ICMR–MRC Workshop

Building Indo–UK Collaboration in Chronic Diseases

2009
ICMR – MRC
Workshop on Chronic Diseases

4-5 November 2009, New Delhi, India

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Global transition patterns in health are being witnessed in developing countries as well, wherein considerable success has been achieved on tackling infectious diseases, nutrition, maternal and child health related issues. Chronic Noncommunicable Diseases (NCD) are gaining importance as causes of premature morbidity and mortality in India, and are likely to impact overall national growth and development.

The Medical Research Council (MRC), UK has contributed to outstanding health research. ICMR is committed to foster research leading to improvement of health status and outcome. The ICMR-MRC Memorandum of Understanding aims to harness the efficiencies of both agencies in addressing the epidemic of NCDs. It will create opportunities for sharing of knowledge, expertise and strengthening capacities of mutual importance.

I am very pleased to note the success of the joint ICMR-MRC workshop organized in New Delhi on 4-5 November 2009 in developing a collaborative research agenda. I wish these efforts best wishes for a fruitful partnership.
In the past millennium, the world has witnessed a gradual and progressive shift in ill-health patterns. Research links this to trends in urbanization, industrialization, globalization occurring in countries, and the emergence of differing disease types. While infectious diseases, maternal and child health were being conquered, the developed countries were burdened with an increasing load of Noncommunicable Diseases (NCDs- cardiovascular diseases, cancers, diabetes, chronic respiratory diseases, mental illnesses, and injuries) in the early decades of this century. It is now well established that the occurrence of these diseases are governed by a cluster of risk factors which in turn are determined by factors influenced by our socio-economic-cultural milieu. The NCD epidemic is posing serious hazards for human health as well as economic progress, while stretching the meagre health systems and economic resources. Lessons and experiences gained during the past decades are a vital asset for utilization through collaboration.

The Indian Council of Medical Research (ICMR) and Medical Research Council, UK (MRC-UK) sought to work together in addressing the increasing problem related to NCDs in populations of both countries. These countries have a long standing era of collaboration in which scientists have been working in various aspects of health research. The ICMR-MRC collaboration is expected to provide a thrust to this endeavour by facilitating interaction amongst investigators from both countries.

This workshop aims to set the agenda for research activities to be pursued over the next few years towards mitigating the chronic disease problems in populations of both countries.
International partnerships are a crucial element of contemporary research, vital to address the enormous problems facing the planet today. This is especially important in the field of biomedical research and MRC views co-operation with agencies outside the UK as central to its mission to improve human health. Such co-operation is now facilitated by the establishment over the last few years of Research Council UK Offices in the USA, China and most recently India.

There is a long history of collaboration between individuals or groups of Indian and UK researchers, based on a long historical relationship, and none more so than in biomedicine. Building on this base, the recent MoU between ICMR and MRC will bring a greater formality and structure to such collaborations. Both agencies have long histories dating back to the early part of the twentieth century and both have shared values and a common vision with regard to the funding of research which will provide a greater understanding of the origins of disease and promote improvements in human health.

Chronic diseases such as cardiovascular disease, stroke, diabetes and chronic obstructive lung disease became the principle causes of death and disability in the UK during the twentieth century. With changing demography, i.e. economic development, urbanisation, nutrition transition etc, there is now a growing epidemic of these diseases in the Indian population.

Both ICMR and MRC recognised the importance of new research to tackle these epidemics by joining the initiative to identify the grand challenges in chronic diseases published in 20071.

ICMR and MRC have now come together in this workshop to try and dissect out some areas from the potentially very broad research agenda, where Indian and UK researchers could, in collaboration, undertake studies which would inform the situation in both countries. We at MRC think that there is a real opportunity to learn from each others experiences to try and make a real difference to health outcomes in this enormously important area.

Introduction and background

The world faces a devastating health crisis. The lives of far too many people are being blighted and cut short by chronic diseases such as heart disease, stroke, diabetes, cancer and chronic respiratory diseases. This is no longer happening only in high income countries. Four out of five chronic disease deaths today occur in low and middle income countries, with people developing disease at younger ages. Chronic disease now accounts for more than 50% of all premature mortality worldwide. What unites all of these is that they are largely preventable and that they are rooted in behaviours in modern society – specifically smoking, poor diet and lack of exercise. The WHO estimates that with appropriate actions, it should be possible to prevent 36 million of deaths globally of which 17 million would be in those under 70 years of age.

An enormous amount of research has already been undertaken in the broad area of chronic disease by both Indian and UK agencies. The purpose of this ICMR-MRC workshop is therefore to consider what has already been achieved and the extent to which past research findings have successfully fed through into policy and practice – what has worked and what has not.

The following questions will be addressed:

- Strengths and weaknesses of current research landscape – unmet needs
- Capacity / capability to respond to unmet needs in chronic disease research in India. What are the roadblocks and how can these be overcome?
- Potential areas for developing evidence – based research programmes in India
  - What are the key research questions that need to be addressed in order to make a significant public health impact?
  - What should be done – scoping and developing specific research activity?

It is hoped that this workshop will identify strengths and weaknesses of the current research landscape and set the agenda for new evidence-based intervention programmes for the two agencies involved.
SESSION I

Burden of Chronic Disease in India and the UK
The Burden of Cardiovascular Disease in India

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Mortality Burden: In India there is paucity of reliable mortality data using vital registration systems. Prior to the year 2000, mortality data from the Registrar General of India were predominantly obtained from rural populations where vital registration varied from <1 to 15%, and was inadequately compiled. The first phase of the Million Death Study has reported mortality statistics from all Indian states using the national Sample Registration System units. Causes of deaths in 113,000 subjects were analysed using a validated verbal autopsy instrument. Cardiovascular diseases accounted for 1.7-2.0 million deaths annually and were the single largest cause of deaths in men (20.3%) as well as women (16.9%).

Mortality Data: Hospital-based statistics have revealed an increasing burden of CVD patients (acute coronary heart disease (CHD) and stroke) in the country. Increasing trends in CVD are observed both in the government and non-government healthcare systems and hospitals. The World Health Organisation (WHO) has predicted that from years 2000 to 2020 Disability-Adjusted Life Years (DALYs) lost from CHD will double in both men and women from 7.7 and 5.5 million. CHD diagnosed using history and ECG changes trebled in both urban and rural adults from mid-1960s to 10% and 5% in 2000. Similar trends are observed for stroke prevalence. There are no long-term CHD incidence data. Stroke incidence registries using population-based surveillance have reported that age-adjusted annual incidence of stroke varies from 100-150/100,000 population. Cross sectional studies provide only limited information on burden of diseases and have multiple limitations.

Risk factors: The increase in CHD and stroke in India is largely an urban phenomenon and only recently reports indicate a rise in rural populations. There are no prospective studies from the country that have identified risk factors of importance. The case-control INTERHEART study reported that standard risk factors such as smoking, abnormal lipids, hypertension, diabetes, high waist-hip ratio, sedentary lifestyle, psychosocial stress, and lack of consumption of fruits and vegetables explained more than 90% of acute CHD events in South Asians. Similar conclusions were reached using urban-rural comparisons in risk factors and smaller case-control studies.

Trends in risk factors: Multiple epidemiological studies to identify prevalence of CHD and stroke risk factors have been performed in different regions of India. Although most suffer from multiple biases inherent to population based prevalence studies, they have provided important information. Tobacco production and consumption has increased significantly in India. It is increasing among the illiterate and declining in the highly literate. Prevalence of hypertension defined using either older or more recent criteria has increased in both urban and rural populations and is 25-40% in urban and 10-20% in rural subjects. Lipid levels are increasing and serial studies from an Indian urban location reported increasing mean levels of total, LDL and non-HDL cholesterol and triglycerides and decreasing HDL cholesterol. Although there are large regional variations in prevalence of diabetes, it has more than quadrupled in the last 20 years in urban as well as rural areas. Studies have reported increasing obesity as well as truncal obesity and increasing sedentary lifestyle and psychosocial stress.

Prevention strategies: Finally, the major challenge for Indian cardiovascular epidemiology is to develop strategies to respond to the threat from these diseases especially in the young.
**Research Needs**

**Mortality Burden:**
1. To improve the vital registration system.
2. Prospective studies in different regions of the country to correctly identify trends in incidence and risk factors.
3. Identification of genetic differences and functional genomics

**Trends in Risk Factors:**
1. Studies, with a national perspective, to identify determinants of risk factors and “causes of the causes” or social determinants of risk factors, using cross-sectional and prospective designs.
2. Population based adult cohorts to track risk factors.
3. Study association of risk factors and CVD using prospective design.
4. Case-control study designs for rapid assessment of risk factors.
5. Studies for risk factor biology and genomics.
6. Validation of developmental origins of adult diseases and utilizing birth cohorts.

**Prevention Strategies:**
1. Studies in Indian subjects that address primordial, primary, and secondary prevention in community-based, high-risk population-group-based or individual-based settings.
2. Population based primary prevention studies that target either multiple risk factors or are focused on individual factors. Interventions include smoking and tobacco control, dietary modifications and measures to enhance physical activity.

**SUGGESTED READING**

Cardiovascular Disease in Indian Asians in the UK

The greater susceptibility of people of Indian Asian descent to cardiovascular disease (CVD) was first clearly identified in studies of migrant populations. In the latter part of the twentieth century, reports emerged of a 1.5 to 2 fold excess mortality from cardiovascular disease in Indian Asian migrants to developed countries such as the UK and Singapore, compared to the host or other populations living in the same setting, or indeed compared to the population of the Indian subcontinent itself. Explanations for this excess risk were unclear, prompting research to explore this phenomenon in more detail. This report focuses on the work performed in the UK to define and better understand cardiovascular disease risks in people of Indian Asian descent.

