

ANALYSIS OF CORONARY HEART DISEASE ABSOLUTE RISK IN DIVISION-BASED DIABETES REGISTER DATA (2000-2002)

National Divisions Diabetes Program
Divisions Diabetes & CVD Quality Improvement Project

*Divisions improving quality of care &
health outcomes in chronic disease*

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Background

Diabetes has a high prevalence worldwide. Current estimates indicate that about 150 million people have type 2 diabetes globally and this figure is expected to double by 2025^{1, 2}. In Australia, the AusDiab survey found that type 2 diabetes affects over 7.4% of the total population aged over 25 year (Female: 6.8%, Male: 8.0%)³. In terms of premature deaths, diabetes was estimated to be responsible for almost 5.3% of the estimated years of life lost in Australia in 1996 for all causes⁴. McCarty et al. estimated that the direct annual health care costs of diabetes in Australia will reach \$2.3 billion by 2010².

Cardiovascular disease (CVD) is responsible for the deaths of 17 million people worldwide each year, or approximately one-third of global deaths annually^{5, 6}. CVD and CHD are not numerically equivalent but highly correlated with a prevalence ratio of 4: 3⁷. Despite their prevalence, many patients who are at high cardiovascular risk remain undetected⁸. In Australia, CVD accounted for 39% of total deaths in 2002⁹. CHD is the most common form of CVD sudden death in Australia¹⁰. Expenditure on cardiovascular drugs under the Pharmaceutical Benefits Scheme totals \$1.2 billion annually, \$629 million of this on lipid lowering drugs, especially statins¹¹.

The Framingham Heart Study¹² and other studies^{13, 14} have identified diabetes, smoking, elevated blood pressure and serum cholesterol, decreased HDL as well as advancing age, as the major CVD risk factors. People with diabetes are two to four times more likely to develop CVD¹⁵, with about 65% of persons with diabetes dying from it¹⁶. Coronary heart disease absolute risk (CHDAR) is the probability of developing CHD over a given time period, (usually over 5 or 10 years). The primary prevention of CHD should be based on assessment of absolute risk (AR) because it acknowledges the multi-factorial causation of cardiovascular disease. Although people with type 2 diabetes already have increased risk, estimation of CHDAR allows multiple risk factors to be considered in decisions about how to prioritize interventions^{12, 17, 18, 19, 20}. The National Institute for Clinical Excellence (NICE) guidelines²⁰ recommended using CHDAR estimation to guide the management of blood pressure and blood lipids in type 2 diabetes. CHDAR estimation based on data from the Framingham study is not ideal for diabetic patients because of the small

number of cases in this study. However, the U.K. Prospective Diabetes Study (UKPDS) with the largest cohort of type 2 diabetes patients and the longest follow up provides a unique diabetes-specific calculator used for estimating CHDAR¹⁹.

GPs play a significant role in primary health care across the continuum of care from prevention of illness to treatment and rehabilitation, and provide consultations to approximately 90% of Australians each year^{21, 22}. Currently, there have been relatively few studies on CHDAR in the Australian general population^{23, 24} and no published reports on CHDAR estimation in patients with type 2 diabetes in clinical practice, particularly in the general practice setting

Aims

Our aims in this study were to estimate the characteristic of CHDAR in Australian general practice patients with type 2 diabetes, to examine the prevalence of individual CHD risk, to evaluate the characteristics of diabetic micro-vascular complications and identify the association between CHDAR and aspects of diabetes care (Medication and Behavior).

Methodology

1. Data resource

Divisions Diabetes and CVD Quality Improvement Project (DDCQIP) is part of the National Divisions Diabetes Program in Australia. Patient data analyzed in this study were extracted from the data collected in 2002 and collated in 2003 by the DDCQIP²⁵ from 16 (250 practices) of the 23 Divisions of General Practice across Australia which had used **CARDIAB**®™ (an electronic registrar system for data collection²⁶) (19 of these 23 Divisions had agreed to participate but 3 Division's data were excluded since the number of patients on the register declined, because the registers were not being maintained adequately or included many non-active patients). Ethical approval for the study was obtained from the Human Ethics Committee of the University of New South Wales (UNSW). Participating patients had consented to data being provided by their GPs to the Divisions and data were de-identified prior to extraction.

2. Inclusion criteria

The patients were excluded if they had diabetes which was not type 2, they were of indigenous descent, they had previous or new MI, stroke, or coronary artery bypass graft, or if their smoking status or gender was not available (see Table 1).

