Int J Public Health
DOI 10.1007/s00038-012-0423-4

ORIGINAL ARTICLE

Mediterranean studies of cardiovascular disease and hyperglycemia: analytical modeling of population socio-economic transitions (MedCHAMPS)—rationale and methods

Wasim Maziak · Julia Critchley · Shahaduz Zaman · Nigel Unwin · Simon Capewell · Kathleen Bennett · Belgin Unal · Abdullatif Husseini · Habiba Ben Romdhane · Peter Phillimore

Received: 15 December 2011 / Revised: 9 October 2012 / Accepted: 10 October 2012

Abstract
Objectives In response to the escalating epidemic of cardiovascular disease (CVD) in the Mediterranean Region (MR), an international collaboration aiming at understanding the burden of CVD and evaluating cost-effective strategies to combat it was recently established. This paper describes the rationale and methods of the project MedCHAMPS to disseminate this successful experience.
Methods The framework of MedCHAMPS is exceptional in combining multiple disciplines (e.g. epidemiology, anthropology, economics), countries [Turkey, Syria, occupied Palestinian territory (oPt), Tunisia, UK, Ireland], research methods (situational and policy analysis, quantitative and qualitative studies, statistical modeling), and involving local stakeholders at all levels to assess trends of CVD/diabetes in the society and attributes of the local health care systems to provide optimal policy recommendations to reduce the burden of CVD/diabetes.
Results and conclusions MedCHAMPS provides policy makers in the MR and beyond needed guidance about the burden of CVD, and best cost-effective ways to combat it. Our approach of building developed–developing countries collaboration also provides a roadmap for other researchers seeking to build research base into CVD epidemiology and prevention in developing countries.

Keywords Cardiovascular disease · Diabetes · Mediterranean Region · Trends · Population · Policies · Interventions

Introduction

Non-communicable diseases (NCDs—particularly cardiovascular diseases (CVD), and type 2 diabetes) are increasing

For the MedCHAMPS collaboration.

W. Maziak
Syrian Center for Tobacco Studies, Aleppo, Syria

W. Maziak (✉)
Department of Epidemiology, Robert Stempel College of Public Health and Social Work, Florida International University, 11200 SW 8th St. AHC-II 590, Miami, FL 33199, USA
e-mail: wmaziak@fiu.edu

J. Critchley
St George's University of London, London, UK

J. Critchley · S. Zaman · P. Phillimore
Institute of Health and Society, Newcastle University, Newcastle Upon Tyne, UK

N. Unwin
Faculty of Medical Sciences, University of the West Indies, Cave Hill Campus, Barbados, West Indies

S. Capewell
University of Liverpool, Liverpool, UK

K. Bennett
Trinity College Dublin, Dublin, Ireland

B. Unal
Dokuz Eylul University, Izmir, Turkey

A. Husseini
Birzeit University, Birzeit, Occupied Palestinian Territory

H. B. Romdhane
Faculté de Médecine de Tunis, Tunis, Tunisia

Published online: 31 October 2012

dramatically in the developing world. The rise of lifestyle-related chronic disease in developing countries is the result of a complex constellation of social, economic, and behavioral factors driven by globalization, urbanization, and aging of populations (Beaglehole and Yach 2003; Yach et al. 2005). For example, the rise in lifestyles characterized by imbalance between nutrition and physical activity and excessive use of tobacco products is casting a heavy toll on the current and future burden of CVD, and type 2 diabetes in these settings (Beaglehole and Yach 2003; Yach et al. 2005). Currently, CVD is the leading cause of morbidity and mortality worldwide accounting for about 30 % of global deaths, with about 80 % of the CVD burden occurring in developing countries (Rodgers and Vaughan 2002). On the other hand, more than one billion adults worldwide are either overweight or obese (World Health Organization 2011b), and 346 million are affected by diabetes (mostly type 2), over two-thirds of whom live in developing countries (World Health Organization 2011a). With future forecasts predicting increasing trends and earlier onset of these diseases (Ezzati et al. 2005; Nugent 2008), the burden of CVD/diabetes will likely wreak havoc on the prospects for economic development in developing countries, as well as on the livelihood of families and communities.