Mortality data from the UK consistently show that both men and women of Indian Asian descent have 1.5 times the mortality from heart disease and stroke compared to the general population. Within the migrant population, there is a gradient of increasing risk from Indians, with around a 20% increase in risk, through people of Pakistani descent, with a 50% increase in risk, to people of Bangladeshi origin, with a 100% increase in risk. Nevertheless, all these subgroups share an excess risk of CVD compared to people of European origin, thus any explanations must also be shared.

Both routine national survey data, and detailed epidemiological studies, demonstrate considerable heterogeneity between these ethnic minority subgroups in terms of conventional cardiovascular risk factors. Smoking rates, for example, are only elevated in Bangladeshi men, and in all subgroups almost non-existent in women compared to their European counterparts. Cholesterol levels are similar, and blood pressure similar or lower in Indian Asian migrants compared to Europeans. But prevalence of diabetes, hypertriglyceridaemia, and central obesity are greater in all Indian Asian subgroups. These are all features of the metabolic syndrome, which is known to increase the risk of CVD, but whether this can also account for the excess CVD risk in Indian Asians requires longitudinal data.

The Southall and Brent cohort, established around 1990, studied over 4000 individuals in middle age from a population sample in West London. Over 20 years of follow-up, mortality from heart disease was indeed elevated in Indian Asian men compared to European origin men. Statistical adjustment for socioeconomic status did not alter this excess risk. The only risk factor that could begin to account for this excess was diabetes. However, when all other components of the metabolic syndrome were accounted for, it was clear that a large amount of the excess risk was unaccounted for. Interestingly, however, there was an indication that the presence of diabetes, or indeed hyperglycaemia, increased the risk of CVD to a greater extent in Indian Asians than Europeans. Stroke mortality is also elevated in Indian Asians in the UK, even though resting blood pressure appears to be lower. Again it is diabetes that better tracks to the inter-ethnic risks of stroke, and may directly increase the risk, overwhelming any protective effect of lower blood pressure.

Paradoxically, risks of peripheral vascular disease are low in Indian Asians compared to Europeans. This can only in part be accounted for by lower smoking rates, and emphasizes that the balance of important risk factors for atherosclerosis vary according to site. The adverse risk factor profile observed in middle age is already established in youth. A study of children, aged between 10 to 12 years, showed increased fasting insulin and triglyceride levels in Indian Asians compared to Europeans.
Longitudinal survey data suggests that Indian Asian adults have not benefited as much as the general population in favourable trends in CVD risk factors, such as blood pressure decline, and may be experiencing a greater impact of adverse trends, such as obesity and diabetes. Thus it is clear that Indian Asians are at greater risk of CVD than people of European origin. This cannot be explained by socioeconomic status, or by dietary factors (as while all ethnic subgroups share an excess risk of CVD, there is considerable heterogeneity in dietary patterns). It is not wholly explained by the metabolic syndrome, although it does appear that diabetes increases CVD risk to a greater extent in Indian Asians, and may explain the excess stroke risk despite favourable blood pressures. Explanations for this are unclear. The adverse CVD risk factor profile that forms the metabolic syndrome is already established in youth in Indian Asians, and there is evidence that the risk factor differential between Indian Asians and Europeans in the UK is increasing.

### Research Needs

1. **Life course studies – impact of combined over/undernutrition on diabetes and cardiovascular risk.** The CVD/diabetes epidemic in India is likely to share many similarities to that already observed in Indian Asian migrant adults to the UK. There are some important differences, one of which is the co-existence of both under and over nutrition in the same population, family, and indeed individual over the life course.

2. **Impact of low cost lifestyle/pharmaceutical interventions to reduce the burden of diabetes and CVD.** Building on the success of the Indian DPP, there is a need to design, test and evaluate complex family based lifestyle interventions, coupled with a feasible, low cost health care delivery service to treat those with established risk factors (eg hypertension, diabetes). This would importantly require economic and policy analysis.

### Suggested Reading


India has the highest population of people with diabetes, with a consistent increase in prevalence over the past few decades. The reasons for this increasing prevalence, the differences in phenotype, the standards of care and the economic impact of diabetes in India are all areas for research.

The latest edition of the Diabetes Atlas of the International Diabetes Federation reports that the estimated prevalence of diabetes in India in 2010 is approximately 51 million, which is likely to rise to 87 million by 2030. This contrasts with the earlier prediction of 57 million people with diabetes by the year 2025 made in 1998. It suggests that the rise of prevalence is significantly in excess of the projections made as recently as a decade ago. The increase in numbers is not only a consequence of increasing population but is also contributed to by an increase in prevalence. The Diabetes Atlas reports an adult prevalence of diabetes to be between 7-9% currently and anticipates an increase to 9-12% over the next two decades. This is consistent with secular trends reported in regional studies performed in India. From an urban prevalence ranging from 1.5-3% in the 1970s, the current prevalence of diabetes in adults from metropolitan India has risen to between 15-18%. Nation-wide studies indicate that the peak prevalence occurs in the 6th and 7th decades of life, with prevalence rates ranging from 27-31%. The other area of concern is the rising prevalence in the socio-economically disadvantaged sections of society. From a situation, a century ago, where diabetes was only reported in the affluent, recent data have shown that within industrial populations, there is a higher prevalence of all coronary heart disease risk factors including diabetes in the those with the lowest educational and economic status. This high disease prevalence has also translated to a significant loss of quality of life. In an assessment by the Indian Council of Medical Research, it was estimated that diabetes results in 1,156,822 YLLs and 2,263,163 DALYs lost annually.

The risk factors associated with diabetes in India are age, BMI, central adiposity, lack of physical activity and family history of disease. The prevailing belief is that the contributory factors for the higher prevalence of diabetes in India include the following: early life influences (including fetal programming), higher body fat and preferential deposition of upper body fat, increased insulin resistance and probable genetic factors. In the presence of these underlying factors, urbanization, industrialization and changes in lifestyle have further driven the increasing prevalence.

An area of concern is the sub-optimal standard of clinical care as evidenced by failure of a significant proportion of patients reaching treatment targets. In a study acquiring information from diabetology clinics, it was reported that the proportion of patients with the following parameters was: 8% with proteinuria; 50% with dyslipidemia; 15-30% with uncontrolled systolic and diastolic blood pressure. Equally disturbing was that even among patients attending specialty diabetes clinics, more than 50% had an HbA1c value more than 2% above the target A1c, and nearly 75% had HbA1c values more than 1% above the target. This suboptimal control of metabolic and vascular parameters probably contributes to the high burden of chronic complications in India. It has been estimated that assuming 50 million people with diabetes live in India, the numbers with various complications would approximate as follows: 9 million with retinopathy, 1 million with nephropathy, 13 million with neuropathy, 10.5 million with coronary heart disease and 3.2 million with peripheral vascular disease.
Despite this, awareness about this disease continues to be low, even in urban India. In a study, 25% of urban Indians were not even aware of a disease called diabetes, only 20% of the general population and 40% of those with diabetes were aware that it is possible to prevent diabetes. Less than one in eight people were aware of the risk factors associated with the disease, and even among people with diabetes only 40% knew that the disease was associated with chronic complications and organ damage.

Probable barriers to improving control were different for health care professionals and patients. Physicians felt that the lack of available guidelines, absence of consensus on targets and parameters to be tested, and clinical "inertia" to address unacceptable parameters contributed to poor metabolic control. In contrast, patients felt that reluctance to take insulin, self-monitor and test frequently, lack of knowledge about the disease and economic constraints contributed to poor control. A few small studies have looked at the cost of disease and it was estimated that the annual cost of care per person (including direct and indirect) was approximately Rs. 20,000 (~$350) annually.

In conclusion, the key issues for concern are high and increasing prevalence in parallel with increasing urbanization, multiple modifiable risk factors associated with disease, high complication rates, and a significant economic cost and adverse impact on quality of life.

**Research Needs**

1. Compare phenotypic differences between patients of Indian and European descent with the view to identifying factors in disease biology contributing to pathogenesis.

2. Gene-environment interactions contributing to disease causation: there are emerging GWAS data in patients with diabetes in India, which can form the basis of planning further studies.

3. Multi-site, multi-approach intervention studies for diabetes prevention: to consider individual (diet, lifestyle), family, community and policy based intervention strategies. In view of early disease onset and the rising prevalence of childhood obesity especially in middle and high income groups, strategies targeting children / adolescents would be preferable.
The Burden of Diabetes in the UK

One in 25 people in England and Wales has diabetes, the equivalent of, on average, at least one child in every school class developing the disease during their lifetime. This equates to 2.35 million people in England (4.7%) with diabetes. The majority have type 2 diabetes, coming on typically in those over forty and those over-weight. Because type 2 diabetes has a slow onset, we know that there are considerable numbers of undiagnosed cases – estimates vary but a conservative view would be that perhaps another quarter million would be found by systematic screening. The number of people with diabetes in England and Wales is predicted to reach 2.5 million (5.05%) this year.

The epidemic
The problem is not that of simply having a higher than normal blood sugar: half of those with diabetes will die from a diabetes-related condition, the average life expectancy is reduced by about six years and the risk of major medical complications is up to eleven times that for people without diabetes. The morbidity includes major amputation, retinopathy, renal failure and myocardial infarction. Those with diabetes are five times as likely to need hospital admission. The result is that huge resources need to be expended on an epidemic which is essentially preventable – preventable because the majority of diabetes is predicated on obesity, the risks increasing 37 fold as the BMI ranges from 23 to 35 (fig).