Table 1: Exclusion criteria

	2000	2001	2002
Total cases on registers	9268	11454	15294
Not type 2 Diabetes	938	1186	1598
Indigenous people	12	60	69
With Stroke, MI, or CABG	210	238	345
Without complete smoking record	6598	8318	9767
Unknown Sex	14	2	3

Note: Some of the exclusion criteria overlapped.

For instance some patients who had stroke also had incomplete smoking records

After screening for exclusion criteria, the eligible cases included in the dataset for analysis were: 2000 year: 1549, 2001 year: 1749, 2002 year: 3286.

3. Statistical methods

For these patients the missing values were imputed using Expectation Maximisation (EM) which is typically used to compute the maximum likelihood estimate given an incomplete sample²⁷. Ten year CHDAR was calculated for all patients using the UKPDS risk spreadsheet for populations²⁸ (Appendix). According to the NICE guidelines²⁰, the CHD AR was dichotomised into two groups:

- Higher risk group: AR>15%
- Lower risk group: ≤15%

3 years' data were merged when analyzing the relationships of CHDAR with other indicators in order to increase the statistical power. SPSS software was used to edit and examine the data. Chi-square was used to analyze the association between two categorical variables. Independent T-Test was used for comparison of quantitative data between two groups, Analysis of Variance (ANOVA) was used for the comparison of continuous data among more than two groups Correlation analysis and

multiple regressions were used to investigate the linear relationships between three or more variables Binary logistic regression was used for the comparison of relationship between dichotomous dependent variables.

Results

1. The characteristics of CHDAR in patients with diabetes in 2000-2002

The mean CHDAR was 0.21 in 2000, 0.20 in 2001, and 0.20 in 2002, and there were no statistical differences between them over the 3 years (ANOVA, P=0.161). The majority of diabetic patients in general practice in this study were in the higher risk group (2000: 60.3%, 2001: 59.6%, and 2002: 57.6%). (See Figure 1 and Table 2)

Figure 1: Mean absolute risk and 95% CI in 2000-2002

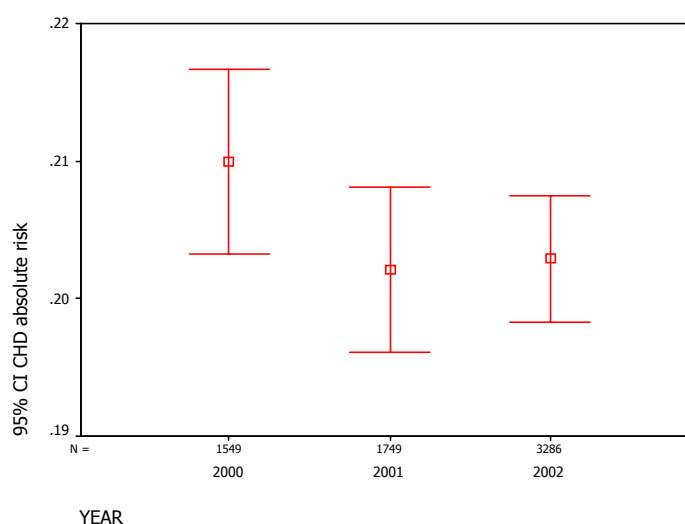


Table 2: Cases in the lower and higher risk groups in 2000-2002

	2000	2001	2002	Total
AR=<0.15	615(39.7%)	706(40.4%)	1303(42.4%)	2714 (41.2%)
AR>0.15	934(60.3%)	1043(59.6%)	1893(57.6%)	3870(58.8%)
Total	1549 (100%)	1749(100%)	3286(100%)	6584(100%)

The mean CHDAR was significantly higher in males than females in each of the 3 years 2000-2002 (P<0.001). There was no statistical difference in AR over the 3 years, separately for

females or males (females: P=0.102, males: P=0.35).

2. The characteristics of risk factors contributing to CHDAR in 2000-2002

For females, there were statistically significant differences in the duration of diabetes (P=0.028), HbA_{1c} (P=0.012) and total cholesterol (P=0.003) over the 3 years, but not in the age, age at diagnosis, systolic blood pressure or HDL. For males, only HbA_{1c} was statistically different over the 3 years (P=0.016).

