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ANALYSING FALLS IN CORONARY HEART DISEASE MORTALITY IN THE WEST BANK BETWEEN 1998 AND 2009

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ABSTRACT

Objectives

To analyse coronary heart disease (CHD) mortality and risk factors trends in the West Bank, occupied Palestinian territory between 1998 and 2009.

Design

Modelling study using CHD IMPACT model

Setting

The West Bank, occupied Palestinian territory

Participants

Data on populations, mortality, patient groups and numbers, treatments and cardiovascular risk factor trends were obtained from national and local surveys, routine national and WHO statistics, and critically appraised. Data were then integrated and analysed using a previously validated CHD model

Primary and secondary outcome measures

CHD deaths prevented or postponed are the main outcome.

Results

CHD mortality rates fell by 20% in the West Bank, between 1998- 2009. Smoking prevalence was initially high in men, 51%, but decreased to 42%. Population blood pressure levels and total cholesterol levels also decreased. Conversely, BMI rose by 1-2kg/m^2 and diabetes increased by 2%-8%.

Population modelling suggested that more than two-thirds of the mortality fall was attributable to decreases in major risk factors, mainly total cholesterol, blood pressure and smoking.

Approximately one third of the CHD mortality decreases were attributable to treatments, particularly for secondary prevention and heart failure. However, the contributions from statins, surgery, and angioplasty were consistently small.

Conclusions

CHD mortality fell by 20% between 1998 and 2009 in the West Bank. More than two-third of this fall was due to decreases in major risk factors, particularly total cholesterol, and blood pressure.

Our results clearly indicate that risk factor reductions in the general population compared save substantially more lives to specific treatments for individual patients. This emphasizes the importance of population-wide primary prevention strategies.

INTRODUCTION

The occupied Palestinian territory comprises the Gaza Strip and the West Bank including East Jerusalem. Some 46% of the Palestinian population of 3.8 million are younger than 15 years while only 3% are older than 65 years. However, the number of older people is increasing gradually and the population is slowly aging. The Palestinians are also undergoing a rapid epidemiological transition. Communicable diseases of childhood have already been controlled with effective immunization programs, and poliomyelitis has been eradicated. However, non-communicable diseases have now overtaken communicable diseases as the main causes of mortality.[1] Thus, cardiovascular disease (CVD) and cancer are now the major causes of morbidity and mortality in Palestine.[2] The Ministry of Heath recently reported that 25% of all deaths are due to cardiovascular diseases in 2010, followed by cerebrovascular diseases (12%), cancer (11%) and diabetes (6%).[3] Increasing levels of adverse risk factors such as diabetes, obesity and physical inactivity have been repeatedly documented. [4, 5]

Chronic disease mortality rates are actually decreasing in the developed world (Western Europe, North America, Australia and New Zealand). However mortality is increasing in the developing countries. It is predicted that by 2020, CVD deaths will exceed infectious and parasitic disease deaths in all regions except sub-Saharan Africa [6]. Furthermore, the Eastern Mediterranean region has been recognized as a hot spot for diabetes and CVD, yet local data to inform policy is severely limited.

The IMPACT CHD model was developed to quantify recent trends in coronary heart disease mortality, in order to help maximize the effective use of existing information and resources to develop appropriate policies and strategies. This study aims to adopt the IMPACT CHD model to the Palestinian context, namely the West Bank population, in order to help explain recent changes in CHD mortality.

METHODS

A validated version of the IMPACT CHD mortality model was further modified and updated to suit the countries in the Middle East and specifically Palestine. The IMPACT model was previously validated in many developed countries[7-10] and in one middle income country (China).[11]

Palestinian data on risk factors levels and current uptake levels of evidence based treatments were identified by extensive searches for published or unpublished data and complemented with specifically designed surveys . All data sources were critically appraised by the local research team and the results are presented in the Technical Appendix. The data needed for the analysis was available for men and women aged 25-75 years in the West Bank, occupied Palestinian territory for the period 1998 – 2009 with some age limitations as described in the Technical Appendix.

The specific data items used to populate the model included: a) Patient numbers in specific CHD groups (Myocardial Infarction (MI), Congestive Heart Failure (CHF), Chronic Angina Pectoris (AP)) b) uptake of specific medical and surgical treatments, c) population trends in major cardiovascular risk factors (smoking, total cholesterol, systolic blood pressure, body mass index, diabetes and physical inactivity).

The main output of the model is the number of deaths prevented or postponed (DPPs) attributed to the changes in specific treatments and or risk factor levels.

Identification and assessment of relevant data

Information on the West Bank ***population demographic changes*** was obtained and validated for the first year from 1997 census based projections and 2007 census based projections for the final year by the Palestinian Central Bureau of Statistics (PCBS).[12] ***Numbers of deaths for both***

years were obtained from the Health Information Management Centre -Palestinian Ministry of Health. ***Population risk factors trend data*** for the year 1998 was obtained from two epidemiological studies conducted in the rural and urban areas of Ramallah governorate in the West Bank. These were the only available published epidemiological studies in the West Bank for that period. They covered a rural and an urban site that were prototypic of many West Bank villages and urban sites.[4, 13]

CHD numbers of hospital admissions in addition to treatment uptake were obtained from our Treatment uptake survey conducted in 2009 which included four hospitals in the north, centre and south of the West Bank. The number of patients undergoing Coronary Artery Bypass Grafting (CABG) and angioplasty were obtained from records in the two hospitals providing this service in the West Bank. The prevalence of angina, heart attack survivors and congestive heart failure in the community were each estimated on the basis of national health surveys and treatment uptake surveys. Information on treatment uptake in the community was also checked by eliciting expert opinion from practising clinicians.

The efficacy of therapeutic interventions were based on recent meta-analyses and randomised controlled trials. The Mant and Hicks approach was used to correct for polypharmacy.[14]

The change in coronary heart disease deaths

First, the number of CHD deaths ***expected*** in 2009 was calculated by indirect age standardisation based on the assumption that 1998 mortality rates had persisted unchanged until 2009. The number of CHD deaths actually **observed** in 2009 was then subtracted. The difference between

the two represents the fall in coronary heart disease deaths (the number of deaths prevented or postponed) that the model needed to explain.

The mortality changes attributed to risk factor trends

The number of deaths prevented or postponed from changes in risk factors were estimated using two approaches. The regression β coefficients approach was used to quantify the population mortality impact of change in those specific risk factors, measured as continuous variables, (blood pressure, total cholesterol and Body mass index (BMI)). The second approach, population attributable risk fraction, was employed for categorical variables- diabetes, physical inactivity and smoking:

$$PAR = \frac{\text{Prevalence} \times (\text{Relative Risk} - 1)}{[\text{Prevalence} \times (\text{Relative Risk} - 1)] + 1}$$

Details of model methodology have been published previously[7] and worked examples are shown in the Technical Appendix.

Estimating the contribution of medical and surgical treatments

The model aimed to include all medical and surgical treatments in 1998 (the base year) and 2009 (the final year). Treatment uptake data was not available for the year 1998 and thus the data included in the model for this year was estimated after consultation with cardiologists and experts working in both hospital and community at that time.

The mortality reduction for each treatment for the number of patients in each group, stratified by age and sex, was calculated as the age-specific case fatality in that group multiplied by the

relative mortality reduction reported in published meta-analyses multiplied by the treatment uptake (the proportion of patients receiving that specific treatment, Appendix 1).

Case-fatality data were obtained from large, unselected, population-based patient cohorts. The survival benefit over a one-year time interval was used for all treatments.

Treatment overlaps

Potential overlaps between different groups of patients were identified and appropriate adjustments were made. Patients group calculations and assumptions are detailed in the Technical Appendix.

Treatment adherence

Adherence, (defined as the proportion of treated patients actually taking therapeutically effective levels of the prescribed medication), was assumed to be 100% among hospital patients, 70% among all symptomatic community patients, and 50% among asymptomatic community patients, based on the literature.[15]

Sensitivity Analyses

Because of the uncertainties surrounding some of the values, multi-way sensitivity analyses using the Brigg's analysis of extremes method was used.[16]

Model validation: comparison with observed mortality falls

The model **estimate** for the changes in deaths attributed to all treatments plus all risk factor changes was summed for men and women in each specific age group. The model fit was then compared with the **observed change** in mortality for that group.

RESULTS

Between 1998 and 2009 CHD mortality in the West Bank fell by 20%. This resulted in approximately 125 fewer CHD deaths compared with the expected number of CHD deaths in 2009 if 1998 mortality rate had persisted unchanged (Table 1).

Table 1. Population sizes and CHD death rates in the West Bank, 1998 and 2009

	Men					
Age groups	**25-34**	**35-44**	**45-54**	**55-64**	**65-74**	**Total**
Population in 1998	132084	80434	41727	28653	19524	302422
Population in 2009	177873	132945	86399	41984	21619	460820
Deaths in 1998 (number)	**9**	**21**	**57**	**101**	**130**	318
Deaths in 2009 (number)	**11**	**30**	**89**	**131**	**133**	394
Death rates per 100,000 in 1998	6.4	26.1	135.4	350.7	665.8	105.2
Death rates per 100,000 in 2009	6.2	22.8	103.4	311.2	616.7	85.5
% Change (crude)	0.0%	-12.6%	-23.6%	-11.3%	-7.4%	-19.0%

	Women					
Age groups	**25-34**	**35-44**	**45-54**	**55-64**	**65-74**	**Total**
Population in 1998	125493	76747	45711	36038	24445	308434
Population in 2009	170942	127590	80883	43693	28424	451532
Deaths in 1998 (number)	**5**	**9**	**22**	**59**	**107**	202
Deaths in 2009 (number)	**5**	**11**	**20**	**51**	**105**	192

Death rates per 100,000 in 1998	3.6	11.1	48.1	162.3	437.7	65.5
Death rates per 100,000 in 2009	3.1	8.9	24.7	116.0	370.6	42.5
% Change (crude)	0.0%	-19.8%	-48.6%	-28.6%	-15.3%	-35.0%

The reduction in CHD mortality among women (35%) was twice as large as the 19% reduction observed among men. The CHD mortality reduction was seen in all age groups with particularly large reductions being observed among those aged 45-54 years, both men (24%) and women (49%).

Major CHD risk factors

Changes in cardiovascular risk factors included in the model were together estimated to prevent or postpone approximately 80 deaths in 2009 *(minimum estimate 75, maximum estimate 140),* which represented approximately 66% of the total CHD mortality fall (**Figure 1**).

Table 2 presents changes in the selected risk factors and the attributed deaths. Changes in risk factors were complex: reduction in total cholesterol (mean reduction 0.34mmol/L in men and 0.22 mmol/L in women), blood pressure (5.27 mmHg in men and 0.01 mmHg in women) and in smoking prevalence (11.5% in men and 2.2% in women). These changes together prevented or postponed approximately 125 deaths (Table 2). Forty percent of the total fall in CHD deaths were thus attributable to cholesterol reduction *(minimum 38% and maximum 77%),* and 36% to blood pressure reduction *(minimum 30% and maximum 50%)* and 33% to smoking reduction *(minimum 22% and maximum 49%)* reduction. However, an additional 45 deaths were attributable to adverse trends **(Figure 2**). Mainly an increase in diabetes prevalence (8.5% in men and 2% in women) generated approximately 30 additional deaths. The mortality effects of increases in physical inactivity and mean body mass index were relatively modest (**Table 2**).