If diabetes is preventable in theory (by avoiding obesity) then can it be prevented in practice? Three trials suggest that prevention is possible – both the Diabetes Prevention Study and the Diabetes Prevention Programme showed that with vigorous and active intervention the incidence of new diabetes was reduced by 58%. The problem with these trials was that the level of intervention needed was intensive and needed to be reinforced. The intervention could never realistically be rolled out to a community.

BMI and risk of diabetes

The solution will lie in using multiple stakeholder interventions. This entails many different individuals and organizations. The process is well illustrated in the campaigns against the use of tobacco. In countries where there is strong taxation, warnings on packets, bans on sales to minors, bans on advertising, bans on smoking in public places and on public transport, tobacco use declines and the health of the nation improves. The knowledge of what part of the campaign is successful is irrelevant – what matters is that the combination of actions results in less smoking. With obesity the problem is more complex because the advice needs to be more complex. In the case of smoking the message is simple: “don’t”. But we all need to eat and most do some exercise. We face a complex problem where we need to encourage more exercise and fewer calories. The issue will need many agencies and significant investment – but it is achievable. Nor must we be captured by the strident voices that demand proof of each facet of any campaign before any concerted action is taken.
Research Needs

The Grand Challenges, written in 2007 and published in Nature¹, delineated how one should approach the research questions. There were six goals, 20 Grand Challenges and 39 steps that would break the problem into manageable aspects. The Goals were:

A. Raise public and political awareness
B. Enhance economic, legal and environmental policies
C. Modify risk factors
D. Engage businesses and community
E. Mitigate health impacts of poverty and urbanization
F. Reorient health systems

The challenges included items such as “Study and address the links between the built environment, urbanization and chronic non-communicable disease” while the steps included finer detail: “Study the motivations behind domestic expenditures, and how these affect lifestyle choices” and “Investigate the impact and effectiveness of food labelling legislation”. The next challenge will be to undertake the work. The epidemic is upon us.

SUGGESTED READING

Chronic Obstructive Pulmonary Disease, COPD, is a major health care burden globally. Its prevalence is increasing each year and this rise is much faster in the developing world. According to WHO estimates, about 80 million people worldwide have moderate to severe COPD and more than 3 million people died of COPD in 2005, which corresponds to 5% of all deaths globally. As projected by the Global Burden of Disease study, COPD is expected to rise to 3rd position as a cause of death and to 5th position as the cause of disability adjusted life years, DALYs, lost by the year 2020. Recent estimates from India suggest that in 2005 chronic diseases accounted for 53% of all deaths and 44% of DALYs lost, with chronic respiratory disease accounting for 7% deaths and 3% DALYs lost. More recent studies suggest that this burden from chronic respiratory diseases (mainly COPD) is rising at an alarming rate.

It is estimated that there are more than 12 million adults with COPD in India with prevalence rates varying depending upon the population studied and the methodology used. In males the prevalence has varied from 2.12% to 9.4% in north India and from 1.4% to 4.08% in south India. Similar patterns are reported in women, with lower rates in the south but the prevalence amongst women is consistently lower in men. There is a strong association between tobacco smoking and COPD and exposure to indoor air pollution, due to use of traditional cooking fuel (biomass), is also an important cause of disease in India. The economic cost of treatment of COPD is significant. It is estimated that more than 103 billion Indian Rupees are spent each year to treat patients with COPD. It is also believed that in India COPD is a widely under diagnosed and under reported. The disease burden therefore may be much more.

Considering the increasing prevalence of tobacco usage in India it is expected that the next decade will see a spiralling increase in the number of cases together with the associated health burden. There is therefore a need to look at different factors contributing to the occurrence of COPD and interventions that may help to decrease the burden of disease or improve prognosis and quality of life.
Research Needs

1. Studies with a standard protocol for accurate detection of prevalence of COPD in rural and urban areas.
2. Studies to look at genetic and ethnic factors that predispose to the development of COPD.
3. Studies to look at the effect of poor socioeconomic status, diet, environmental pollution and childhood infection on development, progression and mortality in COPD.
4. Studies to look at cheaper and more acceptable treatment options like non pharmaceutical intervention (yoga, pranayam etc.) in improving prognosis and quality of life in COPD.
5. Studies to evaluate the economic burden of the disease.

SUGGESTED READING

Chronic Obstructive Pulmonary Disease (COPD): A UK Perspective

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COPD has now become a major global epidemic with rising prevalence and mortality. It is predicted that by 2020 COPD will become the 3rd commonest cause of death and 5th commonest cause of chronic disability in the world. There is a major unmet therapeutic need as currently treatments are only poorly effective and no treatments reduce progression or mortality. The average prevalence of COPD is ~10% in men >40 years and in developed countries is now as frequent in women. There is variability in prevalence between countries, but the most rapid increases in prevalence are in developing countries.

COPD is thought to be due to chronic inflammation of the respiratory tract, which is mainly induced by inhaled irritants such as cigarette smoke. But only ~20% of smokers develop COPD so other factors such as genetic influences are involved. It is now recognised that COPD goes beyond the lungs and there are systemic manifestations, such as muscle weakness and cachexia, as well as an association with several co-morbid diseases, such as ischemic heart disease, heart failure, metabolic syndrome, osteoporosis and depression, all of which may be linked through systemic inflammation.

In the UK cigarette smoking accounts for ~70% of COPD and stopping smoking reduces disease progression. There are several poorly understood non-smoking causes of COPD, including chronic asthma, exposure to other air pollutants, previous lung infections and possibly autoimmunity. COPD is strongly linked to poverty. Non-smoking COPD is more prevalent in developing countries. In the UK (population 60m) there are 30,000 deaths/year in COPD patients – the commonest causes of death are cardiovascular disease, lung cancer and respiratory failure. More women now die from COPD than breast cancer in the UK. The prevalence of COPD is ~10% over 40 years but over 50% of patients are undiagnosed and therefore untreated. COPD is one of the common causes of acute hospital admissions in the UK. The medical costs of COPD in the UK are ~£1bn/year and rising. COPD is also a major reason for loss of time from work (~40% of COPD patients are below retirement age, >24m days lost/year).

COPD is one of the major unaddressed needs in the world. COPD is a major unmet medical need in India; it is currently the second commonest cause of death (million deaths study) and a WHO study (2002) showed that chronic respiratory disease affected approximately 65m people in India, whereas cardiovascular diseases affected 20m, diabetes 25m and stroke 1m. Thus COPD is a major cause of morbidity and mortality in India, and yet there is very little funding spent on research into this important disease. We have already started a productive collaboration with the Chest Research Foundation, Pune to understand the nature of non-smoking COPD.
Research Needs

1. Further UK-Indian collaboration would speed and facilitate understanding of COPD.

2. More accurate epidemiological surveys to assess disease burden together with studies of inexpensive interventions (such as low dose theophylline).

3. Studies of the poorly understood natural history, mechanisms or treatment response of non-smoking COPD in India where smoking accounts for only about 50% of COPD.

SUGGESTED READING


The recognition of the relevance of mental disorders in the larger issue of the burden of health problems for human populations occurred with the introduction of the concept of Disability Adjusted Life Years (DALYs), and the paradigm shift from mortality statistics to morbidity data. The World Development Report (WDR) 1993 highlighted the importance of the burden of health problems in development, including chronic diseases like mental disorders. The World Health Report (WHR) 1999 clearly cited the quantitative information in support of the relevance of mental disorders, with the information that the three major contributors to Global Burden of Diseases were cardiovascular disorders (10%), neuropsychiatric conditions (9%) and cancers (5%), based on 1990 data on DALYs. This led to the World Health Report of 2001 being specifically dedicated to the theme of mental health.

In 1990, it was predicted that by the year 2020 Unipolar Major Depression will be the 2nd ranking contributor to DALYs. This projection has proven to be more than correct, in as much as the 2004 data suggest that unipolar major depression is the top ranking contributor to DALYs across countries and gender. It is now well recognized that the burden of mental disorders is one of the four leading causes of disability, and the most significant contribution is from depression. The contribution to the Global Burden of Diseases (GBD) is already at 12% and is expected to be 15% by the year 2020. If the productive age group of 15 to 44 years is considered, the contribution to the GBD will be 40%. The fact that a sizeable proportion of mental disorders in general, and depressive disorders in particular, are chronic in nature and disabling, has unequivocally brought the acceptance of mental disorders, and specifically depression, as one of the major public health problems.

Some Important Considerations/Trends: Urban Mental Health Service Needs – Treatment Gap, Stress Related Problems, Marginalized Populations: There is definite evidence for mental health problems being higher in prevalence in urban populations as compared to rural populations. Meta analysis of the epidemiological studies in India till the end of the twentieth century reveals that the prevalence for “all psychiatric disorders” was 48.9/1,000 in rural populations and 80.6/1,000 in urban populations. Recent ICMR studies in a multi site research project in urban settings have revealed a treatment gap of 77%, and have also identified contributing factors for the gap. Further, significant proportions of populations are also found to have stress related psychological/mental health problems. This is important for planning mental health services and the interface between psychological ill health and physical health problems. The need for planning mental health services for marginalized populations like the homeless, including destitute women, has been recognized and some workable models of service delivery are being demonstrated.

