

# Diabetes



## Are there economic, as well as clinical, benefits to achieving both HbA<sub>1c</sub> and LDL-C goals?

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**T**2D represents a significant clinical and health economic burden, with cardiovascular disease being the most frequent cause of premature morbidity and mortality in people with T2D. Although the cardiovascular benefits of LDL-cholesterol (LDL-C) control in people with diabetes have been well established, debate persists around whether achieving intensive glucose control alongside an LDL-C control can reduce the cardiovascular risk.

Multifactorial risk factor modifications have been associated with significant micro- and macrovascular outcome benefits when compared with conventional treatments, and, as such, appear to be cost-effective. The primary objective of the study by Shi et al summarised alongside was to assess the clinical and economic benefits associated with the achievement of both a HbA<sub>1c</sub> and LDL-C target goal (<53 mmol/mol [ $<7\%$ ] and <2.6 mmol/L respectively) compared with the achievement of only one of these goals. Additional objectives included comparing the outcomes in dual-goal achievers versus no-goal achievers, as well as single-goal achievers for each target versus no-goal achievers. The authors evaluated the electronic medical records of over 75 000 adults with T2D, and used models to compare microvascular and cardiovascular outcomes, and diabetes-related resource utilisation and medical service costs by goal achievement status.

The main finding from this analysis was that, compared to only LDL-C goal achievement, dual-goal achievement was associated with a lower risk of microvascular complications (adjusted hazard ratio [aHR] 0.79), fewer hospitalisation days (adjusted incidence rate ratio [aIRR] 0.93) and fewer outpatient visits (aIRR 0.88), as well as lower diabetes-related annual medical costs. This is the first study to quantify the differences in clinical and economic outcomes between dual-goal and single-goal HbA<sub>1c</sub> and LDL-C achievement in people with T2D. It clearly demonstrates the clinical and economic value of

achieving a combined LDL-C and HbA<sub>1c</sub> goal of <2.6 mmol/L and <53 mmol/mol (<7%) respectively.

The results of this study support the findings of large clinical trials that have assessed the outcome benefits associated with the achievement of single metabolic goals (HbA<sub>1c</sub> or LDL-C) UKPDS Group, 1998; Shepherd et al, 2006). The results also illustrate that there are additional cardiovascular benefits associated with the achievement of both LDL-C and HbA<sub>1c</sub> goals compared with achieving only the HbA<sub>1c</sub> goal, while there are additional microvascular benefits associated with the achievement of both HbA<sub>1c</sub> and LDL-C goals when compared with only LDL-C goal achievement.

This was a retrospective database study and thus represents observations derived from routine clinical practice and may, therefore, be of greater validity to daily clinical practice than data derived from randomised clinical trials. Furthermore, the longitudinal nature of the study design facilitated the capture of the time-varying nature of laboratory measurements, allowing for better estimation of the association between goal achievement and risk of complications over time.

There are a variety of limitations with any such database observational study, including the effects of missing data on important factors such as disease severity, lifestyle interventions and resource use outside of the specific database used for this analysis. Nevertheless, this study highlights the utility of achieving optimal LDL-C and HbA<sub>1c</sub> levels in people with T2D from a clinical and economic perspective, while also implying that, in UK clinical practice, an LDL-C target of <2.6 mmol/L along with an HbA<sub>1c</sub> target of <53 mmol/mol (<7%) should be advocated as key performance indicators in the management of people with T2D. ■

Shepherd J et al (2006) *Diabetes Care* **29**: 1220–6  
UK Prospective Diabetes Study (UKPDS) Group (1998) *Lancet* **352**: 837–53

## Diabetes Care

### Benefits of dual goal targets: HbA<sub>1c</sub> and LDL-cholesterol

Readability *★★★★*  
Applicability to practice *★★★★*  
WOW! Factor *★★★★*

**1** This study examined the economic and cardiovascular benefit differences when individuals achieved a dual goal target of HbA<sub>1c</sub> and LDL-cholesterol (LDL-C), <53 mmol/mol (<7%) and <100 mg/dL (<2.6 mmol/L) respectively, compared to a singular-goal achievement of only the HbA<sub>1c</sub> or LDL-C goal.

**2** Data from participants of the Veterans Integrated Service Network were enrolled if they had T2D and two or more measurements of HbA<sub>1c</sub> and LDL-C between 2004 and 2010 ( $n=75\,646$ ). In total, 97.4% were men and 84.1% were over the age of 55 years. The average BMI was 31.6 kg/m<sup>2</sup>.

**3** Over the median follow-up of 4.5 years, 35.1% of individuals achieved both goals; 21.6% achieved only the LDL-C goal; 24.6% achieved HbA<sub>1c</sub> goal; and 18.6% did not achieve either goal.

**4** Dual-goal achievement was associated with a lower risk of microvascular complications, acute coronary syndrome and other cardiovascular-related events when compared to LDL-C achievement only.

**5** There were also fewer hospital visits by dual-achievers, and lower diabetes-related annual medical costs compared to only LDL-C goal-achievers (−\$130.89;  $P=0.404$ ). There was no significant difference in the annual medical costs between dual-achievers and only HbA<sub>1c</sub> goal-achievers.

**6** Achieving both goals provided additional benefits when compared with achieving only the LDL-C goal but not with the HbA<sub>1c</sub> goal. This could help decide treatment options.

