North West Adelaide Health Study

Modelling Reduction of Coronary Heart Disease Risk among people with Diabetes

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Executive Summary

Major studies have found that people with diabetes have an increased risk of developing cardiovascular disease (CVD) and lower life expectancy following a CVD-related event. Measures taken to decrease CVD-related mortality are also less effective for people with diabetes. The UK Prospective Diabetes Study (UKPDS) examined 5,102 people with Type 2 diabetes over a 25 year follow up period and found that 44% of deaths were caused by myocardial infarction and 8% by stroke[2]. The UKPDS subsequently developed a coronary heart disease (CHD) risk engine[1], which estimates the risk of a person developing CHD within five, ten and twenty years of diagnosis of type 2 diabetes using a variety of factors, some of which include HbA1c, blood pressure, cholesterol, and smoking status.

Studies have shown that with intensive therapy it is possible to reduce HbA1c by approximately 1%[3], systolic blood pressure by at least 10 mm Hg[4], and total cholesterol by at least 1.0 mmol/L[5,6]. In addition, the downward trend in smoking prevalence over the years in South Australia[7] indicates that cessation of smoking is possible, and it remains an important factor in reducing risk of cardiovascular complications. The UKPDS risk model could therefore be used to determine hypothetical outcomes of reducing diabetes management targets, by values that have been shown to be achievable, with and without the use of medications.

This report examines the risk of developing CHD, as determined by the UKPDS CHD risk engine, among a representative sample of people with diabetes in the North West Adelaide Health Study (NWAHS).

The UKPDS CHD risk engine is applied to the NWAHS population with type 2 diabetes who are aged 25 to 65 years with no self-reported CHD to:

- Identify the characteristics of those most at risk of developing CHD;
- Model the changes in the proportion of people at risk of developing CHD using several proposed situations including:
    - Reducing the systolic blood pressure of people with diabetes by 10 mmHg;
    - Reducing the total cholesterol of people with diabetes by 1 mmol/L;
    - Reducing the HbA1c of people with diabetes by 1%;
    - Simulating cessation of smoking among people with diabetes; and
- Estimate the impact of the hypothetical reductions in key management targets on the proportion of those who are at high risk for developing CHD among those with diabetes in the South Australian population.

For the purposes of these analyses, all those who self-reported being diagnosed by a doctor with type 2 diabetes, who did not self-report having CHD, and who were aged 25 to 65 years were included (n=62). Among participants in the NWAHS aged 25 to 65 years who had no self-reported CHD, the prevalence of diagnosed type 2 diabetes was 2.3% (95% CI 1.8 – 2.9, n=62). This equates to approximately 18,460 people in South Australia.

The UKPDS risk engine calculates risk of developing CHD among those with type 2 diabetes. High risk is identified as 7.5% risk within 5 years, 15% risk within 10 years, or 30% risk within 20 years of diagnosis. The proportion at high risk of developing CHD within 5, 10 and 20 years are shown in Table 1.

Table 1. Proportion of those with type 2 diabetes at high risk for CHD.

	High CHD risk score	Proportion at high risk for developing CHD (%)
Within 5 years	≥ 7.5%	22.1
Within 10 years	≥ 15.0%	29.8
Within 20 years	≥ 30.0%	43.1

Characteristics of those at high risk of CHD

Associations between being at high risk of developing CHD and the factors included in the UKPDS risk model for the NWAHS population were examined. Those at high risk of developing CHD within 10 years of diagnosis were significantly more likely to be aged 55 years or older and to have low HDL cholesterol. Those at high risk of developing CHD within 20 years of diagnosis were statistically significantly more likely to have low HDL cholesterol.

Associations between being at high risk of developing CHD and other demographic and risk factors not included in the UKPDS risk model for the NWAHS population were also examined. There were no additional demographic or risk factors other than those already included in the risk engine model that were significantly associated with being at high risk of developing CHD within 5, 10 or 20 years of diagnosis.

Effect of reduction in diabetes management targets on risk of CHD

Studies have shown that with intensive therapy it is possible to improve diabetes management and reduce risk factors for developing CHD. To estimate the effect of improving diabetes management targets on CHD risk, models were produced by changing management targets among two groups: 1) everyone aged 25 to 65 years with type 2 diabetes, regardless of CHD risk; and 2) those aged 25 to 65 years with type 2 diabetes at high risk of developing CHD according to their risk score as defined in Table 1. The following management targets were changed individually and cumulatively in each model: systolic blood pressure, HbA1c and total cholesterol were decreased by 10 mmHg, 1% and 1.0mmol/L respectively, and smoking status was changed to non/ex-smoker for those who were current smokers.

Reducing total cholesterol had the greatest single effect on reducing CHD risk of any of the risk factors in isolation. The greatest overall reduction in CHD risk however, was observed when all four risk factors were reduced. This was observed regardless of whether risk factors were reduced among everyone, or only those at high risk.

A multifactorial approach focusing on all four risk factors among those at high risk of CHD has the potential to reduce the proportion of people with diabetes who are at risk of a CHD event within ten years from 29.8% to 9.8%. This is equivalent to reducing the number of people at risk of CHD within 10 years by approximately 3690 people in South Australia.

Introduction

Background

Major studies have found that people with diabetes have an increased risk of developing cardiovascular disease (CVD) and lower life expectancy following a CVD-related event, and that measures taken to decrease CVD-related mortality are less effective for people with diabetes. Of note is the UK Prospective Diabetes Study (UKPDS), which examined 5,102 people with Type 2 diabetes over 25 years and found that of the 765 subsequent deaths, 44% were caused by myocardial infarction and 8% by stroke[2]. The UKPDS subsequently developed a coronary heart disease (CHD) risk engine[1], which estimates the risk of a person developing CHD within five, ten and twenty years of diagnosis of type 2 diabetes using a variety of factors, some of which include HbA1c, blood pressure, cholesterol, and smoking status.

Several other equations have also been developed to predict cardiovascular risk, such as the Framingham risk equation[8], which was the first model developed to predict cardiovascular risk based on a large cohort. Since then, several studies[9-13] have been undertaken to validate the equation and to modify it to include different risk factors.

Since the development of these models to predict risk of coronary or cardiovascular disease or events, there have been a number of studies to assess their use in clinical practice for determining those patients who would benefit most from primary prevention of CHD and CVD outcomes by prescribing medication[10,14-16]. In particular, studies have shown that with intensive therapy it is possible to reduce HbA1c by approximately 1%[3], systolic blood pressure by at least 10 mm Hg[4], and total cholesterol by at least 1.0 mmol/L[5,6]. In addition, the downward trend in smoking prevalence over the years in South Australia[7] indicates that cessation of smoking is possible, and it remains an important factor in reducing risk of cardiovascular complications. These risk models could therefore be used to determine hypothetical outcomes of reducing diabetes management targets, by values that have been shown to be achievable, with and without the use of medications.

