well-targeted primary prevention of cardiovascular disease: an underused high-value intervention?

> Rod Jackson University of Auckland, New Zealand October 2015

Mortality trends for coronary heart disease: age 35-69 years, New Zealand (Aotearoa)



Mortality trends for stroke: age 35-69 years, New Zealand (Aotearoa)



Contribution of trends in survival and coronary-event rates to changes in coronary heart disease mortality: 10-year results from 37 WHO MONICA Project populations Lancet 1999; 353: 1547-57

Hugh Tunstall-Pedoe, Kari Kuulasmaa, Markku Mähönen, Hanna Tolonen, Esa Ruokokoski, Philippe Amouyel, for the WHO MONICA (monitoring trends and determinants in cardiovascular disease) Project*

Findings: Contribution to changing CHD mortality varied, but in populations in which mortality decreased, coronary-event rates contributed two thirds and case fatality one third. Interpretation: Over the decade studied (1980-5 through 1991-5), the 37 populations in the WHO **MONICA** Project showed substantial contributions from changes in survival, but the major determinant of decline in CHD mortality is whatever drives changing coronary-event rates.

Rose's 'prevention paradox' the whole population risk axiom

a large number of people at small risk may give rise to more cases in a population than a small number of people at high risk

rationale for a population-based approach: lowering blood pressure & stroke events





↓BP or TC treatment of high BP or TC: population- wide ↓ only if high

has the 'low-hanging fruit' of population-based CVD prevention all been picked?

population

strategies

high-risk

strategies

Rose's high-risk axiom

all policy (including treatment) decisions should be based on absolute measures of risk

rationale for a population-based approach: lowering blood pressure & stroke events



relative stroke risk and usual Blood Pressure

(45 prospective studies: 450,000 people 13,000 events)



BP & absolute IHD mortality risk by age



BP & absolute IHD mortality risk by age



clinical impact of a single risk factor depends on combined effect of multiple risk factors



Systolic Blood Pressure (mmHg)

* 50 yr old woman

patients with high absolute risk benefit most from treatment



avoidable CVD events per 1000 treated by baseline combined risk and extent of systolic blood pressure-lowering



avoidable vascular deaths per 1000 treated by baseline combined risk and extent of LDL lowering with statins



rationale for a population-based approach: lowering blood pressure & stroke events



rationale for high-risk approach: treating high absolute risk patients & CHD events



Voss et al. Int J Epidemiol 2002;31:1253-62

treat absolute risk not single risk factors

hypertension, hypercholesterolemia (and type-2 diabetes?) are not clinically relevant 'diagnoses' only absolute risk is clinically relevant

how can you measure a patient's absolute CVD risk?

NZ risk charts for estimating patients absolute risk (based on Framingham)

Smoker

5 6 7 8

180/105

160/95

140/85

120/75

180/105

160/95

140/85

120/75

180/105

160/95

140/85

120/75

180/105

160/95

140/85

120/75



Total CVD risk per 100 people over 5 years.



Ratio of Total Cholesterol HDL

5 6 7 8

Jackson R. Br Med J. 2000;320:709-10.

Framingham cohort



- 5,215 US White men and women
- Aged 30 to 74
- 1971 to 1983 (12 yrs)
- BP, Smoking, DM, TC, HDL
- CHD events

how often do you use the CVD risk charts? NZ GPs 1999: (n=500, resp. rate=83%)*



*after 5 years of intensive nation-wide education & distribution of multiple risk charts

Arroll et al. NZ Family Physician 2002:29:177-83

how relevant is a US CVD risk prediction study from the 1970s to a multi-ethnic NZ populations in the 21st century?