Most premature CVD and diabetes are avoidable by adopting healthier diets, active lifestyles, and stopping smoking, but intervening at these easy to identify targets has proven to be challenging even in the best equipped health systems. Moreover, knowledge of the most effective interventions to reduce CVD and diabetes comes mainly from industrialized countries, and cannot be applied uncritically in very different socio-cultural settings (Ebrahim and Smith 2001). Furthermore, health systems and services in most developing countries, envisioned to tackle acute infectious diseases, are often not ideally organized to promote effective care and prevention for chronic diseases, and the non-governmental health sector usually focuses on clinical care rather than health care or prevention (Maziak 2009).

The Mediterranean Region (MR) region has been recognized as a hot-spot for CVD and type 2 diabetes, where projections of the burden of these diseases exceed those of other regions, yet local data to inform health policy and intervention are still inadequate (Alwan 1993; Maziak 2006; Murray and Lopez 1996; World health Organization 1999). Six out of the world's top ten countries with the highest prevalence of diabetes are in this region (International Diabetes Federation 2011). The incidence of CVD and diabetes is generally showing an increasing trend in the MR; about 47 % of the region's current burden of disease is considered to be due to NCDs, and the Global Burden of Disease project has estimated that this will rise to about 60 % by the year 2020 (Murray and Lopez 1997).

Deaths from CVD in the MR, moreover, appear to be occurring much earlier than in developed countries and to affect men disproportionately, further compromising the economic livelihood of families and communities in these societies (Maziak et al. 2007; Yusuf et al. 2001). For example in Syria, about half of CVD mortality is occurring before the age of 65 years compared to one-fifth only occurring before the age of 70 years for developed countries (Maziak et al. 2007; Reddy 2002).

Addressing CVD and diabetes in the MR requires intensive work on their proximal individual risk factors (e.g. hypertension, obesity, smoking), as well as wider environmental and societal factors (e.g. policy, culture) (Rose 1985). Therefore, local data about the status of CVD/diabetes in the society and attributes of the local health care systems including planners, providers and customers are needed to guide interventions and policy options. Such local information can be integrated within cutting edge modeling techniques to provide optimal policy recommendations to reduce the burden of CVD/diabetes in MR countries. One of the more extensively studied and refined models is the IMPACT model developed by collaborators on this project (Capewell and colleagues originally in the UK, with validation studies conducted in a variety of populations) (Capewell et al. 2000; Critchley et al. 2004; Ford et al. 2007; Laatikainen et al. 2005; Unal, Critchley and Capewell 2004). Project MedCHAMPS (Mediterranean Studies of Cardiovascular disease and Hyperglycemia: Analytical Modeling of Population Socio-economic transitions) funded by the EU-FP7 involves an international collaboration of institutions in six countries (UK, Ireland, Turkey, Syria, oPt, and Tunisia) to come up with effective policy recommendations, both within and outside the health sector to reduce the burden of CVD and diabetes in each partner MR country.

The importance of MedCHAMPS stems from (1) the need to develop successful models of international collaboration to address the acute health needs of communities in developing countries, (2) the adoption of an iterative participatory approach toward understanding of local health scene in the target MR countries, (3) the coupling of this participatory approach with cutting-edge modeling techniques to evaluate policy options and their feasibility, and (4) the expected relevance of lessons emerging from this project to other countries in the MR, and to developed–developing countries collaborations to reduce the burden of CVD/diabetes worldwide. This paper describes the rationale and methods of MedCHAMPS to inform other potential collaborations to reduce CVD/diabetes morbidity and mortality in developing countries. The framework is exceptional in attempting to pull together scientists and data from multiple disciplines and fields of study (e.g. epidemiology, anthropology, economics) to understand the burden of CVD in partner countries in the MR, as well as recommend best effective and cost-effective policy options to reduce CVD morbidity and mortality in the MR (Fig. 1).

