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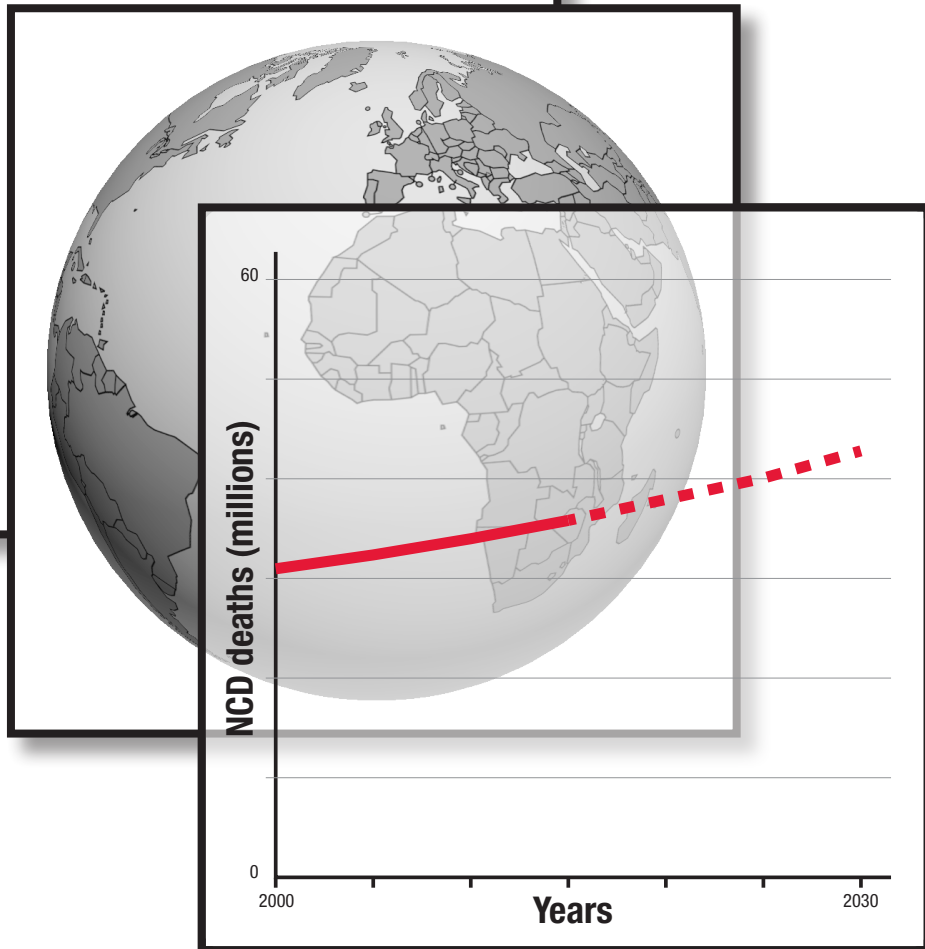
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A Prioritized Research Agenda for Prevention and Control of Noncommunicable Diseases



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A Prioritized Research Agenda for Prevention and Control of Noncommunicable Diseases



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Organization**

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A Prioritized Research Agenda for Prevention and Control of Noncommunicable Diseases was developed under the leadership of Ala Alwan (Assistant Director-General, Noncommunicable Diseases and Mental Health). Shanthi Mendis (Coordinator, Chronic Disease Prevention and Management) was responsible for the technical coordination of the initiative.

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This publication contains the collective views of an international group of experts and does not necessarily represent the decisions or policies of the World Health Organization.

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 - 1.3** Chronic respiratory diseases in low- and middle-income countries. Paper 3. Geneva, World Health Organization, 2011.
 - 1.4** Diabetes prevention and control in low- and middle-income countries. Paper 4. Geneva, World Health Organization, 2011.
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- 1.9** Genetics for prevention and control of noncommunicable diseases. Paper 9. Geneva, World Health Organization, 2011.
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- 2. Reports of Meetings to develop the Prioritized NCD research agenda (2008-2010)**
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- Annexure A.** Research priorities for cardiovascular disease prevention and control which were ranked (as listed in the sixth draft version of the WHO NCD Research Agenda)

Foreword

Currently, noncommunicable diseases (NCD) are responsible for almost two-thirds of all deaths globally. Of the 57 million global deaths in 2008, 36 million, or 63%, were due to NCDs, principally cardiovascular diseases, diabetes, cancers and chronic respiratory diseases. These four groups of diseases share more or less the same risk factors (tobacco use, unhealthy diet, physical inactivity and the harmful use of alcohol). As the impact of NCDs increases and as populations age, annual NCD deaths are projected to continue to rise worldwide.

While popular belief presumes that NCDs afflict mostly high-income populations, the evidence tells a very different story. Nearly 80% of NCD deaths occur in low- and middle-income countries and are the most frequent causes of death in most countries, except in Africa. Even in African countries, however, NCDs are rising rapidly. In fact, projections indicate that while mortality from NCDs will increase in all regions of the world over the next decade, the greatest increase is expected to occur in Africa.

The NCD epidemic strikes disproportionately among people in lower socio-economic groups. NCDs and poverty create a vicious cycle whereby poverty exposes people to behavioural risk factors for NCDs. In turn, the resulting NCDs may become an important driver of the downward spiral that leads families towards poverty.

While the magnitude of the NCD epidemic has been rising in recent years, so has the knowledge and understanding of its control and prevention. Evidence shows that NCDs are to a great extent preventable. Indeed, there is enough knowledge to establish effective NCD prevention programmes capable of arresting the rise in magnitude and reducing the burden. Evidence-based interventions to prevent and manage NCDs are therefore not only achievable, but also cost-effective. Furthermore, the income level of a country or population is not a barrier to success. However, in emphasizing the preventability of NCDs and the existing evidence and opportunities for effective health care, it is essential to recognize the importance of generating additional evidence from research to address gaps and to refine existing knowledge, both in the specific causes of NCD and in terms of how best to intervene, particularly in the context of low- and middle-income countries. Research findings in pathways of disease development will help to scale up prevention strategies and provide fresh ideas and initiatives with respect to prevention.

The Global Strategy for the Prevention and Control of NCDs and its Action Plan endorsed by the World Health Assembly in 2008 provide sound vision and a clear roadmap to prevent and control NCDs and to assist countries in establishing effective programmes.

Objective 4 of the Global Strategy Action Plan calls for a coordinated agenda for NCD research to strengthen the evidence base for cost-effective NCD prevention and control. Research should not only generate more knowledge but also help to translate knowledge into action through innovative approaches. Based on a series of papers commissioned by WHO, and global consultations conducted between 2008 and 2010, key research priority areas have been identified and included as part of a prioritized research agenda for noncommunicable disease. The Agenda, included in this publication, focuses on translational and health system research to expand implementation of proven cost-effective interventions and research to enable affordability of high-cost but effective technologies in the context of various resource settings.

In developing this Agenda, the aim is to enhance international collaboration to promote and support the multidimensional and multisectoral research that is needed in order to generate or strengthen the evidence-base for cost-effective prevention and control.

The research priorities included in this publication have been developed by an extensive network of experts from Member States, WHO Collaborating Centres, research and public health institutions and other partners involved in prioritizing, implementing and funding research projects.

Clearly, this is a living document and the priorities will require regular review as well as updating. In the meantime, I trust that the contents will serve as a useful guide to those implementing and funding research on noncommunicable diseases and their risk factors and determinants.

Dr Ala Alwan

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Executive Summary

To respond to the global public health challenge posed by the rapidly growing burden of noncommunicable diseases (NCDs), the Fifty-third World Health Assembly passed resolution WHA53.17 in May 2000, endorsing the Global Strategy for the Prevention and Control of Noncommunicable Diseases. The Global Strategy states “WHO in close collaboration with other partners, will promote and support research in priority areas of prevention and control, including analytical, operational and behavioural research to facilitate programme implementation and evaluation. Special attention will be given to innovative research on issues of poverty, gender, cost-effective care, and genetic approaches to prevention. WHO will strengthen the role of WHO collaborating centres in supporting implementation of the global strategy, particularly in coordinating collaborative research”.

Subsequently, in May 2008, the Sixty-first World Health Assembly endorsed the Global Strategy Action Plan for the Prevention and Control of Noncommunicable Diseases. The fourth objective of the Action Plan is to “promote research for the prevention and control of noncommunicable diseases”.

To address this objective a Prioritized Research Agenda for Prevention and Control of Noncommunicable Diseases was developed during the period 2008–2010 through a series of consultations, working papers on major NCD research domains, extensive reviews and a survey for ranking research priorities identified by expert groups.

The term “prioritized research agenda” refers to key areas of research that seek to understand and impact policies, programmes and processes for preventing and mitigating the NCD epidemic, with a special focus on low- and middle-income countries.

The main focus of the WHO NCD Research Agenda is on the four major NCDs – cardiovascular disease (CVD), cancer, chronic respiratory disease and diabetes – and shared risk factors and determinants within and outside the health sector. These four NCDs contribute most to the global NCD burden and are mainly responsible for the rapidly rising NCD morbidity and mortality trends in low- and middle-income countries.

The overall goal of the WHO NCD Research Agenda is to ensure that decisions and actions for addressing NCDs are grounded in evidence from research. The aims, as stated in the Global Strategy Action Plan are:

-
- To generate knowledge and help to translate knowledge into action through innovative approaches in the context of low- and middle-income countries and
 - To support low- and middle-income countries in building capacity for epidemiological and health-systems research, including the analytical and operational research required for programme implementation and evaluation in the area of noncommunicable diseases.

In the process of prioritization, research related to policies and interventions that have contributed to declining NCD trends in developed countries have been given special attention. For example, as a result of certain policies and interventions, age-standardized CVD rates have halved over the last two decades in several developed countries. Further, due to similar actions mortality and survival rates from certain cancers have also been declining in some developed countries. Therefore, the following areas have been prioritized.