Shi L, Ye X, Lu M et al (2013) Clinical and economic benefits associated with the achievement of both HbA<sub>1c</sub> and LDL cholesterol goals in veterans with type 2 diabetes. *Diabetes Care* **36**: 3297–304

## Diabetes Care

### Glycaemic control strategies for diabetic neuropathy

Readability ✓✓✓✓  
 Applicability to practice ✓✓✓✓  
 WOW! Factor ✓✓✓✓

**1** In total, 2159 participants of the BARI 2D (Bypass Angioplasty Revascularisation Investigation 2 Diabetes) study (presenting T2D and previously documented coronary artery disease) were randomly assigned to receive either insulin-sensitising (IS) or insulin-providing (IP) drugs.

**2** The authors investigated the prevalence of diabetic peripheral neuropathy (DPN) between the two drug groups.

**3** Participants were followed for an average of 4.5 years and tested annually for DPN. Throughout this time participants could receive drugs from the other drug group if a diabetologist believed it was necessary to achieve the HbA<sub>1c</sub> goal.

**4** At the 4-year follow up, there was no difference in the prevalence of DPN between the IS and IP drug groups.

**5** Among those who did not have DPN at baseline, the cumulative incidence rate of DPN was significantly lower in the IS (66%) than in the IP (72%) therapy group ( $P=0.02$ ) after the follow-up period. The IS therapy provided a greater benefit than the IP therapy in male participants than in female participants (hazard ratio 0.75; 99% Confidence Intervals [CI];  $P<0.01$ ).

**6** The IS strategy significantly reduced the incidence of DPN compared with the IP therapy, but did not supply enough protection for DPN remission among those that had DPN at baseline.

Pop-Busui R, Lu J, Brooks MM et al (2013) Impact of glycaemic control strategies on the progression of diabetic peripheral neuropathy in the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) Cohort. *Diabetes Care* **36**: 3208–15

## Diabetes Care

### Tight BP control associated with increased CHD risk

Readability ✓✓✓✓  
 Applicability to practice ✓✓✓✓  
 WOW! Factor ✓✓✓✓

**1** This study found that aggressive control of blood pressure (BP) (<120/70 mmHg) increased the risk of coronary heart disease (CHD) in African American and white individuals with T2D.

**2** A US database of individuals with T2D and their clinical measurements from 1999 to 2009 was used. In total, 17 536 African Americans and 12 618 white individuals were included in the prospective study to determine the association between BP and CHD prevalence. Participants were followed for a mean of 6 years with an average of 14.6 BP measurements.

**3** During the follow-up period, 3580 white individuals and 3680 African Americans individuals developed incidental CHD.

**4** The multivariable-adjusted hazard ratios of CHD associated with different levels of BP at baseline (<110/65; 110–119/65–69; 120–129/70–80; and 130–139/80–90; 140–159/90–100; and  $\geq 160/100$  mmHg) were 1.73; 1.16; 1.04; 1.00; 1.06; and 1.11 ( $P=0.001$ ), respectively, for the African American group, and 1.60; 1.27; 1.08; 1.00; 0.95; and 0.99 ( $P=0.001$ ) for the white group, respectively.

**5** The study found a U-shaped association between baseline BP and the risk of CHD among both groups.

**6** It is advised that BP be maintained between 130–139 mmHg and 80–89 mmHg, and to recommend less aggressive goals to elderly individuals as the detrimental effect of aggressive BP control was higher.

Zhao W, Katzmarzyk PT, Horswell R et al (2013) Aggressive blood pressure control increases coronary heart disease risk among diabetic patients. *Diabetes Care* **36**: 3287–96

## Diabetes Care

### Different cardiorespiratory fitness regimes for individuals with T2D

Readability ✓✓✓✓  
 Applicability to practice ✓✓✓✓  
 WOW! Factor ✓✓✓✓

**1** Low cardiorespiratory fitness (CRF) is a risk factor for cardiovascular disease (CVD). The authors developed age-predicted, sex-stratified and maximal metabolic equivalent (MET) cut points to determine the risk of CVD events and mortality for people in low CRF categories.

**2** In an ancillary study of the HART-D (Health Benefits of Aerobic and Resistance Training in Individuals With T2D) trial, the authors examined the CRF and proportion of participants who were above the MET cut points before and after 9 months of differing exercise programmes (aerobic training [AT], resistance training [RT], or a combination of both [ATRTR]). There was also a non-exercise control group.

**3** In total, 196 people were included in the study. At baseline, participants were sedentary (defined as aerobic exercise of less than 20 minutes, 3 days a week and no RT). Participants had a mean age of  $57.1 \pm 8.1$  years.

**4** AT consisted of treadmill walking 3–5 days per week at a moderate to vigorous intensity. RT consisted strength training 3 days a week, and the ATRTR group completed both AT and RT.

**5** The study found that AT or ATRTR were particularly effective at improving CRF in sedentary individuals. AT and ATRTR also increased the proportion of people above the MET cut points.

Johannsen NM, Swift DL, Lavie CJ et al (2013) Categorical analysis of the impact of aerobic and resistance exercise training, alone and in combination, on cardiorespiratory fitness levels in patients with type 2 diabetes: results from the HART-D study. *Diabetes Care* **36**: 3305–12

**“It is advised that aggressive blood pressure control should be avoided. It should be maintained between 130–139 mmHg and 80–89 mmHg as aggressive control can lead to an increased risk of cardiovascular disease.”**