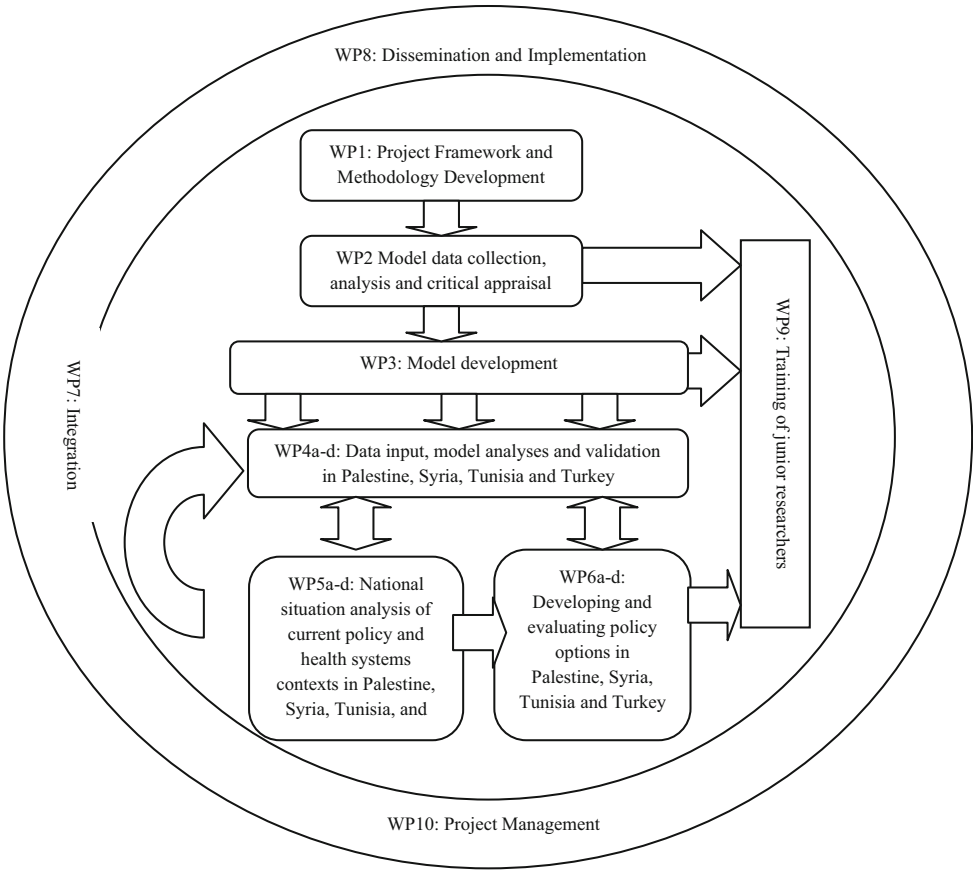

Fig. 1 Schematic depiction of MedCHAMPS project activities (2009–2012; Palestine, Syria, Tunisia and Turkey) and their relationship divided into 10 work packages (WP)

Objectives

Specifically, MedCHAMPS aims at:

1. Identifying data sources and future data requirements in partner MR countries.
2. Developing a CVD/diabetes model for use within the project countries to explain trends and predict likely future impact of disease.
3. Defining the national policy context and characterizing the health systems in partner countries in the MR.
4. Developing and evaluating policy options for partner countries in the MR and supporting their implementation.
5. Disseminating the knowledge obtained in this project to support the design and implementation of sustainable CVD/diabetes prevention and intervention policies in partner as well as other countries in the MR.

Methods

Objective 1: identifying data sources and future data requirements in partner MR countries

The first stage of the project involved obtaining and evaluating existing data sources relevant to CVD and diabetes epidemiology in each of the four partner countries. A data platform was developed to standardize the data requirements across the project. The data platform included the definitions or cutoff points of all the patient groups, risk factors and treatment uptake data. The tool was first developed iteratively by exchanging e-mails then shared with the partners for their comments and discussed with the researchers in a training workshop. Using a pre-designed data collection platform helped to clarify what kind of data was needed to populate the IMPACT Models, and how this data could be found in each study country.

A team of researchers in each country explored a variety of nationally and locally available data sources including census data, mortality data, household surveys, prescribing data and hospital admissions data to identify and collate existing available information on CVD/diabetes morbidity and mortality, major risk factors for CVD/diabetes, and on population and demographic profiles.