- a) Intersectoral and multidisciplinary research to understand and influence the macroeconomic and social determinants of NCDs and exposure to NCD risk factors
- b) Translation research and health system research for global application of proven cost-effective strategies
- c) Research to enable expensive but effective interventions to become accessible and used appropriately in resource-constrained settings.

1. Background

Research is fundamental to generate knowledge and information for formulating evidence-informed policies and practices in support of global public health and health equity. In May 2010, the Sixty-third World Health Assembly, in resolution WHA63.21, endorsed the World Health Organization (WHO) Strategy on Research for Health and laid out the role and responsibilities of WHO in health research (1). WHO Member States welcomed the strategy, particularly with respect to strengthening capacity of national health research systems, and requested the Director-General to implement the strategy within the organization at all levels and with partners, aligned with the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (2). The Prioritized Research Agenda for Prevention and Control of Noncommunicable Diseases (WHO NCD Research Agenda) has been developed in pursuance of this request and in alignment with the 2008–2013 Global Strategy Action Plan (3). The WHO NCD Research Agenda identifies and prioritizes key research needs with a special focus on low- and middle-income countries and is underpinned by the Global Strategy Action Plan, which was endorsed by the World Health Assembly in April 2008 (4). One of the six objectives of the Global Strategy Action Plan is to promote research for the prevention and control of NCDs. The progress of implementation of the Global Strategy Action Plan, including the process of development of the WHO NCD Research Agenda, was reported to the Sixty-third World Health Assembly in May 2010 (5).

2. Scope, goal, objectives and target audience

The WHO NCD Research Agenda uses the same definition of research as the WHO Strategy on Research for Health, which defines research as “the development of knowledge with the aim of understanding health challenges and mounting an improved response to them”.

The term “prioritized research agenda” refers to areas of research that seek to understand and impact policies, programmes and processes for preventing and mitigating the noncommunicable disease (NCD) epidemic, with a special focus on low- and middle-income countries.

The main focus is on the four major NCDs – cardiovascular disease (CVD), cancer, chronic respiratory disease and diabetes – and shared risk factors and determinants within and outside the health sector.¹ These four diseases contribute most to the global NCD burden and are mainly responsible for the rapidly rising NCD morbidity and mortality trends in low- and middle-income countries (6). Furthermore, cost-effective interventions that can be implemented in low-resource settings are available to prevent and control these four major NCDs.

The goal of the WHO NCD Research Agenda is to provide guidance to national NCD research frameworks and to facilitate translation of research findings into policy and practice. The three main objectives of the WHO NCD Research Agenda are:

- to ensure that decisions and actions for addressing NCDs are grounded in evidence from research;
- to identify knowledge gaps and strengthen research required for public health action, prevention of NCDs, priority health needs and health equity;
- to strengthen capacity of low and middle income countries to conduct research on priority NCD issues.

The NCD research priorities identified under each NCD domain are presented in three main activity areas: (i) identification of causes and measurement of magnitude; (ii) analysis of problems and development of solutions; and (iii) application of solutions and evaluation of impact. Due

1. Research related to mental health, violence and injuries, and alcohol and drug abuse will be addressed in other WHO documents.

to the close links between different NCD domains, shared risk factors and determinants, there is a certain degree of repetition and overlap in research priorities between different domains.

The main target audience for the WHO NCD Research Agenda comprises ministries of health, ministries of research, science and technology, development and donor agencies, research institutions, NCD research alliances, policy-makers, the research community, health professionals, nongovernmental organizations (NGOs) and civil society entities.

3. Global burden of NCDs

NCDs caused an estimated 36 million deaths in 2008. This figure represents almost two thirds of all deaths globally, with nearly 80% of deaths due to NCDs occurring in low- and middle-income countries, and approximately 29% of deaths involving people less than 69 years of age (6). The NCD burden is projected to increase disproportionately in lower-income countries and populations over the next 10 years (6). The rapidly increasing magnitude of these diseases disproportionately affects poor and disadvantaged populations, in turn contributing to widening health disparities between and within countries. Current epidemiological evidence indicates that four major NCDs – CVD, cancer, chronic respiratory disease and diabetes – make the largest contribution to the NCD burden in low- and middle-income countries. The current knowledge base related to the etiology and prevention and control of NCDs, if appropriately applied, could prevent the rising trends of NCDs, reduce premature mortality and morbidity and improve the quality of life of those suffering from NCDs (3, 4, 7–9).

4. Role of research in the implementation of the Global Strategy Action Plan

The Global Strategy Action Plan, endorsed by the World Health Assembly in May 2000, focuses on three main areas: (i) mapping the NCD epidemic and determinants; (ii) reducing the level of exposure of individuals and communities to the common risk factors; and (iii) strengthening health care for people with NCDs (3). In May 2008, the World Health Assembly endorsed the implementation of the Global Strategy Action Plan (4).

The fourth objective of the Global Strategy Action Plan focuses on research for the prevention and control of NCDs. The Action Plan of the Global Strategy calls upon the Secretariat to develop a research agenda for NCDs in line with the WHO global research strategy (1), collaborate with partners and the research community and involve major relevant constituencies in prioritizing, implementing and funding research. Research is also an integral component of all the other objectives of the Global Strategy Action Plan, as listed below (4).

Objective 1
To raise the priority accorded to NCDs in development work at global and national levels, and to integrate prevention and control of such diseases into policies across all government departments.
Objective 2
To establish and strengthen national policies and plans for the prevention and control of NCDs.
Objective 3
To promote interventions to reduce the main shared modifiable risk factors for NCDs: tobacco use, unhealthy diets, physical inactivity and harmful use of alcohol.
Objective 4
To promote research for the prevention and control of NCDs.
Objective 5
To promote partnerships for the prevention and control of NCDs.
Objective 6
To monitor NCDs and their determinants and evaluate progress at the national, regional and global levels.

Furthermore, in resolution WHA59.24, the World Health Assembly recognized that the growing burden of diseases and conditions, including NCDs, disproportionately affect developing countries (10). Currently, 2.7 billion, representing 43% of the world population, live on less than US\$ 2 a day (11). There is growing evidence of the association between poverty and NCD risk factors such as tobacco and alcohol abuse (12,13). Poverty, among other factors, directly affects access to diagnostics, medicines, vaccines and medical devices, especially in low- and middle-income countries. In this regard, the Global Strategy on Public Health, Innovation and Intellectual Property aims to provide a framework for securing a sustainable basis for needs-driven essential health research and development relevant to diseases that disproportionately affect low- and middle-income countries, including major NCDs (2).

The need to address NCDs through an evidence-based approach, which requires research is also supported by the resolution unanimously adopted by the United Nations General Assembly in May 2010 (14). The resolution seeks to halt the increasing trends in premature deaths from NCDs worldwide, with a particular focus on low- and middle-income countries.

5. Need for a prioritized research agenda for prevention and control of major NCDs to improve public health

A coherent and coordinated agenda for research is a key requirement for effective prevention and control of NCDs. As resources for health are limited, particularly in low- and middle-income countries, it is essential that NCD policies and programmes be based on sound scientific evidence to ensure effectiveness. The research agenda will provide guidance to Member States in understanding and identifying the key public health research needs related to NCDs, which include:

- What is known to be effective in reducing the NCD burden and disparities?
- What research is needed to apply the evidence base for reducing the burden and disparities in low-resource settings?
- What research is needed to track the NCD burden and its social determinants?
- What research is needed to monitor and evaluate effectiveness of NCD prevention and control?
- What new diagnostics, medicines, technologies and vaccines are required to improve outcomes?
- What are the key research priorities for establishing and scaling up comprehensive national NCD policies and programmes in low- and middle-income countries?

There is a substantial body of knowledge on the causes of the NCD burden and a recognition that its determinants lie outside the health sector. Conducting research on determinants outside the health sector is particularly challenging and requires intersectoral and multidisciplinary efforts.

At present, there is a major mismatch between country demands for conducting research on prevention and control of NCDs and the human resource and financial capacity to respond to those demands. Therefore, the research agenda requires prioritization with the aim of focusing

on key research issues that are likely to have the greatest potential to impact prevention and control of NCDs. The WHO NCD Research Agenda cover the full range of NCD prevention and control activities, including national policy development, programme implementation, tracking of the NCD burden, advocacy to incorporate NCDs in the development agenda, multisectoral actions and partnerships, and monitoring and evaluation. The WHO NCD Research Agenda is meant to generate knowledge where there are gaps and to help translate available knowledge into policy and practice through innovative approaches. In addition, it should improve the use of existing NCD research evidence to impact on the areas in the global health agenda set out by the Member States (15). These include investing in NCDs to reduce poverty, promoting universal coverage for essential NCD interventions, tackling the determinants of NCDs, strengthening health systems governance and accountability for prevention and control of NCDs.

The WHO NCD Research Agenda also reflects the main research functions of WHO, which include stewardship, capacity strengthening and coordination (1). As a facilitator and knowledge manager for research on NCDs, WHO provides a platform for all stakeholders to discuss and harmonize research efforts. It supports needs assessment and priority setting (15). The aim of WHO capacity development activities in NCD research is to strengthen leadership and expertise in order to generate new knowledge and to inform national policy and practice. In addition, WHO coordinates and commissions NCD research when necessary, with a special focus on the needs of low- and middle-income countries.

Research required to address the challenges of NCD prevention and control is broad and spans a wide range of domains, including (i) research on social and economic determinants; (ii) behavioural risk factors (tobacco use, physical inactivity, obesity, unhealthy diet and harmful use of alcohol); (iii) prevention, detection and care of major NCDs (CVD, cancer, chronic respiratory disease and diabetes); and (iv) relevant health policy, health equity and health systems issues.

