Appendix 1) and was adapted from recent published reviews.[22-24] All MeSH subheading were included. No language restrictions were applied to optimise capture of guideline target achievement globally. Online translation tools were used in the first instance to determine if non-English language studies met the inclusion criteria. Where this could not be determined using these tools, external support was planned for translation and data extraction although this was not required. Abstracts were included if sufficient information was available (either online or by contacting the authors) to assess the study against the inclusion and exclusion criteria. The search was supplemented by bibliographic searches of the complete reference lists of all included studies.

After removal of duplicates, an independent review of the titles and abstracts, and then of the full papers of all articles identified by the search strategy was performed by two contributors (AM and JB). Any unresolved conflicts were resolved by the lead author (KK). Data was then independently extracted from the included articles (AM and JB) and collated (AM). No amendments to the pre-specified inclusion and exclusion criteria were required during searching. Data was extracted from the included studies on; study design, location, sample size, comparator guideline(s), comparator thresholds, and achievement outcome. The strengths, limitations, and generalisability of results were also assessed for each study.

Statistical analysis

We have reported the number of people achieving targets for each study in each category measured (HbA1c, blood pressure, LDL-C, HDL-C, and triglycerides). We report the outcome target used for comparison for each study (e.g. HbA1c <7%). Where the study manuscript reported only the proportion of people we have calculated the number achieving targets from the proportion reported. Country-specific proportions were pooled using both fixed and random effects meta-analyses for each category. Random effects meta-analysis was performed using the DerSimonian and Laird method.[25] We report pooled estimates with 95% confidence intervals (CI). We performed pre-specified subgroup analyses for each meta-analysis, grouping studies into three broad locations; Europe, North America, and the rest of the world. We report both the fixed effects and random effects estimates for each subgroup. Heterogeneity between countries in the proportion of people achieving each target was quantified using the I^2 statistic[26] and τ^2 (also estimated using the DerSimonian and Laird method) with an associated p-value for the likelihood of heterogeneity. We also report I^2, τ^2, and p-value for each subgroup. Publication bias was assessed for all pooled analyses where the included number of studies was 10 or more[27] using funnel plots and the Egger's test for asymmetry[28]. Meta-regression was performed to assess the influence of year on the proportion of people achieving targets. Meta-regression was performed using a random-effects model (DerSimonian-Laird estimator)[29]. Statistical analyses were undertaken using the statistical software R version 3.3.2 and the R packages meta[30] and metafor[31].

Study quality was assessed against the Newcastle-Ottowa scale modified for cross-sectional studies (Appendix 2). This scale awards a maximum of 9 points across three domains; selection quality (maximum 4 stars), comparability (2), and outcomes (3).

Results

From 2,491 citations found through electronic database searching, 93 articles were identified for full-text review (Supplementary Figure S1). Of these, 24 studies were included in the final analysis, reporting on 369,251 people from 20 countries; one in North America (USA), 10 in Europe (Belgium, France, Germany, Ireland, Italy, Netherlands, Poland, Spain, Sweden, and the UK), and 9 in the rest of the world (Bangladesh, China, Kuwait, Malaysia, Palestine, Qatar, Saudi Arabia, Thailand, and the Philippines). Only one study reported on outcomes in multiple countries[19]; each country reported on was included separately in the meta-analysis. Sample sizes ranged from 166 people in a regional study in Germany[32] to 238,639 people in a nation-wide study in China[17]. These studies therefore comprised 0.045% and 64.6% of the total sample size respectively. Included studies collected data between 2006 and 2012 inclusive; three studies in 2006, one in 2007, three in 2008, four in 2009, eleven in 2010, five in 2011, and four in 2012. One study was performed as a retrospective cohort analysis[33] and the remaining 23 studies were cross-sectional. The characteristics of included studies are listed in Table 1.

Across the 24 included studies, 28 comparisons with guideline targets were made (Table 2): Most studies (n=19) compared outcomes against the ADA Standards of Medical Care in Diabetes. Three studies[34-37] provided a comparison of glycaemic control against an ADA/EASD joint position statement, four studies[34 38-41] provided a comparison against an ESC/EASD joint guideline, and two studies[41 42] provided a comparison against a NICE guideline. All studies made comparisons against a single contemporary guideline target for each outcome analysed; no studies compared against multiple targets.