Table 2: Deaths Attributable to Population Risk Factor Changes in the West Bank between 1998 and 2009

RISK FACTORS	Risk factor levels		Absolute Change in risk factor 1998-2009	Relative Risk (RR[1]) (or βeta Coefficient)[2]	Deaths prevented or postponed (DPP)			
	1998	2009			Best Estimate	*Minimum estimate*	*Maximum estimate*	Proportion of overall deaths
Cholesterol (total) *mmol/l*					**49**	*46*	*94*	**-40.3%**
Cholesterol (men)	*5.37*	*5.03*	0.34	βετα 0.65				
Cholesterol (women)	*5.25*	*5.03*	*0.22*	βετα 0.65				
Smoking (total) *%)*					**40**	*26*	*59*	**-32.50%**
(% men smoking)	*51.5*	*40*	*11.5*					
(% women smoking)	*5.5*	*3.3*	*2.2*					
BMI (total) *Kg/m²*					**-2**	*-2*	*-5*	**-2.00%**
BMI (men)	*26.95*	*30.88*	-3.93	βετα 0.02				
BMI (women)	*29.12*	*30.99*	-1.87	βετα 0.02				
Diabetes (total) %					**-32**	*-27*	*-60*	**26.20%**
% Diabetes (men)	9.1	*17.6*	*-8.5*	2				
% Diabetes (women)	*12.4*	*14.4*	*-2*	2				
Population systolic BP (total) mm/Hg								
Population bp (men)	*125.57*	*120.3*	5.27	βετα 0.053	**43**	*39*	*84*	**-35.60%**
Population bp (women)	*118.44*	*118.45*	-0.01	βετα 0.053	5	*2*	*68*	-4.1%
Population BP after adjustment for hypertension treatments					**38**	*37*	*61*	**-31.5**
Physical inactivity					**-12**	*-8*	*-17*	**9.7%**
% Physical inactivity men	*79.3*	*91.3*	*12*					
%Physical inactivity women	*87.9*	*93.0*	*5.1*					
Estimated total risk factor effects					**80**	*0*	*0*	**-66.5%**

Medical and surgical treatments (Figure 3)

Medical and surgical treatments together prevented or postponed approximately 35 deaths in 2009 *(minimum estimate 20, maximum estimate 108).* The total treatments thus accounted for approximately 29% *(minimum 17% and maximum 82%)* of the total CHD mortality reduction (**Table 3**). Secondary prevention following acute myocardial infarction explained over 7% *(minimum 3% and maximum 25%)* of deaths prevented or postponed (with ACE inhibitors, aspirin and beta blockers and beta blockers being the main contributors in this group) (Table 3). Smaller contributions came from chronic angina treatment (6%, *minimum 5%- maximum 11%)* and heart failure treatment in the community (5%, *minimum 3% and maximum 10%)* and hypertensive treatment in the community (4%, *minimum 1% and maximum 19%).* Secondary prevention post revascularisation had a very modest effect on CHD mortality reduction with a contribution of 2% (*minimum 1% and maximum 5%).* (Table 3).

Table 3: Deaths Prevented or Postponed by Medical and Surgical Treatments in the West Bank in 2009

TREATMENTS	Patients eligible	Treatment uptake (%)	CHD deaths prevented or postponed Best Estimate	*Minimum estimate*	*Maximum estimate*	*Proportion of overall deaths prevented or postponed (%)*
Acute myocardial infarction	**489**		***2***	***1***	***6***	**-1.9%**
Hospital resuscitation		0.06	*0*	*0*	*1*	-0.3%
Thrombolysis and aspirin						
Aspirin alone		0.90	*5*	*2*	*9*	-3.8%
Thrombolysis alone		0.39	*3*	*1*	*6*	-2.4%
Beta blockers		0.58	*1*	*0*	*2*	-0.6%
ACE inhibitors		0.44	*1*	*0*	*2*	-1.0%
Secondary Prevention post infarction	**2266**		***9***	***4***	***30***	**-7.4%**
Aspirin		0.483	*4*	*1*	*9*	-2.9%
Beta blockers		0.388	*4*	*1*	*11*	-3.6%
Aspirin and beta blockers		0.415	*4*	*1*	*10*	-3.4%
ACE inhibitors		0.472	*5*	*2*	*13*	-4.2%
Statins		0.046	*0*	*0*	*1*	-0.4%
Warfarin		0.100	*1*	*0*	*3*	-0.9%
Rehabilitation		0.483	*1*	*0*	*3*	-.9%
Secondary Prevention post revascularisation	**208**		***2***	***0***	***6***	**- 1.9%**
Angina			***7***	***6***	***13***	**-5.7%**
CABG surgery (2004-5)	208	1.00	*6*	*3*	*10*	-4.6%
Aspirin in the community	22180	0.47	*15*	*13*	*40*	-12.7%
Statin in the community	22180	0.46	***20***	***11***	***50***	**-16.8**
Unstable angina	489		***1***	***2***	***9***	**-1.1%**
Heart Failure	**2811**					
Hospital patients	468		***-2***	***-1***	***-8***	**-1.5%**
Community patients	2342		***-7***	***-4***	***-4***	**-5.4%**
Hypertension Treatments			***-5***	***-2***	***-23***	*-4.1%*
Total treatment effects			**35**	***20***	***108***	**29.0%**

Validation and model fit

In summary, when including all risk factor and treatment data, the model explained approximately 95% of the total CHD mortality reduction observed in the West Bank population between 1998 and 2009. The remaining 5% was unexplained and might reflect other, unmeasured factors. The model estimates of deaths were reasonably consistent with the observed deaths for almost all age groups. Overall, the model fit was better for men than for women. However, in the age group 45-54 the model over-estimated deaths in both men and women (**Table 4**). Moreover, irrespective of whether best minimum or maximum estimates were used, the relative contributions remained relatively consistent.

Table 4. Model validation: estimated versus observed changes in CHD deaths between 1998 and 2009

	Age groups					
Men	**25-34**	**35-44**	**45-54**	**55-64**	**65-74**	**Total**
Estimated fall in CHD deaths	***11***	***35***	***117***	***147***	***144***	***454***
Observed fall in CHD deaths	**11**	**30**	**89**	**131**	**133**	**394**
Discrepancy	**0**	**-5**	**-28**	**-16**	**-11**	**-60**
Estimated fall/ observed fall in CHD deaths	**100%**	**117%**	**131%**	**112%**	**108%**	**115%**
Women						
Estimated fall in CHD deaths	***6***	***14***	***39***	***71***	***124***	***254***
Observed fall in CHD deaths	**5**	**11**	**20**	**51**	**105**	**192**
Discrepancy	**-1**	**-3**	**-19**	**-20**	**-19**	**-62**
Estimated fall/ observed fall in CHD deaths	**120%**	**127%**	**195%**	**139%**	**118%**	**132%**

DISCUSSION

Coronary heart diseases mortality decreased by 20% in the West Bank, oPt between 1998 and 2009. Almost two thirds of this reduction was attributable to changes in major risk factors and approximately one-third was explained by medical and surgical treatments. The recent mortality trends observed in the West Bank were thus characterised by reductions in CHD mortality similar to those observed in the developed rather than developing countries. Other studies have documented similar reductions in CHD mortality in Europe, North America and New Zealand especially since the 1980s.[7, 8, 17, 18]

The biggest CHD mortality reductions attributable to changes in major risk factors came from declines in total cholesterol and smoking, and also blood pressure in men. Interestingly, the implementation efforts of an anti-smoking law in 2005 might have contributed to the substantial declines in smoking prevalence.[19, 20]

However, the increasing Westernisation of diet, particularly junk food and soda represent an ominous future threat. Furthermore, diabetes, obesity and physical inactivity increased substantially between 1998 and 2009.[21-23] The increase in diabetes prevalence generated approximately 30 additional CHD deaths. Rising diabetes and obesity, especially among men, represents a public health priority . Effective evidence-based interventions exist and should be considered, notably junk-food taxes and advertising bans.[24, 25]

The recently developed Palestinian non-communicable diseases (NCDs) strategy adopted an integrated approach encompassing promotion, prevention and control programmes. Population based multi-sectoral effective evidence-based interventions were clearly indicated to control diabetes and

promote physical activity such as health promotion, fiscal measures , market control and community participation. Yet a clear vision and scope of implementation is still evolving.[26]

Modern medical treatments accounted for approximately 30% of the CHD mortality reduction. The scale of effect is similar to that reported in studies using the same methodology in Iceland, Sweden and Finland[9] but lower than the 45%-50% reported for North America,[27] and Europe.[8, 10] The biggest contributions came from community tablets for secondary prevention, chronic angina and heart failure. Treatment uptakes were generally mediocre and need to be improved. However, such treatments create challenges for health providers in terms of identifying patients, providing medications and ensuring their long-term compliance.

Data on both patient groups and treatment uptake levels was scarce. Such data was not available at the national or the hospital level. The required information was therefore collected directly from the hospital patients' records to be utilized in this study. Furthermore, the uptake levels were not consistent among different hospitals and sometimes between physicians. These two findings therefore highlight both a lack of standardised health care provision and important gaps in the NCD health information system.

Modelling strengths and limitations

The modelling approach used in the study was comprehensive, it synthesised all the key risk factors and treatment options to help quantify changes in CHD mortality. Additionally, the model used rigorous sensitivity analyses to systematically examine the potential influence of uncertainties in the data and model assumptions, and hence quantify the potential maximum and minimum effects of these contributory factors

This modelling approach also has obvious limitations. Notably the extent and quantity of available data on CHD risk factor trends and treatment uptake. However, the data used in this model was generally of good quality. Mortality data were obtained from Ministry of Health death registry. Death registry data were evaluated in previous studies as medium quality based on the WHO criteria.[28] The demographic information was obtained from census data, and the risk factor trends were obtained from well designed epidemiological studies and national PCBS, MOH, and WHO surveys. Treatment uptake and patient groups data were obtained from an extensive hospital based survey conducted in 2009. Very scarce data available on treatment uptake was also obtained. However, researchers had to conduct additional surveys to get the timely, accurate data required by the model. Certain assumptions were needed to fill in the gaps for missing information. For instance, assumptions were made for the small group aged 65-74 years where risk factor information were not available. All these assumptions are transparent, being systematically detailed in the Technical Appendix, supported by local expert opinions and literature from the region and included in the sensitivity analyses.

Public health implications

CHD mortality fell by 20% between 1998 and 2009 in the West Bank, oPt. More than two-third of this fall was due to changes in major risk factors mainly total cholesterol, blood pressure and smoking.

Our results clearly indicate that risk factor improvements in the general population saved substantially more lives than specific treatments for individual patients. This emphasizes the importance of population-wide primary prevention strategies.

Contributorship Statement

All authors have fulfilled the following contributions 1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content; and 3) final approval of the version to be published

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Conflict of interest

The authors declare that they have no conflict of interest

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FIGURE LEGENDS

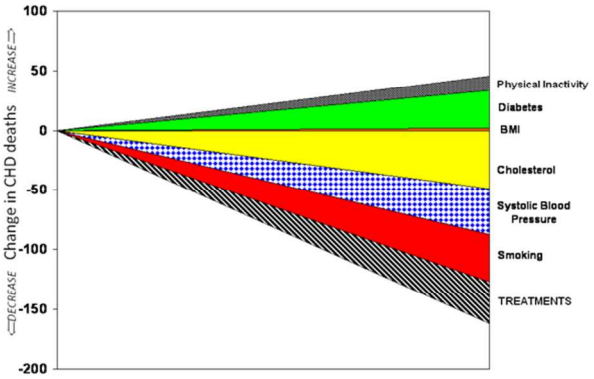
FIGURE 1: Coronary heart disease deaths prevented or postponed by treatment and risk factors changes in the West Bank population between 1998 and 2009.