To address prevention and control of NCDs with a focus on public health and health equity, priority has been given to key research areas within the above mentioned NCD domains. They include, burden of disease, (e.g. incidence, prevalence, economic and social costs); causes and trends, (e.g. risk factor surveillance, mortality trends, causality of social determinants); socioeconomic determinants and non-health sector determinants of NCDs, (e.g. interdisciplinary and intersectoral research for prevention and to address equity issues); effectiveness and impact of prevention policies and programmes; development of solutions for low-resource settings, (e.g.

development and implementation of affordable technologies); translation of evidence into practice in low-resource settings, (e.g. delivery of a core set of essential NCD interventions through a primary health care approach).

6. Achievable outcomes through a prioritized research agenda for prevention and control of major NCDs

The development and implementation of the WHO NCD Research Agenda outlined in this document seeks to achieve the following:

- increased awareness and recognition of the priorities in NCD in global, regional and national research and development efforts;
- incorporation within national NCD policies of NCD research plans that articulate clear research priorities and provide frameworks for NCD research efforts focused on national public health needs;
- increased investment for NCD research and strengthened capacity of low- and middle-income countries to address priority research for prevention and control of major NCDs;
- establishment of institutional mechanisms to facilitate effective use of available research evidence on NCDs for health decision-making, policy development and programme implementation;
- support of the WHO NCD Research Agenda by donor and development agencies with sustainable funding and improved cooperation among research funders and other key partners to align aid with NCD research priorities.

7. Process for the development of the WHO NCD Research Agenda

7.1 Initial phase of development of WHO NCD Research Agenda

As mentioned above, the Global Strategy Action Plan that was endorsed by the World Health Assembly in May 2000 calls for WHO to provide strategic support for research development. The fourth objective of the Global Strategy Action Plan endorsed by the World Health Assembly in May 2008 identifies a coordinated agenda for NCD research as an essential element for prevention and control of NCDs. Informed by previous World Health Assembly resolutions on research (10, 16), a participatory and consultative process has been used to formulate the WHO NCD Research Agenda. The first draft of the WHO NCD Research Agenda was based on the output of a preliminary consultation at WHO headquarters in August 2008 (17). About 200 participants – including leading researchers, representatives from WHO collaborating centres, research institutions, NGOs in official relationships with WHO, development agencies, donor agencies and all levels of WHO – participated in this meeting. Working papers were prepared reviewing the current status of knowledge and research gaps related to key NCD domains: tobacco use, nutrition, physical activity and obesity, CVD, diabetes, cancer, respiratory disease, genetics and cost-effectiveness of interventions. The selection of these research domains was based on priority NCD areas identified in the WHO NCD Research Agenda and the Global Strategy Action Plan. Each paper reviewed what is known, the gaps in knowledge and the research required for prevention and translation of existing knowledge into national policies and programmes.

At the first WHO consultation in August 2008, the papers were presented in a plenary session and further discussed in focused working groups (17). Working groups addressed the following questions in disease-specific group discussions.

The summaries of the working group deliberations were discussed in a plenary session, and the working papers were subsequently revised to form information documents on selected key priority areas for NCD research (18–27). The NCD research agenda went through several revisions over a period of three years (2008–2010). The first outline of the NCD

research agenda was based on the revised working papers and output of the WHO consultation held in 2008. It was presented at the fiftieth session of the WHO Advisory Committee on Health Research in October 2008 for input. The revised second draft was presented at the Ministerial Forum on Health Research in November 2008 in Bamako, Mali (28). The third draft of the WHO NCD Research Agenda was circulated internally and externally to obtain further input in February 2009. The progress of development of the WHO NCD Research Agenda was reported to the fifty-first session of the WHO Advisory Committee on Health Research in March 2009. The working papers were then peer reviewed in preparation for the second WHO consultation held on 12–13 October 2009 (29). The writing groups of the working papers revised them at this consultation into a fourth draft to better focus on research priorities relevant to low- and middle-income countries. During 2010, the working papers were peer reviewed a second time and refined further based on input received from a wider group of experts. The changes were incorporated into the draft of the WHO NCD Research Agenda. It was then circulated to research institutions, WHO collaborating centres, regional offices, WHO country offices and experts for review. The final draft was also presented at the fifty-third session of the WHO Global Advisory Committee on Health Research in May 2010 and circulated to WHO regional offices for input.

7.2 Ranking process

The research priorities contained in the sixth draft of the WHO NCD Research Agenda were also subjected to a process of ranking through a DataCol survey. Research institutions, WHO collaborating centres, WHO regional and country offices, experts and researchers were invited to participate in the survey.

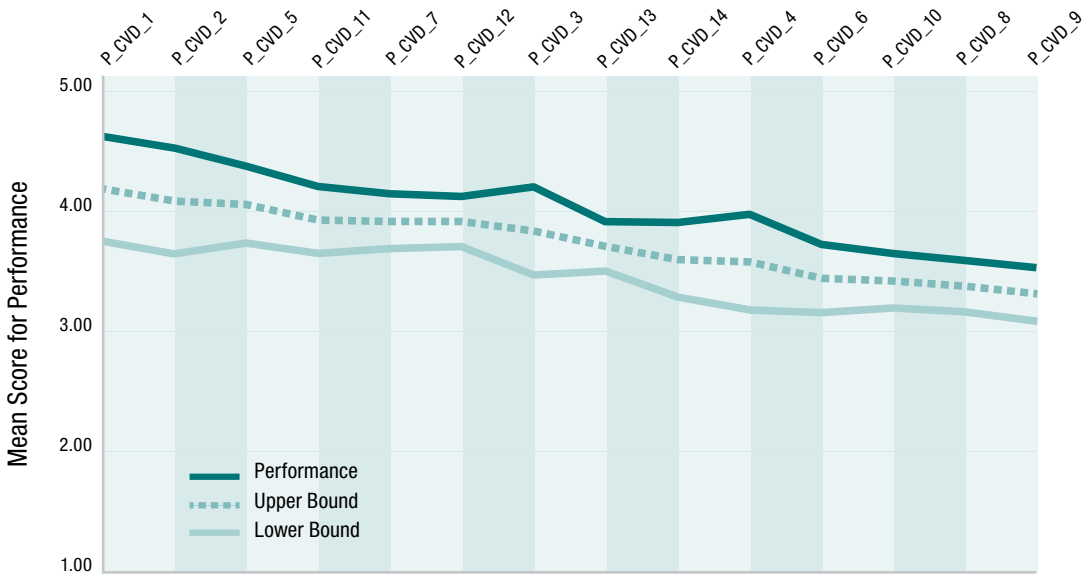
A total of 111 research priorities were identified by expert groups, within 11 specific and cross-cutting NCD domains (CVD, cancer, chronic respiratory disease, diabetes, tobacco, nutrition, obesity and physical activity, social determinants, primary health care approach, human genetics, translation of evidence into policy and programmes), and were ranked. The research priorities were scored for relevance for low- and middle-income countries (score 1–5), feasibility of application in low-resource settings (score 1–5), potential public health impact (score 1–5) and estimated time to see the effect of application of research results (less than 5 years, 5–10 years, more than 10 years).

The results of the ranking exercise for CVD research priorities are shown in Figure 1 as an example. For CVD, 102 researchers ranked 14 research

priorities identified in the sixth draft version of the WHO NCD Research Agenda (Annex A). Figure 1 shows the performance of each priority based on the mean score for relevance, feasibility and public health impact.

As the results indicate, top priorities identified from the ranking process were research related to generation of country-specific information on risk factors and disease burden; monitoring of trends of risk factors and disease; development of models of effective combinations (policy, environment and health system) of interventions; assessment of health system barriers and strengthening of primary health care; and determination of the effectiveness of community education campaigns, community participation and multisectoral action. The results of the ranking process were taken into consideration in the final prioritization of the research areas.

Figure 1 Performance of CVD research priorities ranked by experts (n=112). Performance indicator is based on the means scores of four parameters: relevance, feasibility, public health impact and national health impact.



7.3 Finalization of WHO NCD Research Agenda

A third consultation was convened on 19–21 October 2010 to obtain further input on the seventh draft of the WHO NCD Research Agenda. About 250 participants – including experts, leading researchers, and representatives

from WHO collaborating centres, research institutions, NGOs in official relations with WHO, development agencies, donor agencies and all levels of WHO – participated in this consultation. The expert group identified five top priorities within the list of priorities in each NCD domain. The working papers were discussed and finalized. The top research priorities and finalized working papers were shared with all participants of the consultation. In addition, the implementation of the WHO NCD Research Agenda was also discussed during the third research consultation in October 2010 (30).

Table 1 summarizes the process of development of the WHO NCD Research Agenda.

Table 1 *Process of development of the WHO NCD Research Agenda*

Stage	Actions
Mandate	Global Strategy for NCD prevention and control (World Health Assembly, May 2000) Fourth objective of the Global Strategy Action Plan (World Health Assembly, May 2008)
Milestone 1	WHO consultation, Geneva, Switzerland, 25–26 August 2008 Draft working papers on research priorities
Milestone 2	First draft of the WHO NCD Research Agenda WHO Advisory Committee on Health Research, October 2008
Milestone 3	Draft of the WHO NCD Research Agenda presented to the Ministerial Forum on Health Research, Bamako, Mali, November 2008
Milestone 4	Draft of the WHO NCD Research Agenda presented to the WHO Advisory Committee on Health Research, March 2009 First peer review of working papers
Milestone 5	Revision of working papers and the draft of the WHO NCD Research Agenda WHO consultation, Geneva, Switzerland, 12–13 October 2009
Milestone 6	Second peer review of working papers Draft WHO NCD Research Agenda presented to the WHO Advisory Committee on Health Research, March 2010
Milestone 7	Internal WHO (regional and country office participation) and external review of the WHO NCD Research Agenda Revision of working papers
Milestone 8	Ranking of priorities (researchers, experts, policy-makers)
Milestone 9	Final draft of the WHO NCD Research Agenda and 10 working papers WHO consultation, Geneva, Switzerland, 19–21 October 2010
Milestone 10	Finalization incorporating input from consultation and results of ranking
Product	Prioritized WHO NCD Research Agenda 2011 (for review and revision in 2015)

The WHO NCD Research Agenda has been developed from a global perspective and needs to accommodate regional and national research priorities prior to implementation. It is envisaged that WHO country offices will incorporate the WHO NCD Research Agenda into the Country Cooperation Strategy and facilitate national adaptation and incorporation into National health strategies and NCD Action Plans.