Mental Health as part of Health- Co-morbidity in Medical Practice, Chronic Disability as Multiple Disability: There is a good amount of evidence for co-morbidity of medical conditions with psychiatric disorders not only in clinical practice but also in community studies. Moreover, the course and outcome of the medical conditions is significantly contributed to by the psychiatric disorder and its treatment. The chronic disability being contributed to by multiple conditions of a physical and psychological nature is emerging as a major theme. There is a need to explore the concept of sub-syndromal mental health problem (SMHP) for its impact on disability and chronicity. The oft repeated dictum of mental health being a part of health, needs to be further strengthened.
Cross National and Cross Cultural Issues in a Globalised World – Health Services Research, enlarging definitions of mental disorders, human rights issues, the role of the pharmaceutical industry: The emphasis in cross cultural research has been on clinical presentations and the course of mental disorders but it needs to move to issues of Health Service Research (HSR) and other public health aspects. The strategies for reducing the treatment gap across different countries and cultures need to be compared and contrasted. The controversy of the ever enlarging definition of mental disorders and the criticism of being driven by pharmaceutical industry pressures or psychiatricising normative human experiences is also becoming unavoidable. The clamour for more autonomy driven treatment decisions for mental disorders and disability benefits for persons with mental disorders needs to be addressed.

Research Needs

1. Urbanization and its impact on mental health.
2. Medical and psychiatric co-morbidity and multiple disability.
3. Cross national issues in Health Services Research.
4. Strategies to reduce the treatment gap.
5. Stress related mental health problems.
From Chronic ‘Diseases’ to Chronic ‘Conditions’ – a Primary Healthcare Research Agenda for Low Resource Settings

The over-burdened primary health care systems of low resource settings need pragmatic models of care which address a diverse range of health conditions. In this context, the relevant distinction is not between communicable and non-communicable disorders but between acute and chronic problems. Such a conceptualization offers the most affordable and feasible way ahead to address the large and growing burden of chronic conditions in low and middle income countries in primary care.

I propose a change of terminology from chronic diseases to chronic conditions, based on the criterion of the natural course of the health condition and the expected duration and complexity of the interventions (Panel 1). By replacing the term ‘disease’ the emphasis shifts from a biomedical, top-down, orientation to health systems responses to these conditions. Hallmark examples of chronic conditions include diabetes; hypertension; elevated cholesterol levels; obesity; depressive disorder; alcohol use disorders; tobacco use; post-acute CVS; dementia; HIV/AIDS; and cancers.

Panel 1: What defines a chronic condition

- It is ‘silent’ (i.e. asymptomatic) for extended periods; by the time symptoms appear, the window of opportunity for prevention has been lost
- It requires a package of treatments, both pharmacological and psychosocial, with facility and community based elements, tailored to the needs of the individual,
- These need to delivered over extended periods of time to achieve optimal health outcomes

The conflation of chronic conditions with specific biomedical categories not only undermines the very rationale for the concept, but risks further fragmentation of already weak health systems struggling to scale up comprehensive primary health care. It is simply not realistic, or desirable, to have separate approaches for this diverse range of disorders which, in spite of different aetiologies and biomedical features,
share many characteristics from a health system point of view. Apart from the health system issues, in particular the response in primary care, which justify our conceptual framework; there are many biological reasons too for treating these conditions together: many share similar risk factors and influence each other’s course and outcome (Panel 2).

### Panel 2: Interactions between different chronic conditions

- Co-morbidity due to shared risk factors, for e.g. alcohol and tobacco use
- Co-morbidity due to interactions, for e.g. vascular disease enhancing the risk of dementia
- One condition affecting the course and outcome of another, for e.g. depression worsening the outcomes after an acute CV event
- Co-morbid influences on household members, e.g. stroke leading to depression in caregiver

There are a number of pragmatic advantages of integrating these conditions apart from the potential of leading to scalable interventions. First, the growing evidence base from high income settings on integrated chronic disease management models may become relevant for modification and evaluation in low resource settings. There are a range of approaches to improving delivery of chronic disease care that could be used but they need evaluation including at scale. Second, there can be cross-fertilisation between the disciplines; for example, the growing evidence base on task shifting for complex interventions for mental disorders may be relevant to other chronic conditions.

### Research Needs

1. How to improve detection through opportunistic and pro-active case finding.
2. How to improve initiation of evidence-based treatments, typically a combination of health education, generic drugs and counselling tailored to individual needs.
3. How to maximise optimal outcomes and reduce risk of acute events/relapses through proactive monitoring and adherence support.
4. How to reduce disabilities and support affected family members through community based rehabilitation.
5. How to involve the private and non-profit sector in a population based chronic condition health care program.

### Suggested Reading

SESSION 2
Current Research Activity in Chronic Diseases
ICMR was established in 1911 as an autonomous organization under the Ministry of Health and Family Welfare, Government of India, to undertake and support basic, epidemiological, applied and operational research in the areas of national public health importance using appropriate tools, including those of modern biology. It has a network of 26 permanent institutions spread out across the country. It collaborates with local health departments, universities, medical colleges and other research institutions. Since 5 October 2007, ICMR is one of the ten business allocations of the newly formed Department of Health Research (DHR), Government of India.

The Council has collaboration with agencies, institutions and organizations outside India to promote capacity building of resources and exchange of knowledge. Joint projects are peer reviewed and the Indian investigator is funded under a formal MoU agreed to and signed by both countries. Collaboration is also encouraged through workshops, seminars, delegation visits, and exchange of scientists.

The Division of NCD has been steering multi-disciplinary research throughout the country by funding peer reviewed investigator driven research proposals and commissioning Task Force and Mission Projects. The major subject areas are cancer, cardiovascular diseases, neurosciences, diabetes, mental health, NCD surveillance, environmental and occupational health, while emerging areas like obesity and metabolic syndrome, trauma and injuries have been added. An important aim of its research is to encourage translation of knowledge from basic to applied sciences which can be utilized for public health benefit.

The National Cancer Registry Program (NCRP) was launched in 1982 and currently has 5 hospital and 14 population based registries, and 5 sites in the North-East part of the country. The Cancer Atlas has mapped out cancer related information for the entire country. Thrust areas in oncology research have been cervical, oral and breast cancers, screening of cervical cancer and management guidelines. Tobacco (including smokeless forms) related research includes mechanistic pathways of damage, advocacy for control, economic analysis and supporting the Tobacco Control Act, India. The rheumatic fever/heart disease registry provides epidemiological data amongst school going children at the study sites, and research on vaccine development. Studies of the genetic basis of salt sensitive hypertension and fetal origins of coronary heart diseases are undertaken. Other ongoing and proposed databases and registries focus on acute coronary events, diabetes, stroke and trauma. An ICMR advanced centre on genomics of type 2 diabetes has been established at Chennai. Guidelines on Management of type 2 diabetes have been developed for use at peripheral level. The NCD risk factor surveillance research undertaken has been successfully translated to the national Integrated Disease Surveillance Program (IDSP). An assessment of the Burden of NCDs in India and Causes of Death by Verbal Autopsy provides an insight into the magnitude, and highlights the major causes of adult deaths in different states of the country. The urban Mental Health project has provided an important contribution to the national knowledge and action bank, focused on disaster outcomes especially following the Tsunami and Gujarat earthquakes.
Research Needs

In order to utilize the ICMR-MRC collaboration for building research proposals which address public health needs by addressing knowledge for action we need to:

1. Provide robust evidence on the determinants and pathways from susceptibility to causation of disease through comparable studies in the UK and India.

2. Build systems for effective surveillance and monitoring of trends of diseases and their determinants, and assessing impact of interventions.
Research into the Aetiology and Prevention of Type 2 Diabetes

The rising prevalence of type 2 diabetes and related metabolic disorders is a major public health problem, particularly among populations of people of South Asian origin in whom the disease is especially prevalent. The descriptive epidemiology of the condition suggests that it arises from an interaction between innate susceptibility, either due to genetic predisposition or early programming, and adult lifestyle behaviours particularly dietary and physical activity behaviour. Identification of the underlying basis of these interactions is a major scientific challenge. Previous studies have shown that intensive lifestyle intervention is effective in reducing progression from pre-diabetes to diabetes, demonstrating that diabetes is preventable. However, there is major uncertainty about how to operationalise pragmatic approaches to high risk prevention and also how to appropriately balance investment between high risk and societal approaches to prevention.

Aetiological research into gene-lifestyle interactions on diabetes risk

Although much is known about the broad patterns of lifestyle behaviours that are associated with type 2 diabetes, there is considerable uncertainty about the detail of these associations which limits the precision of public health recommendations. In the case of dietary and nutritional factors, most previous studies have utilized imprecise measurement instruments such as food frequency questionnaires which are inaccurate and potentially biased by under-reporting. Efforts to improve questionnaires or resolve issues of precision and bias by statistical means may be limited, justifying enhanced efforts to develop and apply novel objective biomarkers of nutritional intake. Such biomarkers would be particularly necessary for investigation of nutritional and dietary explanations of ethnic differences in diabetes risk. Similar efforts are also necessary for objective assessment of physical activity behaviour. Questionnaire assessment is a limited approach which is sufficient to demonstrate an overall association but cannot quantify overall activity, distinguish between sub-dimensions or analyse dose-response relationships. Progress has been made in developing and validating objective measures of physical activity and these are now being applied in large scale epidemiological studies. The precision of measurement of these key lifestyle exposures is critical to the study of gene-lifestyle interaction which is likely to be impossible in studies with poor assessment of these important but difficult to measure exposures.

