Clinical *DIGEST 2*

Diabetes journals

Increased CVD event risk with diastolic BP <70 mmHg

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 Blood pressure (BP) control has been shown to significantly reduce the risk of cardiovascular disease (CVD) events in people with T2D; however, evidence on how far the systolic BP (SBP) and diastolic BP (DBP) can be lowered safely, and whether lower BP levels might increase risk, is lacking.

2 The authors aimed to determine whether CVD events could be predicted by baseline and follow-up (On-Study) SBP, DBP, and SBP and DBP combined in 1791 participants from the VADT (Veterans Affairs Diabetes Trial).

3 The primary outcome was the time from randomisation to first occurrence of myocardial infarction, stoke, congestive heart failure, surgery for vascular disease, inoperable coronary disease, amputation for ischaemic gangrene, or CVD death.

4 People with SBP ≥140 mmHg had significant risk both at baseline (hazard ratio [HR], 1.508; $P<0.001$) and On-Study (HR, 1.469; $P=0.002$). DBP <70 mmHg increased CVD events at baseline (HR, 1.482; $P<0.001$) and On-Study (HR, 1.491; $P<0.001$).

5 An increased risk of CVD events was indicated when BP categories were combined: SBP ≥140 mmHg with DBP <70 mmHg at baseline (HR, 1.785; $P=0.03$) and On-Study (HR, 2.042; $P=0.003$) and nearly all SBP with DBP <70 mmHg.

6 It was concluded that a DBP of <70 mmHg, even when combined with guideline-recommended SBP targets, was associated with an increased CVD risk.

Anderson RJ, Bahn GD, Moritz TE et al (2011) Blood pressure and cardiovascular disease risk in the Veterans Affairs Diabetes Trial. *Diabetes Care* **34**: 34–8

Blood pressure control in people with type 2 diabetes: How low is too low?

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Blood pressure control is consistently associated with cardiovascular disease events in studies investigating cardiovascular risk factors in people with type 2 diabetes (UK Prospective Diabetes Study Group, 1998; Mehler et al, 2003). However, the debate continues as to the optimal blood pressure targets for people with type 2 diabetes.

Recently, there has been data from the ACCORD (Action to Control Cardiovascular Risk in Diabetes; ACCORD Study Group et al, 2010) study demonstrating that a reduction of the systolic blood pressure below 140 mmHg down to a target of 120 mmHg improved outcomes in terms of stroke but no other macrovascular end points. This study then reveals potential increased risk for systolic blood pressure elevated to above 140 mmHg either at baseline or during the study. Thus, systolic blood pressure targets appear to be have been elaborated on for people with type 2 diabetes.

The study by Anderson et al (2011; summarised alongside), however, reignites the debate regarding the potential J-shaped curve in the treatment of type 2 diabetes in that those with diastolic blood pressure <70 mmHg were noted to have an increase in cardiovascular risk.

It therefore appears that the threshold for treatment for this population continues to be a systolic blood pressure of ≥140 mmHg and/or a diastolic blood pressure of >90 mmHg, where the treatment target for systolic blood pressure should be at ≤140 mmHg without a major reduction in diastolic blood pressure to <70 mmHg.

> *This study reignites the debate regarding the potential J-shaped curve in the treatment of type 2 diabetes in that those with diastolic blood pressure <70 mmHg were noted to have an increase in cardiovascular risk.*

ACCORD Study Group, Cushman WC, Evans GW et al (2010) Effects of intensive blood-pressure control in type 2 diabetes mellitus. *N Engl J Med* **362**: 1575–85

Mehler PS, Coll JR, Estacio R et al (2003) Intensive blood pressure control reduces the risk of cardiovascular events in patients with peripheral arterial disease and type 2 diabetes. *Circulation* **107**: 753–6

UK Prospective Diabetes Study Group (1998) Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *BMJ* **317**: 703–13

Mean glycaemia and HbA$_{1c}$ strongly associated with CVD risk

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 In this study the authors examined the association between various glycaemic indices (HbA$_{1c}$; mean, postprandial and fasting blood glucose; and blood glucose variability) and metabolic cardiovascular disease (CVD) risk factors.

2 A total of 427 participants were recruited (268 with T1D, 159 with T2D) undertook 16 weeks of blood glucose monitoring.

3 The strongest associations with CVD risk factors in both types of diabetes were seen with mean blood glucose levels and HbA$_{1c}$ levels.

4 Although significant, associations between postprandial and fasting blood glucose and CVD risk factors were weaker; associations with blood glucose variability were non-significant.

5 The authors concluded that mean glycaemia and HbA$_{1c}$ show stronger associations with CVD risk factors than fasting or postprandial blood glucose levels, or glycaemic variability.

Borg R, Kuenen JC, Carstensen B et al (2011) HbA1(c) and mean blood glucose show stronger associations with cardiovascular disease risk factors than do postprandial glycaemia or glucose variability in persons with diabetes: the A1C-Derived Average Glucose (ADAG) study. *Diabetologia* **54**: 69–72

> *"Lower 24-hour sodium excretion was associated with increased all-cause and cardiovascular mortality in people with T2D."*

CV risk profile as a function of diabetes diagnostic criteria

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1. This study aimed to assess the cardiovascular (CV) risk profile of people categorised as newly diagnosed with diabetes using HbA$_{1c}$ and oral glucose tolerance test (OGTT) diagnostic criteria.