Figure 2: CHD deaths prevented or postponed attributable to specific risk factor changes in Palestine 1998-2009: Sensitivity Analysis

(■ = Best estimate, bars indicate minimum & maximum estimates)

Figure 3: CHD deaths prevented or postponed attributable to specific treatments in Palestine 1998-2009: Sensitivity Analysis

(■ = Best estimate, bars indicate minimum & maximum estimates)



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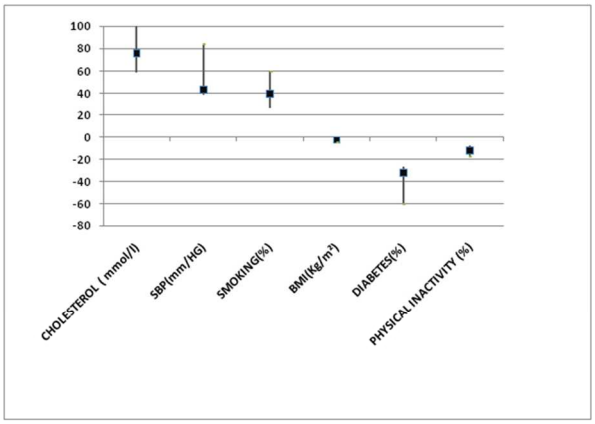

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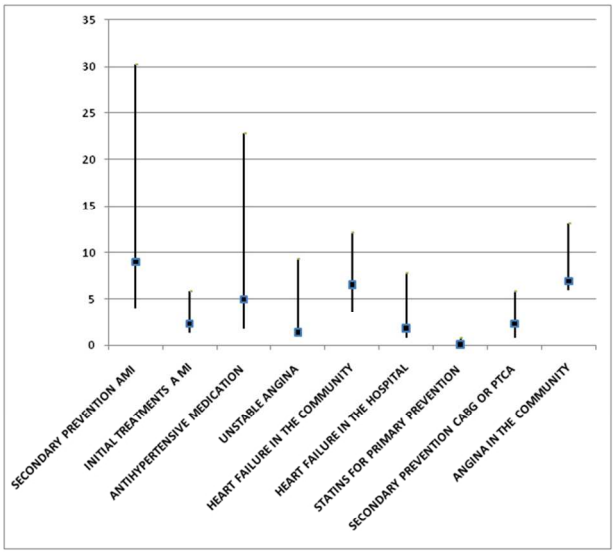

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ANALYSING FALLS IN CORONARY HEART DISEASE MORTALITY IN THE WEST BANK BETWEEN 1998 AND 2009

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ANALYSING FALLS IN CORONARY HEART DISEASE MORTALITY IN THE WEST BANK BETWEEN 1998 AND 2009

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ABSTRACT

Objectives

To analyse coronary heart disease (CHD) mortality and risk factors trends in the West Bank, occupied Palestinian territory between 1998 and 2009.

Design

Modelling study using CHD IMPACT model

Setting

The West Bank, occupied Palestinian territory

Participants

Data on populations, mortality, patient groups and numbers, treatments and cardiovascular risk factor trends were obtained from national and local surveys, routine national and WHO statistics, and critically appraised. Data were then integrated and analysed using a previously validated CHD model

Primary and secondary outcome measures

CHD deaths prevented or postponed are the main outcome.

Results

CHD mortality rates fell by 20% in the West Bank, between 1998- 2009. Smoking prevalence was initially high in men, 51%, but decreased to 42%. Population blood pressure levels and total cholesterol levels also decreased. Conversely, BMI rose by 1-2kg/m^2 and diabetes increased by 2%-8%.

Population modelling suggested that more than two-thirds of the mortality fall was attributable to decreases in major risk factors, mainly total cholesterol, blood pressure and smoking.

Approximately one third of the CHD mortality decreases were attributable to treatments, particularly for secondary prevention and heart failure. However, the contributions from statins, surgery, and angioplasty were consistently small.

Conclusions

CHD mortality fell by 20% between 1998 and 2009 in the West Bank. More than two-third of this fall was due to decreases in major risk factors, particularly total cholesterol, and blood pressure.

Our results clearly indicate that risk factor reductions in the general population compared save substantially more lives to specific treatments for individual patients. This emphasizes the importance of population-wide primary prevention strategies.

INTRODUCTION

The occupied Palestinian territory (oPt) comprises the Gaza Strip and the West Bank including East Jerusalem. Some 46% of the Palestinian population of 3.8 million are younger than 15 years while only 3% are older than 65 years. However, the number of older people is increasing gradually and the population is slowly aging. The Palestinians are also undergoing a rapid epidemiological transition. Communicable diseases of childhood have already been controlled with effective immunization programs, and poliomyelitis has been eradicated. However, non-communicable diseases have now overtaken communicable diseases as the main causes of mortality.[1] Thus, cardiovascular disease (CVD) and cancer are now the major causes of morbidity and mortality in the oPt.[2] The Ministry of Heath recently reported that 25% of all deaths are due to cardiovascular diseases in 2010, followed by cerebrovascular diseases (12%), cancer (11%) and diabetes (6%).[3] Increasing levels of adverse risk factors such as diabetes, obesity and physical inactivity have been repeatedly documented. [4, 5]

Chronic disease mortality rates are actually decreasing in the developed world (Western Europe, North America, Australia and New Zealand). However mortality is increasing in the developing countries. It is predicted that by 2020, CVD deaths will exceed infectious and parasitic disease deaths in all regions except sub-Saharan Africa [6]. Furthermore, the Eastern Mediterranean region has been recognized as a hot spot for diabetes and CVD, yet local data to inform policy is severely limited.

The IMPACT CHD model was developed to quantify recent trends in coronary heart disease mortality, in order to help maximize the effective use of existing information and resources to develop appropriate policies and strategies. This study aims to adopt the IMPACT CHD model to the Palestinian context, namely the West Bank population, in order to help explain recent changes in CHD mortality.

METHODS

A validated version of the IMPACT CHD mortality model was further modified and updated to suit the countries in the Middle East and specifically The oPt. The IMPACT model was previously validated in many developed countries[7-10] and in one middle income country (China).[11]

Palestinian data on risk factors levels and current uptake levels of evidence based treatments were identified by extensive searches for published or unpublished data and complemented with specifically designed surveys . All data sources were critically appraised by the local research team and the results are presented in the Technical Appendix. The data needed for the analysis was available for men and women aged 25-75 years in the West Bank, occupied Palestinian territory for the period 1998 – 2009 with some age limitations as described in the Technical Appendix.

The specific data items used to populate the model included: a) Patient numbers in specific CHD groups (Myocardial Infarction (MI), Congestive Heart Failure (CHF), Chronic Angina Pectoris (AP)) b) uptake of specific medical and surgical treatments, c) population trends in major cardiovascular risk factors (smoking, total cholesterol, systolic blood pressure, body mass index, diabetes and physical inactivity).

The main output of the model is the number of deaths prevented or postponed (DPPs) attributed to the changes in specific treatments and or risk factor levels.

Identification and assessment of relevant data

Information on the West Bank ***population demographic changes*** was obtained and validated for the first year from 1997 census based projections and 2007 census based projections for the final year by the Palestinian Central Bureau of Statistics (PCBS).[12] ***Numbers of deaths for both***

years were obtained from the Health Information Management Centre -Palestinian Ministry of Health. ***Population risk factors trend data*** for the year 1998 was obtained from two epidemiological studies conducted in the rural and urban areas of Ramallah governorate in the West Bank. These were the only available published epidemiological studies in the West Bank for that period. They covered a rural and an urban site that were prototypic of many West Bank villages and urban sites.[4, 13]

CHD numbers of hospital admissions in addition to treatment uptake were obtained from our Treatment uptake survey conducted in 2009 which included four hospitals in the north, centre and south of the West Bank. The number of patients undergoing Coronary Artery Bypass Grafting (CABG) and angioplasty were obtained from records in the two hospitals providing this service in the West Bank. The prevalence of angina, heart attack survivors and congestive heart failure in the community were each estimated on the basis of national health surveys and treatment uptake surveys. Information on treatment uptake in the community was also checked by eliciting expert opinion from practising clinicians.

The efficacy of therapeutic interventions were based on recent meta-analyses and randomised controlled trials. The Mant and Hicks approach was used to correct for polypharmacy.[14]

The change in coronary heart disease deaths

First, the number of CHD deaths ***expected*** in 2009 was calculated by indirect age standardisation based on the assumption that 1998 mortality rates had persisted unchanged until 2009. The number of CHD deaths actually **observed** in 2009 was then subtracted. The difference between

the two represents the fall in coronary heart disease deaths (the number of deaths prevented or postponed) that the model needed to explain.

The mortality changes attributed to risk factor trends

The number of deaths prevented or postponed from changes in risk factors were estimated using two approaches. The regression β coefficients approach was used to quantify the population mortality impact of change in those specific risk factors, measured as continuous variables, (blood pressure, total cholesterol and Body mass index (BMI)). The second approach, population attributable risk fraction, was employed for categorical variables- diabetes, physical inactivity and smoking:

$$PAR = \frac{\text{Prevalence} \times (\text{Relative Risk} - 1)}{[\text{Prevalence} \times (\text{Relative Risk} - 1)] + 1}$$

PAR calculation was stratified by age and sex. Details of model methodology have been published previously[7] and worked examples are shown in the Technical Appendix.

Estimating the contribution of medical and surgical treatments

The model aimed to include all medical and surgical treatments in 1998 (the base year) and 2009 (the final year). Treatment uptake data was not available for the year 1998 and thus the data included in the model for this year was estimated after consultation with cardiologists and experts working in both hospital and community at that time.

The mortality reduction for each treatment for the number of patients in each group, stratified by age and sex, was calculated as the age-specific case fatality in that group multiplied by the

relative mortality reduction reported in published meta-analyses multiplied by the treatment uptake (the proportion of patients receiving that specific treatment, Appendix 1).

Case-fatality data were obtained from large, unselected, population-based patient cohorts. The survival benefit over a one-year time interval was used for all treatments.

Treatment overlaps

Potential overlaps between different groups of patients were identified and appropriate adjustments were made. Patients group calculations and assumptions are detailed in the Technical Appendix.

Treatment adherence

Adherence, (defined as the proportion of treated patients actually taking therapeutically effective levels of the prescribed medication), was assumed to be 100% among hospital patients, 70% among all symptomatic community patients, and 50% among asymptomatic community patients, based on the literature.[15]

Sensitivity Analyses

Because of the uncertainties surrounding some of the values, multi-way sensitivity analyses using the Brigg's analysis of extremes method was used.[16]

Model validation: comparison with observed mortality falls

The model **estimate** for the changes in deaths attributed to all treatments plus all risk factor changes was summed for men and women in each specific age group. The model fit was then compared with the **observed change** in mortality for that group.

RESULTS

Between 1998 and 2009 CHD mortality in the West Bank fell by 20%. This resulted in approximately 125 fewer CHD deaths compared with the expected number of CHD deaths in 2009 if 1998 mortality rate had persisted unchanged (Table 1).