Table 3: Risk factors in females and males by year

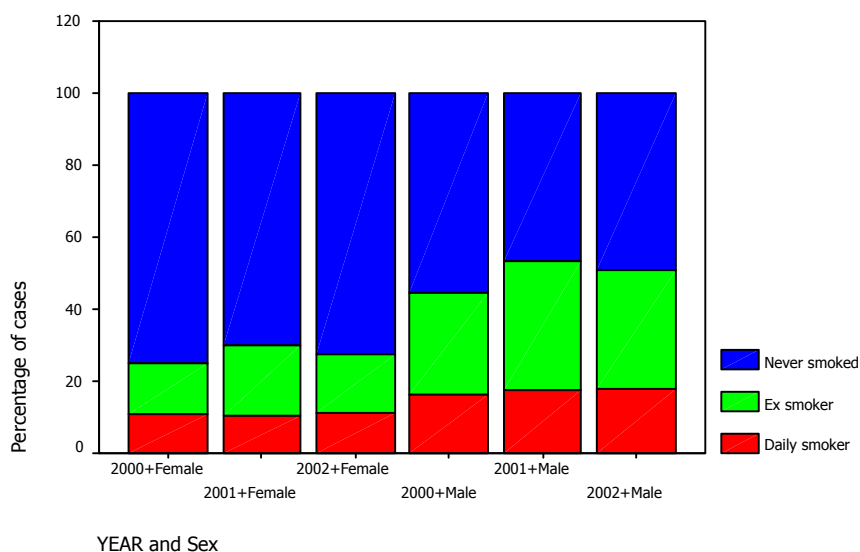
		2000	2001	2002
Female	HbA1c	7.442	7.428	7.302* [▲]
	Total chol	5.27	5.28	5.17* [▲]
Male	HbA1c	7.468	7.566	7.406*

[▲]P<0.05 in the comparison between 2002 and 2000

P<0.05 in the comparison between 2002 and 2001

The percentage of males who were daily smokers (2000: 16.3%, 2001: 17.4%, 2002: 17.9%) was significantly higher than that of females (2000: 11.0%, 2001: 10.4%, 2002: 11.4%) in each of the 3 years (P< 0.05). There were no statistically significant differences over the 3 years for either males or females. The percentage of males who were ex smokers (2000: 28.4%, 2001: 35.8%, 2002: 32.8%) was significantly higher than females (2000: 13.8%, 2001: 19.4%, 2002: 16.2%) in each of the 3 years (P<0.001). There were more than 70% of females who had never smoked (2000: 75.2%, 2001: 70.2%, 2002: 72.4%), and this trend maintained nearly constant over the 3 years (P>0.05). There were nearly half of males who had never smoked. For males, there was a significant difference over the 3 years (P=0.002). The percentage was 55.3% in 2000, decreased to 46.8% in 2001 and increased again to 49.4% in 2002. The percentage of females who never smoked was consistently higher than males in each of the 3 years (P<0.001). (see Figure 2)

Figure 2: Smoking status by gender in 2000-2002



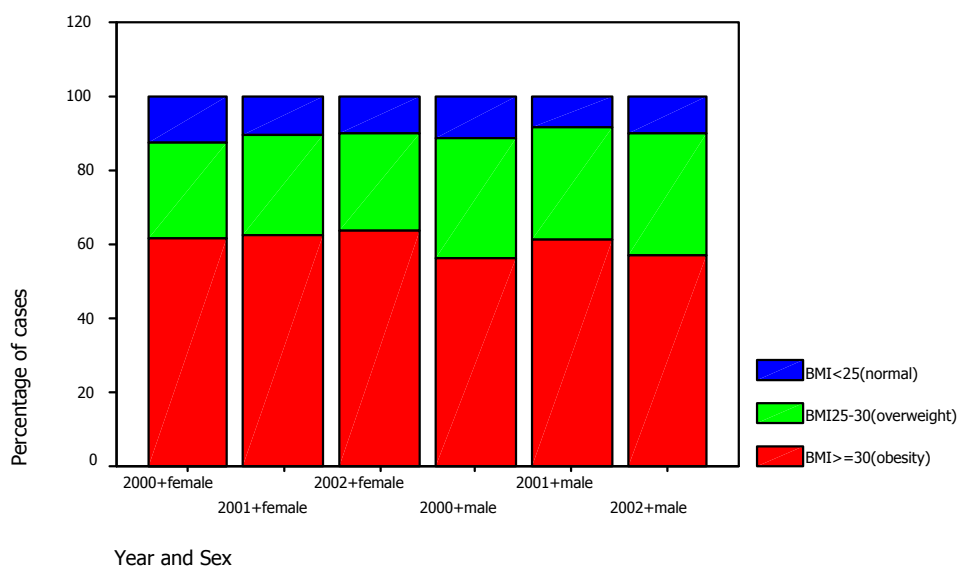
3. The characteristics of other risk factors in 2000-2002