2. Participants (n=964) without known diabetes undertook an OGTT, HbA$_{1c}$ and CV risk factor measurements.

3. Participants diagnosed using HbA$_{1c}$ had higher BMI and waist circumference, lower HDL-cholesterol, higher fasting plasma glucose, insulin resistance and fibrinogen than those diagnosed using OGTT but with an HbA$_{1c}$ level <6.5% (<48 mmol/mol).

4. The authors concluded that a more unfavourable CV risk profile was observed in people diagnosed with diabetes using an HbA$_{1c}$-based criterion than those diagnosed using OGTT.

Boronat M, Saavedra P, López-Ríos L et al (2010) Differences in cardiovascular risk profile of diabetic subjects discordantly classified by diagnostic criteria based on glycated hemoglobin and oral glucose tolerance test. *Diabetes Care* **33**: 2671–3

DIABETES CARE

Dietary salt intake and mortality in people with T2D

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1. The authors of this prospective cohort study aimed to assess the relationship between dietary salt intake and mortality in people with T2D.

2. A total of 638 people were followed-up. Baseline sodium excretion was estimated from 24-hour urinary collections (24 hU$_{NA}$).

3. Over a median of 9.9 years there were 175 deaths, 75 (43%) of which were secondary to cardiovascular (CV) events.

4. There was an inverse association between all-cause mortality and 24 hU$_{NA}$ (P<0.001). After adjustments, 24 hU$_{NA}$ was also associated with CV mortality (P=0.03).

5. It was concluded that lower 24-hour sodium excretion was associated with increased all-cause and CV mortality in people with T2D.

Ekinci EI, Clarke S, Thomas MC et al (2011) Dietary salt intake and mortality in patients with type 2 diabetes. *Diabetes Care* **34**: 703–9

DIABETES CARE

Diet effective in reducing cardio-metabolic risk in T2D

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1. This randomised crossover trial was undertaken to determine the effects of the Dietary Approaches to Stop Hypertension (DASH) eating pattern on cardiometabolic risk in 31 people with T2D.

2. Participants were randomised to a control or DASH diet for 8 weeks.

3. Following the DASH diet, body weight and waist circumference reduced significantly (P=0.007 and P=0.002, respectively), as did fasting blood glucose levels and HbA$_{1c}$ levels (both P=0.04).

4. DASH also had a beneficial effect on HDL-cholesterol (P=0.001), LDL-cholesterol (P=0.02), systolic (P=0.02) and diastolic (P=0.04) blood pressure.

5. The DASH diet was concluded to have beneficial effects on cardiometabolic risk in people with T2D.

Azadbakht L, Fard NR, Karimi M et al (2011) Effects of the Dietary Approaches to Stop Hypertension (DASH) eating plan on cardiovascular risks among type 2 diabetic patients: a randomized crossover clinical trial. *Diabetes Care* **34**: 55–7

DIABETES CARE

Outcomes in high-risk participants of the DIAD study

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1. This study estimated baseline cardiovascular (CV) risk in 1123 participants from the DIAD (Detection of Ischemia in Asymptomatic Diabetes) study to assess cardiac event rates, and the effect of screening in this high-risk population.

2. Participants had T2D, were aged 50–75 years, and had no clinical signs or symptoms of coronary artery disease.

3. Baseline CV risk was measured using the Framingham score, the UKPDS (UK Prospective Diabetes Study) risk engine, criteria of the French-Speaking Association for the Study of Diabetes and Metabolic Diseases, and the presence or absence of the metabolic syndrome. Cardiac death and non-fatal myocardial infarction were assessed during 4.8 years of follow-up in intermediate/high-risk participants.

4. Some 53–75% of participants were defined as being at intermediate or high CV risk; prevalence of inducible ischaemia on screening was 21–24%.

5. There was a higher rate of cardiac events in the intermediate/high-risk group compared with the low-risk group (only significant using the UKPDS risk engine; P=0.002).

6. Annual cardiac event rate was <1% in all groups except the UKPDS high-risk group, which was approximately 2%.

7. The authors concluded that a substantial portion of the DIAD population had intermediate/high CV risk, but that their annual cardiac event rate was low and screening for inducible ischaemia did not alter this.

Bansal S, Wackers FJ, Inzucchi SE et al (2011) Five-year outcomes in high-risk participants in the Detection of Ischemia in Asymptomatic Diabetics (DIAD) study: a post hoc analysis. *Diabetes Care* **34**: 204–9

Cardiovascular disease Clinical *DIGEST*

DIABETOLOGIA

HbA$_{1c}$ ≥ 6.0% and CV risk score useful in high-risk screening programme

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 The authors aimed to assess whether T2D screening using HbA$_{1c}$ or glucose measures alone – or in combination with a cardiovascular (CV) risk assessment – identified people who may benefit from preventive interventions or polypharmacy.