The majority of studies used routinely collected data to determine achievement of targets, although five[37 38 43-45] studies actively measured glycaemic control, blood pressure, or lipids. Proportion of people achieving targets was reported for glycaemic control in all 24 included studies, for blood pressure in 15 studies, LDL-C in 15 studies, HDL-C in eight studies, and triglycerides in eight studies (Table 2). The proportion of people achieving targets varied considerably between countries. Achievement of HbA1c targets ranged from 15.1% in the Philippians[46] to 70.5% in the Netherlands[19], blood pressure targets from 7.4% in Germany[19] to 60.0% in one study in the USA[47], LDL-C targets from 13.3% in one study in Poland[35] to 76.9% in Ireland[48], HDL-C targets from 32.3% in Saudi Arabia[49] to 80.8% in the Philippines[45], and triglyceride targets from 39.2% in Poland[36] to 85.6% in the Philippines[45].

In the pooled sample (random effects model) the proportion of people achieving HbA1c targets was 42.8% (95% CI 38.1-47.5%) with a higher proportion of people meeting targets within Europe and North America than the rest of the world (Figure 1). It should be noted that whilst the study from China contributed to a large proportion of the total sample size, in the random effects model it was only attributed 3.3% of the total weighting. The overall proportion of people achieving blood pressure targets was 29.0% (95% CI 22.9-35.9%) with North America achieving the highest proportion by region (Figure 2). The overall proportion of people achieving targets for LDL-C, HDL-C,

and triglycerides were 49.2% (95% CI 39.0-59.4%), 58.2% (95% CI 51.7-64.4%), and 61.9% (95% CI 55.2-68.2%) respectively (Supplementary Figures S2, S3, and S4).

All groups and subgroups (by region) had a high degree of heterogeneity (I^2 > 75%[26]) between studies (Supplementary Figures S2, S3, and S4). An analysis for small study bias was appropriate for studies measuring achievement of HbA1c, blood pressure, and LDL-C targets (n≥10). Egger's test and forest plots (Supplementary Figures S5, S6, and S7) demonstrated asymmetry in the published studies for each pooled analysis; HbA1c (p=0.0178), blood pressure (p=0.0005), and LDL-C targets (p=0.0040). Smaller studies demonstrated a tendency to report higher target achievement rates for HbA1c and lower target achievement rates for blood pressure and LDL-C.

Meta-regression analysis did not identify any influence of year on the proportion of people achieving HbA1c targets (estimate -1.1%/year; 95% CI -11.1-8.9%/year; p=0.8342), blood pressure targets (estimate 3.4%/year; 95% CI -7.2-14.0%/year; p=0.5266), LDL-C targets (estimate 2.6%/year; 95% CI -8.8-14.0%/year, p=0.6527), HDL-C targets (estimate -4.6%/year; 95% CI -24.1-14.9%/year; p=0.6410), or triglyceride targets (estimate 0.9%/year; 95% CI -20.6-18.7%/year; p=0.9249) (See also Supplementary Figures S8 to S12).

Study quality was limited with most studies having restricted generalisability to all those with T2DM in the community (Supplementary Table S2). Common factors limiting generalisability were; being undertaken in a single secondary care clinic[42 48 50 51], and inclusion only of a subset of people with diabetes e.g. those with long or short duration of disease[34 39 40], elderly people[51], or those on selected treatments[33 52]. Quality scores (Newcastle-Ottowa Assessment Scale) ranged from 0 to 6 (median 4) points. Very few studies stratified targets by the presence of co-morbidities or other clinical features; one study for glycaemic control targets,[37] two studies for lipid targets,[34 39 40] and one study for blood pressure targets.[42] Only one study collected data on recording of individualised targets, but found that no patients (0/305) had a recorded individualised HbA1c target.[42]

The excluded studies included two notable large high quality analyses of achievement of ADA targets for glycaemic, blood pressure and cholesterol control using US data collected from the National Health and Nutrition Examination Surveys (NHANES).[17 18] Both studies were excluded because the dataset used included a small number of people with type 1 diabetes and did not report results separately for those with T2DM.