BMI

The percentage of females who were obese was 61.5% in 2000, 62.3% in 2001 and 63.6% in 2002. The percentage of males who were obese was 56.3 % in 2000, 61.1% in 2001 and 57.0% in 2002. The percentage of people who were obese was higher among females than males in 2000 (P=0.021) and 2002 (P<0.001). The percentage of people who were overweight was significantly higher for males than females in 2000 (P=0.04) and 2002 (P=0.001). The proportion of people who had a normal BMI was less than 12.5% for females and less than 11.4% for males in each of the 3 years.

The percentage of patients at each of the three BMI categories did not change significantly over the 3 years (see Figure 3)

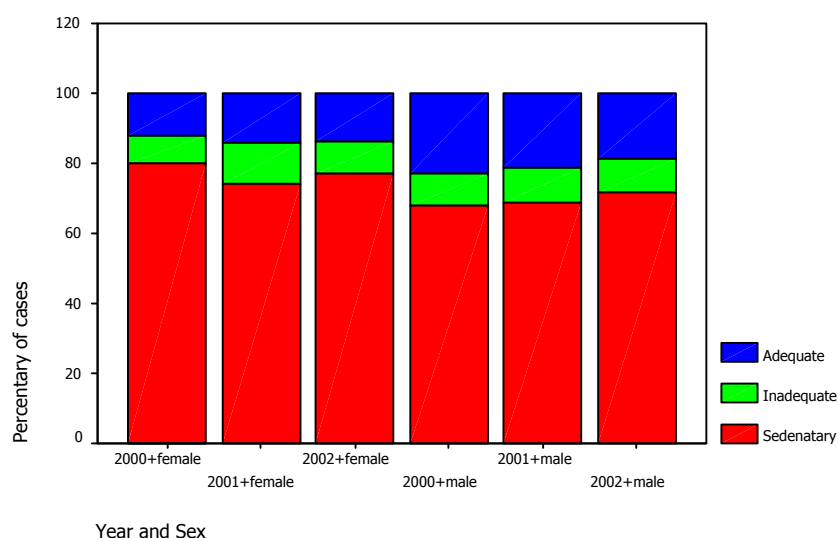
Figure 3: BMI by gender in 2000-2002



Physical activity

The percentage of females whose physical activity status was sedentary was 80.0% in 2000, 74.0% in 2001 and 77.0% in 2002. The percentage of males who were sedentary was 67.9 % in 2000, 68.8 % in 2001 and 71.8 % in 2002. More female tended to live sedentary lives than males in each of the 3 years ($P<0.05$). There were more males who had adequate physical activity levels (2000: 22.9%, 2001: 21.3%, 2003: 18.9%) than females (2000: 12.1%, 2001: 14.3%, 2002: 13.9%) in each of the 3 years ($P<0.05$). There was no significant difference in any of the three categories of physical activity over the three year period for both males and females (see Figure 4).

Figure 4: Physical activity levels by gender in 2000-2002



4. Microangiopathy and its relationship with CHDAR

“Microangiopathy” was derived if the patients had either diabetic retinopathy and/or urinary microalbumin. There were a total of 782 (11.9%) patient records with microangiopathy in the 3 years’ data. There was a significant association between the CHDAR level and microangiopathy ($X^2=43.50$, $P<0.001$). 15.5% of patients with lower AR had microangiopathy compared to 24.3% of those who had higher AR. The binary logistic regression model showed (see Table 4):

- Patients who had higher AR were more likely to have microangiopathy ($B=2.339$, $P<0.001$), even when BMI, systolic BP and HbA1c were included as covariates.
- Patients with higher blood pressure, HbA1c and BMI were more likely to have microangiopathy ($P<0.001$).

Table 4: Logistic regression model for microangiopathy**Variables in the Equation**

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1 ^a	BODY_MAS	.030	.008	15.371	1	.000	1.031
	SBP	.009	.003	13.595	1	.000	1.009
	HBA1C	.134	.027	24.192	1	.000	1.144
	CHD_AR	2.339	.306	58.306	1	.000	10.376
	Constant	-5.098	.449	128.924	1	.000	.006

^a. Variable(s) entered on step 1: BODY_MAS, V21, HBA1C, CHD_AR.