8. Key domains for research

The brief summaries below under each NCD domain deal only with priority research issues of importance in policy and programme development and do not encompass the full range of research questions related to each area. The rationale for prioritizing specific research issues in each NCD domain is provided in respective background papers (18–27). Among the research priorities listed below under each NCD domain, five key priorities shortlisted as top priorities by the expert group at the third research meeting in October 2010 are highlighted.

Major NCDs

8.1 Cardiovascular disease (CVD)

8.1.1 What is known?

CVD is the leading NCD, contributing to 17 million deaths (48% of NCD deaths) annually and 10% of the global disease burden (18). The knowledge base related to the etiology and treatment of CVDs (coronary heart disease, cerebrovascular disease, rheumatic heart disease) and major cardiovascular risk factors (tobacco use, physical inactivity, unhealthy diet, obesity, hypertension, hyperlipidemia, diabetes) is substantive and informs effective prevention and treatment efforts.

Population-wide primary prevention interventions that have been identified as very cost effective include price and non-price related demand reduction elements of the FCTC, population-wide salt reduction, alcohol taxation in countries with high levels of consumption, reductions in salt, saturated fat, trans fats in the diet and public awareness / mass media campaigns for promoting a healthy diet and physical activity. In addition, delivery of low-cost multi-drug treatment to people with high cardiovascular risk and diabetes, through a primary health care approach is a highly cost-effective and affordable individual health care intervention in many low- and middle-income countries.

Many developed countries have effectively applied this existing knowledge base to bring about a downward trend in CVD. In low- and middle-income countries, however, CVD trends are rapidly rising due to ageing of

populations, unplanned urbanization and globalization. Furthermore, many constraints, barriers and competing communicable, maternal and child health priorities result in major gaps in applying existing knowledge of CVDs in low- and middle-income countries. Innovative approaches are required to apply what is known about CVDs to resource-constrained settings. These approaches also need to be informed by implementation research.

Existing data on the effectiveness of medical interventions on drug treatment and surgery are mostly derived from studies in high-income populations. In general, they should also be applicable in low- and middle-income countries. Therefore, limited research resources would be most usefully invested to generate new knowledge on the best way to translate the vast body of existing scientific knowledge into action in those countries.

8.1.2 Which aspects require further research?

Table 2 *Research priorities in CVD in the context of NCD prevention and control*

Thematic area	Research priorities (top five priorities are in bold italics and are marked with *)
Identification of causes and measurement of magnitude	<p>* <i>Generate country-specific information about risk factors, the disease burden, economic and social costs and impact of globalization and urbanization on behaviours, to make compelling arguments to political leadership for placing CVD high on the development agenda and for policy development.</i></p> <p>Develop methods for monitoring trends of CVD morbidity, mortality and risk factors and for evaluating the effectiveness of policies and programmes</p> <p>Develop observational cohorts to study social, cultural and economic determinants of behavioural and other cardiovascular risk factors</p>
Analysis of problems and development of solutions	<p>* <i>Develop models of combinations of interventions (policy, environmental, health systems) to address cardiovascular risk factors in diverse settings and evaluate their effectiveness.</i></p> <p>* <i>Investigate and define health system-related opportunities and barriers to care and develop feasible approaches to apply cost-effective interventions for primary and secondary prevention with a special focus on primary care and non-physician health workers.</i></p> <p>Develop and validate screening programmes based on absolute risk in an intervention trial using fixed-dose combinations at different thresholds of coronary risk</p> <p>Develop appropriate resource allocation models for medical technologies required for CVD interventions in order to maximize health benefits and equity</p> <p>Develop vaccines and safer and affordable medicines for addressing neglected CVDs such as rheumatic heart disease and Chagas disease</p> <p>Investigate and define barriers and solutions to develop and implement health-supporting policies in sectors outside health (e.g. trade, education, agriculture, industry)</p>

Thematic area	Research priorities (top five priorities are in bold italics and are marked with *)
Application of solutions and evaluation of impact	Determine the effectiveness of community education campaigns, community participation and multisectoral action for CVD prevention in different cultural and economic settings * <i>Validate cost-effective screening approaches, risk prediction methodologies and clinical algorithms applicable in low- and middle-income country settings</i> * <i>Evaluate the macroeconomic impact and the impact on social inequities of cardiovascular policies and interventions</i>

8.2 Cancer

8.2.1 What is known?

The known major causes of cancer include tobacco use, chronic infections, dietary factors, obesity, physical inactivity, harmful use of alcohol, hormonal and reproductive factors, ionizing and non-ionizing radiation, and occupational and environmental exposures to carcinogens (19). There is evidence on the benefits from control of most of these factors. Cost effective interventions are available across the four broad approaches to cancer prevention and control: primary prevention, early detection, treatment (surgery, chemotherapy, and radiotherapy) and palliative care. With regard to vaccines, significant advances have been made with the development and application of a vaccine against hepatitis B, with some evidence of a reduction in liver cancer. Current vaccines for prevention of cancer of cervix are expensive and only effective against two of the known oncogenic human papilloma viruses. Early detection (through awareness about early symptoms or organized screening programmes) will benefit patients with most types of cancer. There is convincing evidence that screening is effective for breast, cervical, colorectal and oral cancer.

For cancer treatment, improvements in the outcome of testis, breast, ovary and colorectal cancer and Hodgkin's lymphoma, as well as childhood cancer, have been demonstrated. The challenge is to develop innovative approaches that will enable this potential to be achieved in low- and middle-income countries. In many of these countries, most cancer patients die without even adequate pain relief as access to palliative care, oral morphine and staff trained in palliative care is limited. Benefits sought in cancer control can best be obtained by integrating a comprehensive national cancer control programme with multisectoral involvement into the existing health system.

8.2.2 Which aspects require further research?

Table 3 *Research priorities in cancer in the context of NCD prevention and control*

Thematic area	Research priorities (top five priorities are in bold italics and are marked with *)
Identification of causes and measurement of magnitude	<p>* <i>Track the cancer burden and risk factors and collect data (e.g. staging, treatment, use of opiates, economic impact of cancer, human resources for cancer control) needed to strengthen cancer programmes</i></p> <p>Establish or improve cancer registration, especially in Africa</p>
Analysis of problems and development of solutions	<p>* <i>Develop methods for applying cancer prevention strategies in relation to local culture and local resources (including primary prevention, effective early detection, vaccination programmes)</i></p> <p>Identify means for downstaging detectable cancers through public awareness programmes and local successes, e.g. in downstaging and treatment, and apply more widely</p> <p>* <i>Develop means to train health professionals on all aspects of cancer control, including leadership and management of cancer control programmes with a public health approach at the national and district levels</i></p> <p>* <i>Study cost-effectiveness of modalities of different surgical procedures and radiotherapies given varying resource settings and health care systems</i></p> <p>Develop effective approaches to influence politicians on the needs for cancer control</p> <p>Develop innovative ways to facilitate the development or reinforcement of cancer control programmes and accelerate their scaling up in low- and middle-income countries</p> <p>Identify the determinants that result in cancer being diagnosed at an advanced stage</p> <p>* <i>Identify means to reduce barriers to access to diagnosis, treatment, rehabilitation for curable and palliative care for non-curable cancers</i></p> <p>Develop cost-effective and feasible models of alternative technologies for teleimaging and telepathology as tools for improved diagnosis and education in low- and middle-income countries</p>
Application of solutions and evaluation of impact	<p>Evaluate models for implementing effective screening programmes in different socioeconomic settings</p> <p>Establish and evaluate the impact of a comprehensive vaccination programme for hepatitis B and oncogenic human papilloma viruses</p>

8.3 Chronic respiratory diseases

8.3.1 What is known?

It is estimated that 4 million people died prematurely from chronic respiratory diseases in 2005, and it is projected that the global death rate and burden due to chronic respiratory diseases will increase considerably in the future (20). Major chronic respiratory diseases include asthma and chronic obstructive pulmonary disease (COPD). COPD alone was responsible for 3.7 million deaths and will rank as the third leading cause of death in 2030. Asthma and COPD both share common risk factors, including tobacco smoking and indoor air pollution. Smoking is estimated to cause about 42% of chronic respiratory disease (20). The reliance by nearly 3 billion people on solid fuels (coal, wood, animal dung, crop wastes) and traditional stoves for cooking and heating needs, leads to high levels of indoor air pollution. Indoor air pollution increases the risk of COPD (20). Tobacco control and reducing indoor air pollution are key measures for prevention of COPD. Although there are cost effective new stove and fuel technologies, progress with implementation of effective policy and interventions for indoor air pollution has been slow. Morbidity and mortality due to asthma and COPD could be prevented by the application of simple technologies and cost-effective interventions through a primary health care approach. However, at present there are major gaps in the application of these interventions, particularly in low- and middle-income countries.