Discussion

Considerable variation exists in the achievement of glycaemic control, blood pressure, and lipid targets in people with T2DM globally with no evidence of improvement between 2006 and 2012 inclusive. The majority do not achieve glycaemic targets, although target achievement was better in studies conducted in Europe and America than the rest of the world. Less than a third of people achieved blood pressure targets globally although this varied substantially by region (Europe 23%, America 52%, and the rest of the world 34%). Around half of people achieve LDL-C targets and over half achieve targets for HDL-C and triglycerides. Small study bias demonstrated asymmetry in the published studies for the groups amenable to analysis (glycaemic control, blood pressure, and LDL-C).

Implications

The low proportion of people achieving targets in T2DM and the large amount of variation globally are cause for concern. As demonstrated by high quality trial data, people with T2DM and uncontrolled blood glucose have increased risk for microvascular and macrovascular events.[3] Similarly those with uncontrolled blood pressure and lipids have increased risk for macrovascular events.[4 6-8 53] With the global burden of diabetes now estimated to be 422 million people,[54] and growth vastly exceeding previous predictions,[55] this failure to meet targets means a vast number of people are exposed to these excess risks. Substantial improvements to guideline target achievement are required. Moreover, to reach and keep the target for all the above mentioned risk factors as early as possible seems to pay in terms of reducing the risk for future complications, avoiding the "Metabolic memory" effect.[56 57]

A wide variety of patient, physician, and healthcare system related factors have previously been identified as contributing to lack of adherence to clinical guidelines. Many patients do not consider diabetes to be a chronic illness or to pose a threat to their health.[58] They may also lack the motivation or personal resources to adhere to treatment strategies[58] including lifestyle modification and medication use. Patient perceptions of diabetes management also contrast with guidelines; patients have negative perceptions of treatment intensification, view addition of medication as associated with higher risk of adverse health outcomes, and view addition of medication as a personal failure.[59]

Whilst clinicians generally have a positive attitude towards clinical guidelines, finding them helpful resources and a method to improve care quality,[60] physicians often consider guidelines to be impractical or too rigid to apply to individual patients.[60-62] An algorithm to devise individualised glycaemic targets has been previously proposed[63] but nothing has yet been incorporated into guidelines. Lack of provider knowledge of current guideline targets may also be an important contributing factor. Lack of clinician time, lack of clinical support staff, and lack of access to healthcare, particularly for low income patients, may also contribute.[62 64]

Many methods to improve guidelines target attainment have been suggested. A synthesis of systematic reviews of the effectiveness of guideline implementation strategies suggested that effective methods to improve guideline adherence include; interactive education, clinical reminder systems, audit and feedback, benchmarking, and multifaceted interventions.[65-67] The Anglo-Danish-Dutch Study of Intensive Treatment In People with Screen-Detected Diabetes in Primary Care (ADDITION)-Denmark trial has recently demonstrated that training general practitioners to provide target-driven intensive management of glycaemic control and cardiovascular risk can improve cardiovascular outcomes long term.[68] The universal implementation of these effective methods is required to improve target attainment in people with T2DM. The sustainability of any intervention should also be considered.[69] Despite broad consistency across guidelines, there are some minor differences (Table 1). The lack of uniform guidance may weaken potential effectiveness and achieving consensus across these major guidelines may help improve uptake.

Strengths and limitations

The primary strength of this review is the identification of a relatively large number of studies providing recent comparisons with guidelines across all domains assessed. The included studies were

also moderately large with 11 studies including more than 1000 people although only three studies[33] [70 71] included more than 10,000 people.

There are several limitations. The quality of the studies, when considered in the context of the study question, was generally low with generalisability of results to all people with T2DM in many studies. The heterogeneity of outcomes between studies may also limit the reliability of the pooled estimates.[26] Whilst this is the first systematic review and meta-analysis to assess the achievement of guideline targets in people with T2DM, heterogeneity in guideline adherence rates have been identified in other studies: A systematic review of adherence to management guidelines for the treatment of Non-ST-Elevation Acute Coronary Syndromes found large variation in guideline adherence rates.[72] A systematic review of the effectiveness of lifestyle interventions for the prevention of T2DM also found a high level of variation in adherence to guideline recommendations.[73] Some the heterogeneity in our results may also arise from the differences in guideline targets which were compared against across the studies (table 2).