PREDICT in PHOs: electronic decision support for CVD risk prediction & management



2002



NZ CVD / DIABETES PROGRAMME

DEMOGRAPHICS	CVD RISK ASSESSMENT	CVD RISK	MANAGEMENT	DIABETES MANAGEME	ти		
Due stities a							
	<u>NZMC / NZN</u>	<u>C number</u>					
Demographics (All to be prepopulated from PMS)							
	Ē	<u>First name</u>]			
	l	<u>ast name</u>]			
		<u>NHI</u>					
	рнв с	atchment	Please Select		*		
	Quintile of d	eprivation					?
	Meshbloc	k geocode					?
	Da	te of birth		dd/mm/yyyy			?
		<u>Aqe</u>	Yea	rs			
		<u>Gender</u>	Please Select		*		?
Ethnic Grou	<u>p (1 or more self-identified etl</u> <u>may b</u>	nic group e chosen)	Not Stated		*		?
	Ethni	c Group 2	Not Stated		*		
	Ethni	c Group 3	Not Stated		*		
			NEXT				
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DEMOGRAPHICS CYD RISK ASSESSMENT CVD RISK	MANAGEMENT DIABETES MANAGEMENT					
This page should be completed for all patients. A After submitting this form, additional follow up m management form will become available depend	ll underlined items are required. anagement forms become available to you. The secondary Diabetes ant upon the status of the Diabetes field on this form.					
NOTE: It is inappropriate to do CVD risk assessment in pregnancy.						
ASSUME	ASSUME NEGATIVE DEFAULTS					
Clinical History						
Family History of Premature CVD	Yes 🔿 - 🔿 No 📲					
Angina/MI	Yes 🔿 - 🔿 No 📲					
PTCA/CABG	Yes 🔿 - 🔿 No					
Ischaemic Stroke or TIA	Yes 🔿 - 🔿 No 📲					
PVD	Yes 🔿 - 🔿 No 📕					
Diabetes	Please select					
ECG confirmed Atrial Fibrillation	Yes 🔿 - 🚫 No 📲					
Diagnosed Genetic Lipid Disorder	Please select					
Diagnosed metabolic syndrome	Yes O - O No					
Smoking History	Please select					
Pregnant?	Yes 🔿 - 💿 No 📲					
Examination						
Most recent BP (Sitting)	/ mmHg					
Previous BP (Sitting)	/ mmHg					
TC/HDL ratio	- Date: dd/mm/yyyy					
Total Cholesterol	mmol/L - Date: dd/mm/yyyy					
This data is the patient's real clinical information	Yes 💿 - 🔘 No					

a





get current best evidence on risk & management into clinical practice



PREDICT 1° care recruitment 2002-15







1° prevention cohort by ethnicity aged 30-74 years: 2002-2012

	Men	Women
Total (205,274)	114,463	90,811
European/other	74,002	57,757
Maori	14,142	12,583
Pacific	16,372	13,490
Indian	9,947	6,981

with no hx of CVD, renal disease or AF
1° prevention cohort events by type

	non fatal	fatal
All CVD (4,595)	4,188	404
MI	1,428	92
Other CHD	1,128	152
Stroke	723	110
TIA	309	0
PVD	281	22
CHF	466	28
Coronary procedures	116	0
Peripheral procedures	37	0

612,000 person-years follow-up; average 3 years & range 0-10 years

observed vs predicted risk: Framingham score



1° prevention score

observed vs predicted risk: PREDICT score



1° prevention score

CVD events during follow-up in PREDICT population 30-74 years, by clinical history



2002-2012

-----PREDICT (M) ------Anderson Framingham (M) Proportion of all CVD events occurring during follow-up (%) Proportion of all CVD events occurring during follow-up (%) **Deciles of predicted risk Deciles of predicted risk**

Figure 3a & b: Discrimination plots* of proportions of CVD events occurring during follow-up by decile of risk predicted using PREDICT-CVD 1° & Anderson Framingham models in women (a) and men (b)

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2002-2012

rationale for high-risk approach: treating high absolute risk patients & CHD events



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vascular risk management: Auckland 2006-9



Mehta et al. Eur J Prevent Cardiol. 2014;21:192–202

CVD events during follow-up in PREDICT population 30-74 years, by clinical history



CVD events during follow-up in PREDICT population 30-74 years, by clinical history



CVD events by history of CVD in NZ: 2002-12 (PREDICT n=270,000)



CVD events by history of CVD in NZ: 2002-12 (PREDICT n=270,000)



vascular risk management: Auckland 2006-9



Mehta et al. Eur J Prevent Cardiol. 2014;21:192–202

how should we choose treatment thresholds?