Table 1. Population sizes and CHD death rates in the West Bank, 1998 and 2009

	Men					
Age groups	**25-34**	**35-44**	**45-54**	**55-64**	**65-74**	**Total**
Population in 1998	132084	80434	41727	28653	19524	302422
Population in 2009	177873	132945	86399	41984	21619	460820
Deaths in 1998 (number)	**9**	**21**	**57**	**101**	**130**	318
Deaths in 2009 (number)	**11**	**30**	**89**	**131**	**133**	394
Death rates per 100,000 in 1998	6.4	26.1	135.4	350.7	665.8	105.2
Death rates per 100,000 in 2009	6.2	22.8	103.4	311.2	616.7	85.5
% Change (crude)	0.0%	-12.6%	-23.6%	-11.3%	-7.4%	-19.0%
	Women					
Age groups	**25-34**	**35-44**	**45-54**	**55-64**	**65-74**	**Total**
Population in 1998	125493	76747	45711	36038	24445	308434
Population in 2009	170942	127590	80883	43693	28424	451532
Deaths in 1998 (number)	**5**	**9**	**22**	**59**	**107**	202
Deaths in 2009 (number)	**5**	**11**	**20**	**51**	**105**	192

Death rates per 100,000 in 1998	3.6	11.1	48.1	162.3	437.7	65.5
Death rates per 100,000 in 2009	3.1	8.9	24.7	116.0	370.6	42.5
% Change (crude)	0.0%	-19.8%	-48.6%	-28.6%	-15.3%	-35.0%

The reduction in CHD mortality among women (35%) was twice as large as the 19% reduction observed among men. The CHD mortality reduction was seen in all age groups with particularly large reductions being observed among those aged 45-54 years, both men (24%) and women (49%).

Major CHD risk factors

Changes in cardiovascular risk factors included in the model were together estimated to prevent or postpone approximately 80 deaths in 2009 *(minimum estimate 75, maximum estimate 140),* which represented approximately 66% of the total CHD mortality fall (**Figure 1**).

Table 2 presents changes in the selected risk factors and the attributed deaths. Changes in risk factors were complex: reduction in total cholesterol (mean reduction 0.34mmol/L in men and 0.22 mmol/L in women), blood pressure (5.27 mmHg in men and 0.01 mmHg in women) and in smoking prevalence (11.5% in men and 2.2% in women). These changes together prevented or postponed approximately 125 deaths (Table 2). Forty percent of the total fall in CHD deaths were thus attributable to cholesterol reduction *(minimum 38% and maximum 77%),* and 36% to blood pressure reduction *(minimum 30% and maximum 50%)* and 33% to smoking reduction *(minimum 22% and maximum 49%)* reduction. However, an additional 45 deaths were attributable to adverse trends **(Figure 2**). Mainly an increase in diabetes prevalence (8.5% in men and 2% in women) generated approximately 30 additional deaths. The mortality effects of increases in physical inactivity and mean body mass index were relatively modest (**Table 2**).

Table 2: Deaths Attributable to Population Risk Factor Changes in the West Bank between 1998 and 2009

RISK FACTORS	Risk factor levels		Absolute Change in risk factor 1998-2009	Relative Risk (RR) (or βeta Coefficient)	Deaths prevented or postponed (DPP)			
	1998	2009			Best Estimate	*Minimum estimate*	*Maximum estimate*	Proportion of overall deaths
Cholesterol (total) *mmol/l*					**49**	*46*	*94*	**-40.3%**
Cholesterol (men)	*5.37*	*5.03*	0.34	βετα 0.65				
Cholesterol (women)	*5.25*	*5.03*	*0.22*	βετα 0.65				
Smoking (total) *%)*					**40**	*26*	*59*	**-32.50%**
(% men smoking)	*51.5*	*40*	*11.5*					
(% women smoking)	*5.5*	*3.3*	*2.2*					
BMI (total) *Kg/m²*					**-2**	*-2*	*-5*	**-2.00%**
BMI (men)	*26.95*	*30.88*	-3.93	βετα 0.02				
BMI (women)	*29.12*	*30.99*	-1.87	βετα 0.02				
Diabetes (total) %					**-32**	*-27*	*-60*	**26.20%**
% Diabetes (men)	9.1	*17.6*	*-8.5*	2				
% Diabetes (women)	*12.4*	*14.4*	*-2*	2				
Population systolic BP (total) mm/Hg					43	39	84	-35.60%
Population bp (men)	*125.57*	*120.3*	5.27	βετα 0.053				
Population bp (women)	*118.44*	*118.45*	-0.01	βετα 0.053				
Population BP after adjustment for hypertension treatments					**38**	*37*	*61*	**-31.5**
Physical inactivity					**-12**	*-8*	*-17*	**9.7%**
% Physical inactivity men	*79.3*	*91.3*	*12*					
%Physical inactivity women	*87.9*	*93.0*	*5.1*					
Estimated total risk factor effects					**81**	*73*	*138*	**-66.5%**

Medical and surgical treatments (Figure 3)

Medical and surgical treatments together prevented or postponed approximately 35 deaths in 2009 *(minimum estimate 20, maximum estimate 108).* The total treatments thus accounted for approximately 29% *(minimum 17% and maximum 82%)* of the total CHD mortality reduction (**Table 3**). Secondary prevention following acute myocardial infarction explained over 7% *(minimum 3% and maximum 25%)* of deaths prevented or postponed (with ACE inhibitors, aspirin and beta blockers and beta blockers being the main contributors in this group) (Table 3). Smaller contributions came from chronic angina treatment (6%, *minimum 5%- maximum 11%)* and heart failure treatment in the community (5%, *minimum 3% and maximum 10%)* and hypertensive treatment in the community (4%, *minimum 1% and maximum 19%).* Secondary prevention post revascularisation had a very modest effect on CHD mortality reduction with a contribution of 2% (*minimum 1% and maximum 5%).* (Table 3).

Table 3: Deaths Prevented or Postponed by Medical and Surgical Treatments in the West Bank in 2009

TREATMENTS	Patients eligible	Treatment uptake (%)	CHD deaths prevented or postponed Best Estimate	*Minimum estimate*	*Maximum estimate*	*Proportion of overall deaths prevented or postponed (%)*
Acute myocardial infarction	**489**		***2***	***1***	***6***	**-1.9%**
Hospital resuscitation		0.06	*0*	*0*	*1*	-0.3%
Thrombolysis and aspirin						
Aspirin alone		0.90	*5*	*2*	*9*	-3.8%
Thrombolysis alone		0.39	*3*	*1*	*6*	-2.4%
Beta blockers		0.58	*1*	*0*	*2*	-0.6%
ACE inhibitors		0.44	*1*	*0*	*2*	-1.0%
Secondary Prevention post infarction	**2266**		***9***	***4***	***30***	**-7.4%**
Aspirin		0.483	*4*	*1*	*9*	-2.9%
Beta blockers		0.388	*4*	*1*	*11*	-3.6%
Aspirin and beta blockers		0.415	*4*	*1*	*10*	-3.4%
ACE inhibitors		0.472	*5*	*2*	*13*	-4.2%
Statins		0.046	*0*	*0*	*1*	-0.4%
Warfarin		0.100	*1*	*0*	*3*	-0.9%
Rehabilitation		0.483	*1*	*0*	*3*	-.9%
Secondary Prevention post revascularisation	**208**		***2***	***0***	***6***	**- 1.9%**
Angina			***7***	***6***	***13***	**-5.7%**
CABG surgery (2004-5)	208	1.00	*6*	*3*	*10*	-4.6%
Aspirin in the community	22180	0.47	*15*	*13*	*40*	-12.7%
Statin in the community	22180	0.46	***20***	***11***	***50***	**-16.8**
Unstable angina	489		***1***	***2***	***9***	**-1.1%**
Heart Failure	**2811**					
Hospital patients	468		***-2***	***-1***	***-8***	**-1.5%**
Community patients	2342		***-7***	***-4***	***-4***	**-5.4%**
Hypertension Treatments			***-5***	***-2***	***-23***	*-4.1%*
Total treatment effects			**35**	***20***	***108***	**29.0%**

Validation and model fit

In summary, when including all risk factor and treatment data, the model explained approximately 95% of the total CHD mortality reduction observed in the West Bank population between 1998 and 2009. The remaining 5% was unexplained and might reflect other, unmeasured factors. The model estimates of deaths were reasonably consistent with the observed deaths for almost all age groups. Overall, the model fit was better for men than for women. However, in the age group 45-54 the model over-estimated deaths in both men and women (**Table 4**). Moreover, irrespective of whether best minimum or maximum estimates were used, the relative contributions remained relatively consistent.

Table 4. Model validation: estimated versus observed changes in CHD deaths between 1998 and 2009

	Age groups					
Men	**25-34**	**35-44**	**45-54**	**55-64**	**65-74**	**Total**
Estimated fall in CHD deaths	***11***	***35***	***117***	***147***	***144***	***454***
Observed fall in CHD deaths	**11**	**30**	**89**	**131**	**133**	**394**
Discrepancy	**0**	**-5**	**-28**	**-16**	**-11**	**-60**
Estimated fall/ observed fall in CHD deaths	**100%**	**117%**	**131%**	**112%**	**108%**	**115%**
Women						
Estimated fall in CHD deaths	***6***	***14***	***39***	***71***	***124***	***254***
Observed fall in CHD deaths	**5**	**11**	**20**	**51**	**105**	**192**
Discrepancy	**-1**	**-3**	**-19**	**-20**	**-19**	**-62**
Estimated fall/ observed fall in CHD deaths	**120%**	**127%**	**195%**	**139%**	**118%**	**132%**

DISCUSSION

Coronary heart diseases mortality decreased by 20% in the West Bank, oPt between 1998 and 2009. Almost two thirds of this reduction was attributable to changes in major risk factors and approximately one-third was explained by medical and surgical treatments. The recent mortality trends observed in the West Bank were thus characterised by reductions in CHD mortality similar to those observed in the developed rather than developing countries. Other studies have documented similar reductions in CHD mortality in Europe, North America and New Zealand especially since the 1980s.[7, 8, 17, 18]

The biggest CHD mortality reductions attributable to changes in major risk factors came from declines in total cholesterol and smoking, and also blood pressure in men. Interestingly, the implementation efforts of an anti-smoking law in 2005 might have contributed to the substantial declines in smoking prevalence.[19, 20]

However, the increasing Westernisation of diet, particularly junk food and soda represent an ominous future threat. Furthermore, diabetes, obesity and physical inactivity increased substantially between 1998 and 2009.[21-23] In the year 1998, the prevalence of obesity was 49% for women and 30% for men aged 35-64 years old. [24] Since then, the prevalence of obesity has increased mainly among men. [25, 26] The increase in diabetes prevalence generated approximately 30 additional CHD deaths. Rising diabetes and obesity, especially among men, represents a public health priority . Effective evidence-based interventions exist and should be considered, notably junk-food taxes, labelling and reformulation issues, and advertising bans.[27, 28]

The recently developed Palestinian non-communicable diseases (NCDs) strategy adopted an integrated approach encompassing promotion, prevention and control programmes. Population based

multi-sectoral effective evidence-based interventions were clearly indicated to control diabetes and promote physical activity such as health promotion, fiscal measures , market control and community participation. Yet a clear vision and scope of implementation is still evolving.[29]

Modern medical treatments accounted for approximately 30% of the CHD mortality reduction. The scale of effect is similar to that reported in studies using the same methodology in Iceland, Sweden and Finland[9] but lower than the 45%-50% reported for North America,[30] and Europe.[8, 10] The biggest contributions came from aspirin and community-based medications for secondary prevention, chronic angina and heart failure. Treatment uptakes were generally mediocre and need to be improved. However, such treatments create challenges for health providers in terms of identifying patients, providing medications and ensuring their long-term compliance.

Data on both patient groups and treatment uptake levels was scarce. Such data was not available at the national or the hospital level. The required information was therefore collected directly from the hospital patients' records to be utilized in this study. Furthermore, the uptake levels were not consistent among different hospitals and sometimes between physicians. These two findings therefore highlight both a lack of standardised health care provision and important gaps in the NCD health information system.