A second step was to critically appraise the quality of available data, comparing these with standard international guidelines (such as WHO STEPwise surveillance guide, WHO Health Metrics Network) and making recommendations regarding future collection of data, based on current availability, and level of economic development. Summaries of the data availability and quality within each country were prepared by the MedCHAMPS researchers for each

country (detailed tables are available from the authors upon request).

Objective 2: developing a CVD/diabetes model for use within the project countries

During this second stage, data already collated and appraised were used to populate a series of chronic disease models (for CHD, ischemic stroke, and type 2 Diabetes), to explain past trends in disease, and predict the likely future impact of disease, under a number of different policy scenarios.

The existing CHD IMPACT model was further developed and adapted to deal with an MR situation where CHD rates may be increasing, using different absolute levels of risk (based on case-fatality data from Tunisia). Two "new" Markov models were also developed to cover trends in ischemic stroke and type 2 diabetes; these were validated first with data readily available from Western populations, and then with data from one of the partner countries (Tunisia) before wider dissemination. Each of the three models was then populated with data from the project countries (collated during Objective 1). Each model was then validated against observed trends or CVD levels in each MR project country, performing sensitivity analysis (using both simple methods, such as analysis of extremes, and probabilistic methods) to identify key variables and areas of uncertainty to which the models are particularly sensitive. Data collection and entry are to some extent an iterative process, as efforts were made to refine data estimates for parameters shown to be most critical in the model evaluations.

The IMPACT CHD model

Data on populations, mortality, patient groups and numbers, treatments and risk factor trends were collated and critically appraised. The data were then integrated and analyzed using IMPACT, a previously validated CHD policy model (Capewell et al. 2000; Critchley et al. 2004; Ford et al. 2007; Laatikainen et al. 2005; Unal, Critchley and Capewell 2004). The model was initially used to explain past CHD mortality trends in each of the four countries, and validated by comparing with observed trends.

The diabetes model

The model integrates population, obesity and smoking trends for adults in each population, to estimate future diabetes prevalence using a Markov approach. Model parameters were derived from the literature. Diabetes incidence was estimated using DISMOD II from the baseline estimation of diabetes prevalence. The model outputs were compared with subsequent diabetes prevalence surveys. The agreement was generally good.

Objective 3:defining the national policy context and characterizing the health systems in partner countries in the MR

This objective involved a "situation analysis", which sought to integrate perspectives at different 'levels' of the health system in each partner country, reflecting the contexts in which health systems manage CVD and diabetes. This aimed to identify both gaps in policies as well as the gaps on the ground or limitations in existing delivery of services. Starting with established schematic frameworks of potentially effective policy measures and health system interventions for the prevention of CVD/diabetes, we adopted a variety of techniques including document analysis, key informant interviews, clinic observation and patient interviews to characterize the health service response to CVD/DM. The first level (document analysis), involved identifying, collating and systematically reviewing relevant documentary materials on policies and health services provision, with support from senior project members and local stakeholders at various levels. Key informant analysis (the second level) was then used to explore perceptions and knowledge of relevant national policies, and the constraints on their implementation through interviews with senior personnel involved in organizing or influencing the health system, clinicians in the public and private sectors, members of professional associations, non-governmental organizations, members of the pharmaceutical industry, and the specialist media. Finally, direct clinic observation (the third level) was carried out in four selected clinics in each partner country, including interviews with clinic staff to explore their experience in treating NCD patients. The health beliefs and treatment experience of NCD patients and their family members were also explored through interviews, assessing also whether these differed according to demographic, gender or socio-economic stratification. The rationale for this three-level design was to integrate a level of conceptualization as evidenced in policy documents, a level of awareness as displayed by key informants, and a level of practice revealed through clinic fieldwork. Document analysis, taken on its own, portrays aspects of the health system and the ways it is intended to function (whether exemplified in an institutional organogram or a set of protocols to guide treatment); but the portrayal is invariably incomplete and depicts a situation in theory. Key informants can help us to put flesh on the bones of this theoretical depiction: they provide commentary on how the health system works and is intended to work, and where the