Realising the potential health benefits of diabetes prevention

Previous studies have demonstrated that pharmacological therapy and lifestyle intervention are effective in reducing the risk of progression from impaired glucose tolerance to diabetes, showing that diabetes is preventable. However, there are considerable uncertainties about how to prevent diabetes in the real world. In the case of pharmacological interventions, the major uncertainty is related to the impact of treatment on the long term clinical endpoints rather than simply change in glucose levels. There is a major need to evaluate the long term benefits of cheap and safe glucose lowering therapy in people at high cardiovascular risk who have non-diabetic hyperglycaemia. The impact of lifestyle intervention, in contrast to that of pharmacological treatments, is sustained beyond the duration of the intervention, but its impact on long term clinical outcomes has also not been demonstrated. The choice of appropriate target group for high risk prevention strategies (rather than people with IGT) and the demonstration of effectiveness of simplified interventions are important and researchable topics. Finally, the same lifestyle behavioural targets apply not only to individuals at high risk, but also...
to whole populations. Indeed, the impact of preventive interventions on diabetes risk is likely to be greatest at the population level for strategies that are aimed at entire sub-sections of society at moderate risk rather than smaller groups at high risk. Although the notion of societal shift in key behavioural factors is critical to dealing with the public health epidemic of diabetes, little research effort has been aimed at understanding the determinants of the population distribution of those behaviours nor in evaluating population-level interventions. A critical issue is the development of approaches to balancing investment in individual approaches, which have a high evidence base as they are amenable to evaluation by randomized controlled trial experiments, compared to the potentially more important societal prevention strategies that are supported by weaker forms of data such as natural experiments rather than RCTs.

### Research Needs

1. Comparable studies in India and the UK of the association between objectively assessed diet and physical activity behaviour and risk of progression to diabetes, to provide the basis for public health recommendations and to allow the investigation of these behaviours as the explanation for differences in diabetes risk between ethnic groups.

2. Studies in India and the UK of the long term health impact of cheap and safe glucose-lowering therapies in people at high risk of cardiovascular disease who have non-diabetic hyperglycaemia.

3. Studies in India of the population determinants of objectively measured diet and physical activity behaviour as a step towards the development of population approaches to diabetes prevention.

4. Development of evaluation strategies for major population-level natural experiment interventions which impact on dietary and physical activity behaviour.

5. Development in the UK and India of strategies for balancing investment in individual and societal approaches to chronic disease prevention.
Fetal Programming of Chronic Disease

Professor Chittararanjan Yajnik
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Current models of diabetes and related disorders suggest a genetic predisposition and precipitation by obesogenic lifestyles, usually in adult life. Diabetes prevention trials have concentrated on post-reproductive men and women with obesity and impaired glucose tolerance. This strategy has been thought of as ‘primary’ prevention. However, the escalating epidemic of obesity and diabetes now affects younger and poorer populations. This may be substantially related to intrauterine programming. The pioneering research in this field has been done in the UK and in India. Active groups in this area belong to an organization SNEHA (Society for Natal Effects on Health of Adults), which was started 15 years ago.

Two well known intrauterine programming influences for obesity and diabetes are: 1) maternal obesity and diabetes (Freinkel’s ‘fuel-mediated teratogenesis’) and 2) maternal undernutrition (‘nutrient-mediated teratogenesis’). Thus, both low and high birth weight are associated with diabetes. However, the real interest is in the programming events related to intrauterine environment which cause fetal programming. Research in Pune has shown that maternal dietary factors like green leafy vegetables, milk and fruit have a programming effect. Further analysis revealed that nutrition of vitamin B12 and folate which influence 1-C (methyl) metabolism could be at the heart of fetal programming of adiposity and insulin resistance. Moreover, vitamin B12 deficiency may predispose to gestational diabetes and thus contributes to the ‘dual teratogenesis’ which will accelerate fetal programming of obesity and diabetes. An additional risk factor for diabetes is rapid childhood growth, especially in those born small. Maternal 1-C metabolism is also an important determinant of fetal neuro-cognitive development, thus making an important contribution to human capital.

Fetal programming in rapid transition

Given their pioneering role, India and UK are well placed to contribute to this important research. This will have long term effects on the health of the populations.
**Research Needs**

1. The formation of a consortium of related research groups from India and UK to provide a platform for regular meetings and discussions.

2. Continued follow up of established cohorts, include advanced methodology to study the biology of programming.

3. Interventions in the young to improve the health of the next generation.

4. Setting up a new large cohort of pregnant women in India and the UK (migrant Indians and white Europeans) to study genetic, intrauterine and postnatal environmental contributions to the risk of chronic disease.

5. Genetic and epigenetic studies to define the mechanisms of fetal programming.


**SUGGESTED READING**


Obesity Research: Indo-UK Collaborations

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India is undergoing an epidemic of obesity, diabetes and coronary heart disease. Indians, living in India or the UK, appear to be particularly vulnerable to obesity, which has major cost implications for the health resources of these countries. Adoption of urban lifestyles is clearly important, while the role of genetics and early undernutrition needs to be elucidated further. At the same time as the obesity epidemic, substantial proportions of the population suffer from undernutrition leading to the double burden of disease, with one exaggerating the other.

The collaborative studies in which I am involved with several of my UK and Indian colleagues have included follow up of children born in nutritional supplementation trials and of families migrating from rural to urban areas. They have delivered some important insights, such as amelioration of excess cardiovascular risk in undernourished adolescents who received nutritional supplement in childhood, and in the case of urban migrants, a discordant rise in obesity in early years of migration, particularly in those from lower socio-economic groups. Further work on these cohorts is now being carried out to examine the phenotypic changes in greater detail and to look at the genetic make-up, seeking clues on how the environment interacts with genes. It appears that interaction between undernutrition in early life and overnutrition in later life may hold the key to the increased risk of obesity and related conditions in Indians. These studies were characterised by large scale collaborations, the use of innovative study designs and value for money.

Both undernutrition and overnutrition in childhood appear to lead to the same end result of heart disease, diabetes and other chronic conditions; childhood nutrition appears to be at the cross-roads of most adult chronic conditions. These conditions are important both in India and the UK and any potential gains in knowledge will benefit both countries and their health budgets. Addressing nutrition in childhood is also likely to prove more cost-effective in long term because of longstanding impact.
Research Needs

1. Studies on nutrition, particularly childhood under- and over-nutrition.

2. Focus on intervention studies and delivery of interventions: one central question (for which we have no prior models to learn from) is: how does one address undernutrition and overnutrition simultaneously in a population through public health programmes where both co-exist, since addressing one may worsen the other?
Life-course Influences on Chronic Disease

Consideration of life-course influences on later outcomes involves the full panoply of potential factors that can affect disease risk. As figure 1 shows social and biological processes are seen in reciprocal relationships – for example adverse social circumstances in childhood can influence lung development through, for example, exposure to passive smoking and/or influences on growth in utero. This will in turn lead to increased susceptibility to childhood chest illnesses, which may be detrimental to educational achievement. The latter will impact on the socioeconomic trajectory related to exposures such as occupational hazards, poor adult diet and smoking, further exacerbating the rapidity of decline in lung function.

Given the all-encompassing nature of life course influences on later outcomes, the following studies outline ways of strengthening causal inference. It is clear that identifying such processes from within the highly inter-correlated net of potential influences is problematic.

An important issue in investigating how factors acting before conception, through fetal development and infancy into adult life, can influence health outcomes is the separation of causal from confounded associations. This can be illustrated by considering possible outcomes of breastfeeding. In rich countries, such as the UK, breastfeeding is strongly associated with favourable socioeconomic circumstances, and therefore it is unsurprising that for many outcomes – from risk of infection, through blood pressure and obesity, to respiratory function and cognition – babies who are breast fed do better as children, adolescents and adults. It is, however, possible to carry out investigations in contexts where breastfeeding is not associated with socioeconomic position. We have compared the association of breastfeeding with various outcomes in the ALSPAC birth cohort (from mothers recruited when pregnant in 1991-1992 in Bristol, UK, with ongoing follow-up) and the Pelotas 1993 cohort (involving long-term follow-up of infants born in 1993 in South Eastern Brazil). In ALSPAC breastfeeding is very strongly related to family income, whereas in Pelotas this is not the case. Blood pressure, body mass index and IQ were examined as outcomes. Income in ALSPAC is related to lower body mass index in children, whereas in Pelotas it is related to higher body mass index; in ALSPAC higher income is related to lower blood pressure in childhood whereas in Pelotas there is no consistent association of family income with blood pressure. In both contexts higher family income is related to better cognitive function. Therefore, if confounding by socio-economically patterned factors generated the associations, it would be expected that breastfeeding would be related to lower body mass index in ALSPAC, but would not be related to body mass index in Pelotas; similarly it would be expected that breastfeeding would be related to lower blood pressure in ALSPAC but not in Pelotas. Finally it would be expected that breastfeeding would be related to higher IQ in ALSPAC, but not in Pelotas. The findings are that breastfeeding is indeed related to lower body mass index and lower blood pressure in ALSPAC but not in Pelotas. However in both contexts breastfeeding is related to higher IQ. This pattern of results suggests that associations of breastfeeding and body mass index/obesity and blood pressure are due to confounding, whereas the associations with IQ are not. A large-scale randomized controlled trial of breastfeeding promotion in Belarus, where by-randomization data are available, suggests that there is no causal effect of breastfeeding on either blood pressure or body mass index/obesity, but there is a causal effect on IQ. Thus comparing the associations in the two contexts produces evidence in line with data from randomized controlled trials.
With respect to intrauterine exposures the degree of confounding can sometimes be estimated by comparing the association between exposures experienced by the mother during pregnancy and outcomes among the offspring, with the association of exposures experienced by the father during the pregnancy period and offspring outcomes. If the effects are due to an intrauterine exposure, then maternal exposure during pregnancy should have a clearly greater influence than paternal exposure. A different approach is that of Mendelian randomization, which utilizes genetic variants of known functional effect that can proxy for modifiable exposures. If carried by the mother, these variants would influence the intrauterine environment experienced by her offspring. These genetic variants are stable over time, are not related to confounding factors and can be assessed after pregnancy is complete or even after outcomes in the offspring have been observed.