who should have their risk predicted?



choose the most efficient way of identifying those meeting treatment criteria (e.g. by age, sex, medical hx)



Reference: 50 yr old females

Jackson et al. Lancet 2005. 365:434-41

key questions on CVD risk prediction

- why treat predicted (combined) risk rather than individual risk factors?
- which prediction tool for which population?
- how should we choose treatment thresholds?
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- should predicted risk be modified for patients already on treatment?
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age-specific mortality in men according to SBP & age: relative risk of death



Geoffrey Rose. BMJ 1981;282:1847-51

age-specific mortality in men according to SBP & age: (a) relative & (b) absolute risk



Geoffrey Rose. BMJ 1981;282:1847-51

relative & absolute benefits from treating hypertension according to age & presence of CV-renal abnormality

Age (yr)	Cardiovascular -renal abnormality	Relative treatment effectiveness (%)	Lives saved per 100 treated (absolute)
< 50	-	59	6
	+	62	14
> 50	-	50	15
	+	60	29

Geoffrey Rose. BMJ 1981;282:1847-51



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Jackson et al. Lancet 2005. 365:434-41



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absolute CVD risk & glycaemia: HbA1c ± other CVD risk factors



Epic Norfolk unpublished



CVD events by history of CVD in NZ: 2002-12 (PREDICT n=270,000)



CVD events by history of CVD in NZ: 2002-12 (PREDICT n=270,000)



blood pressure & IHD mortality by age



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differences in cardiovascular risk in different ethic groups & different regions



using the original Framingham functions in a Chinese population

Figure 2. Ten-Year Prediction of CHD Events in CMCS Men and Women Using the Original Framingham Functions



using <u>recalibrated</u> Framingham functions in a Chinese population

Figure 3. Ten-Year Prediction of CHD Events in CMCS Men and Women Using the Recalibrated Framingham Functions

Laboratory-based versus non-laboratory-based method for assessment of cardiovascular disease risk: the NHANES I Follow-up Study cohort

Thomas A Gaziano, Cynthia R Young, Garrett Fitzmaurice, Sidney Atwood, J Michael Gaziano

Summary

Background Around 80% of all cardiovascular deaths occur in developing countries. Assessment of those patients at high risk is an important strategy for prevention. Since developing countries have limited resources for prevention strategies that require laboratory testing, we assessed if a risk prediction method that did not require any laboratory tests could be as accurate as one requiring laboratory information.

Methods The National Health and Nutrition Examination Survey (NHANES) was a prospective cohort study of 14 407 US participants aged between 25–74 years at the time they were first examined (between 1971 and 1975). Our follow-up study population included participants with complete information on these surveys who did not report a history of cardiovascular disease (myocardial infarction, heart failure, stroke, angina) or cancer, yielding an analysis dataset N=6186. We compared how well either method could predict first-time fatal and non-fatal cardiovascular disease events in this cohort. For the laboratory-based model, which required blood testing, we used standard risk factors to assess risk of cardiovascular disease: age, systolic blood pressure, smoking status, total cholesterol, reported diabetes status, and current treatment for hypertension. For the non-laboratory-based model, we substituted body-mass index for cholesterol.

Findings In the cohort of 6186, there were 1529 first-time cardiovascular events and 578 (38%) deaths due to cardiovascular disease over 21 years. In women, the laboratory-based model was useful for predicting events, with a c statistic of 0.829. The c statistic of the non-laboratory-based model was 0.831. In men, the results were similar (0.784 for the laboratory-based model and 0.783 for the non-laboratory-based model). Results were similar between the laboratory-based and non-laboratory-based models in both men and women when restricted to fatal events only.

Interpretation A method that uses non-laboratory-based risk factors predicted cardiovascular events as accurately as one that relied on laboratory-based values. This approach could simplify risk assessment in situations where laboratory testing is inconvenient or unavailable.