The UKPDS risk engine for CHD remains the only model developed specifically for predicting coronary disease risk in people with diabetes, and can be modified to predict CHD risk within the North West Adelaide Health Study (NWAHS) cohort. Providing an epidemiological description of those at risk could help health professionals, those with diabetes, and the wider population to prevent or delay a CHD event.

This report examines the risk of CHD among a representative sample with diabetes in the NWAHS. The focus of the NWAHS is on chronic disease, including diabetes and CVD, and health-related risk factors from both self-reported and biomedically measured data. The study's primary purpose is to study progression or regression of study participants along a disease continuum. The NWAHS is a collaboration between the North Western Adelaide Health Service (The Queen Elizabeth Hospital and Lyell McEwin Health Service campuses), the South Australian Department of Health, The University of Adelaide, the University of South Australia, and the Institute of Medical and Veterinary Science. Further information about the NWAHS can be downloaded from www.health.sa.gov.au/pros.

Aims

The aim of this report is to apply the UKPDS CHD risk engine to the NWAHS population with type 2 diabetes who are aged 25 to 65 years with no self-reported coronary heart disease. Specifically, this report aims to:

- Identify the characteristics of those most at risk of developing CHD;
- Model the changes in the proportion of people at risk of developing CHD using several proposed situations including:
    - Reducing the systolic blood pressure of people with diabetes by 10 mmHg;
    - Reducing the total cholesterol of people with diabetes by 1 mmol/L;
    - Reducing the HbA1c of people with diabetes by 1%; and
    - Simulating cessation of smoking among people with diabetes.
- Estimate the impact of the hypothetical reductions in key management targets on the proportion of those who are at high risk for CHD among those with diabetes in the South Australian population.

Ethics

Ethics approval for the NWAHS has been granted by the Ethics of Human Research Committee of the Central Northern Adelaide Health Service.

Methodology

Sample selection

The NWAHS is a cohort study of a random, representative sample of people aged 18 years and over living in the north west region of Adelaide (n=4060). The sample for the NWAHS was recruited in two phases between November 1999 and July 2003. All households in the north western area of Adelaide with a telephone connected and the telephone number listed in the Electronic White Pages (EWP) were eligible for selection. The sample was stratified into the two health regions: western Adelaide and northern Adelaide. Within each household, the person who had their birthday last, and was 18 years or older, was selected for interview and invited to attend the clinic. Detailed methodology of the NWAHS has been reported previously[17].

Respondents were recruited to the study via a CATI telephone interview, during which they answered questions about their health. Self-reported data were also collected in a self-administered questionnaire that participants completed before they attended the clinic. Biomedical data were collected from participants at their clinic appointment. Socio-demographic data were collected via telephone interview and self-completed questionnaire.

This report examines the risk of CHD, including heart attack and angina, among those with self-reported doctor-diagnosed type 2 diabetes, who have not reported having CHD and who are aged between 25 and 65 years (n=62). People with diabetes were defined as those who had a fasting plasma glucose level of at least 7.0mmol/L, and/or who self-reported being told by a doctor that they had type 2 diabetes.

Data collection

The QPL (Questionnaire Programming Language) system was used to conduct the interviews. At least ten call-backs were made to the telephone number selected to interview household members. Different times of the day or evening were scheduled for each call-back. If a person could not be interviewed immediately they were re-scheduled for interview at a time suitable to them. Replacement interviews for persons who could not be contacted or interviewed were not permitted.

Clinic appointment

Respondents were given the option of attending a clinic at either The Queen Elizabeth Hospital or the Lyell McEwin Health Service. Appointments were made from 7:30am and took approximately 45 minutes.

Measurements conducted at the clinic included:

- Blood pressure
- Height and weight
- Waist and hip circumference
- Fasting blood sample (glucose, lipid profile, glycated haemoglobin)
- Lung function tests (spirometry followed by Ventolin inhalation and retesting)
- Skin allergy tests (to rye grass, cat, house dust mite, alternaria, feather, and cockroach).

Response rate

Response and participation rates are shown for each recruitment phase and the total cohort in Table 2. The overall response rate was 49.4%.

Table 2. Participation and response rate

	Total cohort	
	n	%
Initial sample	**10096**	
Sample loss[a]	1883	
Eligible sample	**8213**	
Non-contact and refusals	2363	
Completed interview[b]	**5850**	**71.2**
Refused or did not attend clinic	1790	
Attended clinic[c]	**4060**	**49.4**

[a] Sample loss of ineligible telephone numbers due to business numbers, not in area, modems/fax numbers, disconnected numbers
[b] Participation rate = completed interview / eligible sample
[c] Response rate = attended clinic / eligible sample

Statistical analysis

Data was analysed using SPSS Version 14.0. Chi-square tests, analysis of variance, and logistic regression analysis were used, and p-value of <0.05 was taken to be significant.

Weighting

The data presented in this report were weighted by region (western and northern health regions), age group, gender, and probability of selection in the household to the Australian Bureau of Statistics 1999 Estimated Residential Population and the 2001 Census. Probability of selection of the adult in the household was calculated from the number of adults in the household and the number of telephone listings in the Electronic White Pages that reach the household.

The Model

The UKPDS risk engine formula was calculated as follows:

$$R(t) = 1 - \exp(-q[(1-d^t)/(1-d)])$$

where t = time, d = risk ratio for duration of diagnosed diabetes, and q = the product of the risk ratios for age at diagnosis, sex, ethnicity, smoking, HbA1c, blood pressure, and lipids[1].

Box 1. UKPDS risk engine model

One parameter in the risk engine was modified for use with the NWAHS data. The risk ratio for ethnicity was set at 1.00 (indicating that ethnic background is not a risk factor) as the ethnic backgrounds in the original model were not relevant to this population.

The model produces a risk score out of 100 for each individual in the sample, which is expressed as a percentage. This risk score indicates a person's risk of developing CHD within a specified period of time after diagnosis of diabetes. In this report, risk scores are generated to indicate the risk of developing CHD within 5, 10, and 20 years of diagnosis of type 2 diabetes.

For example, a person might have a 5-year risk score of 14.3. That individual therefore has a 14.3% chance of developing CHD within 5 years of being diagnosed with type 2 diabetes. A mean risk score is calculated from the sum of all the individual risk scores, divided by the number of individuals. The mean 5-year risk score might be, for example, 12.0. This means that, on average, people have a 12.0% chance of developing CHD within 5 years of being diagnosed with type 2 diabetes. Another way to express this is to say that approximately 1 in every 8 people diagnosed with type 2 diabetes will develop CHD within 5 years of diagnosis.