Modelling strengths and limitations

The modelling approach used in the study was comprehensive, it synthesised all the key risk factors and treatment options to help quantify changes in CHD mortality. Additionally, the model used rigorous sensitivity analyses to systematically examine the potential influence of uncertainties in the data (quality and sources) and model assumptions, and hence quantify the potential maximum and minimum effects of these contributory factors

This modelling approach also has obvious limitations. Notably the extent and quantity of available data on CHD risk factor trends and treatment uptake. Furthermore, the model tended to overestimate the number of deaths averted in almost all age groups, especially among women. This may reflect less precision in female data. However, the data used in this model was generally of good quality. Mortality data were obtained from Ministry of Health death registry. Death registry data were evaluated in previous studies as medium quality based on the WHO criteria.[31] The demographic information was obtained from census data, and the risk factor trends were obtained from well designed epidemiological studies and national PCBS, MOH, and WHO surveys. Treatment uptake and patient groups data were obtained from an extensive hospital based survey conducted in 2009. Very scarce data available on treatment uptake was also obtained. However, researchers had to conduct additional surveys to get the timely, accurate data required by the model. Certain assumptions were needed to fill in the gaps for missing information. For instance, assumptions were made for the small group aged 65-74 years where risk factor information were not available. Assumption on treatment uptake at the starting point were also based on expert opinions working in the system for more than 10 years. Estimates of treatment uptake were collated from international and regional literature then validated with the expert opinions. The generalization of efficiency estimates from meta-analysis of controlled clinical trials to effectiveness in clinical practice in the West Bank setting were clearly optimistic, and may have resulted in an over-estimate of the true treatment benefits.

All these assumptions are transparent, being systematically detailed in the Technical Appendix, supported by local expert opinions and literature from the region and included in the sensitivity analyses. By good luck, the overall model fit approached 100%. However, it should be noted that fit within specific age groups was much less perfect.

Public health implications

CHD mortality fell by 20% between 1998 and 2009 in the West Bank, oPt. More than two-third of this fall was due to changes in major risk factors mainly total cholesterol, blood pressure and smoking.

Our results clearly indicate that risk factor improvements in the general population saved substantially more lives than specific treatments for individual patients. This emphasizes the importance of population-wide primary prevention strategies. Such strategies should also emphasize the risk factors which had a negative effect on the reduction of CHD in the model especially, diabetes, BMI and increased levels of physical inactivity. The Palestinian policy and strategic plan for NCD had focused on health diet and physical activity as its 2nd a 3rd policy objectives (MOH, 2010). [32]

Contributorship Statement

All authors have fulfilled the following contributions 1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content; and 3) final approval of the version to be published

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Conflict of interest

The authors declare that they have no conflict of interest

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FIGURE LEGENDS

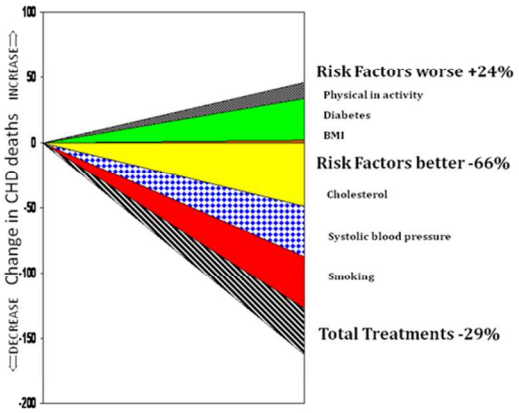
FIGURE 1: Coronary heart disease deaths prevented or postponed by treatment and risk factors changes in the West Bank population between 1998 and 2009.

Figure 2: CHD deaths prevented or postponed attributable to specific risk factor changes in Palestine 1998-2009: Sensitivity Analysis

(■ = Best estimate, bars indicate minimum & maximum estimates)

Figure 3: CHD deaths prevented or postponed attributable to specific treatments in Palestine 1998-2009: Sensitivity Analysis

(■ = Best estimate, bars indicate minimum & maximum estimates)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50
0
-50
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INCREASE
DECREASE
Change in CHD deaths
Risk Factors worse +24%
Physical in activity
Diabetes
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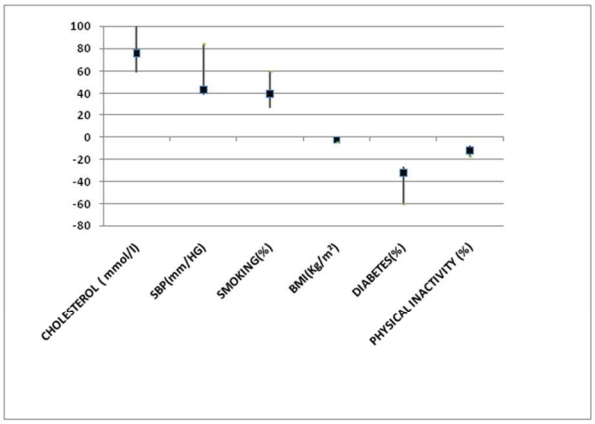
Risk Factors better -66%
Cholesterol
Systolic blood pressure
Smoking
Total Treatments -29%



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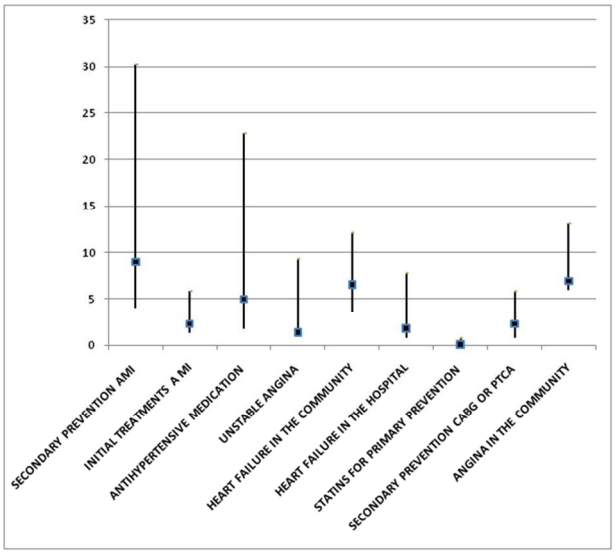

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MedCHAMPS Technical Appendix

Supplementary Online Content

eAppendix. The Palestine IMPACT Model

We evaluated the Palestine population aged from 25 to 75 years using an updated version of the IMPACT model. This is a cell-based model, constructed using Microsoft Excel, which integrates available country-specific epidemiological data to explain an observed decrease in CHD mortality. The tables included in this supplementary appendix document provide details about these methods. This model has been validated in Europe, New Zealand, China and the United States (1-6).

I. Population data

The population data was obtained from census 1997 and 2007 census projections. The two censuses were conducted by the Palestinian Central Bureau of Statistics (PCBS) following standardised methodology. A reliability analyses were conducted for the two census using 20% post census survey.

II. Changes in mortality rates from Coronary Heart Diseases (CHD) in Palestine from 1998 to 2009

The data sources used are shown in eTable 1. Mortality data was obtained from the ministry of health-health information centre for the years 1997 up to 2009. Mortality data for the year 1998 was not complete. The numbers used for the year 1998 were the average number for the previous (1997) and next (1999) years. Mortality rates from CHD were calculated using the underlying cause of death: International Classification of Diseases ICD-10 codes I20-I25, I50. As we were only interested in deaths from coronary artery disease we only included heart failure deaths with the code of I50. (See below and eTable 1 for details.)

a. Expected and observed number of deaths from CHD, then calculating the DPPs:

We first calculated the expected CHD number of deaths in 2009 had 1998 mortality rates remained constant from 1998 (the base year). This was calculated using indirect standardisation, by multiplying age and gender specific mortality rates in 1998 by the population size for each 10-year age-gender stratum in 2009.

The primary output of the IMPACT model is the number of **deaths prevented or postponed** (DPPs) in 2009 due to the reduction in CHD mortality rates since 1998. This was then calculated as the difference between the number of CHD deaths expected in 2009, and the number CHD deaths actually observed in 2009.

b. Estimating DPP attributable to evidence based treatments:

The number of DPPs attributable to treatments, information on the size of the clinically relevant patients groups, each intervention relative risk reduction reported in systematic reviews (SR) and meta-analysis (MA) and their uptakes and case fatality rates.

III. Patient Groups

The treatment arm of the Model includes the following groups:

- Hospitalized patients with an acute myocardial infarction (AMI) within the last year (2009)
- Hospitalized patients with Unstable Angina Pectoris (AP) within the last year (2009)
- Community-dwelling patients who have survived an AMI in the past 5 years (2005-2009)
- Community-dwelling patients with chronic Angina who have undergone revascularisation procedure (Coronary Artery Bypass Grafting (CABG), or a Percutaneous Coronary Intervention(PCI), within the last year for chronic Angina.
- Community-dwelling patients with chronic angina (no revascularisation and/or previous MI)
- Hospitalized patients with heart failure within the last year,
- Community-dwelling patients with heart failure,
- Hypertensive patients eligible for pharmacological therapy and have not suffered any of the above events.
- Hypercholesterolemic patients eligible for cholesterol lowering therapy (Statin) and have not suffered any of the above events.

a. Data Sources for Patients Groups

Hospital patient groups: were calculated based on the number obtained from three hospitals included in the Treatment Uptake Survey (TUS, Annex 1) separately for AMI, AP ~~and~~and congestive heart failure CHF. These hospitals are assumed to serve the population in the north, centre and south of the West Bank. The number obtained from each hospital was then extrapolated to the population in that region and then combined to represent the number from the whole West Bank. The numbers calculated were AMI=489, unstable angina=489, and heart failure=468.

Chronic angina: was calculated based on Palestinian Family Health Survey (PFHS) and TUS. The PFHS provides estimate of cardiac diseases in the community. Chronic angina was estimated based on cardiac diseases excluding all hospital CHD cases, CABG, MI survivals and community heart failure. The estimate was similar to estimates reported in neighbouring countries. The number included in the model was 23167.

Community heart failure: was calculated based on TUS and estimates from the literature. Two estimates were used one based the results of a study conducted in Kingdom of Saudi Arabia, and the second estimate was based on the assumption that CHF/Hospital HF equal 5X. Both gave similar estimates. The number used in the model was 2342 which was based on community-hospital ratio.

Statins for primary prevention: was calculated based on PFHS which provides estimates of hypercholesterolemia patients receiving medications. This estimate might be underestimated as this number refers only to diagnosed patients only. The underestimation arises first from the proportion of undiagnosed patients. Also because the question used was proxy-self reported.

Antihypertensive medication: was estimated base on two sources. First, Stepwise survey which provides estimates of hypertensive patients and receiving medication for it. The estimated number based on this method was 465639. Second, PFHS, which provides

estimates of hypertensive patients with receiving medication (self-reported). The estimated number was 81894. This number was used in the model although it might be under-estimated for the reasons mentioned above for hypertensive group. The numbers estimated based on the first method was used in the sensitivity analysis.

Secondary prevention post MI: was calculated based on the number of hospitalised AMI in 2009. We assumed 10% fewer in each preceding year and 10% case fatality rate every year. These assumptions were supported by local expert opinions. The estimated number was 2266.

Secondary prevention following CABG/PTCA: was calculated based on hospitalised AMI and CABG in 2009. We assumed 5% annual increase in CABG since 1998. This assumption was based on expert opinion. Half the estimated number was assumed as MI survivals and the final number included in the model was 208. Similar calculation was done for PTCA.

b. Potential overlaps between patient groups:

There are potential overlaps between patient groups (meaning that one person may belong to more than one patient group at the same time) . Hospital patient groups were selected based on one-year case fatality and overlapping between groups was avoided. Community patients groups were calculated based on the numbers of hospitalized patients groups with assumptions based on the literature.