Lancet 2008; 371: 923-31 See Comment page 878 Division of Cardiovascular Medicine (T A Gaziano MD), Division of Social Medicine and Health Inequalities (S Atwood BA), Brigham & Women's Hospital, Boston, MA, USA; Harvard Medical School, Boston, MA, USA (C R Young MSc); Laboratory for Psychiatric Biostatistics, McLean Hospital, Belmont, MA, USA (G Fitzmaurice DSc); and Brigham & Women's Hospital, VA Boston Healthcare System, Boston, MA, USA (J M Gaziano MD)

Correspondence to: Dr Thomas A Gaziano, Division of Cardiovascular Medicine, Brigham & Women's Hospital, Boston, MA 02115, USA tgaziano@partners.org

key questions on CVD risk prediction

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35 yr old male **Overweight smoker** Non diabetic BP 140/ 80 mmHg TC 6.0 mmol/L HDLC 1.0 mmol/L TC/HDL = 6.0**5-yr CVD risk = 4%** but long-term risk 1

Why predict short-term CVD risk?

Blood pressure lowering & stroke

Figure 3: Cumulative incidence of stroke among participants assigned active treatment and those assigned placebo

Progress Lancet 2001; 358: 1033-41

Lipid lowering & CVD

Figure 6: Life-table plot of effects of simvastatin allocation on percentages having major vascular events

See figure 5 for numbers of participants having a first event during each year of follow-up.

HPS Lancet 2002; 360: 7–22

Lifetime risk of CVD to age 95 yrs: Framingham

Predicting life-time CVD risk

....is clinically irrelevant

Ratio of Total Cholesterol:HDL

Ratio of Total Cholesterol:HDL

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NUMBERS. Drs Sue Wells & Andrew Kerr (UoA)

WHAT ARE THEY?

Your heart numbers are two of the most important numbers you need to know because they give an insight into how healthy your heart is and also reflect the effect that your lifestyle is having on your body.

The two numbers are your blood pressure (BP) and your cholesterol ratio (TC/HDL). If you know your numbers, we can predict your risk of heart disease using the Heart Forecast tool on this site.

Read on to learn more about why these numbers are so important and how to find out YOUR numbers.

>> More

www.knowyournumbers.co.nz

Introduction		Step 1	
Your Pick Eactors		Step 7	
Tour Risk Pactors		Step 2	
Gender:	• male • female	Do you have diabetes?: yes on no Either Type 1, Type 2 or Type unknown diabetes. Not Gestational diabetes.	
Do you belong to any high risk ethnic group? The following ethnic groups may be at h Maori, Samoan, Cook Island Maori, Ton Fijian, Other Pacific Islands, Indian, Sri I	yes ono igher risk: New Zealand gan, Niuean, Tokelauan, Lankan, Pakistani,	Family history of early heart attack yes ono or stroke?: A brother or father below 55 years old or a sister or mother below 65 years old.	
Average BP:	an. 140 / <mark>80 mmHg</mark>	Next ►	
TC/HDL Ratio:	6		
Are you a current smoker or have you recently quit? Recently quit is any time within the last a	● yes ● no 12 months.		

Your Heart Forecast

Your current risk right now

Point where heart pills are recommended (15% risk

Your current risk right now

Your projected risk if no changes are made

Point where heart pills are recommended (15% risk)

Your ideal risk zone

(Based on Non-Smoker, TC/HDL ratio:4, BP: 120/80)

Your current risk right now

Your projected risk if no changes are made

Point where heart pills are recommended (15% risk)

 Your ideal risk zone (Based on Non-Smoker, TC/HDL ratio:4, BP: 120/80)

Your current risk right now - - Point where heart pills are recommended (15% risk)

Your projected risk if no changes are made

Your ideal risk zone (Based on Non-Smoker, TC/HDL ratio:4, BP: 120/80)

Risk level women No diabetes Diab

deaths from heart disease & other causes: NZ

population-based approach

high-risk approach

treatment of high BP or TC: ↓ only if high Mortality trends for all causes of death: age 35-69 years, New Zealand (Aotearoa)

relative stroke risk and usual Blood Pressure

(45 prospective studies: 450,000 people 13,000 events)