We did not include studies which compared adherence to other diabetes guidelines which may have influenced our results. Comparison with locally adapted diabetes targets may have found different levels of attainment than our comparison with widely applied guidelines.

Whilst no influence of year was found on the number of people achieving targets, it should be noted that data collection in the identified studies was clustered in the middle of observation period. This limits the ability of the review to assess the changes in target achievements over time. As there are large confidence intervals around our estimates of the rate of change in target attainment the current data is underpowered to detect small improvements since 2006.

Assessment for small study bias demonstrated asymmetry, however the direction of bias was variable; small studies reported higher target achievement rates for HbA1c and lower achievement rates for blood pressure and LDL-C targets. Whilst publication bias is potentially a contributing factor, variation in clinical care quality, differing comparison target values, population characteristics and socioeconomic variation between countries and studies are all likely to contribute.

Another limitation of the existing literature is that most comparisons were against a fixed target rather than individualised targets as described in the most recent guidelines.[13 16] The only study to attempt to collect data on recording of individualised targets was unable to identify a recorded target for participants.[42] Another study, which derived individualised targets from clinical characteristics including age, duration of diabetes, and diabetes complications, found the highest proportion (64%) of people achieving glycaemic targets of all the European studies.[37] This suggests that, in studies where comparison is made against a uniform target, a substantial proportion of people are misclassified as not achieving target when they are nevertheless below an appropriate (higher) individualised target.

Recommendations for future research

Further large-scale studies are needed to compare current practice against individualised targets, particularly for glycaemic control. Future studies should also aim to improve on the generalisabilty of existing studies with collection of data on unselected populations of people with T2DM. Population based databases are a possible appropriate for these analyses. Additional investigation into the

factors underlying the heterogeneity in outcome achievement is merited; why are there such considerable differences between countries in the levels of targets achieved? Studies exploring this could include assessment of the impact of socioeconomic factors and reimbursement for medication. There is also a need for high standard quality improvement studies to identify ways to improve guideline adherence.

Conclusions

A minority of people with T2DM achieve targets for glycaemic control and blood pressure. Lipid targets are achieved for LDL-C in around half of people and more than half for HDL-C and triglycerides. Considerable variation exists between countries in the achievement of targets. Whilst many contemporary studies were identified which measured achievement of guideline targets, these studies were mostly of limited quality and did not consider achievement of individualised targets. Whilst the existing data support the assertion that substantial global improvement is needed in the attainment of targets in T2DM, further high quality studies are needed to fully quantify the problem.

Word count: 3072/5000

Contributions

KK had the original idea for the study design and supervised the review and meta-analysis. AC, XC and CDB critically appraised the study design. KK drafted the manuscript with critical appraisal and additions from AC, XC, and CDB. KK is the guarantor of this work. All authors have read and approved the final manuscript.

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Competing interests

KK has received funds for research, honoraria for speaking at meetings and or served on Advisory Boards for Amgen, Astra Zeneca, BMS, Lilly, Novartis, Pfizer, Servier, Sanofi Aventis, MSD and Novo Nordisk.

AC disclosed the following conflict of interest: Advisory Board membership: Astra Zeneca, Boehringer Ingelheim, DOC Generici, Eli Lilly, Janssen, Novo Nordisk, OM Pharma. Consultancy: Eli Lilly. Lecture fees: Astra Zeneca, Boehringer Ingelheim, Eli Lilly, Merck, Novartis, Novo Nordisk, Sanofi, Servier and Takeda. Research Grants: Eli Lilly, Mitsubishi, Novartis and Novo Nordisk.

XC disclosed the following conflicts of interest: Consultant: AstraZeneca, Boehringer Ingelheim, Lilly, Novartis, Novo Nordisk and Sanofi. Research Support: AstraZeneca, Novartis, Sanofi, Boehringer Ingelheim, MSD. Speaker's Bureau: AstraZeneca, Boehringer Ingelheim, Lilly, Novartis, Novo Nordisk and Sanofi.