8.3.2 Which aspects require further research?

Table 4 *Research priorities in chronic respiratory diseases in the context of NCD prevention and control*

Thematic area	Research priorities (top five priorities are in bold italics and are marked with *)
Identification of causes and measurement of magnitude	Estimate attributable fraction of risk of chronic respiratory disease related to tobacco smoke, solid fuel combustion, outdoor air pollution, allergens and other environmental factors * Determine the prevalence of asthma, COPD and occupational respiratory diseases and track the disease burden, risk factors and comorbidities
Analysis of problems and development of solutions	* Develop evidence-based approaches for early diagnosis and treatment of asthma and COPD through a primary health care approach with a special focus on children and elderly groups Develop evidence-based approaches for early detection of occupational chronic respiratory disease and interventions to prevent progression of disability

Thematic area	Research priorities (top five priorities are in bold italics and are marked with *)
Application of solutions and evaluation of impact	<p>* <i>Assess gaps in access to and affordability of essential technologies and medicines for asthma and COPD</i></p> <p>Estimate the impact of early detection of occupational chronic respiratory disease and interventions to prevent disability</p> <p>* <i>Study the feasibility and effectiveness of low-cost and integrated prevention and management approaches of chronic respiratory diseases through a primary health care approach concomitant with other NCDs</i></p> <p>* <i>Evaluate the impact of interventions for reducing the use of solid fuels and mitigating their effects in cooking and heating in homes and outdoor air pollution</i></p> <p>Estimate impact of interventions to reduce morbidity and mortality due to severe or uncontrolled asthma in children and disadvantaged populations</p> <p>Assess the benefits of large-scale community education campaigns and community participation in the prevention and control of chronic respiratory disease in different cultural and economic settings</p>

8.4 Diabetes

8.4.1 What is known?

There is compelling evidence that in people with impaired glucose tolerance type 2 diabetes could be prevented by lifestyle modification or medication (21). Improved metabolic control has been shown to prevent or delay complications in type 1 and type 2 diabetes. Lowering blood pressure, controlling glycaemic status, screening for high-risk feet and pre-pregnancy control of diabetes, screening and treatment of retinopathy, and screening for nephropathy have been shown to be cost effective. There is no evidence at present on how to prevent type 1 diabetes.

8.4.2 Which aspects require further research?

Table 5 *Research priorities in diabetes in the context of NCD prevention and control*

Thematic area	Research priorities (top five priorities are in bold italics and are marked with *)
Identification of causes and measurement of magnitude	<p>Determine the prevalence of diabetes and previously diagnosed and undiagnosed type 2 diabetes, including cross-sectional assessment of complications and prevalence and risk factors of gestational diabetes</p> <p>* Monitor trends in rates of major complications of type 1 and type 2 diabetes, including CVD, lower extremity amputations and blindness and end-stage renal disease</p>
Analysis of problems and development of solutions	<p>* Investigate how to identify and overcome barriers to translation of evidence-based knowledge into improved management of diabetes (medication use, technologies, health systems, culture, gender, literacy)</p> <p>Develop low-cost, reliable, non-invasive tests and blood tests for screening and diagnosis, and validation of risk prediction algorithms in different countries</p> <p>* Develop cost-effective technologies for glucose monitoring and insulin delivery, including stable insulin preparations</p> <p>* Develop models for optimal delivery of diabetes education and clinical management in low- and middle-income countries – testing and comparing different models and assessing cost-effectiveness</p> <p>Develop a cost-effective, fixed-dose combination pill to manage diabetes and other risk factors for CVD and renal disease and test its safety, efficacy, tolerance and adherence in various settings</p> <p>Develop low-risk prevention programmes with lifestyle intervention in high-risk individuals, including elderly individuals</p> <p>Develop a programme for prevention and management of gestational diabetes with lifestyle intervention during pregnancy and after delivery</p>
Application of solutions and evaluation of impact	<p>* Investigate optimal implementation and evaluation of community-based primary prevention models (for diabetes and for CVD) with particular attention to the effects of rural–urban migration and changing food preferences, physical activity patterns and transportation policies. Target high-risk individuals within the community, where appropriate</p>

NCD risk factors

8.5 Tobacco control

8.5.1 What is known?

Tobacco control measures that have been demonstrated to reduce the NCD burden and disparities include monitoring tobacco use and prevention policies, protecting people from tobacco smoke, offering help to quit tobacco use, warning about the dangers of tobacco, enforcing bans on tobacco advertising, promotion and sponsorship, and raising taxes on tobacco (22). All these measures are embedded in the WHO Framework Convention on Tobacco Control recommendations for action. Available evidence is largely from high-income countries, but evidence on the impact of each of the above measures is growing in low- and middle-income countries. Future research should prioritize design and evaluation of interventions to reduce tobacco consumption, especially in low- and middle-income country settings.

8.5.2 Which aspects require further research?

Table 6 *Research priorities in tobacco control in the context of NCD prevention and control*

Thematic area	Research priorities (top five priorities are in bold italics and are marked with *)
Identification of causes and measurement of magnitude	<p>Assess the economic impact of tobacco use and evaluate the economic impact of tobacco control (e.g. on jobs, health care costs and productivity)</p> <p>Generate information about taxation and pricing, including country-specific estimates of price elasticity</p> <p>Collate data on the use of various tobacco products, contribution of tobacco use to NCDs, implementation and enforcement of tobacco control policies, and activities of tobacco industry (marketing, pricing, lobbying, etc.)</p> <p>* Study the interrelationships between tobacco use and poverty, including the role of tobacco use in causing poverty and compromising other spending and the differential effect of tobacco control policies and programmes on the poor</p>

Thematic area	Research priorities (top five priorities are in bold italics and are marked with *)
Analysis of problems and development of solutions	<p>* <i>Optimize cessation interventions, including adaptation of effective interventions in high-income settings to low- and middle-income countries, identification of most cost-effective interventions for resource-constrained settings and integration of cessation into health systems</i></p> <p>* <i>Develop messages effective in overcoming misinformation spread by tobacco companies, building and strengthening social norms against tobacco, and building support for tobacco control policies and programmes</i></p> <p>* <i>Develop economically viable alternatives to tobacco growing and manufacturing in countries with relatively high economic dependence on tobacco</i></p>
Application of solutions and evaluation of impact	<p>* <i>Estimate the impact of tax and price policies, taking into account price elasticity, differential impact, tax structure, and effective tax administration to curb tax avoidance and tax evasion</i></p> <p>Evaluate the economic impact of tobacco control, including the impact on jobs, effects of smoke-free area policies in the hospitality sector, reduced health care costs and benefits from increased productivity</p> <p>Estimate the impact of tax increases on tobacco use (consumption, prevalence, cessation, initiation, differences for priority populations) and revenues from taxation, and the effects of tax increases on illicit trade</p> <p>In countries highly dependent on tobacco, carry out research on developing economically viable alternatives to tobacco growing and manufacturing</p>

8.6 Nutrition, physical activity and obesity

8.6.1 What is known?

The key role of nutrition and physical activity in the development and prevention of NCDs is undisputed (23, 24). Previous research has identified a wide range of dietary and physical activity behaviours that have been shown to greatly influence the risk of developing NCDs that are amenable to change and thus could make a major contribution to NCD prevention. These include high intakes of saturated and trans fat, salt and sugar; harmful use of alcohol; and a low intake of vegetables, fruit and fibre. Poor maternal diet and undernutrition in utero have also been identified as greatly influencing chronic disease risk. In addition, high levels of inactivity (especially associated with a shift to sedentary occupations) and low levels of physical activity greatly increase the risk of most major

NCDs. These factors are particularly relevant to low- and middle-income countries as they move through an economic transition.

A key pathway for the influence of diet and physical activity on the risk of NCDs is through the increasing trend towards overweight and obesity. Rates of obesity are rising rapidly across the world and it now affects a high proportion of the population of low-income countries. A diet with a high energy density, rich in fats and sugars, or both, has been associated with a greater likelihood of unhealthy weight gain. Food intake is subconsciously regulated to a surprisingly accurate degree. However, environmental pressures to eat more (including widespread marketing of inappropriate foods, price barriers to healthy selections and larger portion sizes) are now intense and these pervasive influences readily overwhelm the biological, neurohormonal attempts to regulate energy intake. In addition, energy expenditure has fallen greatly with economic development and rapid urbanization, contributing to a shift to sedentary occupations, increased sedentary leisure options, greater use of motorized transport and less activity in daily chores.

Positive effects on the risk and incidence of NCDs have been achieved through programmes that have reduced total and saturated fat intakes, reduced salt intake, reduced sugary drinks and foods and increased fibre, vegetables and fruit. Improving the level and intensity of physical activity has also had profound effects on the risk of developing NCDs. However, there is less evidence on effective strategies for achieving these changes at the population level. Social marketing programmes have been shown to be an important element in a strategy that improves awareness and supports efforts to change behaviours. There have also been successful programmes increasing fruit and vegetable intake, reducing salt and fat and controlling weight, but there is still much to be learned to make these more effective. There is a paucity of evidence around influencing maternal diet to improve health outcomes in children. There is a strong body of evidence that indicates that trying to increase physical activity by advocating leisure time physical activity would not result in population changes in activity that is sufficient to stop increases in body weight. This has major implications for urban design and other environmental and social policy measures designed to make everyday walking a routine feature of life.