gaps and shortcomings are to be found. In doing so they may take us a step toward understanding better how the health system actually works. But key informants generally speak from privileged positions, and are often selected because of their ability to give an overview. Such a perspective is not well suited to understanding local realities, especially outside the capital. For that, direct observation and enquiry are necessary to gain an insight into local practices, local obstacles and dilemmas, and the local understanding of different kinds of actors (staff and patients). In the context of MedCHAMPS, brief fieldwork in four clinics per country was an attempt to provide a preliminary 'reading' of clinic-based realities. No claims can be made about the 'representative' sampling of clinics, though the design envisaged a spread of public and private, primary and secondary services, and urban and rural. But we judged it a vital element in a situation analysis to provide some details of the situation 'on the ground', to triangulate with findings from the document analysis and key informants. The concept of adherence in diabetes treatment is a case in point, tracking from documents to key informants to local practices and frustrations.

Objective 4: developing and evaluating policy options and supporting their implementation in partner countries

Following the completion of Objectives 2 and 3, a mixed method approach was utilized to identify and evaluate a series of potential policy options. This was based on the results of the situation analysis and epidemiological modeling described above. The situation analysis was used to identify possible relevant policy options and to test the feasibility and potential uptake of these policies, while the epidemiological modeling allowed us to explore the likely range of effectiveness of various selected policy options. The exact policy options considered thus depended on the results of health system situational analysis in each of the partner countries. Based on the input from previously defined stakeholders, priorities were set for each country. Selected policy options that can be modeled were then evaluated using the adapted IMPACT models, to undertake "what if" analyses in each study country, quantifying their likely effectiveness. A full economic evaluation was performed for one cross cutting policy option (salt reduction): combinations of different interventions such as labeling, reformulation and educational campaigns were costed based on methods developed in the WHO Global Burden of Disease Project, and WHO-CHOICE project (see www.who.int/choice/en/).

Costs of specific interventions for salt reduction were collected in each country and combined with outcomes to generate cost-effectiveness ratios, and subjected to probabilistic sensitivity analyses to generate cost-effectiveness acceptability curves based on net benefit (quantifying uncertainty around each estimate). Outcomes were expressed as deaths prevented or postponed (DPPs) or life years gained (LYG) for resources expended. These results were compared with other methodologies and published studies to arrive at optimal policy recommendations for partner countries. Having completed an assessment of the costs of implementation of these selected policy options, we were able to recommend policy changes to relevant government departments based on considerations of feasibility and effectiveness, and/or cost-effectiveness, and finally assist with drawing up detailed country specific plans for the implementation and evaluation of the chosen high priority policy options. All these processes were supported with empirical evidence.

Objective 5: dissemination and involvement of policy makers

Major stakeholders (particularly international policy makers and researchers, national policy makers, and primary stakeholders such as community members and organizations, health care providers, local health advocacy groups, non-governmental organizations) have been involved and targeted through consultation during the project and at critical stages in particular. This activity is built into the knowledge management strategy of MedCHAMPS to maximize the relevance, acceptability and impact of the findings disseminated. These key policy makers have been explicitly involved in the project management and advisory group, which met at least annually to review and discuss the progress of the project. They also took part as "key informants" in the situation and policy analysis, and have also assisted with identifying and retrieving relevant documents for document analysis. Most critically, national stakeholders were approached with results from the epidemiological modeling and situation analysis, before commencing Objective 4 (option appraisal), to shape and comment on the policy options to be budgeted and planned.

Specific activities were planned and conducted to disseminate our findings, seek feedback about our work, and induce policy changes. These included identification of key project stakeholders in each of the partner countries; consultation with national policy makers at all stages of the project; conducting national meetings and workshops aimed at sharing project findings and seeking feedback from professionals and stakeholders; consultation with health providers in each country about their experiences; lectures, abstracts presented at national and international scientific meeting; media and press releases devoted to the dissemination of project findings; website development for MedCHAMPS as a portal for information about the project

and dissemination of project findings and experiences (http://research.ncl.ac.uk/medchamps/index.html); scientific publications in peer-reviewed journals; production of policy-briefings for national and international policy makers; organization of national meetings for the dissemination of project findings and stimulation of policy action.