5. Diabetes care and its relationship with CHDAR***Glucose lowering pharmaco-therapy***

In the 3 years, there were 3819 patient records (58.0% of the total records) data who were on glucose lowering therapy (medication). There was a significant association between glucose lowering pharmaco-therapy and CHDAR ($X^2=43.52$, $P<0.001$). 66.6% of patients who were in the higher risk group were taking glucose lowering therapy, while 33.4% of patients who were in higher AR risk were not. The binary logistic regression showed (see Table 5):

- Patients who had higher AR were more likely to be taking glucose lowering pharmaco-therapy ($B= 1.854$, $P<0.001$).
- Patients who had higher BMI or lower blood pressure were more likely to be taking glucose lowering pharmaco-therapy ($P<0.01$).

Table 5: Logistic regression model for glucose lowering pharmaco-therapy**Variables in the Equation**

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1 ^a	BODY_MAS	.016	.006	8.217	1	.004	1.016
	SBP	-.006	.002	10.062	1	.002	.994
	TCHOL	-.243	.033	55.745	1	.000	.784
	HBA1C	.502	.028	317.887	1	.000	1.651
	CHD_AR	1.854	.244	57.924	1	.000	6.383
	Constant	-1.916	.364	27.676	1	.000	.147

^a. Variable(s) entered on step 1: BODY_MAS, V21, V40, HBA1C, CHD_AR.

Anti-hypertensive therapy

In the 3 years, there were 1,894 patient records who were on anti-hypertensive therapy (28.8% of the total records). There was a significant association between anti-hypertensive therapy and the CHDAR ($X^2=53.76$, $P<0.001$). Only 40.5% of patients who had a higher AR were on anti-hypertensive therapy, while 59.5% of patients who were at higher AR risk were not on

anti-hypertensive therapy. The binary logistic regression model showed (see Table 6):

- Patients who had higher AR were less likely to be taking antihypertensive therapy (B= -0.696, P<0.05).
- Patients who were older, or had higher BMI, and/or systolic blood pressure were more likely to be taking antihypertensive therapy (P<0.01).
- Patients with higher total cholesterol were less likely to be taking antihypertensive therapy (P<0.05).

Table 6: Logistic regression model for anti-hypertensive therapy

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AGE	.039	.003	125.501	1	.000	1.040
	BODY_MAS	.041	.006	45.359	1	.000	1.041
	SBP	.016	.002	64.987	1	.000	1.016
	TCHOL	-.093	.036	6.651	1	.010	.911
	CHD_AR	-.696	.296	5.535	1	.019	.498
	Constant	-5.856	.426	189.219	1	.000	.003

a. Variable(s) entered on step 1: AGE, BODY_MAS, V21, V40.

Lipid therapy

In the 3 years, there were 1,436 patient records who were on lipid therapy (21.8% of the total records). There was a significant association between lipid therapy and the level of absolute risk ($X^2=11.92$, $P<0.01$). Only 29.4% of patients who were in the higher risk group were taking lipid therapy, while 70.6% of patients who were in higher AR risk were not on lipid therapy. The binary logistic regression model showed (see Table 7):

- Patients who had higher AR were less likely to be taking lipid therapy (B= -1.294, P<0.0001).
- Patients who had higher total cholesterols were less likely to be taking lipid therapy (P<0.0001).
- Patients who were older and/or had higher HbA1c were more likely to be taking lipid therapy (P<0.001).

Table 7: Logistic regression model for lipid therapy

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	age	.025	.004	46.318	1	.000	1.026
	TCHOL	-.155	.039	16.116	1	.000	.856
	hba1c	.099	.025	15.318	1	.000	1.104
	chd_ar	-1.294	.342	14.352	1	.000	.274
	Constant	-2.235	.380	34.617	1	.000	.107

a. Variable(s) entered on step 1: age, v40, hba1c, chd_ar.

Referred rate by GPs and Attended rate of patients

In the 3 years, the rates of referral to ophthalmologists (23.3%) and podiatrists (8.5%) were low in the records of diabetic patients in our sample, and the rates of attendance to ophthalmologists (6.2%) and podiatrists (1.8%) were much lower. The rate of attendance to diabetes educators was also low (8.7%), and the lowest rate of attendance was with dieticians (1.7%) (see Table 8).