2 A population-based, high-risk screening programme was undertaken in 193 primary care practices. Individuals (n=163 185; age 40–69 years) were sent a T2D risk questionnaire.

3 Of the respondents, 20 916 who were at risk of T2D were stratified by: (i) glucose measures (normal glucose tolerance; impaired fasting glucose; impaired glucose tolerance; and diabetes); (ii) HbA$_{1c}$ (<6.0% [<42 mmol/mol]; 6.0–6.4% [42–46 mmol/mol]; or ≥6.5% [≥48 mmol/mol]); and CV risk (heart SCORE <5 or ≥5). Median follow-up was 7 years.

4 SCORE ≥5 identified 91.7% (95% confidence interval [CI], 91.1–92.3%) of those who might benefit from preventive interventions. SCORE ≥5 in combination with an HbA$_{1c}$ ≥6.0% (≥42 mmol/mol) identified 96.7% (95% CI, 96.3–97.0%), which rose to 97.6% (95% CI, 97.2–97.9%) in combination with blood glucose measures.

5 The authors concluded that an HbA$_{1c}$ level ≥6.0% (≥42 mmol/mol) combined with an elevated CV risk assessment (SCORE ≥5) is a good identifier of those who may benefit from preventive lifestyle or drug interventions.

Lauritzen T, Sandbaek A, Skriver MV, Borch-Johnsen K (2011) HbA(1c) and cardiovascular risk score identify people who may benefit from preventive interventions: a 7 year follow-up of a high-risk screening programme for diabetes in primary care (ADDITION), Denmark. *Diabetologia* **54**: 1318–26

DIABETOLOGIA

HbA$_{1c}$ value provides information on myocardial infarction odds

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 Diabetes is an established risk factor for myocardial infarction (MI) and the authors hypothesised that a reliable index of ambient blood-glucose levels (i.e. HbA$_{1c}$) may provide information on MI risk.

2 The relationship between HbA$_{1c}$ levels in people who had experienced an MI and controls from 52 countries who participated in the INTERHEART study were analysed.

3 HbA$_{1c}$ levels in 15 780 participants (1993 had diabetes) were taken. The mean HbA$_{1c}$ level was 6.2% (44 mmol/mol) in the 6761 people with MI, and 5.9% (41 mmol/mol) in controls.

4 After adjustment (age, sex and nine major MI risk factors including diabetes), HbA$_{1c}$ values ≥5.4% (≥36 mmol/mol) were associated with progressively higher odds ratio (OR) of MI; OR for MI in those with HbA$_{1c}$ levels ≥6.12% (43 mmol/mol) being 1.55 (95% confidence interval [CI], 1.37–1.75).

5 When analysed as a continuous variable, every 1.0% increase in HbA$_{1c}$ was associated with a 19% (95% CI, 14–23) increase in the odds of MI, while every 0.5% increase in HbA$_{1c}$ was associated with a 9% increase in the odds of MI (95% CI, 7–11).

6 These risks were consistent across certain subgroups including younger people, people without diabetes and hypertension, and some ethnic groups.

7 It was concluded that HbA$_{1c}$ values provide more information on the odds of MI than self-reported diabetes status and a range of other established risk factors.

Gerstein HC, Islam S, Anand S et al (2010) Dysglycaemia and the risk of acute myocardial infarction in multiple ethnic groups: an analysis of 15,780 patients from the INTERHEART study. *Diabetologia* **53**: 2509–17

DIABETES CARE

Raised pulse pressure risk of CV complications, but not nephropathy

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 Pulse pressure (PP) is an estimate of arterial stiffness and has previously been associated with incident cardiovascular disease (CVD) in people with T1D.

2 Diabetic nephropathy has not previously been taken into account in PP assessments and the authors sought to prospectively investigate the associations between PP and nephropathy in people with T1D.

3 Participants (n=4509) were from the FinnDiane cohort, for whom follow-up (median 5.3 years) data on incident CVD events and renal status were available in 69% and 76% of participants, respectively.

4 In total, 269 (8.6%) participants experienced a CVD event and 370 (10.8%) progressed to a higher level of albuminuria or to end-stage renal disease.

5 PP was significantly higher at baseline in those who went on to experience a CVD event (66±18 vs 52±14 mmHg; P<0.001) or worsened in renal status (58±18 vs 54±15 mmHg; P<0.01) during follow-up.

6 PP was independently associated with a first ever CVD event (hazard ratio per 10 mmHg, 1.22; 95% confidence interval [CI], 1.10–1.34) but not with progression of renal disease (HR, 1.00; 95% CI, 0.89–1.12) after adjustments for traditional risk factors.

7 The authors concluded that, although a risk factor for CVD, PP was not associated with nephropathy among this cohort with T1D.

Gordin D, Wadén J, Forsblom C et al (2011) Pulse pressure predicts incident cardiovascular disease but not diabetic nephropathy in patients with type 1 diabetes (The FinnDiane Study). *Diabetes Care* **34**: 886–91

> *"… every 1.0% increase in HbA$_{1c}$ was associated with a 19% increase in the odds of myocardial infarction …"*