CDB reports having received honoraria for consulting, advisory boards, and lecture fees from Abbott, AstraZeneca, A. Menarini Diagnostics, Johnson & Johnson, Lilly, Merck Sharp & Dohme (MSD), Novartis, Novo Nordisk A/S, and Sanofi.

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Tables

Study	Study period*	Location	Study type	Participants (N)	Comparator guideline(s)
Europe					
Bala et al. (2013)[34]	2012	Poland	Questionnaire-based cross-sectional study	People with T2DM duration <2 years (1,636)	ADA/EASD 2012
Bala et al. (2014)[39 40]	2012	Poland	Questionnaire-based cross-sectional study	People with T2DM duration >10 years (1,740)	ESC/EASD 2013
Bala et al. (2011)[35 36]	2009	Poland	Questionnaire-based cross-sectional study	People with T2DM duration <2 years (1,714)	ADA/EASD 2009
Cahill et al. (2010)[48]	2010	Ireland	Prospective cross-sectional study at a single diabetes clinic in Ireland	People with T2DM (466)	ADA 2010
Miñambres et al. (2016)[37]	2011-2012	Spain	Cross-sectional study in multiple centres across Spain	People with T2DM (5,382)	ADA/EASD 2012
Rodríguez et al. (2011)[52]	2007	Spain	Cross-sectional study in multiple centres across Spain	People with T2DM aged 30+ attending participating centres (2,271)	ADA 2010
Stark et al. (2011)[32]	2008	Germany	Cross-sectional study comparing guideline adherence in those in a disease management programme to those in usual care	People with T2DM insured with social insurance aged 25-74 (166)	ADA 2009
Stone et al. (2013)[19]	2009-2010	Europe (multiple countries)	Cross-sectional study patients recruited from eight countries; primary and specialist care	People with T2DM attending participating centres (7,597)	ADA 2009
Vaccaro et al. (2008)[38]	2004-2006	Italy	Cross-sectional study at 10 large hospital outpatient clinics	People with T2DM aged 50-75 with no CVD history (2,465)	ADA 2007 and EASD/ESC 2007
North America					
Davidson et al. (2008)[33]	1997-2006†	USA	Retrospective cohort analysis of a large electronic records database	People with T2DM aged 30-75 and on oral therapy with metformin, a sulphonylurea, or a thiazolidinedione (60,296)	ADA 2006
Lian and Liang (2014)[74]	2009-2011	USA	Cross-sectional analyses of US insurance claims data	Adults with T2DM on antidiabetic medicine started after an HbA1c value >7% and retested at 1 year (1,337)	ADA 2009
Meyer et al. (2010)[51]	Not reported	USA	Cross-sectional study in a geriatric clinic	Elderly (65+) people with T2DM (165)	ADA 2008
Rao et al. (2015)[47]	2010-2012	USA	Cross-sectional study at three clinics in Michigan USA	People with T2DM (390)	ADA 2014
Wong et al. (2013)[75]	1999-2010‡	USA	Cross-sectional series (National Health and Nutrition Examination Survey; NHANES)	Adults with T2DM (2,403)	ADA 2010
Woodard et al. (2011)[71]	2007-2008	USA	Cross-sectional study (Veterans Affairs National Patient Care Database)	Veterans with diabetes registered with the database (35,872)	ADA 2009
Rest of the world					
Al Harbi et al. (2015)[49]	2010-2011	Saudi Arabia	Cross-sectional study at a large family medicine centre in Saudi Arabia	People with T2DM (450)	ADA 2010
Ali et al. (2013)[50]	2012	Palestine	Cross-sectional sample from a single secondary care centre in Palestine	People with T2DM (450)	ADA 2013
Al-Taweel et al. (2013)[41]	2010	Kuwait	Cross-sectional study in outpatient diabetes clinics in 8 primary care centres and 4 secondary care centres	People with T2DM on diabetes treatment for >6 months (652)	ADA 2009, ESC/EASD 2007, NICE 2008
Issam Diab et al. (2013)[42]	2011	Qatar	Cross-sectional study at a single out-patient centre serving the whole population of Qatar	People with T2DM and no history of CVD (305)	NICE 2009