8.6.2 Which aspects require further research?

Table 7 *Research priorities in nutrition and obesity in the context of NCD prevention and control*

Thematic area	Research priorities (top five priorities are in bold italics and are marked with *)
Identification of causes and measurement of magnitude	<p>* <i>Develop feasible and affordable methodologies to monitor individual intakes of salt, fruit and vegetables, red meat, total energy, fats and fatty acids and total carbohydrate quality and quantity</i></p>
Analysis of problems and development of solutions	<p>Develop economic models of structural change and behavioural programmes to demonstrate the potential benefits of specific actions to improve nutrition at the population level as well as the cost to various stakeholders</p> <p>Develop models of impact of different sectoral policies on nutrition (e.g. agriculture, trade, transport, social welfare)</p> <p>Develop methods to ensure that nutrition interventions achieve sustainable changes in behaviour</p> <p>* <i>Study the appropriate use of food regulation, legislation and price controls to improve nutrition and reduce the risk of obesity (e.g. eliminate trans fat, reduce salt in processed food and improve access to fruit and vegetables and low-fat products)</i></p> <p>Identify effective ways to address inequitable social gradients in diet in low- and middle-income countries</p> <p>Analyse the roles that the public and private sectors could play in improving nutrition in the community and identify potential positive contributions</p> <p>* <i>Determine effective programmes and policies for inclusion in a portfolio of actions to improve dietary quality and food security and prevent weight gain and obesity. These programmes may be at the individual level (e.g. behaviour modification) or at the policy level (e.g. agriculture and trade), but all should include measures of economic viability, overall effectiveness, sustainability and differential social impact</i></p> <p>* <i>Develop and validate health promotion approaches to improve nutrition programmes in schools, worksites and government institutions</i></p> <p>Develop mechanisms to reduce the impact of marketing of energy-dense, nutrient-poor foods to children</p> <p>Validate criteria and tools for defining and measuring the energy density of foods in low- and middle-income countries</p> <p>Study the effects of folic acid and vitamins B12, A and D on the development and prevention of major NCDs</p> <p>* <i>Study the role of specific food products on the development and prevention of major NCDs (palm oil, coconut oil, dairy products, meat)</i></p>
Application of solutions and evaluation of impact	<p>Evaluate the effectiveness of food labelling and signposting</p>

Table 8 *Research priorities in physical activity in the context of NCD prevention and control*

Thematic area	Research priorities (top five priorities are in bold italics and are marked with *)
Identification of causes and measurement of magnitude	<p>* <i>Develop measurement and surveillance methods for physical inactivity and sedentary behaviours (using self-report, objective methods and combinations of both) to collect population prevalence and trend data and support estimates of disease burden attributable to physical inactivity and economic cost of inactivity in adults and young people</i></p> <p>* <i>Define the individual, social and environmental determinants of physical activity and sedentary behaviours across the life course, with a special emphasis on critical developmental periods in early life (under 5 years), young life and adolescence (5–18 years) and in later life (over 65 years)</i></p>
Analysis of problems and development of solutions	<p>Develop economic models of structural change and behavioural programmes to demonstrate the potential benefits of specific actions to improve physical activity at the population level as well as the cost to various stakeholders</p> <p>* <i>Test whole-of-community, multicomponent approaches aimed at increasing physical activity and reducing sedentary behaviour (e.g. individual, social, environmental and policy actions across school, primary health care, worksite, local neighbourhood settings)</i></p> <p>Develop methods to ensure that physical activity interventions achieve sustainable changes in behaviour</p> <p>Analyse the roles that the public and private sectors could play in improving physical activity in the community and identify potential positive contributions</p> <p>Validate criteria and simple and accurate tools for assessing physical activity levels in low- and middle-income countries</p> <p>Identify components of physical activity that should be targeted to best improve physical activity levels and help prevent weight gain</p> <p>* <i>Carry out research to identify the most effective mechanisms for the adoption and implementation of the 2010 Global Physical Activity Guidelines in low- and middle-income countries</i></p>
Application of solutions and evaluation of impact	<p>* <i>Evaluate prospective cohort, quasi-experimental and opportunistic “natural experiments” involving changes in the urban and peri-urban environments, including studies of urban redevelopment, installation and modification of transport systems, changes in regulations and legislation in sectors other than health (e.g. transportation, community development, finance) to assess their impacts on physical activity and sedentary behaviours</i></p>

Cross-cutting domains

8.7 Primary health care approach for prevention and control of NCDs

8.7.1 What is known?

Cost-effective interventions are available for prevention and control of all major NCDs and have been effectively utilized in developed countries. The challenge is to deliver them equitably, within the fragile health systems of low- and middle-income countries where there are many barriers related to governance, health care financing, service delivery, health care workforce and community participation. This has resulted in major gaps in the provision of equitable care resulting in recurrent hospitalizations, catastrophic health expenditure due to complications and premature mortality. The nature and extent of these gaps have to be identified, and methods to close the gaps should be explored and evaluated through research. Only a primary health care approach can ensure patient-oriented care best suited to the long-term needs of NCDs (25). Donors need to give priority to research needs relevant to integration of NCDs into a primary health care-based health system. In resource-constrained settings, non-physician health care providers have to be trained and provided with simple aids for diagnosis of prevalent NCDs. Common service delivery models have to be developed while being aware of commonalities and synergies between HIV/AIDS and other chronic conditions.

8.7.2 Which aspects require further research?

Table 9 *Research priorities: primary health care approach for prevention and control of NCDs*

Thematic area	Research priorities (top five priorities are in bold italics and are marked with *)
Identification of causes and measurement of magnitude	<p>Develop context-specific approaches to improve the accuracy and validity of health information systems to ensure continuity of care and inform policy development</p> <p>Quantify gaps in public spending and donor support for addressing NCDs in primary care and increase their visibility in order to leverage political commitment to action</p> <p>Determine the roles and functions of all levels of the primary health care-based system as a means of explicitly defining the technologies, equipment, infrastructure, medicines and health workforce requirements for good quality NCD prevention and care</p>

Thematic area	Research priorities (top five priorities are in bold italics and are marked with *)
<p>Analysis of problems and development of solutions</p>	<p>* <i>Develop context-specific solutions to overcome health system barriers, including weak referral system and limited access to medical technology, medicines and skilled health workforce</i></p> <p>Develop health financing models that reduce out-of-pocket health care expenditure and catastrophic spending related to NCDs</p> <p>* <i>Carry out research to determine the key requirements (human resources, technologies and medicines), cost estimates and impact of implementing a core set of essential NCD interventions (e.g. for prevention of heart attacks and strokes in high-risk people, for prevention of diabetes complications including renal disease, for early detection of curable cancers, for support to tobacco cessation, for treatment of bronchial asthma) with a special focus on primary care</i></p> <p>* <i>Determine the requirements for implementing a core set of cost-effective NCD interventions at various levels of the health system, including human resources and health and biomedical technology</i></p> <p>Develop cost-effective approaches for promotive, preventive, early detection of NCD and health behaviour counselling in primary health care settings</p> <p>* <i>Develop cost-effective models for optimal delivery of patient education, improving adherence and self-care</i></p> <p>Develop means of training and improving performance of the health workforce to deliver good-quality NCD care</p> <p>Design and validate models for enabling NCD patients to become self-reliant in monitoring and managing their conditions using innovative methods, e.g. mobile phones to address issues related to health literacy, self-care, adherence to long-term therapy</p> <p>Assess the potential contribution of traditional medicine to prevention and control of NCDs</p>
<p>Application of solutions and evaluation of impact</p>	<p>* <i>Evaluate the impact of integrated service delivery models aimed at securing continuity of care across different NCDs, comorbidities, pregnancy, through various levels of health care delivery systems and through public, NGO and private sectors</i></p> <p>Conduct sector analysis studies to evaluate the role of the private health sector for prevention and management of NCDs and its impact on health equity</p> <p>Design and validate simple and reliable audit systems to monitor the impact and quality of NCD programmes in primary care in low-resource settings</p>

8.8 Social determinants and NCDs

8.8.1 What is known?

Causal pathways to NCDs are strongly influenced by social advantages and disadvantages across societies, which in turn are shaped by macroeconomic and political factors, legislation, tax systems and policies of governments and international financial institutions (11, 31). The resulting social gradients related to NCDs are seen worldwide. Most of the determinants of NCDs lie in the non-health sectors. Intersectoral action that coordinates policies among health and non-health sectors, such as education, trade, agriculture, transport and social services, is fundamental for addressing health equity as well as NCD prevention and control.

8.8.2 Which aspects require further research?

Table 10 *Research priorities in social determinants in the context of NCD prevention and control*

Thematic area	Research priorities (top five priorities are in bold italics and are marked with *)
Identification of causes and measurement of magnitude	<p>* <i>Understand the role of social determinants in prevention and control of NCDs, partly through better disaggregation of population health data in order to identify vulnerable groups</i></p>
Analysis of problems and development of solutions	<p>* <i>Develop ways of getting policies of different government departments to complement each other (whole-of-government approaches) for NCD prevention and control and health equity</i></p> <p>* <i>Study the impact of social, economic and political factors (including social protection, health services, education) on NCD outcomes and inequalities</i></p> <p>Develop legislative and regulatory frameworks that ensure means of public revenue generation and greater equity in access to health and education services</p> <p>* <i>Develop mechanisms for community participation in the design, delivery and priority setting of NCD policies, and develop mechanisms to enable civil society to play a role in advocacy, monitoring and social mobilization for addressing NCDs</i></p> <p>Conduct a systematic analysis of all NCD policies and services to improve gender equity and rural–urban gradients</p> <p>Identify means of cultivating responsible media that encourage social dialogue and debate on issues of inequity and social responsibility</p>
Application of solutions and evaluation of impact	<p>Generate evidence on the effectiveness of measures to reduce health inequities related to NCDs through action on social determinants</p> <p>* <i>Design, implement and evaluate pro-poor NCD prevention and control programmes</i></p>

8.9 Genetics

8.9.1 What is known?

Globally at least 7.6 million children are born annually with severe genetic or congenital disorders. Nearly 90% of these infants are born in low- and middle-income countries. In high-income countries a range of interventions, including folic acid food fortification, routine administration of anti-D for rhesus negative mothers, genetic counselling, carrier screening programmes, prenatal diagnosis, newborn screening and curative paediatric surgery, have considerably reduced the prevalence of congenital and genetic disorders (26). These programmes have shown that the introduction of genetic approaches requires a pervasive adjustment in health care systems, and offer some useful but scattered models of how to meet this need. Requirements include (i) basic genetic education for primary health care professionals; (ii) adaptation of medical information systems to hold family histories and retain lifelong genetic information; (iii) surveillance of disease prevalence and the effects of interventions through registries; and (iv) community involvement in genetic screening. They also show an inescapable need for trained community-based genetic counsellors to support primary and secondary care by taking genetic family histories, providing genetic information and counselling, and linking primary and secondary care, and the community, with specialist services and DNA laboratories.