The risk scores in this report are generally presented as mean risk scores, which are the average of all individual risk scores. The standard deviation (SD) and standard error (SE) are also provided to give a measure of variability of the mean scores.

Characteristics of those at high risk of coronary heart disease

Prevalence of type 2 diabetes

For the purposes of these analyses, all those who self-reported being diagnosed by a doctor with type 2 diabetes, who did not self-report having CHD, and who were aged 25 to 65 years were included (n=62). The prevalence of type 2 diabetes in the NWAHS overall was 3.9% (95% CI 3.4 – 4.5). This compares with the overall South Australian prevalence of type 2 diabetes in 2001 of 3.5% (95% CI 2.9 – 4.2) for people aged 18 years and over[18]. Among those aged 25 to 65 years in the NWAHS population, who had no self-reported CHD, the prevalence of type 2 diabetes was 2.3% (95% CI 1.8 – 2.9). This equates to approximately 18,460 people in South Australia. This represents approximately one quarter of the total number of people with all types of diabetes aged 18 years and over in South Australia.

Risk of CHD among those with diabetes

The estimated mean percentage risk scores for developing CHD within 5, 10 and 20 years of diabetes diagnosis among those aged 25 to 65 years with self-reported doctor-diagnosed type 2 diabetes are shown in Table 3. The mean percentage risk scores shown in Table 3 indicate the average risk of developing CHD 5, 10 and 20 years after being diagnosed with type 2 diabetes. For example, for people aged 25 to 65 years with diagnosed type 2 diabetes who have not previously been diagnosed with CHD, the average risk of developing CHD 10 years after being diagnosed with type 2 diabetes is 12.5%. This means that there is a 1 in 8 chance of people in this group developing CHD 10 years after being diagnosed with diabetes.

Table 3. Estimated mean percentage risk of coronary heart disease within 5, 10 and 20 years of diagnosis (n=62).

	Mean percentage risk score	SD	SE	Number of people at risk
5 year risk	5.7	7.7	1.0	1 in 18
10 year risk	12.5	10.3	1.3	1 in 8
20 year risk	31.5	18.1	2.3	1 in 3

Characteristics of those at high risk of coronary heart disease

In order to be clinically meaningful, risk scores generated by risk equations have generally been categorised into 'low risk' and 'high risk' groups. The clinical relevance of this categorisation is in identifying people where active intervention and risk factor monitoring are indicated[19]. It would be clinically appropriate then for those people categorised as being at high risk of CHD to receive some form of lifestyle modification counselling and preventative treatment with medication.

The Heart Foundation suggests that people who have an absolute risk of ≥15% in the next 5 years should be targeted for treatment[20]. However this cut off applies only to those without diabetes, because people with diabetes are already at higher absolute risk for CHD. The national *Diabetes management in General Practice* guidelines[19] suggest that for those with diabetes, absolute risk of >15% in the next 10 years identifies those where active intervention and risk factor monitoring are indicated.

The most widely suggested score for initiation of preventative treatment for CHD when diabetes is present is an absolute 10-year risk score of >15%[20-23], or a cumulative risk of approximately 1.5% per year after diagnosis of diabetes[12,19,24]. The limitation to using these risk cut offs is that the risk of CHD events increases with increasing age[23], meaning that risk actually increases exponentially over time, not at a steady rate of 1.5% per year. However, the cut offs are arbitrary, and for the purposes of this report, simply define low and high risk groups for comparison.

The absolute risk scores used in this report to indicate that an individual with type 2 diabetes is at high risk of CHD are 7.5% risk within 5 years, 15% risk within 10 years, and 30% risk within 20 years of diagnosis. The proportion of the sample at high risk of CHD within 5, 10 and 20 years are shown in Table 4.

Table 4. Proportion of those with type 2 diabetes at high risk for CHD (n=62).

	High CHD risk score	Proportion at high risk for CHD (%)
Within 5 years	≥ 7.5%	22.1
Within 10 years	≥ 15.0%	29.8
Within 20 years	≥ 30.0%	43.1

Characteristics of those at risk of CHD within 5, 10 and 20 years of diagnosis: Factors included in the risk model

Associations between being at high risk of CHD and the factors included in the UKPDS risk model for the NWAHS population were examined by univariate odds ratios (Table 5 to Table 7). The management targets used were taken from the national *Diabetes management in General Practice* guidelines[19].

While few significant associations were found, overall, those at high risk of CHD within 10 years of diagnosis (Table 6) were statistically significantly more likely to be aged 55 years or older and to have low HDL cholesterol, and those at risk of CHD within 20 years of diagnosis (Table 7) were statistically significantly more likely to have low HDL cholesterol. It is likely that there were no other significant associations found due to the small sample size.

Table 5. Univariate odds ratios associated with being at high risk of CHD within 5 years (n=62).

	n	%	OR	(95% CI)	p value
Age at diagnosis of diabetes					
Less than 55 years	4/41	8.4	1.00		
55 years or older	10/20	51.0	-	-	**-**
Sex					
Male	12 /39	31.9	1.00		
Female	1/22	5.0	-	-	-
Smoking status					
Non-/Ex-smoker	11/53	21.0	1.00		
Current smoker	2/8	29.2	-	-	-
HbA1c					
Normal (≤7.0%)	6/30	20.3	1.00		
High (>7.0%)	7/31	23.9	1.23	(0.37 – 4.12)	0.74
Systolic blood pressure					
Normal (<130 mmHg)	3/22	13.8	1.00		
High (≥130 mmHg)	10/39	26.9	-	-	-
HDL Cholesterol					
Normal (≥1.0 mmol/L)	8/44	17.0	1.00		
Low (<1.0 mmol/L)	6/17	35.1	2.63	(0.74 – 9.30)	0.13
Total Cholesterol					
Normal (<4.0 mmol/L)	2/9	25.0	1.00		
High (≥4.0 mmol/L)	11/53	21.7	-	-	-

Note: associations may not be significant due to small sample sizes.