**Fig. 1 Lifecourse influences on respiratory disease**
Adapted from Ben-Shlomo & Kuh 1999

**Research Needs**

1. Investment in a large birth cohort study, recruited antenatally, with complete family follow-up and comprehensive biological sample, exposure and outcome assessment, would provide a powerful resource for investigating lifecourse influences on chronic disease in adults and their offspring.

**SUGGESTED READING**


NHLBI Centres of Excellence for Chronic Diseases

Chronic diseases, especially heart disease and stroke, diabetes, lung diseases, and cancer, account for around 60% of all deaths globally, twice the number of deaths from infectious diseases, maternal and perinatal conditions, and nutritional deficiencies combined. Populations in developing countries are disproportionately affected by chronic diseases, with 80% of deaths occurring in low- and middle-income countries and more individuals developing chronic diseases at younger ages than those in higher income countries.

With action, however, 36 million premature deaths worldwide could be averted by 2015, according to the World Health Organization (WHO), with nearly half prevented in people under 70 years old.

In a response to this global challenge, the National Heart Lung and Blood Institute (NHLBI) of the US National Institutes of Health (NIH) has established a network of nine collaborating centres of excellence, with funding for five years, to combat chronic diseases in developing countries. UnitedHealth (Ovations) is co-funding six of these centres and also two others. Each centre is a partnership between a developing country and a developed country institution. The centres are shown in the diagram below, and as an illustration, the structure and proposed activities of the New Delhi centre are briefly described.

New Delhi Centre Activities: The New Delhi Centre for Cardiometabolic Risk Reduction in South Asia (CARRS) is led by the Public Health Foundation of India with Emory University as the developed country partner. The All India Institute of Medical Sciences in Delhi and the Madras Diabetes Research Foundation in Chennai are network partners in India, and Emory also has a sub-contractual arrangement with the Aga Khan University in Karachi.

Given the emergent proportion of disease burden from the South Asia region, the serious dearth of research capacity, inadequate surveillance data, gaps in implementation of proven interventions, as well as heterogeneity in access and care delivery in the region, the New Delhi Center (CARRS) will concentrate on population-based applied research and training. It will primarily focus on establishing a robust applied science base through two complementary activities: (a) development and implementation of a model sentinel surveillance scheme capturing population-based cardiometabolic risk factor data among representative samples of 4,000 each in Delhi and Chennai (a similar scheme will be implemented in Karachi), with follow-up for incident events, and a repeat cross-sectional survey on independent samples after four years to assess population changes and (b) a randomized controlled translation trial to evaluate implementation of low-cost, multifactorial, multi-faceted, innovative, scalable and sustainable delivery improvement strategies (incorporating a low-cost care coordinator and a decision support system) for CVD risk reduction among 1,200 people with diabetes at eight sites. CARRS will leverage its infrastructure and other opportunities to build local capacity and leadership by offering opportunities for training in applied research. In addition to strengthening inter-disciplinary applied research infrastructure and capacity in care delivery, it will connect science with policy and programs, achieving realistic, demonstrable gains in disease prevention and control.
NHLBI/Ovations Centers of Excellence and Developed Country Partners

Centre of Excellence Country
Developed Country Partner
Administrative Coordinating Center
Research Needs

1. Expand population-based surveillance and applied research for cardiovascular disease and diabetes. A large cohort study, which can serve as a laboratory for interdisciplinary collaborations – combining the benefits of large population studies with small carefully characterized investigations that are locally relevant.

2. Implement translational research trials aimed at testing low-cost innovative strategies for effectively delivering proven efficacious interventions (e.g., primary prevention of diabetes; secondary prevention of cardiovascular disease through better control of blood pressure, lipids, glucose, and better use of aspirin, ace-inhibitors/ARBs). The strategies for improving delivery could include low-cost pharmacology (e.g., polypill or wider use of generics) or testing of disease management approaches (e.g., care coordinator, decision support systems, referral methods, shared care between primary and secondary services).

3. Utilize and leverage existing research networks (e.g., NHLBI COE) so that duplication can be avoided.

Suggested Reading


Translating Gene Identification into Biological Insights and Clinical Advance

Despite the global importance of type 2 diabetes (T2D), in terms of consequences for both health and economic wellbeing, there remains poor understanding of the biology involved in diabetes development and profound uncertainty over the ways in which genetic predisposition and environmental exposures jointly contribute to disease risk. Although many of the key environmental risk factors are known, capacity to manipulate these effectively to achieve prevention is manifestly limited, and, once diabetes has been diagnosed, available treatments are unable to remove the spectre of serious complications.

Given this scenario, basic research into the biology of disease causation has the potential to underpin future clinical translation, and needs to be considered hand in hand with urgent efforts to forestall the impact of diabetes using currently available tools. Genetic research offers one of the routes to achieving this, and recent technological advances in susceptibility gene discovery give confidence that substantial inroads into a molecular understanding of T2D pathogenesis are possible. Whilst improvements in biology are the principal focus of these endeavours, genetic discoveries also have the potential to inform personalized medicine: this may extend to enumeration of the mechanisms underlying the particularly strong propensity of South Asians to develop diabetes and its complications.

So far, discovery efforts (predominantly in European-descent populations) have identified close to 40 common variant signals with proven roles in T2D susceptibility (around 20 of these have been published to date, the others represent as yet unpublished data). By and large, when these signals have been evaluated in samples of East and/or South Asian origin, the risk-alleles have been found to have very similar effects. This suggests that, despite recent divergence of non-African descent populations, the common variant effects are shared, and reflect our shared ancestry. It seems more likely therefore that the genetic contribution to explaining qualitative and quantitative differences in diabetes presentation lies in the low frequency and rare variants that are the current focus of much genetic discovery research.

The mutual strengths of research in the UK and India should ensure that research makes an important contribution to the development of effective and appropriate strategies for clinical translation in terms of diagnostics, therapeutics and public health measures. It is important that this exciting potential effort at international research collaboration does not focus exclusively on currently available measures to forestall the impact of diabetes, but also builds infrastructure and research capital that can underpin the future advances that will be necessary.
Research Needs

1. Extend the search for common variants to major population groups. Several such studies are underway in samples from South Asian populations resident in the UK and Singapore, but there would be great merit in combining these with equivalent studies in samples from India.

2. Extend the search for rare and low frequency variants to all major population groups.

3. Make use of different population histories to map causal variants.

4. Explore the biology of the signals identified.

5. Understand the joint effects of genes and environment and the ways these map onto differences in risk, prevalence, phenotype, complications and therapy, so that we can ensure that the translational lessons learned have local relevance. Several of the key studies underway within India (including for example the Indian Migration Study, and the Pune collections) provide unique resources for extending such research.
The South Asia Network for Chronic Disease (SANCD)

South Asia Network for Chronic Disease (SANCD) is funded by the Wellcome Trust (WT) through a £4.5m strategic award to the LSHTM and the Public Health Foundation of India (PHFI). SANCD is based in New Delhi and comprises existing research groups led by University of London and Bristol investigators and Indian partner organizations in Mumbai, Goa, Chennai and Pondicherry. It has developed links with ICDDR,B Dhaka Bangladesh and Aga Khan University, Pakistan. Our mission is to promote and strengthen chronic disease research capacity in South Asia through sharing skills and knowledge between network partners with the aim of improving the prevention and control of chronic disease in the region.

**Building large collaborations for genetic epidemiology.** We currently work with an NIH funded diabetes initiative (Mark McCarthy, Oxford) and an EU initiative (GeoCode, University of Bristol) using our existing studies of rural urban migrants (n=8000) and long-term follow up of a randomized trial of pregnancy/childhood nutritional supplementation (n=2000).

**Establishing large scale population cohorts of households** including entire families to examine the causes and consequences of common risk factors and chronic diseases on households. The cohorts will be used for surveillance and monitoring, health services evaluation and conduct of randomized controlled trials. We are currently piloting a study with Matlab, Bangladesh to add a chronic disease component to their existing demographic surveillance of over 210,000 people who have been followed for over 40 years.

**Trials and health service evaluations.** A range of public health interventions, currently recommended for use in developing countries, will be evaluated: reducing dietary salt for blood pressure control; health promotion for detection and management of CVD risk factors in the workplace; household smoking cessation and indoor smoke reduction.

**PhD fellows, post-doctoral researchers and small-scale research grant funding.** We provide mentoring and long-term support to UK and Indian PhD and post-doctoral research fellows. For example, we are providing pilot study funding for a psychiatrist working on long-term follow up of problem alcohol drinkers in Goa to determine the feasibility of methods.

**Improving research infrastructure.** Our activities currently include development of methods for field epidemiology (e.g. nutritional assessment, physical activity), integrating blood/DNA collection in existing large-scale population studies, archives of population data, financial and research governance, ethical oversight, and procurement of equipment. We are expanding the use of hand-held devices for data capture and the use of bar-coding for biological sample identification. We intend to help researchers make better use of existing databases and have recently conducted analyses of the National Family Household Survey III data demonstrating the marked variation in diabetes prevalence.