Ji et al. (2013)[70]	2011	China	Cross-sectional survey of outpatients conducted in 606 hospitals across China	People with T2DM on oral or injectable therapy (238,639)	ADA 2009
Jimeno et al. (2012)[45]	2008-2009	The Philippines	Cross-sectional study (Diabcare) in 40 centres across the Philippines	People with T2DM (724)	ADA 2010
Latif et al. (2011)[44]	2009	Bangladesh	Cross-sectional study (Diabcare) in 100 centres across Bangladesh	People with T2DM aged 18-85 (1,860)	ADA 2009
Mafauzy et al. (2011)[43]	2009	Malaysia	Cross-sectional study (Diabcare) in multiple secondary care clinics throughout the country	People with T2DM (1,549)	ADA 2010
Sriwijitkamol et al. (2011)[76]	2006	Thailand	Cross-sectional study in a single secondary care centre	People with T2DM attending the study centre (722)	ADA 2006

Table 1. Characteristics of the studies included (n=24). *Period of data collection, †Only baseline data included for analysis, ‡Only results from 2009-2010 cross-section included for analysis. ADA, American Diabetes Association; CVD, cardiovascular disease; EASD, European Association for the Study of Diabetes; ESC, European Society of Cardiology; NICE, National Institute for Health and Clinical Excellence.

Study	Treatment targets					Country	Achievement of targets n/N (%)				
	HbA1c (%)	Blood pressure (mmHg)	LDL-C (mmol/l)	HDL-C (mmol/l)	Trigly-ceride (mmol/l)		HbA1c	Blood pressure	LDL-C	HDL-C	Trigly-ceride
Europe											
Bala et al. (2013)[34]	≤6.5	<140/90	<2.6 or <1.8 in CAD	-	-	Poland	**398/1,060 (37.5)**	410/819 (50.1)	217/819 (26.5)	-	-
Bala et al. (2014)[39 40]	≤7%	<140/90	<2.6 or <1.8 in CAD	-	-	Poland	**570/1,1431 (39.8)**	542/1,136 (47.7)	312/1,136 (27.5)	-	-
Bala et al. (2011)[35 36]	<6.5%	<130/90	<2.6	>1.0 (M) >1.3 (F)	<1.7	Poland	**231/798 (28.9)**	243/1,684 (19.9)	225/1,689 (13.3)	731/1,684 (55.3)	660/1,684 (44.3)
Cahill et al. (2010)[48]	< 7%	<130/80	<2.6	-	-	Ireland	199*/466 (42.7)	197*/466 (42.3)	355*/466 (76.2)	-	-
Miñambres et al. (2016)[37]	Variable (as per guidelines)	-	-	-	-	Spain	3,550/5,267 (67.4)	-	-	-	-
Rodríguez et al. (2011)[52]	≤7%	-	-	-	-	Spain	1,247/2,271 (55.0)	-	-	-	-
Stark et al. (2011)[32]	<7%	-	<2.6	-	-	Germany	106/166 (63.9)	-	36/166 (21.7)	-	-
Stone et al. (2013)[19]	<7%	<130/80	<2.6	>1.0 (M) >1.3 (F)	<1.7	Belgium	606*/1,016 (59.7)	180*/1,021 (17.6)	494*/994 (49.7)	692*/1,016 (68.1)	612*/1,006 (60.8)
						France	677*/1,037 (65.3)	1,048*/156 (14.9)	486*/928 (52.4)	615*/937 (65.7)	609*/945 (64.4)
						Germany	446*/919 (48.6)	948*/70 (7.4)	197*/642 (30.7)	356*/578 (61.6)	309*/716 (43.2)
						Ireland	480*/900 (53.4)	894*/223 (24.9)	635*/826 (76.9)	418*/860 (48.6)	486*/810 (60.0)
						Italy	347*/973 (35.7)	975*/203 (20.8)	297*/736 (40.4)	647*/954 (67.8)	639*/951 (67.2)
						Netherlands	715*/1,014 (70.5)	1,014*/206 (20.3)	582*/988 (58.9)	571*/1,010 (56.5)	636*/1,005 (63.3)
						Sweden	306*/542 (56.5)	547*/148 (27.1)	165*/349 (47.3)	231*/390 (59.3)	252*/407 (61.9)
						UK	397*/1,015 (39.1)	1,024*/256 (25.0)	573*/769 (74.5)	348*/796 (43.7)	480*/920 (52.1)
Vaccaro et al. (2008)[38]	<7%	<130/80	<2.6	-	-	Italy	912*/2,465 (37.0)	254*/2,465 (10.3)	407*/2,465 (16.5)	-	-
North America											
Davidson et al. (2008)[33]	<7%	-	-	-	-	USA	2,487/5,356 (46.4)	-	-	-	-
Lian and Liang (2014)[74]	< 7%	-	-	-	-	USA	912/1,337 (68.2)	-	-	-	-
Meyer et al. (2010)[51]	<7%	-	<2.6	-	-	USA	101/159 (63.5)	-	86/164 (52.4)	-	-
Rao et al. (2015)[47]	<7%	<130/80	<2.6	>1.0 (M) >1.3 (F)	<1.7	USA	145/386 (38.6)	234/390 (60.0)	261/358 (72.9)	173/390 (44.3)	240/390 (61.5)
Wong et al. (2013)[75]	<7%	<130/80	<2.6	-	-	USA	289/531 (55.5)	261/531 (52.8)	133/254 (54.4)	-	-