Table 6. Univariate odds ratios associated with being at high risk of CHD within 10 years of diagnosis (n=62).

	n	%	OR	(95% CI)	p value
Age at diagnosis of diabetes					
Less than 55 years	8/41	19.1	1.00		
55 years or older	10/20	52.4	4.68	(1.44 – 15.15)	**0.01**
Sex					
Male	17/39	43.9	1.00		
Female	1/22	5.0	-	-	-
Smoking status					
Non-/Ex-smoker	15/53	28.5	1.00		
Current smoker	3/8	38.5	-	-	-
HbA1c					
Normal (≤7.0%)	8/30	26.0	1.00		
High (>7.0%)	10/31	33.5	1.43	(0.48 – 4.32)	0.52
Systolic blood pressure					
Normal (<130 mmHg)	6/22	26.8	1.00		
High (≥130 mmHg)	12/39	31.6	1.26	(0.40 4.02)	0.69
HDL Cholesterol					
Normal (≥1.0 mmol/L)	10/44	22.1	1.00		
Low (<1.0 mmol/L)	9/17	49.4	3.44	(1.06 -11.23)	**0.04**
Total Cholesterol					
Normal (<4.0 mmol/L)	2/9	25.0	1.00		
High (≥4.0 mmol/L)	16/53	30.6	-	-	-

Note: associations may not be significant due to small sample sizes.

Table 7. Univariate odds ratios associated with being at high risk of CHD within 20 years of diagnosis (n=62).

	n	%	OR	(95% CI)	p value
Age at diagnosis of diabetes					
Less than 55 years	15/41	35.8	1.00		
55 years or older	12/20	58.6	2.54	(0.85 – 7.62)	0.10
Sex					
Male	25/39	63.1	1.00		
Female	2/22	8.0	-	-	-
Smoking status					
Non-/Ex-smoker	21/53	39.2	1.00		
Current smoker	6/8	68.3	3.35	(0.70 – 16.03)	0.13
HbA1c					
Normal (≤7.0%)	12/30	38.6	1.00		
High (>7.0%)	15/31	47.6	1.44	(0.52 – 3.99)	0.48
Systolic blood pressure					
Normal (<130 mmHg)	8/22	35.1	1.00		
High (≥130 mmHg)	19/39	47.7	1.69	(0.58 – 4.95)	0.34
HDL Cholesterol					
Normal (≥1.0 mmol/L)	15/44	33.4	1.00		
Low (<1.0 mmol/L)	12/17	67.9	4.23	(1.29 – 13.89)	**0.02**
Total Cholesterol					
Normal (<4.0 mmol/L)	4/9	41.5	1.00		
High (≥4.0 mmol/L)	23/53	43.4	-	-	-

Note: associations may not be significant due to small sample sizes.

Characteristics of those at high risk of CHD within 5, 10 and 20 years of diagnosis: Factors not included in the risk model

In order to assess whether or not there were factors other than those included in the risk model that were associated with being at high risk for CHD, associations between various demographic and biomedical risk factors and risk of CHD were examined.

Table 8 to Table 10 show the univariate odds ratios for factors not included in the model associated with being at high risk of CHD within 5, 10 and 20 years of diagnosis. Due to small numbers, significant results may not be found, therefore caution is advised when interpreting the results

There were no additional demographic or risk factor variables other than those already included in the risk engine model that were significantly associated with being at high risk of CHD within 5, 10 or 20 years of diagnosis. While family history of CHD is a recognised risk factor for development of CHD, it was not significantly associated with being at high risk for CHD in this sample. This could be because those with a family history had already developed CHD and were therefore not included in these analyses.

Table 8. Demographic and risk factor odds ratios associated with being at high risk of CHD within 5 years of diagnosis (n=62).

	n	%	OR	(95% CI)	p value
Country of birth					
Australia	7/30	24.6	1.00		
Outside Australia	6/30	20.0	0.77	(0.23 – 2.57)	0.67
Income					
Up to $20,000	3/18	18.5	1.00		
$20,001 or more	9/36	23.8	-	-	-
Highest education level					
Up to secondary education	7/34	21.8	1.00		
Post secondary education	5/26	21.4	1.00	(0.28 – 3.39)	0.97
Marital status					
Married/Living with partner	10/42	23.7	1.00		
Separated/Divorced/Widowed/Never married	4/19	18.6	-	-	-
Work status					
Full time employed	6/20	31.0	1.00		
Not full time employed	7/39	17.7	0.48	(0.14 – 1.67)	0.25
Alcohol risk					
Non drinker/No risk	13/48	26.2	1.00		
Drinker/Low to very high risk	1/13	7.1	-	-	-
Physical activity level					
Sedentary	2/15	11.6	1.00		
Undertakes some exercise	10/40	25.3	-	-	-
Body mass index					
Underweight/Normal/Overweight (BMI<30.0)	2/18	11.4	1.00		
Obese (BMI≥30.0)	11/43	26.8	-	-	-
Waist circumference					
Normal	0/6	0.0	1.00		
High (Males≥95cm; Females≥80cm)	14/55	24.4	-	-	-
Waist to hip ratio					
Normal	9/37	24.9	1.00		
High (Males>1.0; Females>0.85)	4/24	17.7	-	-	-
Family history of heart disease					
No	5/24	20.0	1.00		
Yes	9/37	23.6	1.24	(0.35 – 4.33)	0.74

Note: associations may not be significant due to small sample sizes.

Table 9. Demographic and risk factor odds ratios associated with being at high risk of CHD within 10 years of diagnosis (n=62).

	n	%	OR	(95% CI)	p value
Country of birth					
Australia	10/30	31.3	1.00		
Outside Australia	9/30	28.8	0.89	(0.30 – 2.66)	0.83
Income					
Up to $20,000	5/18	26.1	1.00		
$20,001 or more	11/36	30.0	1.22	(0.34 – 4.36)	0.77
Highest education level					
Up to secondary education	9/34	27.2	1.00		
Post secondary education	8/26	32.6	2.30	(0.42 – 3.96)	0.65
Marital status					
Married/Living with partner	13/42	30.0	1.00		
Separated/Divorced/Widowed/Never married	6/19	29.4	0.97	(0.30 – 3.19)	0.96
Work status					
Full time employed	7/20	34.7	1.00		
Not full time employed	11/39	27.8	0.72	(0.23 – 2.29)	0.58
Alcohol risk					
Non drinker/No risk	17/48	35.9	1.00		
Drinker/Low to very high risk	1/13	7.1	0.14	(0.02 – 1.23)	0.08
Physical activity level					
Sedentary	4/15	24.6	1.00		
Undertakes some exercise	13/40	31.5	-	-	-
Body mass index					
Underweight/Normal/Overweight (BMI<30.0)	3/18	17.6	1.00		
Obese (BMI≥30.0)	15/43	35.1	-	-	-
Waist circumference					
Normal	0/6	0.0	1.00		
High (Males≥95cm; Females≥80cm)	18/55	32.9	-	-	-
Waist to hip ratio					
Normal	13/37	34.6	1.00		
High (Males>1.0; Females>0.85)	5/24	22.3	0.54	(0.17 – 1.76)	0.31
Family history of heart disease					
No	8/24	33.8	1.00		
Yes	10/37	27.2	0.74	(0.24 – 2.23)	0.59

Note: associations may not be significant due to small sample sizes.