**Networking.** SANCD provides a networking function for researchers, faculty of PHFI and partner field based organizations – medical colleges, NGOs or private research organizations – in the region. Activities include scientific meetings, seminars and short courses on research methods.
**Collaborative research.** Household cohort: Our pilot studies will provide a strong foundation for conducting a large scale blood based study of 50,000+ households that will generate intergenerational observational data for future genetic and epigenetic studies. It will also provide the framework for conducting cluster randomized trials of interventions relevant to households (e.g. dietary salt restriction; reduction of indoor household smoke pollution).

**Factories CVD prevention trial.** Our preliminary evaluation of the effects of a tailored comprehensive health promotion package has demonstrated large effects of risk factors (3-5mmHg fall in systolic blood pressure; 0.7mmol/l fall in total cholesterol; 10% reduction in smoking prevalence) in a non-randomized comparison (Prabhakaran et al, 2009).

**Research Needs**

1. Conducting a large scale, cluster randomized (by factory) of the Factories CVD prevention trial (above) factored with a CVD prevention drug regimen and powered for risk factor changes (early outcomes) and events (later outcomes) would make a major contribution (either scaling up or avoiding wasting resources) to workplace health in India.

**Suggested Reading**


SESSION 3
Experience from Interventions and Programmes
The World Health Report of 2002 states that cardiovascular diseases (CVD) will be the largest cause of death and disability in India by 2020. Non Communicable Diseases (NCDs), especially cardiovascular diseases (CVD), diabetes mellitus, cancer, stroke and chronic lung diseases have emerged as major public health problems in India, due to an ageing population and unhealthy lifestyles. It is estimated that in 2005 NCDs accounted for 5,466,000 (53%) of all deaths (10,362,000) in India. According to WHO estimates, there were 32 million diabetics in India in the year 2000 and these are likely to increase to 80 million by the year 2030. The number of ischemic heart disease (IHD) patients is estimated to have increased from 18.6 million in 1998 to 22.37 million in 2004. Meta analysis on studies (1962 – 2000) on hypertension indicates an increasing prevalence of hypertension and cardiovascular disease (CVD) amongst both rural and urban populations. It has been estimated that total economic cost of the 3 tobacco related diseases (CVD, Cancer & COPD) in India is Rs. 27,760 crore ($6034 million US) per year.

The pilot phase of the National Programme for Prevention and Control of Diabetes, Cardiovascular Diseases and Stroke (NPDCS) was launched in January, 2008, to prevent and control these chronic diseases. An outlay of Rs. 1660.50 crore ($350 million US) has been allotted for the NPDCS in the 11th Five Year Plan. On a pilot basis, the NPDCS has been initiated in 10 districts in 10 States. NPDCS is aimed at prevention and control of NCDs using health promotion and health education advocacy. Early detection of people with high levels of risk factors will be done through ‘opportunistic screening’. Capacity building of health systems at all levels will be carried out to tackle NCDs and improve the quality of care. Trained manpower at various levels in health care delivery system will be developed.

District NCD Programmes will include ‘District Health Promotion Centres’ and the ‘District NCD Cells’ for creating awareness on lifestyle related diseases with a focus on the adoption of healthy lifestyles at schools, community, work places etc. and providing opportunistic screening and targeted intervention to reduce mortality and morbidity due to diabetes, CVD and stroke. It is intended that nearly half of all districts will be involved in a phased manner: Dedicated units of CVD/ Diabetes/ Stroke centres at 54 Government Medical Colleges will be established and strengthened. An Information and Education Campaign, IEC, will be undertaken using mass media. There are schemes for financial assistance for cardiac surgeries and involvement of NGOs. Research in related areas of NCDs will also be supported under NPDCS.

NPDCS will be integrated with the National Rural Health Mission (NRHM). NRHM was launched in 2005 and provides an overarching umbrella, subsuming the existing programmes of the Ministry including all the NCD control programmes. The core strategy of the NRHM includes decentralization of villages and district level Rural Planning and Management. In addition, states have the flexibility to project operational modalities in their State Action Plans which have further strengthened decentralized programming at village and district levels. At the district level, District Health Missions have been formed under the chairmanship of a District Collector. To bring more accountability and reorient the services to local needs, many of the states under the NRHM programme have set up committees involving representatives from the public. The Rogi Kalyan Samiti (Patient Welfare Committee) is a registered society (group of trustees) for the government hospitals to manage the affairs of these hospitals.
Common NCDs are managed in the healthcare delivery system up to primary health centre level and NPDCS would augment the activities and facilities for prevention and control of NCDs. There are several other initiatives for other NCDs e.g. Mental Health, Tobacco control etc. which are in addition to NPDCS and NRHM. The Cigarette and other Tobacco Product Act was implemented in 2003 to reduce tobacco consumption. The National Tobacco Control Programme has also been started. Involvement of other sectors has been initiated. Efforts are also being made to integrate various NCD programmes through policy corrections and structural changes.

Research Needs

1. Applied research in the various fields related to NCDs.
2. Community based interventions for feasibility and effectiveness in prevention and control of common NCDs.
3. Surveillance of NCDs and risk factors for monitoring of trends in causation and control of NCDs.

Suggested Reading

Tobacco Control Policies of the Indian Government

India is the second largest consumer of tobacco in the world, with 10% of all smokers globally. It is in addition the third largest tobacco producer. The prevalence in the age group 15-49 is 57% in men and 11% in women, with a high prevalence amongst the socially disadvantaged, poor and illiterate. Tobacco attributable deaths are projected to be one million in 2010. As in other south Asian countries, there are multiple forms of tobacco consumption with 85% in non-cigarette categories. The forms of smoking are also diverse: beedis, cigarettes, cigars, chuttas, cherrots, pipes, hookahs, dhumtis and chillum. Tobacco is also chewed in a variety of forms, taken as snuff, sucked and gargled in water. In 2002 an ICMR study estimated the healthcare costs of the three major tobacco-related diseases in India to be Rs 308.33 billion in 2002.

There is a need to discuss and understand the forces acting for and against tobacco control in India. Efforts of those trying to limit consumption include activism and advocacy by civil society organisations, the judiciary, some parts of the media helping to build a positive attitude towards tobacco control (eg some newspapers), commitment by the Government, especially the Ministry of Health and Family Welfare and the support of well informed Parliamentarians and policy-makers. Those lobbying against control include the tobacco industry, which resists and violates laws and regulations (eg advertisement bans are flouted) and distorts economic considerations relating to tobacco production and taxation, trade unions which have concerns about employment in the tobacco industry, and those concerned with equity – bidi smoking is seen as “the poor man’s luxury” which should not be taxed.

The process to control tobacco use has been long and protracted starting in 1975 with statutory health warnings on cigarette packets (Cigarettes Act). The Superior Courts intervened to prohibit smoking in public places (1999, 2001) and in 2004 a comprehensive tobacco control bill received Presidential Assent, the same year that the Framework Convention on Tobacco Control was ratified. The main provisions of the act are: a prohibition of smoking in public places; prohibition of advertisement, sponsorship and promotion of tobacco products; prohibition of the sale of tobacco products to minors or the sale within 100 yards of an educational institution; the display of pictorial health warnings on tobacco products and the regulation of tar and nicotine content of tobacco products. Following the legislation, the Government introduced the National Tobacco Control Programme to complement and implement the law. This was expanded from an initial 9 pilot states to 21 in 2009. The programme is focused at the District level and involves: the training of teachers, health workers, health professionals, law enforcers, NGOs, women’s groups; an IEC, Information and Education Campaign, using cable TV, street shows, exhibitions, melas etc- all in the regional language; schools programmes; monitoring of enforcement and Tobacco Cessation Centres.

A major challenge has been that of providing alternative livelihoods for tobacco farmers and bidi-rollers. This has needed partnerships between different parts of Government eg the Ministries of Health and Family Welfare, Rural Development and Labour.
There have however been industry challenges to enforcement such as: the violation of the ban of advertisements through indirect product placements in films; the violation of the ban on smoking in public places and the dilution and delay of health warnings on tobacco product packaging. The Government is currently seeking new measures to counter such challenges.

**Research Needs**

1. Studies of the health effects of smokeless tobacco.
2. Studies of the effectiveness of community-based tobacco cessation programmes.
4. Health systems research-tobacco control in primary care, integration into National Health Programmes.
5. Economic considerations – taxation, impact of tobacco use and tobacco control.
6. Tobacco control in youth – prevention of primary uptake, cessation programmes for youth.
Workplace Wellness Programme: An Effective Approach to Prevent Cardiovascular Disease in the Organised Work Sector in India

Intervention and prevention strategies are being sought to curb the rise in burden of cardiovascular disease in India. The workplace is an important location for successful prevention strategies because employees’ behaviour can be influenced by providing a supportive environment and leveraging existing infrastructure to offer low-cost but effective interventions.

The objective of our study was to decrease the mean levels of cardiovascular risk factors significantly in the intervention population.

Six out of ten industries participating in a baseline cross sectional survey were selected as the intervention arm of the study. One industry from the remaining four was selected as control arm of the study. Repeat risk factor measurements were carried out after four years of interventions among employees and their family members.

Thematic concepts on the role of physical activity, tobacco use, salt consumption, fruits and vegetable consumption, and other dietary factors on blood pressure, were communicated to the target population using various media. All high risk individuals were referred to a health care facility for further risk stratification and treatment. Individual and group counselling sessions on diet, tobacco use and physical activity were also conducted for those with established risk factors.