IV. Treatments uptake

The data was obtained from Treatment Uptake Survey 2009. This survey included four hospital located in the north, centre and south of the West Bank. Three out of the four were governmental hospitals. The ministry of health services serve more than 75% of the population in the West Bank. Two were referral hospitals providing CABG and PTCA services.

Treatment uptake was collected from hospital records for the events of interest (MI, CHF, AP and survivals of CABG and PTCA) for most age groups. Few cases in younger age groups were not captured in this survey because of low Frequency of cardiac diseases in these age groups. Average treatment uptake was used for this age group.

Treatment uptake for patients groups in the community was collected from hospital records, specifically from the discharge sheet. More than 10 interviews were conducted with experts in this field and treatment uptake estimates calculated based on the data from the discharge sheet were modified based on expert opinion when needed. The numbers used in the model were the modified estimates with 50% reduction.

Calculating treatments DPPs

For each of the groups, we estimated the number of DPPs that were attributable to various treatments. All treatments of interest are listed in eTable 2.

The deaths prevented or postponed associated with a specific CHD treatment within a disease subgroup was estimated by taking the product of the number of people in the subgroup (eTable 1), the proportion of those patients who received a particular treatment (eTable 2), case fatality rates, DPPs for at least one year were considered in the calculation based on

survival benefit over a one year time interval (eTable 3), and the relative risk reduction attributed to that specific treatment based on the published literature (eTable 4). We assumed that compliance defined as the proportion of patients prescribed medications on therapeutic doses of medication, was 100% among hospital patients, 70% among symptomatic community patients and 50% in asymptomatic individuals taking statins or anti-hypertensives for primary prevention (7-10).
All these assumptions were tested in subsequent sensitivity analyses.

EXAMPLE 1: estimation of DPPs from a specific treatment
In Palestine in 2009, 112 men aged 55-64 were hospitalized with AMI. Utilization of aspirin was 49% (11). Efficacy of aspirin is 15% (12) 1-year case-fatality rate was 7.9%.13
The deaths prevented or postponed (DPPs) was calculated as:
Patient numbers x treatment uptake x relative mortality reduction x one-year case fatality **=** 112x 49% x 15% X 6.4% = 25deaths prevented or postponed.

V. Risk factors

The IMPACT model calculates the DPPs associated with changes in CHD risk factors, including smoking, total cholesterol, systolic blood pressure, body mass index, diabetes mellitus, and physical inactivity. Data sources are shown in eTable 1.The data obtained for the first point was two epidemiological studies conducted in rural and urban areas within Ramallah governorates the years 1996 and 1998. The data for the second point was obtained from the Stepwise survey 2009 which is a national survey. Smoking and physical inactivity were self reported in both data sources, blood pressure, total cholesterol, Weight and heights were measured by trained nurses in both surveys.

To assess the validity of these assumptions, we compared the reductions in systolic blood pressure and total cholesterol over the time horizon of the Palestine IMPACT model to those observed in previous IMPACT models. Further, trends and age gradients were compared with neighbouring countries.

Two approaches were used to calculate DPPs, the **regression approach** and the **population-attributable risk factor (PARF) approach;** The regression approach was used for continuous variables (systolic blood pressure, total cholesterol, and body mass index). The number of expected deaths from CHD occurring in 2005 (the end year) was multiplied by the absolute change in risk factor prevalence, and by a regression coefficient quantifying the change in CHD mortality that would result from the change in risk factor level. Natural logarithms were used, assuming a log-linear relationship between changes in risk factor levels and mortality.

EXAMPLE 2: estimation of DPPs from risk factor change using the regression method:
Mortality fall due to reduction in systolic blood pressure in women aged 55-64
In 2009, there were 20 CHD expected deaths (had 1998 mortality rates remained constant) among 43,693 women aged 55-64 years. Mean systolic blood pressure decreased by 3.4 mmHg (from 137.9 in 1998 to 134.5 mmHg in 2009). For every 20 mmHg reduction in systolic blood pressure, we estimated an age- and sex specific reduction in mortality of 50 percent. This generates a logarithmic coefficient of –0.035 (14).
The number of deaths prevented or postponed:

= (1-(EXP(coefficient*change))*expected deaths in 2009)
= (1-(EXP(-0.035*3.4))* 71)
= 8 DPPs

Data sources for the number of CHD deaths and risk factors are shown in eTable 1, and sources for the coefficients in eTable 5.

The PARF approach was used for categorical variables (smoking, diabetes, and physical inactivity). PARF was calculated as:
(P x (RR-1)) / (P x (RR-1)) +1
where P is the prevalence of the risk factor and RR is the relative risk for CHD mortality associated with that risk factor. DPPs were then estimated as the expected CHD deaths in 2009 multiplied by the difference in the PARF for 1998 and 2009.

EXAMPLE 3: estimation of DPPs from risk factor change using the PARF method
The prevalence of diabetes among men aged 65-74 years was 22% in 1999 and 28% in 2009. Assuming a Relative Risk of 1.93 (15), the PARF was 0.17 in 1998 and 0.21 in 2009. The number of deaths attributable to the increase in diabetes prevalence from 1998 to 2009 was therefore:
(144) * (0.21-0.17) = 6 DPPs
Data sources for the prevalence of risk factors and for the number of CHD deaths are shown in Table e1. The relative risks used in these PARF analyses were obtained from the INTERHEART study (15), which provides independent RR values, adjusted for other major risk factors.

VI. Other Methodological Considerations

a. Systolic BP and Hyperlipidemia

In order to separate the DPPs from pharmacological versus non-pharmacological primary prevention of hypertension and hyperlipidemia, we subtracted the age-gender specific DPP's calculated in the treatment section (i.e. for primary hyperlipidemia and hypertension patient groups), from the DPP's calculated in the risk factor section.

b. Polypharmacy Issues

There is a paucity of data on the efficacy of treatment combinations. Simply assuming that the efficacy of multiple treatments was additive would over-estimate the treatment effect; we therefore we used the Mant and Hicks method to estimate case-fatality reduction by polypharmacy for all treatments evaluated.16 This approach
was subsequently endorsed by Yusuf (17) and Law and Wald.(18) This approach estimates a cumulative relative benefit as follows:
Relative Benefit = 1 - ((1-relative reduction in case-fatality rate for treatment A) X (1-relative reduction in case-fatality rate for treatment B) X ...X (1- relative reduction in case-fatality rate for treatment N).

EXAMPLE 4: estimation of reduced benefit if patient taking multiple medications (Mant and Hicks approach)

For AMI survivors, applying relative risk reductions (RRR) for aspirin, beta-blockers ACE inhibitors statins and rehabilitation then gives:

Relative Benefit = 1 - [(1 –aspirin RRR) X (1 - beta-blockers RRR) X (1 - ACE inhibitors RRR) X (1- statins RRR) X (1- rehabilitation RRR)]
= 1 - [(1- 0.15) X (1-0.23) X (1-0.20) X (1- 0.22) X (1- 0.26)]
= 1 - [(0.85) X (0.77) X (0.80) X (0.78) X (0.74)]
= 0.70 i.e. a 70% lower case fatality

c. Sensitivity Analyses

Because of the uncertainty surrounding many of the values, multi-way sensitivity analyses were performed (19). For each model parameter, a maximum and minimum plausible value was assigned using the 95% confidence intervals from the source documentation; if this was unavailable, we defined these limits as 20% above and below the best estimate. The maximum and minimum plausible values were fed in to the model generating maximum and minimum estimates for deaths prevented or postponed.

eTable 1. Main Data Sources for Populating the Palestine IMPACT Model

Information	1998	2009	Comments
Population Statistics	Palestinian Central Bureau of Statistics	Palestinian Central Bureau of Statistics	Projections from 1997 census and 2007 census. Reliability analysis was conducted using 20% post census survey.
Deaths by Age and Sex Number	Health information centre- Ministry of Health	Health information centre- Ministry of Health	ICD 10 codes (I20-I22-I24-I50) Good quality data[1]
Number of patients admitted yearly			
AMI		Treatment uptake survey 2009	Survey conducted in four hospital in the West Bank. Data obtained from patients records. Over lapping was avoided by selecting the case base on the case fatality.
Acute Angina		Treatment uptake survey 2009	
Heart failure		Treatment uptake survey 2009	
Number of patients treated yearly with			
CABG		hospital records	Two main hospital provide CABG services. The number of patients treated in 2009 was obtained from Makassed and Ramallah hospitals
PCI		hospital records	One main hospital provide PCI services. The number of patients treated in 2009 was obtained from Makassed hospitals
Post-MI		Hospital records	
Community chronic angina		Hospital records and 2006 Family Health survey	Cardiac disease (self-reported) excluding hospital CHD cases and community heart failure
Community Heart Failure		Hospital records and (2001). "Prevalence	

[1] Abu-Rmeileh NME, Husseini A, Abu-Arqoub O, Hamad M, Giacaman R. Mortality patterns in the West Bank, Palestinian Territories, 1999- Prev Chronic Dis. 2008 Oct;5(4):A112. Epub 2008 Sep 15

		and aetiology of heart failure in an Arab population." Eur J Heart Fail 3(3): 301-5.	
Hypertension (primary prevention)		2006 Family Health Survey and 2010 Stepwise survey	FHS is a national survey conducted every 4 years using standardised methodology. Stepwise survey is a national health survey conducted using WHO standardised methodology
Hyperlipidemia (primary prevention)		2006 Family Health Survey	Same as above
Population Risk Factor Prevalence	**1998**	**2009**	**Comments**
Current cigarette smoking	HUSSEINI, A. (2002)[2] ABDUL-RAHIM, H. F. (2002)[3]	2010 Stepwise survey	The data for the year 1998 was based on two epidemiological studies conducted in urban and rural areas of Ramallah governorate.
Systolic Blood Pressure	HUSSEINI, A. (2002) ABDUL-RAHIM, H. F. (2002)	2010 Stepwise survey	Same as above
Total cholesterol	HUSSEINI, A. (2002) ABDUL-RAHIM, H. F. (2002)	2010 Stepwise survey	Same as above
Physical inactivity	HUSSEINI, A. (2002) ABDUL-RAHIM, H. F. (2002)	2010 Stepwise survey	Same as above
BMI	HUSSEINI, A. (2002) ABDUL-RAHIM, H. F. (2002)	2010 Stepwise survey	Same as above
Diabetes	HUSSEINI, A. (2002) ABDUL-RAHIM, H. F. (2002)	2010 Stepwise survey	Same as above

[2] HUSSEINI, A. (2002) Type 2 Diabetes Mellitus and selected associated factors in an adult Palestinian population: an epidemiologic study of type 2 Diabetes Mellitus and impaired glucose tolerance (IGT) in Kobar and Ramallah, Palestine. Faculty of Medicine. Oslo, University of Oslo.