NZ CVD / DIABETES PROGRAMME

DEMOGRAPHICS	CVD RISK ASSESSMENT	CVD RISK	MANAGEMENT	DIABETES MANAGEME	ти	
Due stities a						
Practiculier	rs uetalis					
	<u>NZMC / NZN</u>	<u>C number</u>				
Demograph	ics (All to be prepopula	ated from	PMS)			
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	l	<u>ast name</u>]		
		<u>NHI</u>				
	рнв с	atchment	Please Select		*	
	Quintile of d	eprivation				?
	Meshbloc	k geocode				?
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		<u>Gender</u>	Please Select		*	?
Ethnic Grou	<u>p (1 or more self-identified etl</u> <u>may b</u>	nic group e chosen)	Not Stated		*	?
	Ethni	c Group 2	Not Stated		*	
	Ethni	c Group 3	Not Stated		*	
			NEXT			
l						J

DEMOGRAPHICS CYD RISK ASSESSMENT CVD RISK	MANAGEMENT DIABETES MANAGEMENT
This page should be completed for all patients. A After submitting this form, additional follow up m management form will become available depend	ll underlined items are required. anagement forms become available to you. The secondary Diabetes ant upon the status of the Diabetes field on this form.
NOTE: It is inappropriate to do CVD risk ass	sessment in pregnancy.
ASSUME	NEGATIVE DEFAULTS
Clinical History	
Family History of Premature CVD	Yes 🔿 - 🔿 No 📲
Angina/MI	Yes 🔿 - 🔿 No 📲
PTCA/CABG	Yes 🔿 - 🔿 No
Ischaemic Stroke or TIA	Yes 🔿 - 🔿 No 📲
PVD	Yes 🔿 - 🔿 No 📕
Diabetes	Please select
ECG confirmed Atrial Fibrillation	Yes 🔿 - 🚫 No 📲
Diagnosed Genetic Lipid Disorder	Please select
Diagnosed metabolic syndrome	Yes O - O No
Smoking History	Please select
Pregnant?	Yes 🔿 - 💿 No 📲
Examination	
Most recent BP (Sitting)	/ mmHg
Previous BP (Sitting)	/ mmHg
TC/HDL ratio	- Date: dd/mm/yyyy
Total Cholesterol	mmol/L - Date: dd/mm/yyyy
This data is the patient's real clinical information	Yes 💿 - 🔘 No

a

PF		Risk	RISK ASSESSMENT INFO		
CL	This	This	Note the BMI calculator on this page calculates th are required.	he BMI value automatically from height an	d weight. All underlined items
DEMOG	After		Examination		
	man		Height	170 cm	
	NOT			20 ka - Data	
Pr			RMI (Auto-calculated)	27.7 kg/m²	2
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		C e		. Please review carefully before proceeding.	_
		•	Aspirin	No	?
			Clopidogrel	No	?
			Warfarin	No	?
			ACE Inhibitor	No	?
			Angiotensin II Receptor Blocker	No	?
			Beta Blocker	No	?
			Thiazide	No	?
			Calcium Antagonist	No	?
			Other drug therapy for Hypertension	No	?
	Еха		Statin	No	?
			Fibrate	No	?
			Other Lipid lowering drugs	No	?
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			Investigation		
			Fasting glucose	6.1 mmol/L - Date: 26/10/2004 dd/mm,	/9999
			LDL Cholesterol (fasting)	3.3 mmol/L - Date: 26/10/2004 dd/mm,	/yyyy 2
			<u>Triglyceride (fasting)</u>	2.2 mmol/L - Date: 26/10/2004 dd/mm,	/9999 2
			HDL Cholesterol	1 mmol/L - Date: 26/10/2004 dd/mm,	/9999
			Lifectule management		