Discussion

Several features of MedCHAMPS are methodologically novel in terms of enhancing evidence-based policy making within the Mediterranean Region. Most notably, it is the combination of a detailed qualitative situation analysis, epidemiological modeling using the best local data available (and making assumptions to "fill in the gaps" where needed), and a cost-effectiveness analysis that is unique in a middle income region with increasing burden of CVD and diabetes (Murray et al. 2003) (Fig. 1).

In industrialized nations, disease models have been used for some time to guide policy and strategy development at various levels, but the approach is novel in the MR. In the recent study by some in our team in a middle-income city (Beijing, China) explored the feasibility of examining CHD trends in the whole Beijing population of 13.8 million (Critchley et al. 2004). Between 1984 and 1999, age adjusted CHD mortality rates increased by approximately 50 % in men and 27 % in women aged 35–74, mostly as a result of a substantial increase in total cholesterol levels (1.05 mmol/l) consistent with an increasingly 'Westernized' diet (Critchley et al. 2004). While these results demonstrate the feasibility of using the IMPACT methodology in a middle income setting, its application to the local risk factor profile and culture of the MR brings insights to guide CVD/diabetes prevention in this region and cautiously beyond. We have also developed new modeling platforms for type 2 diabetes and stroke for this project, which allowed us to explore a greater range of disease outcomes than previously and to base our chosen policy options on estimates of the effectiveness and cost-effectiveness of different interventions on risk factors for a wide range of health outcomes related to CVD/diabetes.

The most extensive collection of original data for MedCHAMPS was in the qualitative part of the research, combining a national overview of health policy for CVD/diabetes with the organization and provision of local health services. The inclusion of an element of local data collection in clinics, in the qualitative part of the research, is guided by the need to understand how the guidelines and interventions may be interpreted and applied in different clinical and cultural contexts, as well as the need to balance concerns with primary and secondary prevention. Crucial as a focus on risk factors and primary prevention is for MedCHAMPS' overall aim, it was also important to keep in mind the challenge for health systems which have to manage the treatment of those who already have CVD/diabetes. What are the pressures on services? How well trained are staff to deal with the particular demands of these chronic health problems? And how do patients access services? These were questions addressed through brief fieldwork in a number of clinics in each country. And while such questions have been asked in other national contexts, these are still new topics of research in the MR, involving methodological skills and perspectives which are still relatively novel and unfamiliar.

This in-depth understanding of local health care systems coupled with the application of modeling techniques allows us to identify prevention strategies that are most likely to be effective and acceptable in reducing the burden of CVD/diabetes in the MR. By quantifying the current and likely future burden of CVD/diabetes and their related risk factors in the target populations, MedCHAMPS maximizes the effectiveness of existing resources (surveys of major CVD and diabetes risk factors) in developing appropriate CVD/diabetes policies in partner MR countries. The experience from model building and policy analysis in Palestine, Syria, Tunisia and Turkey is of great importance for other countries in the MR, which share similar social, economic, and cultural attributes. Moreover, our use of variety of approaches (situation analysis, policy analysis, key informant interviews, secondary analyses of quantitative surveys, qualitative and participatory studies, reviews of documents and literature, model development and analysis; Fig. 1) is generating much needed local capacity that can take on the collection and analysis of data in key health areas beyond the life of this project. Finally, MedCHAMPS goes further than generating reliable evidence to guide policy and local capacity by developing the implementation and future evaluation plans for recommended policies in partner MR countries.

Conclusions

In summary, our results provide policy makers in partner MR countries with a clear picture about the burden of CVD in their countries, and best cost-effective ways to combat it. They are likely to be of great importance for other countries in the MR, which share similar social, economic, and cultural attributes. Finally, our approach of building developed–developing countries collaboration taking advantage of local expertise and knowledge coupled with the application of advanced research methods provides a roadmap for other researchers in developing countries aiming to build research base into CVD epidemiology and prevention.

Acknowledgments The Project MedCHAMPS is funded by EC FP7 (grant no 223075).