Table 10. Demographic and risk factor odds ratios associated with being at high risk of CHD within 20 years of diagnosis (n=62).

	n	%	OR	(95% CI)	p value
Country of birth					
Australia	16/30	51.3	1.00		
Outside Australia	11/30	35.5	0.52	(0.19 – 1.46)	0.21
Income					
Up to $20,000	7/18	41.6	1.00		
$20,001 or more	13/36	36.6	0.81	(0.25 – 2.59)	0.72
Highest education level					
Up to secondary education	14/34	42.3	1.00		
Post secondary education	11/26	43.5	1.05	(0.37 – 2.95)	0.93
Marital status					
Married/Living with partner	18/42	43.5	1.00		
Separated/Divorced/Widowed/Never married	8/19	42.4	0.96	(0.32 – 2.86)	0.94
Work status					
Full time employed	9/20	45.8	1.00		
Not full time employed	17/39	43.0	0.89	(0.30 – 2.62)	0.84
Alcohol risk					
Non drinker/No risk	24/48	48.8	1.00		
Drinker/Low to very high risk	3/13	22.1	-	-	-
Physical activity level					
Sedentary	6/15	39.3	1.00		
Undertakes some exercise	18/40	44.6	1.24	(0.37 – 4.20)	0.73
Body mass index					
Underweight/Normal/Overweight (BMI<30.0)	6/18	32.1	1.00		
Obese (BMI≥30.0)	20/43	47.9	1.94	(0.62 – 6.12)	0.26
Waist circumference					
Normal	0/6	0.0	1.00		
High (Males≥95cm; Females≥80cm)	26/55	47.6	-	-	-
Waist to hip ratio					
Normal	19/37	51.5	1.00		
High (Males>1.0; Females>0.85)	7/24	30.0	0.40	(0.14 – 1.20)	0.10
Family history of heart disease					
No	12/24	50.9	1.00		
Yes	14/37	38.0	0.59	(0.21 – 1.67)	0.32

Note: associations may not be significant due to small sample sizes.

Effect of reduction in diabetes management targets on risk of coronary heart disease

Effects of reduction in management targets

Studies have shown that with intensive therapy it is possible to reduce HbA1c by approximately 1%[3], systolic blood pressure by at least 10 mm Hg[4], and total cholesterol by at least 1.0 mmol/L[5,6]. In addition, the downward trend in smoking prevalence over the years in South Australia[7] indicates that cessation of smoking is possible, and it remains an important factor in reducing risk of cardiovascular complications. The Heart Foundation outlines various methods to help patients quit smoking, and suggests that even three to five minutes of time taken to encourage smokers to attempt to quit can increase smoking cessation rates[20].

To estimate the effect of reducing diabetes management targets among everyone with diabetes regardless of CHD risk, systolic blood pressure, HbA1c and total cholesterol values were decreased by 10 mmHg, 1%, and 1.0 mmol/L respectively, and for those who were current smokers, smoking status was changed to non/ex-smoker to simulate cessation of smoking. The reduced values for HbA1c, blood pressure and total cholesterol were used in the risk engine to determine the effect of a reduction in these values among everyone with diabetes on 5, 10 and 20 year risk of CHD. Mean risks were compared to the 'no change' scenario (ie. assuming no reduction in management targets was achieved) using paired samples t-tests.

Table 11 to Table 13 present the mean risk of developing CHD within 5, 10 and 20 years of diagnosis, resulting from various scenarios. These scenarios include no change (in management targets), reduction in systolic blood pressure by 10 mmHg, reduction in HbA1c by 1%, reduction in total cholesterol by 1.0 mmol/L, cessation of smoking, and a reduction in all four targets. The mean percentage risks shown in Table 11 to Table 13 indicate the average risk of developing CHD 5, 10 or 20 years after being diagnosed with type 2 diabetes, when changes in diabetes management targets are modelled.

For example, for people aged 25 to 65 years with diagnosed type 2 diabetes who have not previously been diagnosed with CHD, the average risk of developing CHD 5 years after being diagnosed with type 2 diabetes is 5.7%. This means that there is around a 1 in 18 chance of people in this group developing CHD 5 years after diagnosis. However, if everyone in this group were to reduce their total cholesterol by 1.0 mmol/L, the average risk would drop to 4.5%, or around a 1 in 22 chance of developing CHD 5 years after being diagnosed with type 2 diabetes.

Table 11. Estimated mean percentage risk of coronary heart disease within 5 years of diagnosis for various scenarios, and significance of paired t-test in comparison to 'No change' scenario for all with type 2 diabetes & no CHD (n=62).

	Mean percentage risk score	SD	Number of people at risk	p-value
No change	5.7	7.7	1 in 18	
Reduction in HbA1c by 1%	5.0	7.5	1 in 20	**<0.001**
Reduction in systolic blood pressure (SBP) by 10 mmHg	5.3	7.6	1 in 19	**<0.001**
Reduction in total cholesterol (TChol) by 1.0 mmol/L	4.5	7.4	1 in 22	**<0.001**
Cessation of smoking	5.5	7.7	1 in 18	**0.009**
Reduction in SBP, HbA1c & TChol & cessation of smoking	3.7	7.3	1 in 27	**<0.001**

Note: estimated number of people at risk is rounded to the nearest integer.

Table 12. Estimated mean percentage risk of coronary heart disease within 10 years of diagnosis for various scenarios, and significance of paired t-test in comparison to 'No change' scenario for all with type 2 diabetes & no CHD (n=62).

	Mean percentage risk score	SD	Number of people at risk	p-value
No change	12.5	10.3	1 in 8	
Reduction in HbA1c by 1%	11.1	9.7	1 in 9	**<0.001**
Reduction in systolic blood pressure (SBP) by 10 mmHg	11.7	9.9	1 in 9	**<0.001**
Reduction in total cholesterol (TChol) by 1.0 mmol/L	9.9	9.2	1 in 10	**<0.001**
Cessation of smoking	12.0	10.1	1 in 8	**0.008**
Reduction in SBP, HbA1c & TChol & cessation of smoking	8.0	8.5	1 in 13	**<0.001**

Note: estimated number of people at risk is rounded to the nearest integer.

Table 13. Estimated mean percentage risk of coronary heart disease within 20 years of diagnosis for various scenarios, and significance of paired t-test in comparison to 'No change' scenario for all with type 2 diabetes & no CHD (n=62).