There was a significant association between CHDAR and the rate of referral to ophthalmologists ($P=0.004$). More patients who were in the higher risk group (59.7%) were referred to ophthalmologists compared with those in the lower risk group (40.3%). Also there was a similarly significant association between CHDAR and the rate of attendance to ophthalmologists ($P=0.005$). Among patients who attended ophthalmologists, there were more in higher risk group (64.9%) than those in lower risk group (35.1%). There was no significant association between CHDAR and the rate of referral to podiatrists ($P=0.262$). Similarly, there was no significant association between CHDAR and the rate of attendance to podiatrists ($P=0.070$). There was no significant association between the CHDAR and the rate of attending diabetes educators ($P=0.318$). There was a significant association between CHDAR and the rate of attending dieticians ($P=0.006$). Among patients who attended dieticians, there were more in the lower risk group (53.0%) than in the higher risk group (47.0%) (see Table 8)

Table 8: Rates of referral / attendance to other health Professionals and AR level

		Number (%)	Percentage of cases		Chi-square P
			AR=<0.15	AR>0.15	
Referral to ophthalmologists	N	5048(76.7%)	40.3%	59.7%	0.004
	Y	1536(23.3%)	44.1%	55.9%	
Attendance to ophthalmologists	N	6179(93.8%)	41.6%	58.4%	0.005
	Y	405(6.2%)	35.1%	64.9%	
Referral to podiatrists	N	6027(91.5%)	41.3%	58.7%	0.262
	Y	557(8.5%)	39.9%	60.1%	
Attendance to podiatrists	N	6467(98.2%)	41.3%	58.7%	0.070
	Y	117(1.8%)	34.2%	65.8%	
Attendance to diabetes Educators	N	6011(91.3%)	41.1%	58.9%	0.318
	Y	573(8.7%)	42.2%	57.8%	
Attendance to dieticians	N	6469(98.3%)	41.0%	59.0%	0.006
	Y	115(1.7%)	53.0%	47.0%	

Appendix

UKPDS Risk Engine (Excel Spreadsheet)

Age at Diagnosis	Duration	Sex	Atrial Fibrillation	Ethnicity	Smoking	SysBP	HbA1c	Total Chol	HDL Chol	Regression dilution H	BP	Chol	Time	Risk	CHD Lower CI	Upper CI
55	0	F	N	1	0	140	6.0	4.0	1.0	2	6	2	10	5.7%	4.6%	7.1%
55	0	F	N	1	0	140	6.0	8.0	1.0	2	6	2	10	13.9%	11.1%	17.2%
55	0	F	N	1	0	160	6.0	4.0	1.0	2	6	2	10	6.7%	5.3%	8.4%
55	0	F	N	1	0	160	6.0	8.0	1.0	2	6	2	10	16.2%	12.9%	20.1%
55	0	F	N	1	2	140	6.0	4.0	1.0	2	6	2	10	7.6%	5.9%	9.7%
55	0	F	N	1	2	140	6.0	8.0	1.0	2	6	2	10	18.2%	14.4%	22.9%
55	0	F	N	1	2	160	6.0	4.0	1.0	2	6	2	10	8.9%	6.9%	11.6%
55	0	F	N	1	2	160	6.0	8.0	1.0	2	6	2	10	21.2%	16.7%	26.6%
55	0	M	N	1	0	140	6.0	4.0	1.0	2	6	2	10	10.6%	8.8%	12.6%
55	0	M	N	1	0	140	6.0	8.0	1.0	2	6	2	10	24.8%	20.6%	29.5%
55	0	M	N	1	0	160	6.0	4.0	1.0	2	6	2	10	12.4%	10.2%	15.0%
55	0	M	N	1	0	160	6.0	8.0	1.0	2	6	2	10	28.6%	23.5%	34.2%
55	0	M	N	1	2	140	6.0	4.0	1.0	2	6	2	10	14.0%	11.5%	17.0%
55	0	M	N	1	2	140	6.0	8.0	1.0	2	6	2	10	31.9%	26.5%	37.8%
55	0	M	N	1	2	160	6.0	4.0	1.0	2	6	2	10	16.4%	13.1%	20.3%
55	0	M	N	1	2	160	6.0	8.0	1.0	2	6	2	10	36.5%	30.0%	43.6%
55	0	F	Y	1	0	150	6.0	4.0	1.0	2	6	2	10	6.2%	5.0%	7.7%
55	0	M	Y	1	2	160	6.0	8.0	1.0	2	6	2	10	36.5%	30.0%	43.6%

<http://www.dtu.ox.ac.uk/index.htm?maindoc=/ukpds/>

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