In the context of NCDs, “cascade” family testing and DNA genotyping for risk of family cancer syndromes is an example of a successful intervention. Recently, cascade testing for risk of familial hypercholesterolaemia, including carrier diagnosis by DNA genotyping, has been officially recommended in the United Kingdom. The experience from these programmes confirms the need for an organized infrastructure for community genetics services.

Successful interventions are not limited to high-income countries. Recessively inherited haemoglobin disorders (sickle cell disease and thalassaemia), which are common in sub-Saharan Africa and Asia, have been successfully managed in some countries by rather simple interventions including prevention programme, early diagnosis and the provision of adequate treatment. Oculocutaneous albinism is an easily recognized genetic risk factor for skin cancer, but risk could be prevented by simple interventions such as wearing a broad-brimmed hat and long-sleeved clothing and the use of sunscreen. However, these simple and cost-effective approaches will be generally applied only if the value of genetic approaches in health care is recognized in lower-income as well as high-income countries.

8.9.2 Which aspects require further research?

Table 11 *Research priorities in genetics in the context of NCD prevention and control*

Thematic area	Research priorities (top five priorities are in bold italics and are marked with *)
Identification of causes and measurement of magnitude	<p>* <i>Develop methods and instruments for assessing the health and economic burden of genetically determined disorders</i></p> <p>Assess the country-specific distribution of carrier prevalence, affected births and outcomes for affected children in terms of survival and access to and quality of care for sickle cell anaemia and thalassaemia</p> <p>* <i>Monitor ethical, social and legal issues concerned with implementation of new genetic knowledge in health care practice</i></p>
Analysis of problems and development of solutions	<p>* <i>Develop approaches applicable in primary health care for genetic risk assessment, information and counselling</i></p> <p>Investigate the role of genetic risk factors in targeting drug treatments in primary health care</p> <p>Develop approaches to facilitate equitable access to low-cost genetic testing and treatment of genetic disorders</p> <p>Adapt medical record systems to include genetic and family history information</p> <p>Develop informatics approaches for delivering information for health decision-makers, and instruments for professional education and information for patients and the community</p> <p>* <i>Develop community genetics services, based on genetic approaches in health care at all stages of life</i></p> <p>Develop service models for control of single gene disorders in low- and middle-income countries</p> <p>Develop locally appropriate approaches for carrier screening of haemoglobinopathies and information about reproductive risk and availability and acceptability of options for reducing it</p> <p>Investigate requirements for patient care and cost-effective models of care to address birth defects, including haemoglobinopathies</p> <p>* <i>Develop cost-effective tools for delivering information on genetic disorders for health decision-makers, for patients and the community and for professional education</i></p> <p>Design an integrated service combining patient care and prevention through carrier identification and genetic counselling in relation to birth defects, including haemoglobinopathies</p>
Application of solutions and evaluation of impact	<p>Implement and evaluate preventive approaches for birth defects: (i) before pregnancy (e.g. folic acid food fortification, detection and counselling for carriers, such as sickle cell anaemia or thalassaemia); (ii) during pregnancy (e.g. fetal anomaly scanning and other forms of prenatal diagnosis); (iii) at the end of pregnancy (anti-D to prevent rhesus haemolytic disease in subsequent pregnancies); (iv) in the newborn period (neonatal screening)</p> <p>Assess changes in affected birth prevalence and patient outcomes in response to interventions addressing birth defects, including haemoglobinopathies</p>

8.10 Promoting use of research findings to policies and practice for prevention and control of noncommunicable diseases.

8.10.1 What are the factors that affect research utilization?

There are a number of issues beyond the actual research that affect research utilization – many of them relating to context (27). Studies from low- and middle-income countries show that research has the highest impact when it is of high quality and based on good empirical data and simple analysis. A facilitating factor for producing high-quality research is long-term collaboration with an international research institute. Personal contact between researchers and policy-makers during the research, and the production of research briefs focused on decision-makers' needs, also assist success. Research should be timely and balance immediate with longer-term issues in order to be utilized by policy-makers. Cross-country comparisons are viewed as particularly useful, and it is a plus if the research is perceived as independent. Preferably, the interventions should have multiple outcomes (for example, target barriers and facilitators or operate at different levels in society). Research should be carried out with the appropriate collaborators so that the research could be used to build consensus for change among stakeholders. Furthermore, those presenting the research must carry authority in order to make an impact.

Various networks, such as the Evidence-Informed Policy Network (EVIPNet) launched by WHO, may serve as important sources of information for policy-makers, together with sources such as the Cochrane Library, which contains systematic reviews of health system research. Think tanks that can deliver timely and credible research and advice in the right format, and regional networks and supranational organizations that can enhance policy leverage of national and local civil society organizations, could serve as two institutional models that would be effective.

8.10.2 Which aspects require further research?

Table 12 *Research priorities in promoting use of research findings to policies and practice for prevention and control of noncommunicable diseases in low- and middle-income countries*

Research priorities (top five priorities are in bold italics and are marked with *)
<ul style="list-style-type: none">* <i>Study contextual factors in relation to knowledge translation and research utilization to inform measures to facilitate research use, including policy diffusion and readiness and capacity of (health) systems to accept and implement policies and programmes</i>* <i>Study the interactions of competing interests groups, actor networks, and policy frames and their impact on utilization of evidence</i>* <i>Investigate the relationship between different sectors in society in dealing with NCDs, including how links between research institutions and public health agencies can contribute to NCD prevention and control</i>* <i>Investigate how lifestyle measures and policies (regulatory and legislative) affect personal choices, business opportunities and societal organization and how they in turn impact action</i>* <i>Develop cost-effective approaches for translation of evidence-based health promotion interventions</i>
Develop conceptual frameworks and analyses of research–policy–practice processes to better understand research utilization (or lack thereof)
Investigate how links between research institutions, public health agencies and other public agencies related health can contribute to NCD prevention and control
Better understand the political realities and power relations between various stakeholders that may hinder research uptake

9. Top 20 priority areas for NCD research

Based on the three consultations conducted in 2008/2009, the extensive review in 2010, the results of the ranking process conducted in 2010, the key research priorities identified in different NCD domains have been condensed and summarized below as the top 20 priority areas for research in NCD prevention and control.

a) Research for placing NCDs in the global development agenda and for monitoring NCDs and NCD risk factors

- Research to monitor country-specific information on risk factors, disease burden, and time trends and their economic and social costs and impact of globalization and urbanization on behaviours, in order to make the policy case for political leadership to give high priority for NCD on the development agenda
- Research to assess the economic impact of tobacco use, to evaluate the economic impact of tobacco control (e.g. on jobs, health care costs, and productivity) and to investigate the interrelationships between tobacco use and poverty

b) Intersectoral and multidisciplinary research to understand and influence the macroeconomic and social determinants of NCDs and exposure to NCD risk factors

- Research to determine the impact of NCD prevention and control policies on social inequities in populations and to develop Interventions for reducing them, e.g. design, implement and evaluate pro-poor NCD prevention and control programmes
- Research to develop comprehensive and cost-effective sets of interventions (policy, environmental and health systems) to address NCD risk factors (tobacco use, indoor air pollution from solid fuel combustion, harmful use of alcohol, physical inactivity and unhealthy diet) in diverse cultural and economic settings and evaluate their effectiveness
- Research to estimate the impact of tax and price policies, on tobacco use and tobacco control, taking into account country-specific price elasticity, differential impact, tax structure, and effective tax administration to curb tax avoidance and tax evasion

- Research to determine effective programmes and policies to improve dietary quality and food security and prevent weight gain and obesity (e.g. behaviour modification programmes, agriculture and trade policies), including measures of economic viability, overall effectiveness, sustainability and differential social impact
- Research to investigate the appropriate use of food regulation, legislation and price controls to improve nutrition and reduce the risk of obesity (e.g. eliminate trans fat, reduce salt in processed food and improve access to fruit and vegetables and low-fat products)
- Research to understand the individual, social and environmental determinants of physical activity and sedentary behaviours across the life course
- Research on optimal implementation and evaluation of community-based primary prevention models (e.g. for prevention of CVD and diabetes), with particular attention to the effects of rural–urban migration and changing food preferences, physical activity patterns and transportation policies
- Research on ways to mobilize community resources (e.g. develop mechanisms for community participation in the design, delivery and priority setting of NCD policies), and develop mechanisms to enable civil society to play a role in social mobilization for addressing NCDs
- Research to evaluate changes in the urban and peri-urban environments, including studies of urban redevelopment, installation and modification of transport systems, changes in regulations and legislation in sectors other than health (e.g. transportation, community development, finance) to assess their impacts on physical activity and sedentary behaviours

c) Translation research and health system research for global application of proven cost-effective strategies

- Research to validate cost-effective screening approaches (e.g. for cancer and other NCDs), risk prediction methodologies and clinical algorithms (e.g. to identify people at high risk of developing diabetes and CVD) that are applicable to low- and middle-income country settings
- Research to establish and evaluate cancer prevention strategies in the context of local culture and local resources (including primary prevention, effective early detection, cost-effective vaccination programmes for hepatitis B and oncogenic human papilloma viruses)

- Research to assess gaps in availability and affordability of essential medicines and basic technologies and develop strategies to address these gaps
 - Research to identify contextual factors in relation to knowledge translation and research utilization to inform measures to facilitate research use, including policy diffusion and readiness and capacity of (health) systems to accept and implement policies and programmes
 - Research to determine the key requirements (human resources, technologies and medicines), cost estimates and impact of implementing a package of essential NCD interventions (e.g. for prevention of heart attacks and strokes in high-risk people, for prevention of diabetes complications including renal disease, for early detection of curable cancers, for support of tobacco cessation, for treatment of bronchial asthma) with a special focus on primary care
 - Research to define health system-related opportunities and barriers to access for early detection, diagnosis, treatment, rehabilitation and palliative care and develop feasible and integrated approaches to apply cost-effective NCD interventions at all levels of health care
 - Research to develop effective tools for training of health workers for NCD prevention and control and innovative approaches for evaluation and improvement of their performance with a special focus on the primary care workforce
 - Research to develop cost-effective approaches to deliver patient education, improve adherence and strengthen self-care
- d) Research to enable expensive but effective interventions to become accessible and used appropriately in resource-constrained settings**
- Research to improve affordability of expensive but effective technologies for diagnosis and treatment of NCDs in the context of varying resource settings and health care systems (e.g. cost-effective investigative and surgical procedures for CVD and cancer and radiotherapy techniques for cancer)