21

CVD / DIABETES ECDS	۵	NZ (PRO	CVD / GRAN	/ Diabet /ime	'ES
DEMOGRAPHICS CVD RISK ASSESSMENT CVD RISK MANAGEMENT					
ACTIONS RECOMMENDATIONS PATIENT INFORMATION RISK ASSESSMENT IN	NFO				
Actions: This page was made specifically for JOE BLOGGS (ABC1235): 26-Feb-	2007	12:30 ŀ	⊠ Sen ìrs	d 🖨 Print	
Test/Retest Considerations					
 Re-test fasting glucose today 					
Lifestyle					
 Reassess dietary pattern and physical activity today 					
 Refer to dietitian 					
 Discuss weight management 					
Blood Pressure					
BP therapy - check compliance, optimise dosage or add another agent					
Lipids					
 Repeat lipid test (fasting) if required to establish accurate baseline 					
 Start a statin after 3-6 months of specific lifestyle interventions (take transaminase level [ALT]) 	baselii	ne			
 Check fasting lipids and LFTs in 3 months (if start a statin) 					
	<u>P</u> ri	int	<u>S</u> ave	<u>C</u> ancel	<u>H</u> elp
VD / DIABETES ECDS	۵	PR	OGRAMM	IE	
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PREDICT CVD / DIABETES ECDS		۵	NZ CVD PROGRAÍ	/ Diabe Mme	TES
DEMOGRAPHICS CVD RISK ASSESSMENT CVD RISK MANAGEMENT					
ACTIONS RECOMMENDATIONS PATIENT INFORMATION RISK ASS	ESSMENT II	NFO			
Recommendations: This page was made specifically for JOE BLOGGS (ABC1235):	26-Feb-	2007 1	⊠ sei 2:30 hrs	nd 🖨 Print	
CVD Risk					
 Patient has an estimated 5-year CVD risk of 17%. CVD risk cat [(NZGG CVD) Estimating CVD risk] 	tegory: H	igh.			
 Patient has one or more of the criteria not included in the Framay confer additional risk (see Risk Assessment Info tab). The patient has been moved up one risk category (+5%). [(NZGG CVD) Estimating CVD risk] 	mingham (equatio	on which		
 Aim to lower CVD risk to less than 15% via lifestyle advice and of several risk factors. 	d simultan	eous r	eduction		
 Patient has metabolic syndrome (also called insulin resistance ATP III NCEP diagnostic criteria (see below). [(NZGG CVD) The Metabolic syndrome] 	syndrome	e) acco	ording to		
	d.	ted ev	ery 6		
 Fasting glucose (5mmol/L) is normal but test date not recorde Since patient has metabolic syndrome, fasting glucose should months. If the last test was performed more than 6 months a rechecking glucose and rerunning decision support. 	be re-tes Igo, recon	nmend			
 Fasting glucose (5mmol/L) is normal but test date not recorde Since patient has metabolic syndrome, fasting glucose should months. If the last test was performed more than 6 months a rechecking glucose and rerunning decision support. Lifestyle 	be re-tes igo, recon	nmend			

	REDICT DIABETES ECDS
	PREDICT
DEM	PREDICT CVD / DIABETES ECDSNZ CVD / DIABETESAPROGRAMME
	DEMOGRAPHICS CVD RISK ASSESSMENT CVD RISK MANAGEMENT
	ACTIONS RECOMMENDATIONS PATIENT INFORMATION RISK ASSESSMENT INFO
	Patient Information: Send A Print This page was made specifically for JOE BLOGGS (ABC1235): 26-Feb-2007 12:30 hrs
	 You have a high risk (15-20%) of developing heart disease or blood vessel disease or having a stroke in the next 5 years. The good news is that there are plenty of things that you can do to reduce this risk and your doctor or nurse can help you with this. [NHF booklet- reducing the risk of heart attack and stroke (www.nhf.org.nz)]
	Lifestyle
	 Regular physical activity and a diet that protects your heart will improve your general health, help to lower your blood pressure, improve your cholesterol and triglycerides (blood fats), blood sugar and other factors. Your doctor may refer you for special dietary advice so that it will be tailored just for you. [Tackling your risk factors-Eating and Nutrition (www.nhf.org.nz)] [Tackling your risk factors-physical activity (www.nhf.org.nz)]
	 Well done! You are doing 30 minutes or more physical activity on most days of the week. Keep it up and if possible do a little more!
<u>) </u>	 Your weight is above the recommended healthy weight. If you are not already involved in a healthy lifestyle programme, ask your doctor or practice nurse about your options. The target is to lose 10% of your initial weight. This may take some
	Print <u>S</u> ave <u>C</u> ancel <u>H</u> elp