Woodard et al. (2011)[71]	<7%	<130/80	<2.6	-	-	USA	16,444/35,872 (45.8)	17,013/35,872 (47.4)	25,491/35,872 (71.1)	-	-
Rest of the world											
Al Harbi et al. (2015)[49]	≤7%	<130/80	<2.6	>1.0 (M) >1.3 (F)	<1.7	Saudi Arabia	109/450 (24.2)	145/450 (32.2)	227/388 (58.5)	125/388 (32.2)	258/413 (62.5)
Ali et al. (2013)[50]	<6.5%	<130/80	-	-	-	Palestine	131/450 (29.1)	122/450 (27.1)	-	-	-
Al-Taweel et al. (2013)[41]	<7%	<130/80	-	-	-	Kuwait	125*/652 (19.2)	300*/652 (46.0)	-	-	-
Issam Diab et al. (2013)[42]	<7%	<140/80 or <130/80 in CKD	-	-	-	Qatar	**68/305 (22.3)**	72/236 (30.5)	-	-	-
Ji et al. (2013)[70]	<7%	-	-	-	-	China	75,829/238,639 (31.78)	-	-	-	-
Jimeno et al. (2012)[45]	< 7%	-	<2.6	>1.0	<2.2	the Philippines	**109/724 (15.0)**	-	416/724 (57.5)	585/724 (80.8)	620/724 (85.6)
Latif et al. (2011)[44]	< 7%	-	<2.6	>1.0	<2.2	Bangladesh	412/1,784 (23.1)	-	543*/1,860 (29.2)	1,040*/1,860 (55.9)	1,045*/1,860 (56.2)
Mafauzy et al. (2011)[43]	< 7%	<130/80	<2.6	>1.0	<2.2	Malaysia	341/1,549 (22.0)	605/1,549 (39.1)	837/1,549 (54.0)	1,125/1,549 (72.6)	1,242/1,549 (80.2)
Sriwijitkamol et al. (2011)[76]	<7%	<130/80	<2.6	>1.2 (M) >1.4 (F)	<1.7	Thailand	244*/498 (49.0)	194*/625 (31.0)	296*/463 (64.0)	280*/437 (64.0)	269*/463 (58.0)

Table 2. Treatment targets and the proportion of people achieving targets for the included studies (n=24). *Calculated value. ADA, American Diabetes Association; CAD, coronary artery disease; CKD, chronic kidney disease; CVD, cardiovascular disease; EASD, European Association for the Study of Diabetes; ESC, European Society of Cardiology; NICE, National Institute for Health and Clinical Excellence.

Figure captions

Figure 1. A forest plot of the proportion of people achieving guideline derived targets for HbA1c. Subgroup analysis by region are included.

Figure 2. A forest plot of the proportion of people achieving guideline derived targets for blood pressure (BP). Subgroup analysis by region are included.