[3] The metabolic syndrome in a rural and an urban Palestinian population: an epidemiological study of selected components of the metabolic syndrome, including diabetes, hypertension, dyslipidemia, and obesity in the adult population of a rural and an urban Palestinian community. Faculty of Medicine. Oslo, University of Oslo.

eTable 2. Treatment Utilization Data Sources

	1998	Source	2009	Source
MI (DG:1)				
Thrombolysis	46.5%	Assumption: 50% of final year (2009)	92.5%	TUS
Primary PCI	0%	Assumption: 100% of final year (2009)	0%	TUS
Aspirin	92.5%	Assumption: 100% of final year (2009)	92.5%	TUS
Beta Blockers	29.7%	Assumption: 50% of final year (2009)	59.40%	TUS
ACE Inhibitor	22.7%	Assumption: 50% of final year (2009)	45.3%	TUS
Primary CABG	0%	Assumption: 100% of final year (2009)	0%	TUS
Community CPR	0.5%	Assumption: 50% of final year (2009)	1%	????
Hospital CPR	2.9%	Assumption: 50% of final year (2009)	5.70%	TUS
Rehabilitation	28.5%	Assumption: 100% of final year (2009)	28.5%	
Unstable Angina (DG2)				
Aspirin alone	5.6%	Assumption: 50% of final year (2009)	11.1%	TUS
Aspirin and heparin	41.5%	Assumption: 50% of final year (2009)	83.0%	TUS
Platelet glycoprotein IIB/IIIA inhibitors	0%	Expert opinion	0%	TUS
PCI	0%	Expert opinion	0%	TUS
CABG surgery	0%	Expert opinion	0%	TUS
2nd Prevention post AMI (DG3a)				
Aspirin	24.6%	Assumption: 50% of final year (2009)	**49.2%**	50% reduction of treatment uptake upon discharge obtained as expert opinion.
Beta Blockers	19.8%	Assumption: 50% of final year (2009)	**39.5%**	50% reduction of treatment uptake upon discharge obtained as expert opinion.
ACE inhibitors	21.1%	Assumption: 50% of final year (2009)	**42.2%**	50% reduction of treatment uptake upon discharge obtained as expert opinion.
Statins	24.1%	Assumption: 50% of final year (2009)	48.1%	50% reduction of treatment uptake upon discharge obtained as expert opinion.
Warfarin	2.4%	Assumption: 50% of final year (2009)	4.7%	50% reduction of treatment uptake upon discharge obtained as expert opinion.
Rehabilitation	0%	Expert opinion	0%	Expert opinion
2'prevention				

following CABG/PTCA (DG4)				
Statins	23.6%	Assumption: 50% of final year (2009)	47.2%	50% reduction of treatment uptake upon discharge obtained as expert opinion.
Aspirin	24.9%	Assumption: 50% of final year (2009)	49.8%	50% reduction of treatment uptake upon discharge obtained as expert opinion.
ACE inhibitors	18.0%	Assumption: 50% of final year (2009)	36.0%	50% reduction of treatment uptake upon discharge obtained as expert opinion.
Beta-blockers	21.3%	Assumption: 50% of final year (2009)	42.5%	50% reduction of treatment uptake upon discharge obtained as expert opinion.
Warfarin	0.5%	Assumption: 50% of final year (2009)	0.9%	50% reduction of treatment uptake upon discharge obtained as expert opinion.
Rehabilitation	0%	Expert opinion	0%	Expert opinion
Chronic angina (DG5)				
CABG surgery	100%		100%	
Angioplasty	100%		100%	
Aspirin	24.3%	Assumption: 50% of final year (2009)	48.6%	50% reduction of treatment uptake upon discharge obtained as expert opinion.
Statins	23.6%	Assumption: 50% of final year (2009)	47.2%	50% reduction of treatment uptake upon discharge obtained as expert opinion.
Hospital heart failure (DG6)				
ACE inhibitors	44.0%	Assumption: 66% of final year (2009)	66.7%	TUS
Beta blockers	22.0%	Assumption: 66% of final year (2009)	33.3%	TUS
Spiroolactone	44.0%	Assumption: 50% of final year (2009)	66.7%	TUS
Aspirin	69.2%	Assumption: Same as the final year (2009)	69.2%	TUS
Statins	45.5%	Assumption: 50% of final year (2009)	45.5%	TUS
Heart failure in the community (DG7)				
Statins	17.5%	Assumption: 50% of final year (2009)	35.0%	50% reduction of treatment uptake upon discharge obtained as expert opinion.
Aspirin	19.5%	Assumption: 50% of final year (2009)	39.1%	50% reduction of treatment uptake upon discharge

				obtained as expert opinion.
ACE inhibitors	20.6%	Assumption: 50% of final year (2009)	41.3%	50% reduction of treatment uptake upon discharge obtained as expert opinion.
Beta-blockers	17.2%	Assumption: 50% of final year (2009)	34.4%	50% reduction of treatment uptake upon discharge obtained as expert opinion.
Spironolactone	10.6%	Assumption: 50% of final year (2009)	21.3%	50% reduction of treatment uptake upon discharge obtained as expert opinion.
Primary prevention hypertension (DG8)	**1998**	**Source**	**2009**	
Treated % of total population	0%	Assumption: Treatment was not available	1%	PFHS
Primary prevention hyperlipidemia (DG9)				
Treated %				
Statins	0%	Assumption: Treatment was not available	40%	???

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eTable 3. Age-Specific Case Fatality Rates for Each Patient Group

	AMI	POST AMI	Unstable angina	CABG	Angioplasty	HF in hospital	HF in community	Hypertension	Statins for primary prevention
M 25-34	0.0110	0.0080	0.0160	0.0030	0.0030	0.0340	0.0110	0.0000	0.0000
M 35-44	0.0120	0.0090	0.0240	0.0050	0.0050	0.0680	0.0220	0.0010	0.0010
M 45-54	0.0230	0.0170	0.0340	0.0070	0.0070	0.0960	0.0320	0.0020	0.0020
M 55-64	0.0540	0.0340	0.0560	0.0120	0.0120	0.1400	0.0450	0.0060	0.0060
M 65-74	0.1010	0.0730	0.0700	0.0230	0.0250	0.2830	0.0930	0.0140	0.0140
M 75+	0.1640	0.1220	0.0910	0.0420	0.0420	0.3370	0.1110	0.0350	0.0350
F 25-34	0.0110	0.0040	0.0160	0.0030	0.0030	0.0340	0.0110	0.0000	0.0000
F 35-44	0.0130	0.0060	0.0240	0.0050	0.0050	0.0680	0.0220	0.0010	0.0010
F 45-54	0.0260	0.0100	0.0340	0.0070	0.0070	0.0960	0.0320	0.0010	0.0010
F 55-64	0.0610	0.0190	0.0560	0.0120	0.0120	0.1400	0.0450	0.0020	0.0020
F 65-74	0.1140	0.0840	0.0700	0.0230	0.0270	0.2220	0.0810	0.0070	0.0070
F 75+	0.1670	0.1160	0.0910	0.0420	0.0390	0.2890	0.0940	0.0210	0.0210

Table 4: Clinical Efficacy of Interventions: Relative Risk Reductions Obtained From Meta-Analyses, and Randomized Controlled Trials

TREATMENTS	Current Relative Risk Reduction	Source paper: First author (year)	IN USE CURRENT MODELS	Previous Value	Notes
Acute myocardial infarction					
Thrombolysis	31% (95% CI: 14, 45)	Estess(2002)(1), FTT, Collins(1996)(2)			<55 yrs: OR=0.692; RRR=30.8 (95% CI: 14-45) 55-64 yrs: OR=0.736; RRR=26.4 (95% CI: 17-40) 65-74 yrs: OR=0.752; RRR=24.8 (95% CI: 15-37) >75 yrs: OR=0.844; RRR=15.6 (95% CI: 4-30)
Aspirin	15% (95% CI: 11, 19)	Antithrombotic Trialists' Collaboration (2002)(3)			OR=0.85 (95% CI: 0.81, 0.89). RRR 15% (95% CI: 11,19) page 75:outcome is vascular and nonvascular deaths
Primary angioplasty STEMI	41% (95% CI: 5, 50)	Cucherat (2000) (4)			OR 0.68 (95% CI: 0.50, 0.95). RRR 32% (95% CI: 5,50) outcome compares primary angioplasty to thrombolytics, not specific to STEMI, in results on page 3.
Primary PTCA Non-STEMI	25% (95% CI: 5, 51)	RITA 3 (Fox 2005)(5)			OR 0.65 (95% CI: 0.49, 0.95). RRR 32% (95% CI: 5,51) for cardiovascular death on page 917. [RRR for cardiovascular death or MI was 26 (95% CI: 3,44) and was 24 (95% CI: 0,42) for any death] A recent SR suggest benefit only in a composite outcome including death and MI, but with wide CI (6) Mehta showed that an early invasive strategy for NSTEMI ACS is

					not better than a delayed one(7) However, there is a mortality benefit for doing this sometime after the ACS.
Primary CABG surgery	39% (95%CI: 23, 52)	Yusuf (1994)(8)			OR 0.61 (95% CI: 0.48, 0.77). RRR 39% (95% CI: 23,52) on page 565, 0-5 yr mortality
Beta blockers	4% (95% CI: -8, 15)	Freemantle (1999)(9)			OR 0.96 (95% CI: 0.85, 1.08), RR 4% (95% CI: -8,15) on page 1732.
ACE inhibitors	7% (95% CI: 2, 11)	Latini (1995) (10)		OR 0.93, (0.89, 0.98), RR 7% (2,11) for 30 day mortality in MI.	
Cardio-pulmonary resuscitation (CPR)					
Community CPR USA	5%-15%** (95%CI:4, 15.3)	Rea (2001)(11) Nichol (1999)(12)		Nichol study reports overall median survival to discharge at 7.4% in this multi-country/site review, page 520 The Model focuses on 30/7 survival. Discharge survival will therefore provide an over-estimate, which we have explicitly addressed by assuming 5% at 30/7. Rea looks at odds of bystander dispatcher assisted CPR and bystander CPR without dispatch assistance and compares to No bystander CPR. 7265 out-of-hospital arrests attended. OR 0.59 - 0.69 for these two groups which would give RRRs of 41% and 31%. [Consider as crude equivalent of CPR to no CPR comparison]. 15.3% survival to discharge in Kingcounty, WA; consider as maximum value. Use Nichol (1999)28	

				5% as USA average. Graham et al 1999 meta anlysis of papers 1973 - 1996 report 6.4% at discharge. Assume better in 2000, thus 6.4% at 30/7 OPALS RCT reports only 5.2%. Bottiger: 15% maximum uptake for CPR. NEJM 2008 359:2651-2662	
Hospital CPR USA	33% *** (95%CI: 10, 36)	NHDS discharge codes (2000) Tunstall-Pedoe(1992)(13)		AMI accounted for 35% of adult total cases. Adult survival to discharge 36% post VF or VT (majority of post AMI cases, only 10.6% post Asystole, Adult survival to discharge 18% overall, but this reflected ALL Medical arrests in hospital. (varied from 10-36%) depending on type of initial rhythm) (tables 4 &5 page 55) Review of 36,000 adults with cardiac arrests in the 253 US/Canadian Hospitals National Registry of CPR. Nadkarni, JAMA, 2006:295 (1) 50-57) Older article from Tunstall-Pedoe on page 1350 shows survival at 24 hrs to be 32%, discharge to home at 21%, and 1 year survival to be 15% overall. (16% and 8% in general wards, 31% and 16% in coronary care unit (page 1349), etc. Assume in USA 2000 is better. Corroboration: Model assumes that approximately 2% AMI admissions have primary VF	