	Mean percentage risk score	SD	Number of people at risk	p-value
No change	31.5	18.1	1 in 3	
Reduction in HbA1c by 1%	28.5	17.0	1 in 4	**<0.001**
Reduction in systolic blood pressure (SBP) by 10 mmHg	29.9	17.5	1 in 3	**<0.001**
Reduction in total cholesterol (TChol) by 1.0 mmol/L	25.9	16.1	1 in 4	**<0.001**
Cessation of smoking	30.5	17.8	1 in 3	**0.006**
Reduction in SBP, HbA1c & TChol & cessation of smoking	21.2	14.3	1 in 5	**<0.001**

Note: estimated number of people at risk is rounded to the nearest integer.

Compared to the 'no change' scenario, reducing HbA1c by 1%, systolic blood pressure by 10mmHg, total cholesterol by 1.0 mmol/L, and ceasing smoking, and the combination of all four scenarios, all resulted in significantly decreased risk of developing CHD within 5, 10 and 20 years of diagnosis of diabetes.

For CHD risk 5, 10 and 20 years after diagnosis of diabetes, the greatest reduction in mean percentage risk resulted from reducing all four risk factors. Reducing total cholesterol among all with diabetes resulted in the greatest decrease in mean percentage risk for a single risk factor.

Effects of reduction in management targets among those at high risk of coronary heart disease

To estimate the effect of reducing diabetes management targets only among those at high risk of developing CHD, systolic blood pressure, HbA1c and total cholesterol values were decreased by 10 mmHg, 1%, and 1.0 mmol/L respectively, and for those who were current smokers, smoking status was changed to non/ex-smoker to simulate cessation of smoking, for those who had a CHD risk of ≥7.5% in 5 years, ≥15% in 10 years, and ≥30% in 20 years. The mean risk scores after modeling these reductions in management targets were then compared to the no change scenario (assuming no reduction in management targets was achieved). Everyone with diabetes was included in the analysis, but only those at high risk of CHD had their management targets reduced in the model.

As mentioned in the previous section, the risk scores used for the purposes of this report to indicate high risk of CHD among those with type 2 diabetes are 7.5% within 5 years, 15% within 10 years, and 30% within 20 years of diagnosis. The proportion at high risk of CHD within 5 years was 22.1% (n=14), the proportion at high risk of CHD within 10 years was 29.8% (n=18), and the proportion at high risk of CHD within 20 years was 43.1% (n=26).

Table 14. Estimated mean percentage risk of coronary heart disease within 5 years of diagnosis for various scenarios, and significance of paired t-test in comparison to 'No change' scenario for those at high risk of CHD (n=62).

	Mean percentage risk score	SD	Number of people at risk	p-value
No change	5.7	7.7	1 in 18	
Reduction in HbA1c by 1% among those at high risk	5.4	7.5	1 in 19	**<0.001**
Reduction in systolic blood pressure (SBP) by 10 mmHg among those at high risk	5.5	7.6	1 in 18	**<0.001**
Reduction in total cholesterol (TChol) by 1.0 mmol/L among those at high risk	5.1	7.3	1 in 20	**<0.001**
Cessation of smoking among those at high risk	5.6	7.7	1 in 18	0.12
Reduction in SBP, HbA1c & TChol & cessation of smoking among those at high risk	4.7	7.2	1 in 21	**<0.001**

Note: estimated number of people at risk is rounded to the nearest integer.

Table 15. Estimated mean percentage risk of coronary heart disease within 10 years of diagnosis for various scenarios, and significance of paired t-test in comparison to 'No change' scenario for those at high risk of CHD (n=62).

	Mean percentage risk score	SD	Number of people at risk	p-value
No change	12.5	10.3	1 in 8	
Reduction in HbA1c by 1% among those at high risk	11.7	9.4	1 in 9	**<0.001**
Reduction in systolic blood pressure (SBP) by 10 mmHg among those at high risk	12.1	9.8	1 in 8	**<0.001**
Reduction in total cholesterol (TChol) by 1.0 mmol/L among those at high risk	11.1	8.8	1 in 9	**<0.001**
Cessation of smoking among those at high risk	12.2	10.1	1 in 8	0.08
Reduction in SBP, HbA1c & TChol & cessation of smoking among those at high risk	10.1	8.0	1 in 10	**<0.001**

Note: estimated number of people at risk is rounded to the nearest integer.

Table 16. Estimated mean percentage risk of coronary heart disease within 20 years of diagnosis for various scenarios, and significance of paired t-test in comparison to 'No change' scenario for those at high risk of CHD (n=62).

	Mean percentage risk score	SD	Number of people at risk	p-value
No change	31.5	18.1	1 in 3	
Reduction in HbA1c by 1% among those at high risk	29.7	16.4	1 in 3	**<0.001**
Reduction in systolic blood pressure (SBP) by 10 mmHg among those at high risk	30.6	17.2	1 in 3	**<0.001**
Reduction in total cholesterol (TChol) by 1.0 mmol/L among those at high risk	28.1	14.9	1 in 4	**<0.001**
Cessation of smoking among those at high risk	30.7	17.6	1 in 3	**0.02**
Reduction in SBP, HbA1c & TChol & cessation of smoking among those at high risk	25.1	12.5	1 in 4	**<0.001**

Note: estimated number of people at risk is rounded to the nearest integer.

Compared to the 'no change' scenario, reducing HbA1c by 1%, systolic blood pressure by 10mmHg, and total cholesterol by 1.0 mmol/L, and the combination of those three scenarios plus cessation of smoking, resulted in significantly decreased risk of developing CHD within 5, 10 and 20 years of diagnosis of diabetes. In addition, cessation of smoking significantly reduced the risk of developing CHD among those with diabetes within 20 years of diagnosis.

For CHD risk 5, 10 and 20 years after diagnosis of diabetes, the greatest reduction in risk of developing CHD resulted from reducing all four risk factors. Reducing total cholesterol among all with diabetes resulted in the greatest decrease in risk for a single risk factor.

Estimated reductions in proportion of people at high risk when management targets are reduced

The proportion of the population at high risk of developing CHD when management targets are reduced, and the number of people this proportion would represent in South Australia (among those aged 25 to 65 with type 2 diabetes and without CHD), are shown in Table 17 to

Table 19. Population figures were estimated using the 2003 Estimated Residential Population.

Table 17. Estimated proportion at high risk of developing coronary heart disease within 5 years of diagnosis for various scenarios, and estimated number of people this equates to in South Australia (n=62).