10. Key elements required for strengthening the research capacity of low- and middle-income countries for implementation of the WHO NCD Research Agenda

The basic prerequisites for health research systems are well recognized and include a national research policy, leadership, a competent research workforce, adequate financing, priority-setting mechanisms, regulatory frameworks, ethical oversight mechanisms, adequately equipped research institutions and effective information and dissemination systems (32). Nevertheless, there is presently a serious mismatch between the rising NCD burden and the research capacity and research output in many low- and middle-income countries (33, 34). The reasons for the low output of research include (i) inadequate training of professionals and poor infrastructure for research; (ii) lack of funds for research; (iii) absence of effective leadership and peer support in research; and (iv) absence of a tradition of research in many low- and middle-income countries. Furthermore, in low- and middle-income countries, research is often funded from external sources and addresses donor-driven research priorities that may not be appropriate for the local context.

If support can be provided to build indigenous research capability, then local studies can be undertaken to translate the results of studies carried out elsewhere into individual national settings. The critical elements required for strengthening research capacity in low- and middle-income countries are:

- strengthening the competence of researchers through appropriate training;
- strengthening the infrastructure, equipment and supplies in research institutions;
- providing sustainable funding for research;

- assisting researchers to identify priority national problems that require research solutions;
- leveraging and aligning the activities of all societies, associations, networks and partners dealing with NCDs to strengthen national NCD research efforts.

Research capacity development should also enhance research sustainability and train national professionals and scientists in order to obtain competitive grants and discourage brain drain. National research institutions should draw up a roadmap for NCD research and the associated research capacity needs for the country in the medium-to-long term. One important mechanism for addressing research capacity in low- and middle-income countries for prevention and control of NCDs is to create international collaboration through the development of partnership research projects of high quality similar to the ones that have been used in tropical disease research with good results (35). Partnership grants could link one or a number of research groups in low- and middle-income countries that have developed a high level of scientific competence with one or more partners in high-income or low- and middle-income countries with a similar research agenda. In this way, the resources and strengths of the institutions are pooled for the greater benefit of low- and middle-income country institutions. Such partnerships would provide more opportunities for training younger scientists from low- and middle-income countries. It would also help them increase the capacity of the individual scientists and their institutions to conduct quality research. This process is not as one-sided as is sometimes believed. Researchers from developed countries who go to work in developing countries are on a steep learning curve and gain capacity from the skills and experience of their collaborators. Thus, partnerships are mutually beneficial to scientists from both high-income and low- and middle-income countries.

It is important that donors and partners build and support international collaborations at the institutional level rather than just at the project or individual levels. Donors need to provide sufficient funds to develop country institutions to enable them to generate and support research activities, such as creating offices to manage contracts and grants, and schemes for faculty development.

The professional training of NCD specialists in low- and middle-income countries should include training in research so as to enable them to practise evidence-based decision-making in their professional work, to read research publications critically and to engage in relevant research. They should also be the ones to develop norms about diseases and health

problems that occur in their own environment, while using norms and standards from high-income countries for comparison. Results of research are also needed by governments to enable them to determine how to spend scarce resources on prevention and control of NCDs. This means that training in research and research methods should be at the forefront of efforts to strengthen capacity for prevention and control of NCDs in low- and middle-income countries. Such training should cover key areas, including writing research proposals, research methods, protocol development, data collection and analysis, report writing and presentation and writing of research results for publication and summaries as policy briefs. The required training could take the form of short workshop-type training for clinicians to introduce them to methods and techniques of research, while longer training (such as PhD) is appropriate for those wishing to undertake careers in teaching and research. After this type of longer-duration training, research clinicians should benefit from a re-entry grant (or similar facility) to enable them to initiate research in their institutions. Experience in training for research has also shown that it is advisable to invest in high-level training of long duration for young people who are more likely to have long and productive periods doing research. There is an urgent need for each low- and middle-income country to develop a dynamic policy for training and sustaining the indigenous research capacity with a focus on priority research areas to address the growing burden of NCDs.

There must be plans for the deployment of staff after training and establishment of suitable research career structures. In addition, all health personnel working at the district level should be given research orientation. There should be strong commitment of governments to the entire process of having their own strong national research groups for undertaking relevant research, including research in NCDs needed for national development.

In 1990, the Commission on Health Research for Development found that only 5% of the total funds spent on research were addressing the problems of the developing world, which was bearing 93% of the global burden of disease (36). The Commission called for an increase in investment in research and set targets of 2% of national health expenditure and 5% of international official development assistance. Very few low- and middle-income countries have demonstrated progress towards the 2% target. Two decades later, the situation has not changed appreciably. Currently, under 10% of the world's biomedical research funds are allocated to address problems behind 90% of the world disease burden, which occurs in low- and middle-income countries (28).

On the positive side, health research funding has increased fivefold over the last two decades to the current level of approximately 160 billion euros per year (37). The public sector accounts for 41%, the private for-profit sector for 51% and the private not-for-profit sector for 8% of the funding. Despite the overall increase in resources for research and development, significant gaps have emerged. First, investment in NCD research does not match the public health threats posed by the rapidly rising NCD epidemic. Second, there is a gap between what is known to maximize NCD outcomes and what is being delivered in practice. Third, there is inadequate research investment to address the needs of currently underserved populations. It is, therefore, essential that public research funding is coherently aligned with the WHO NCD Research Agenda and is geared to making an impact on the NCD burden.

The European Commission supports WHO on implementing certain elements of the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property. Global health research is also supported by the European Commission under the Framework Programmes of the European Union (38). Currently, the main focus of these programmes includes HIV/AIDS, malaria, tuberculosis and emerging epidemics and support for the European and Developing Countries Clinical Trials Partnership.

WHO is an observer of the Global Alliance for Chronic Diseases, which was formed in 2009 to support research on NCDs. Charter members of the alliance are the Australian National Health and Medical Research Council, the Canadian Institutes of Health Research, the Chinese Academy of Medical Sciences, the United Kingdom Medical Research Council, and the United States National Institutes of Health (specifically its National Heart, Lung, and Blood Institute and the Fogarty International Center). WHO will facilitate Alliance support for implementation of the Global Strategy Action Plan (39).

Enhanced investment in NCD research remains an urgent need, particularly to address training, retention of research workforce and the weak research capacity in low- and middle-income countries. Given the major shortfall for NCD research, it is necessary to avoid fragmentation of funding and align all available funds, public subsidies and incentives for meaningful research on the key areas identified by the WHO NCD Research Agenda.

The WHO NCD Research Agenda has been developed to address the fourth objective of the Global Strategy Action Plan. The objective is to provide guidance to national NCD research activities so that public health action and priority health needs related to NCDs are grounded in high-quality scientific evidence. For effective implementation of the WHO NCD

Research Agenda, it will be necessary to have the resources and commitment to NCD research at regional, national and global levels, results-based collaboration with partners, and adequate staffing and funding at all levels of WHO. Before the WHO NCD Research Agenda is moved from development into implementation it needs to be aligned with regional research priorities (40–42). Context-specific national adaptations will also be required. Based on the input from the third WHO consultation in October 2010, an implementation plan is being developed to define roles and responsibilities and to identify the outcomes and impacts expected within a defined time frame.

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List of Working papers

(Please see compact disc)

Paper 1. Research priorities: *Prevention and control of cardiovascular diseases, with a focus on low- and middle-income countries.* Geneva, World Health Organization, 2011.

Paper 2. Research priorities: *Cancer – prevention, early detection, screening, treatment and palliative care.* Geneva, World Health Organization, 2011.

Paper 3. Research priorities: *Chronic respiratory diseases in low- and middle-income countries.* Geneva, World Health Organization, 2011.

Paper 4. Research priorities: *Diabetes prevention and control in low- and middle-income countries.* Geneva, World Health Organization, 2011.

Paper 5. Research priorities: *Tobacco control.* Geneva, World Health Organization, 2011.

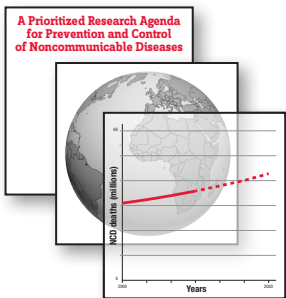
Paper 6. Research priorities: *Nutrition and obesity, with a focus on low- and middle-income countries.* Geneva, World Health Organization, 2011.

Paper 7. Research priorities: *Physical inactivity, with a focus on low- and middle-income countries.* Geneva, World Health Organization, 2011.

Paper 8. Research priorities: *Primary health care approach for prevention and control of noncommunicable diseases.* Geneva, World Health Organization, 2011.

Paper 9. Research priorities: *Genetics for prevention and control of noncommunicable diseases.* Geneva, World Health Organization, 2011.

Paper 10. Research priorities: *Promoting use of research findings to policies and practice for prevention and control of noncommunicable diseases in low- and middle-income countries.* Geneva, World Health Organization, 2011.



Key messages

- NCD policies and programmes need to be based on sound scientific evidence generated by research, particularly in resource constrained settings.
- Research is essential to bridge the “knowledge translation” and “implementation” gaps.
- Investment in implementation research can improve effectiveness of programs and save resources.
- The prioritized NCD research agenda provides a basis for strengthening cooperation among the research community.

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