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				(Olmsted County study). This is consistent with NHDS discharge code of CPR in 0.74% (2000), suggesting approximately 1/3 survive.	
Secondary Prevention in CHD Patients					
Aspirin	15% (95%CI: 11, 19)	Antithrombotic Trialists' Collaboration (2002)(3)		OR 0.85 (95% CI: 0.49, 0.95), RR 15% (95% CI: 11, 19) outcome is vascular and nonvascular deaths on page 75. This data seems to be appropriate to this outcome in CHD patients	
Beta blockers	23% (95%CI: 15, 31)	Freemantle (1999)(9)		OR 0.77 (95% CI: 0.85, 0.69), 23% (95% CI: 15,31) on page 1734. Odds of death in long term trials.	
ACE inhibitors	23% (95%CI: 13, 26)	Flather (2000)(14)		OR 0.80 (95% CI: 0.74, 0.87), 20% (95% CI: 13,26) on page 1577, death up to 4 years [endpoint of study looking at those with heart failure or LV dysfunction.]	
Statins	22% (95%CI: 10, 26)	Baigent (2005)(15), Wilt (2004) (16)	29%, Pignone (2000)(17)	OR=0.78 (95% CI: 0.74—0.84). RRR=22% (95% CI: 10, 26) RR=0.77 (95% CI: 0.68—0.87). RRR=23% (95% CI: 13,30) in those with other CHD OR=0.77 (95% CI: 0.71-0.83). RRR=23% (95% CI: 17, 29) Wilt (2004) Section CHD mortality, page 1430.	
Warfarin	22% (95%CI: 13, 31)	Lau (1992)(18) ,Anand (1999) (19)		OR=0.78 (95% CI: 0.67-0.90), RRR=22% (95% CI: 10, 33) Meta-analysis looking at oral	

				anticoagulant therapy in coronary artery disease (31 trials about 18,000 patients) by intensity of INR control: High intensity (INR>2.8) warfarin vs. control for outcome of death had OR of 0.78(95% CI: 0.69-0.87) corresponding to a RRR of 22% (95% CI: 13, 31); Moderate intensity warfarin (INR 2-3.0) vs. control had OR of 0.82 (95% CI: 0.23-2.33) not significant but corresponding RRR of 18% (95% CI: -133, 77)	
Rehabilitation	27% (95%CI: 10, 39)	Brown (2003)(20)		OR= 0.74 (95% CI: 0.61-0.90), RRR = 26% (95% CI: 10, 39) in Fig 1, page 685 Taylor reference.	
Chronic Angina					
CABG surgery years 0-5	39% (95% CI: 23,52)	Yusuf (1994)(8)		OR= 0.61 (95% CI: 0.48-0.77), RR 39% (95% CI: 23,52) on page 565, 5 yr mortality	
CABG surgery years 6-10	17% (95% CI: 2, 30)	Yusuf (1994)(8)		OR= 0.83 (95% CI: 0.70-0.98), RR 17 (95% CI: 2,30) on page 565, 10 yr mortality OR= 0.68 (95% CI: 0.56-0.83), RR 32 (95% CI: 17,44) on page 565, 7 yr mortality CABG compared to medical treatment	
CABG vs PCI, severe CHD (three vessels, main left)	Combined endpoint:Death or myocardial Infarction	Serruys(2009)(21)	NO	Rates of major adverse cardiac or cerebrovascular events at 12 months were significantly higher in the PCI group (17.8%, vs. 12.4% for CABG; P=0.002), in large part because of an increased rate of repeat revascularization (13.5% vs.	

				5.9%, P<0.001); as a result, the criterion for noninferiority was not met. At 12 months, the rates of death and myocardial infarction were similar between the two groups; stroke was significantly more likely to occur with CABG (2.2%, vs. 0.6% with PCI; P=0.003). These results support the assumption that CABG is superior to PCI for revascularization in angina high risk patients. Limitations: Short followup (1 yr), few women, not optimal medical therapy in CABG patients (which might decrease effectiveness and explain higher rates of stroke.	
Angioplasty in Chronic angina, with stents	NO EFFECT ON CHD mortality. (compared to medical therapy)	Schomig 2008 (22) However this metanalysis provide a significant effect for all cause mortality (OR 0.8, 0.64-0.69)	Previous value: 13% (95% CI: 0, 16) RRR from: BASKET (23) Yusuf (1994)(8); Pocock (1995)(24), Folland (1997)(25). Maximum benefit, assume equivalent to CABG surgery for two vessel disease CABG, OR 0.84, (RR 16% 2, 30) 5 year survival 88% in controls. Minimum	No difference with CABG in a metaanalysis comparing PCI vs CABG(26)	

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			assumption: NIL benefit.		
Aspirin	15% (95% CI: 11, 19)	Antithrombotic Trialists' Collaboration (2002)(3)		OR= 0.85 (95% CI: 0.81-0.89), RR 15% (95% CI: 11,19) outcome is vascular and nonvascular deaths on page 75.	
Statins	**22%** (95% CI: 10-26)	Baigent (2005) (15)	29% Pignone (2000)(17)	RR=0.78 (95% CI: 0.74—0.84). RRR=22% (95% CI: 10, 26) RR=0.77 (95% CI: 0.68—0.87). RRR=23% (95% CI: 13,30) in those with other CHD	
ACEI	**17% (6%-28%)**	Al Mallah (2006)(27)		ACEI in CAD without abnormal LVF	
Unstable Angina					
Aspirin alone	15% (95%CI: 11, 19)	Antithrombotic Trialists' Collaboration (2002)(3)		OR= 0.85 (95% CI: 0.81-0.89), RR 15% (95% CI: 11,19) outcome is vascular and nonvascular deaths on page 75. Assume appropriate for unstable angina patients	
Aspirin & Heparin	33% (95% CI: -2,56)	Oler (1996)(28)		OR 0.67 (95% CI: 0.48,1.02) RR 33% (95% CI: -2, 56) in table 2. The study outcome is composite MI death and non fatal MI, compares those on ASA+Hep to ASA only	
Platelet glycoprotein IIB/IIIA inhibitors	9% (95% CI: 2,16)	Boersma(2002)(29)		RR 0.91 (95% CI: 0.84, 0.98) RR 9% (95% CI: 2,16) study looked at acute coronary syndrome without persistent ST elevation	
Primary PTCA Non-STEMI	32% (95% CI: 5-51)	RITA 3 (Fox 2005)(5)		OR 0.68 (95% CI: 0.49, 0.95). RRR 32% (95% CI: 5, 51) for Cardiovascular deaths, table 3. A recent SR suggest benefit only in	

				a composite outcome including death and MI, but with wide CI (6) Mehta showed that an early invasive strategy for NSTEMI ACS is not better than a delayed one(7) However, there is a mortality benefit for doing this sometime after the ACS.	
Primary CABG surgery	**43%** (95% CI: 19,60)	Yusuf (1994)(8)		OR 0.57 (95% CI: 0.40, 0.81). RR 43% (95% CI: 19,60) reduction in mortality at 5 years in those with class III/IV angina, table 4, page 566.	
Heart failure in patients requiring hospitalisation					
ACE inhibitors	20% (95% CI:13,26)	Flather (2000)(14)		OR 0.80 (95% CI: 0.74, 0.87). RR 20% (95% CI: 13,26) on page 1577, [death up to 4 years was study endpoint for those with heart failure or LV dysfunction].	
Beta blockers	35% (95% CI:26,43)	Shibata (2001)(30)		OR 0.65 (95% CI: 0.57, 0.74). RR 35% (95% CI: 26,43) : all cause mortality	
Spironolactone	30% (95%CI: 18, 41)	Pitt (1999)(31)		OR 0.70 (95% CI: 0.59, 0.82). RR 30% (95% CI: 18,41) in those that had at least one cardiac related hospitalization. [31% (95% CI: 18-42) in entire study population of those with CHF, page 711]	
Aspirin	15% (95% CI: 11,19)	Antithrombotic Trialists' Collaboration (2002)(3)		OR= 0.85 (95% CI: 0.81, 0.89), RR 15% (95% CI: 11,19) outcome is vascular and nonvascular deaths on page 75.. A recent review from the ESC says that there is no evidence of benefit	

				of aspirin in heart failure patients. See Dickenstein 2008 (32)	
Statins	NO EFFECT	GISSI HF 2008 (33), Kjekshus 2008 (CORONA)(34).	29%, Pignone (2000)(17) 22%, Baigent (2005) (15) : OR=0.78 (95% CI: 0.74, 0.84). RRR=22% (95% CI: 10-26),post AMI OR=0.77 (95% CI: 0.68, 0.87). RRR=23% (95% CI: 13,30) inthose with other CHD	Two recent negative trials suggest that there may be no benefit. Trials with selected population, no subgroup analysis for CHD etiology. See GISSI HF 2008 (33), Kjekshus 2008 (CORONA)(34). The current assumption is that statins have the same effect as in secondary prevention in CHD patients. This is still recommended (class B) in the most recent European guideline on the management of heart failure. See Dickenstein 2008 (32)	
Heart failure in the community					
ACE inhibitors	20% (95%CI: 13,26)	Flather (2000)(14)		OR 0.80 (95% CI: 0.74, 0.87). RR 20% (95% CI: 13,26) on page 1577, death up to 4 years [in those with heart failure or LV dysfunction].	
Beta blockers	35% (95% CI:26,43)	Shibata (2001)(30)		OR 0.65 (95% CI: 0.57, 0.74). RR 35 (95% CI: 26,43). Section 3.3 page 353	
Spironolactone	31% (95%CI: 18, 42)	Pitt (1999)(31)		OR 0.69 (95% CI: 0.58, 0.82). RR 31% (95% CI: 18-42) in entire study population consisting of those with CHF, page 711 [30 (95% CI: 18, 41) in those with a cardiac related hospitalization].	
Aspirin	15% (95%CI: 11, 19)	Antithrombotic Trialists' Collaboratio		OR= 0.85 (0.81, 0.89), RR 15% (11,19) outcome is vascular and	

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		n (2002)(3)		nonvascular deaths on page 75. Assume appropriate for patients with CHF due to CHD. A recent review from the ESC says that there is no evidence of benefit of aspirin in heart failure patients. See Dickenstein 2008(32)	
Statins	NO EFFECT	GISSI HF 2008 (33), Kjekshus 2008 (CORONA)(34).	29%, Pignone (2000)(17) 22%, Baigent (2005) (15) : OR=0.78 (95% CI: 0.74, 0.84). RRR=22% (95% CI: 10-26), post AMI OR=0.77 (95% CI: 0.68, 0.87). RRR=23% (95% CI: 13,30) in those with other CHD	Two recent negative trials suggest that there may be no benefit. Trials with selected population, no subgroup analysis for CHD etiology. See GISSI HF 2008 (33), Kjekshus 2008 (CORONA)(34). The current assumption is that statins have the same effect as in secondary prevention in CHD patients. This is still recommended (class B) in the most recent European guideline on the management of heart failure. See Dickenstein 2008(32)	
Hypertension treatment					
	13% (95% CI: 6,19)	Law (2003),(35)	11%, Collins (1990)(36)	OR 0.87 (95% CI: 0.81, 0.94). RRR 13% (95% CI: 6, 19) in those with high blood pressure without disease at entry. [RRR 29% (95% CI: 17, 37) those with average blood pressure and CHD, treated with ACEI]	
Therapies for primary prevention of raised cholesterol					
Statins	29%	Pignone (2000)(17)		OR 0.65 (95% CI: 0.48, 0.89).	

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				35% (95% CI: 11,52) for CHD mortality (only trials using statins), figure 3 on page 4	
Gemfibrozil	7% (95% CI: -8, 19)	Studer (2005)(37)	Used only in the US Model	OR 0.93 (95% CI: 0.81, 1.08); RRR 7% (95% CI: -8, 19)	
Niacin	5% (95% CI: -10, 18)	Studer (2005)(37)		OR 0.95 (95% CI: 0.82, 1.10); RRR 5% (95% CI: -10, 0.18)	
Aspirin in primary prevention					
Aspirin, primary prevention	NO EFFECT	ATC (2009)(38)		NO effect on vascular mortality in primary prevention.	

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