	Proportion at high risk for CHD (5-year risk score ≥7.5%)	Estimated number of people in SA
No change	22.1	4080
Reduction in HbA1c by 1% among those at risk	20.1	3710
Reduction in systolic blood pressure (SBP) by 10 mmHg among those at risk	21.5	3970
Reduction in total cholesterol (TChol) by 1.0 mmol/L among those at risk	15.7	2900
Cessation of smoking among those at risk	20.6	3800
Reduction in SBP, HbA1c & TChol & cessation of smoking among those at risk	4.8	890

Note: population estimations are rounded to the nearest 10.

Table 18. Estimated proportion at high risk of coronary heart disease within 10 years of diagnosis for various scenarios, and estimated number of people this equates to in South Australia (n=62).

	Proportion at high risk for CHD (10-year risk score ≥15%)	Estimated number of people in SA
No change	29.8	5500
Reduction in HbA1c by 1% among those at risk	25.3	4670
Reduction in systolic blood pressure (SBP) by 10 mmHg among those at risk	27.0	4980
Reduction in total cholesterol (TChol) by 1.0 mmol/L among those at risk	21.5	3970
Cessation of smoking among those at risk	27.5	5080
Reduction in SBP, HbA1c & TChol & cessation of smoking among those at risk	9.8	1810

Note: population estimations are rounded to the nearest 10.

Table 19. Estimated proportion at high risk of coronary heart disease within 20 years of diagnosis for various scenarios, and estimated number of people this equates to in South Australia (n=62).

	Proportion at high risk for CHD (20-year risk score ≥30%)	Estimated number of people in SA
No change	43.1	7960
Reduction in HbA1c by 1% among those at risk	34.2	6310
Reduction in systolic blood pressure (SBP) by 10 mmHg among those at risk	37.7	6960
Reduction in total cholesterol (TChol) by 1.0 mmol/L among those at risk	31.7	5850
Cessation of smoking among those at risk	40.3	7440
Reduction in SBP, HbA1c & TChol & cessation of smoking among those at risk	24.2	4470

Note: population estimations are rounded to the nearest 10.

Achieving changes in all four risk factors among those at high risk of developing CHD has the potential to reduce the number of people aged 25 to 65 years with type 2 diabetes at risk of developing CHD within 5, 10, and 20 years by 3190, 3690, and 3490 people respectively in South Australia. In other words, the proportion of people at high risk of developing CHD within 10 years could be reduced by 67%.

Discussion

Reduction of CHD risk

The Steno-2 study[25] found that a long-term, targeted, intensive intervention involving multiple risk factors, including hyperglycaemia, hypertension, and dyslipidaemia, reduced the risk of both cardiovascular and microvascular events by approximately 50 percent among patients with type 2 diabetes and microalbuminuria. The effect of a multifactorial approach to risk reduction is evident from the results presented here, which show that reducing HbA1c by 1%, systolic blood pressure by 10 mmHg, and total cholesterol by 1.0 mmol/L in combination, contributes to significantly decreased mean absolute risk of developing CHD within 5, 10 and 20 years of diagnosis of diabetes. In addition, cessation of smoking significantly reduced the mean risk of developing CHD among those with diabetes within 20 years of diagnosis.

If a reduction in management targets was achieved for everyone with type 2 diabetes, regardless of CHD risk, a reduction in any one single factor significantly decreased the mean risk of developing CHD in the short term (>7.5% risk within 5 years of diagnosis), medium term (>15% risk within 10 years of diagnosis) and long term (>30% risk within 20 years of diagnosis).

If a reduction in management targets was achieved only for those who are at high risk of developing CHD in the short, medium and long term, a reduction in HbA1c, systolic blood pressure, or total cholesterol (or a reduction in all three factors plus the cessation of smoking) would significantly decrease the risk of developing CHD. Cessation of smoking did not significantly decrease the risk of developing CHD in the short or medium term, but it did contribute to a significant reduction in long term risk of developing CHD.

The greatest effect on risk of developing CHD in the short, medium and long term resulted from a reduction in all four factors. This is consistent with the Steno-2 study which evaluated the effect of a multifactorial intervention on cardiovascular disease[25]. The greatest single effect on CHD risk in the short, medium and long term in this analysis resulted from a reduction in total cholesterol.

Studies examining the effect of lipid lowering therapies on cardiovascular outcomes have found that treatments for reducing total[5] and LDL[6] cholesterol are effective in reducing risk of cardiovascular outcomes, regardless of pretreatment cholesterol levels[6]. In terms of high blood pressure and HbA1c, treatments have been shown to be effective in reducing HbA1c by approximately 1%[3], and blood pressure by at least 10 mm Hg[4]. Importantly, it has been suggested that while it is important to work towards meeting management targets, any significant reduction in blood pressure[26] and HbA1c[19] levels will improve patient outcomes, even if management targets are not met.

Effects of reduction – what does it mean in population terms

In terms of the effects of reducing management targets on the proportion of people at high risk of developing CHD, a reduction in total cholesterol by 1.0 mmol/L would decrease the proportion at high risk of developing CHD within 10 years of diagnosis by 8.3 percentage points, or by approximately 1530 people in South Australia. If all management targets were achieved, the proportion at high risk of developing CHD within 10 years of diagnosis would be reduced by 20.0 percentage points, or by approximately 3690 people in South Australia.

Costs

Several analyses undertaken by the UKPDS team have shown that intensive interventions to reduce blood pressure and blood glucose are cost effective[27-30]. In addition, intensive interventions have been shown to improve quality of life[30] and increase the years of life free from cardiovascular end points without a significant increase in total cost[28]. However it has been suggested that there is a need to

undertake country-specific cost-effectiveness analyses where costs differ significantly between health care systems.

Strengths and Limitations

The analysis was limited by the small sample of people from the NWAHS who matched the UKPDS sample based on having type 2 diabetes, being aged 25 to 65 years, and having no previous history of CHD. Further studies could assess the use of the risk engine in people aged under 25 and over 65 years.

The only factors in the risk model that were shown to be significantly associated with being at high risk of developing CHD in this sample were low HDL cholesterol and being aged 55 years and over for 10-year risk, and low HDL cholesterol for 20-year risk. It would be expected that all the factors included in the model would be associated with being at high risk for CHD, so it could be that there were not as many significant factors due to the small sample size.

There were no additional factors not already included in the risk model that were significantly associated with being at high risk of CHD in the short (5-year), medium (10-year), and long (20-year) term. It is possible that these additional factors did not reach statistical significance because of the small sample size. However, it could also be that regardless of sample size, these factors are not important in contributing to risk of developing CHD among people with type 2 diabetes. Our data did not confirm this either way.

The strength of the NWAHS is that because it is a cohort study, further analyses may be able to validate the use of the UKDPS risk engine within an Australian population. In addition, further research in this cohort may lead to other risk factors being included in a risk model which are specific to this population.