References

Alwan AA (1993) Cardiovascular diseases in the eastern Mediterranean region. World Health Stat Q 46(2):97–100

Beaglehole R, Yach D (2003) Globalisation and the prevention and control of non-communicable disease: the neglected chronic diseases of adults. Lancet 362(9387):903–908

Capewell S, Beaglehole R, Seddon M, McMurray J (2000) Explanation for the decline in coronary heart disease mortality rates in Auckland, New Zealand, between 1982 and 1993. Circulation 102(13):1511–1516

Critchley J, Liu J, Zhao D, Wei W, Capewell S (2004) Explaining the increase in coronary heart disease mortality in Beijing between 1984 and 1999. Circulation 110(10):1236–1244

Ebrahim S, Smith GD (2001) Exporting failure? Coronary heart disease and stroke in developing countries. Int J Epidemiol 30(2):201–205

Ezzati M, Vander Hoorn S, Lawes CM, Leach R, James WP, Lopez AD, Rodgers A, Murray CJ (2005) Rethinking the "diseases of affluence" paradigm: global patterns of nutritional risks in relation to economic development. PLoS Med 2(5):e133

Ford E, Ajani U, Croft J, Critchley JA, Labarthe D, Kottke T (2007) Explaining the decrease in mortality from coronary heart disease in the United States between 1980 and 2000. N Engl J Med 356:2388–2398

International Diabetes Federation 2011, Diabetes Atlas. (http://www.idf.org/atlasmap/atlasmap). Accessed 16 Nov 2011

Laatikainen T, Critchley J, Vartiainen E, Salomaa V, Ketonen M, Capewell S (2005) Explaining the decline in coronary heart disease mortality in Finland between 1982 and 1997. Am J Epidemiol 162(8):764–773

Maziak W (2006) Health in the middle East. BMJ 333(7573):815–816

Maziak W (2009) The crisis of health in a crisis ridden region. Int J Public Health 54(5):349–355

Maziak W, Rastam S, Mzayek F, Ward KD, Eissenberg T, Keil U (2007) Cardiovascular health among adults in Syria: a model from developing countries. Ann Epidemiol 17(9):713–720

Murray CJ, Lopez AD (1996) The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020. Harvard Univ Press, Boston

Murray CJ, Lopez AD (1997) Alternative projections of mortality and disability by cause 1990–2020: global Burden of Disease Study. Lancet 349(9064):1498–1504

Murray CJ, Lauer JA, Hutubessy RC, Niessen L, Tomijima N, Rodgers A, Lawes CM, Evans DB (2003) Effectiveness and costs of interventions to lower systolic blood pressure and cholesterol: a global and regional analysis on reduction of cardiovascular-disease risk. Lancet 361(9359):717–725

Nugent R (2008) Chronic diseases in developing countries: health and economic burdens. Ann N Y Acad Sci 1136:70–79

Reddy KS (2002) Cardiovascular diseases in the developing countries: dimensions, determinants, dynamics and directions for public health action. Public Health Nutr 5(1A):231–237

Rodgers A, Vaughan P (2002) 'World Health Report 2002: Reducing Risks, Promoting Healthy Life. World Health Organization, Geneva

Rose G (1985) Sick individuals and sick populations. Int J Epidemiol 14(1):32–38

Unal B, Critchley JA, Capewell S (2004) Explaining the decline in coronary heart disease mortality in England and Wales between 1981 and 2000. Circulation 109(9):1101–1107

World health Organization (1999) The world health report 1999: making a difference. WHO, Geneva

World Health Organization 2011a, Diabetes Programme. [http://www.who.int/diabetes/en/]. Accessed 2 Dec 2011

World Health Organization 2011b, 'Obesity and overweight. Fact sheets. Available at: [http://www.who.int/mediacentre/factsheets/fs311/en/] Accessed 2 Dec 2011

Yach D, Leeder SR, Bell J, Kistnasamy B (2005) Global chronic diseases. Science 307(5708):317

Yusuf S, Reddy S, Ounpuu S, Anand S (2001) Global burden of cardiovascular diseases: part I: general considerations, the epidemiologic transition, risk factors, and impact of urbanization. Circulation 104(22):2746–2753