Conclusion

These analyses have been able to provide evidence that practical, achievable reductions in key management targets for people with diabetes can have a significant effect on reducing absolute risk of coronary heart disease. The results show that reduction in total cholesterol in isolation has a significant influence on reduction of absolute risk for coronary heart disease, but that the greatest effect on risk for developing CHD is gained through a multifactorial approach where interventions focus on all key risk factors for CHD.

Research into the validity of applying the UKDPS model in an Australian population would enhance current clinical practice guidelines in the management of cardiovascular risk in people with diabetes. Further analyses may also include an examination of the addition of microalbuminuria to the risk model, as well as cost-effectiveness analyses of interventions to reduce risk of developing CHD among people with diabetes in Australia, which would be beneficial in optimising health care resource utilisation.

References

1. Stevens RJ, Kothari V, Adler AI, Stratton IM. The UKPDS risk engine: a model for the risk of coronary heart disease in Type II diabetes (UKPDS 56). Clin Sci (Lond). 2001;101(6):671-9.

2. Bloomgarden ZT. American Diabetes Association Annual Meeting, 1998: cardiac disease and related topics. Diabetes Care. 1998;21(10):1764-73.

3. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. Lancet 1998;352(9131):837-53.

4. Group UKPDS. Efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 39. BMJ 1998;317(7160):713-720.

5. Hippisley-Cox J, Cater R, Pringle M, Coupland C. Cross sectional survey of effectiveness of lipid lowering drugs in reducing serum cholesterol concentration in patients in 17 general practices. Bmj 2003;326(7391):689.

6. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. Lancet 2002;360(9326):7-22.

7. TCRE. Key smoking statistics for SA - 2006. Adelaide: Tobacco Control Research and Evaluation, 2007.

8. Anderson KM, Odell PM, Wilson PW, Kannel WB. Cardiovascular disease risk profiles. Am Heart J 1991;121(1 Pt 2):293-8.

9. Ramachandran S, French JM, Vanderpump MP, Croft P, Neary RH. Using the Framingham model to predict heart disease in the United Kingdom: retrospective study. BMJ 2000;320(7236):676-7.

10. Haq IU, Jackson PR, Yeo WW, Ramsay LE. Sheffield risk and treatment table for cholesterol lowering for primary prevention of coronary heart disease. Lancet 1995;346(8988):1467-71.

11. Joint British recommendations on prevention of coronary heart disease in clinical practice. British Cardiac Society, British Hyperlipidaemia Association, British Hypertension Society, endorsed by the British Diabetic Association. Heart 1998;80(Suppl 2):S1-29.

12. Jackson R. Updated New Zealand cardiovascular disease risk-benefit prediction guide. Bmj 2000;320(7236):709-10.

13. Simons LA, Simons J, Friedlander Y, McCallum J, Palaniappan L. Risk functions for prediction of cardiovascular disease in elderly Australians: the Dubbo Study. Med J Aust 2003;178(3):113-6.

14. Ramsay LE, Haq IU, Jackson PR, Yeo WW, Pickin DM, Payne JN. Targeting lipid-lowering drug therapy for primary prevention of coronary disease: an updated Sheffield table. Lancet 1996;348(9024):387-8.

15. Sanmuganathan PS, Ghahramani P, Jackson PR, Wallis EJ, Ramsay LE. Aspirin for primary prevention of coronary heart disease: safety and absolute benefit related to coronary risk derived from meta-analysis of randomised trials. Heart 2001;85(3):265-71.

16. Baker S, Priest P, Jackson R. Using thresholds based on risk of cardiovascular disease to target treatment for hypertension: modelling events averted and number treated. Bmj 2000;320(7236):680-5.

17. Grant JF, Chittleborough CR, Taylor AW, Dal Grande E, Wilson DH, Phillips PJ, Adams RJ, Cheek J, Price K, Gill T, Ruffin RE. The North West Adelaide Health Study: detailed methods and baseline segmentation of a cohort for selected chronic diseases. Epidemiol Perspect Innov. 2006;3:4.

18. Population Research and Outcome Studies. Diabetes in South Australia, 2001. Brief Report No. 2002-19. Adelaide: Department of Health, 2002.

19. Diabetes Australia & The Royal Austarlian College of General Practitioners. Diabetes Management in General Practice. 12 ed Diabetes Australia, 2006.

20. Tonkin A, Barter P, Best J, Boyden A, Furler J, Hossack K, Sullivan D, Thompson P, Vale M, Cooper C, Robinson M, Clune E. National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand: position statement on lipid management--2005. Heart Lung Circ 2005;14(4):275-91.

21. The National Prescribing Centre. Type 2 diabetes (part 2): the management of cardiovascular risk factors. NHS; UK, 2004.

22. Song SH, Brown PM. Coronary heart disease risk assessment in diabetes mellitus: comparison of UKPDS risk engine with Framingham risk assessment function and its clinical implications. Diabet Med 2004;21(3):238-45.

23. Joint British recommendations on prevention of coronary heart disease in clinical practice. British Cardiac Society, British Hyperlipidaemia Association, British Hypertension Society, endorsed by the British Diabetic Association. Heart. 1998;80(Suppl 2):S1-29.

24. Haq IU, Jackson PR, Yeo WW, Ramsay LE. Sheffield risk and treatment table for cholesterol lowering for primary prevention of coronary heart disease. Lancet. 1995;346(8988):1467-71.

25. Gaede P, Vedel P, Larsen N, Jensen GV, Parving HH, Pedersen O. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. N Engl J Med 2003;348(5):383-93.

26. National Heart Foundation of Australia. Hypertension Management Guide for Doctors. 2004.

27. Gray A, Raikou M, McGuire A, Fenn P, Stevens R, Cull C, Stratton I, Adler A, Holman R, Turner R. Cost effectiveness of an intensive blood glucose control policy in patients with type 2 diabetes: economic analysis alongside randomised controlled trial (UKPDS 41). BMJ 2000;320(7246):1373-1378.

28. Group UKPDS. Cost effectiveness analysis of improved blood pressure control in hypertensive patients with type 2 diabetes: UKPDS 40. BMJ 1998;317(7160):720-726.

29. Gray A, Clarke P, Farmer A, Holman R. Implementing intensive control of blood glucose concentration and blood pressure in type 2 diabetes in England: cost analysis (UKPDS 63). BMJ 2002;325(7369):860-865.

30. Clarke PM, Gray AM, Briggs A, Stevens RJ, Matthews DR, Holman RR. Cost-utility analyses of intensive blood glucose and tight blood pressure control in type 2 diabetes (UKPDS 72). Diabetologia 2005;48(5):868-77.