Although all of the risk factors, except triglycerides, showed favourable changes in the intervention population, all of them had worsened in the controls with the exception of high-density lipoprotein (HDL) cholesterol. In the intervention group, the highest reduction was noted for blood sugar, with the lowest reduction for systolic blood pressure (SBP). Similarly, in the control group the highest increase was observed for blood glucose and the lowest increase was observed for waist circumference. The favourable change of 6.6% increase in HDL cholesterol was statistically significant in the control group. Positive changes of interventions for mean levels of SBP and total cholesterol were observed across all age groups. By contrast, across all age groups the control population had a worsening of their SBP and total cholesterol mean levels.

The proportion above Framingham ten year risk score of >=10% dropped down from 34.1% at baseline to 26.8% at the final survey in the intervention arm. Although, the baseline proportion of individuals in the Framingham risk category of >=10% was lower in control arm (25.4%), it was increased to 34.7% at the final survey. In the cohort analysis, after adjustment for all potential confounding factors the mean difference in change between the intervention arm and control arm in weight was -2.8 Kg and in waist circumference was -3.5 cm. Similarly, the mean differences in change between intervention arm and control arm in SBP and DBP were -11.8 mm of Hg and -8.4 mm of Hg.
respectively. The relative differences in change mean plasma glucose, and total cholesterol levels were also in favour of the intervention arm. The mean HDL cholesterol increased by 4.1 mg/dl in the intervention arm.

The majority of trials have been performed in North America, Western Europe, Japan, and Australia. There have been several limitations. These include single-component interventions, interventions of short duration, self-reporting of endpoints and at times measurement of surrogates for CVD risk factors. In a systematic review involving 18 trials, Ebrahim and Davey-Smith concluded that community based interventions resulted in only small reductions in systolic blood pressure, diastolic blood pressure, smoking and total cholesterol with no effect on mortality. In developing countries such as India, it is possible that a combination of primary prevention strategies and selective high risk approaches can effectively bring down population level intermediate risk factors of cardiovascular disease. This may be because of the early phase of demographic transition in India with a rising burden of cardiovascular diseases.

**Research Needs**

1. Cluster randomized trial of worksite interventions to reduce chronic diseases.

2. Evaluation of quality improvement in reducing short and long term adverse outcomes after acute coronary syndromes.

**SUGGESTED READING**


Polypill (TIPS) and CVD Prevention in Developing Economies

Dr Denis Xavier
• Professor and Head, Pharmacology, St. John’s Medical College Coordinator, Division of Clinical Trials, St. John’s Research Institute, St. John’s National Academy of Health Sciences, Bangalore, India

At the St. John’s Research Institute we have conducted some of the largest observational studies and interventional trials in cardiovascular disease (CVD) for over a decade. Over 20 large studies have to date included over 40,000 patients from a collaboration of over 170 centres. The Indian Polycap Study (TIPS) to evaluate the Polypill concept is one such study.

Wald and Law using meta-analyses estimated that a combination of BP lowering drugs, statin, aspirin and folic acid, given to all above the age of 55 would reduce the risk of a cardiovascular event by over 80% (BMJ 2003). With the advantages of a fixed dose combination (cheaper, better compliance, fewer medication errors), the Polypill was advocated to all with vascular disease and those with a risk for a vascular event.

TIPS considered the following issues to be addressed, (a) can we formulate a Polypill with 4-5 drugs, (b) how will it act when given to individuals at average risk, (c) will it be well tolerated and (d) can it substantially reduce cardiovascular risk factors? A combination of aspirin, simvastatin, ramipril, atenolol and hydrochlorothiazide (we did not include folic acid as the clinical trial evidence on homocysteine lowering with folic acid is not conclusive) was developed. This combination was contained in a regular size capsule and we called it the ‘Polycap’.

The Indian Polycap Study (TIPS): design and results
The objectives of TIPS were to test if the Polycap was (a) equivalent in reducing BP, heart rate, modifying lipids and inhibiting platelet function when compared to its individual components in different combinations and (b) to compare its tolerability. The randomized, double blinded, controlled trial with the Polycap and 8 other arms had non-inferiority and superiority comparisons.

St. John’s coordinated the trial in 53 centres in different parts of India. McMaster University, Canada centrally managed the data and carried out statistical analyses. The subjects were between 45 and 80 years of age and had at least one CV risk factor and did not have a clear indication or a contraindication to any one of the 5 drugs in the Polycap.

Compared with groups not receiving blood-pressure-lowering drugs, the Polycap reduced systolic blood pressure by 7.4 mm Hg and diastolic blood pressure by 5.6 mm Hg, which was similar when three blood-pressure-lowering drugs were used, with or without aspirin. Reductions in blood pressure increased with the number of drugs used. Polycap reduced LDL cholesterol by 0.7mmol/L, which was less than that with simvastatin alone both reductions were greater than for groups without simvastatin. The reductions in heart rate with Polycap and other groups using atenolol were similar (7.0 beats per min), and both were significantly greater than that in groups without atenolol. The reductions in 11-dehydrothromboxane B2 were similar with the Polycap compared with the three blood-pressure-lowering drugs plus aspirin, and aspirin compared with groups without aspirin.

TIPS demonstrated the safety and efficacy of the Polycap in those at moderate cardiovascular risk as well as the incremental effect of added BP lowering drugs (1, 2 and 3 drugs). Based on the risk reductions we estimated that the Polycap could reduce cardiovascular outcomes (ischemic heart disease and strokes) by approximately 50%.

Current status and next steps
The next steps now are to get the support of the medical profession and patients, to evaluate the economic issues in a developing country setting and
to assess adherence, long-term safety and benefits on clinical end points in a large pragmatic trial. Our group has secured a Wellcome Trust Grant for a large clinical outcomes trial that is planned in 2010, to demonstrate the safety and efficacy of the Polypill (see above). This trial will take a minimum of 5 years. The Polycap is now approved for marketing in India. We understand that a few other pharma companies have produced and are marketing their version of a Polypill. The Polypill has the potential to significantly reduce the burden of CVD, especially in developing countries.

In addition, our group is presently funded by the NHLBI (NIH, USA) to conduct two projects. (a) PREPARE – a cluster RCT on strategies for primary prevention in a rural setting in 3 regions of India; screen 15,000 subjects and intervene on 1,250 at risk individuals for 2 years to estimate reductions in CVD risk factors, and (b) SPREAD – an urban hospital-based secondary prevention RCT in acute coronary syndromes; 1,000 patients followed up for one year to estimate reductions in risk factors and adherence to evidence-based medications and lifestyle modifications. Trained non-medical health workers will implement the interventions in both of these studies. These studies will demonstrate feasibility and estimate risk reductions. Using these data, we recommend the conduct of larger clinical outcomes studies in different health care settings in India.

### Research Needs

1. To conduct translational research on effective strategies for primary and secondary prevention of CVD.

2. To evaluate strategies to improve affordability and accessibility to chronic CVD care, and especially to low cost evidence-based medications. In the meantime we recommend the conduct of research projects and programmes to evaluate strategies to improve affordability and accessibility to evidence-based medications for CVD prevention. Alongside lifestyle modification, uptake of low-cost evidence-based medications has the potential for significant and rapid reductions in CVD especially in a developing country setting.

### Suggested Reading


Health-risk behaviours, including tobacco use, unhealthy diets, inadequate physical inactivity, alcohol and other drug use, are often established during childhood and adolescence, extend into adulthood, are interrelated, and are preventable. These behaviours contribute to chronic disease and other health conditions which are the leading cause of death, disability and social problems. Establishing healthy behaviours during childhood and maintaining them is easier and more effective than trying to change unhealthy behaviours during adulthood. Children in schools are more receptive to health promotion based interventions as their perceptions and practices are being etched during these formative years. Effective “child to child” approaches in promoting health education and motivating for health advocacy, with the help of peer leaders, can bring about immense positive change among the youth. Schools play a critical role in promoting the health and safety of young people and helping them establish lifelong healthy behaviour patterns. They provide students with an opportunity and place to learn about health and practice the skills that promote healthy behaviours such as eating healthy foods and participating in physical activity. Schools, in partnership with community agencies and organizations, improve the health and well-being of young people by assessing health needs; setting priorities; and planning, implementing, and evaluating school health activities. They bring together school administrators, teachers, other staff, students, families, and community members to solve the most serious health and social problems. Research has shown that these school health programmes can reduce the prevalence of health risk behaviours among young people and have a positive effect on academic performance too.

School Health Programmes by HRIDAY-SHAN

HRIDAY-SHAN has been involved in various health promotion programmes at school, college, home and community level. It comprises two components: HRIDAY (Health Related Information Dissemination Amongst Youth) and SHAN (Student Health Action Network). The HRIDAY programme focuses on enhancing health awareness among school students aged 10-13 years, whereas the SHAN component promotes informed health activism among high school students aged 14-17 years. School based health programmes by HRIDAY aim to promote health awareness and informed health activism among youth in India. Diet and nutrition (including healthy diets, food safety, food policies), physical activity promotion, avoidance of addictions such as tobacco and alcohol, environment protection (water and air safety), healthy gender relations (including prevention of HIV-AIDS), road safety, peace and non-violent conflict resolution are its major areas of focus. A number of innovative educational activities and strategies including awareness, community outreach programmes (COP), policy-maker advocacy, skill building interventions, watchdog activities, global youth meetings have been adopted by HRIDAY-SHAN to create the ownership among youth. Components of HRIDAY’s school based health programmes involve sensitization of students and parents, poster display on healthy diet and importance of physical activity, and generating awareness on consequences of tobacco, promoting tobacco-free norms in schools and homes. All these components undertaken by HRIDAY have led to adoption of healthy living habits among youth, especially in the area of tobacco avoidance.
HRIDAY- CATCH, a group randomized trial conducted by HRIDAY with students in grade VII of 30 elementary schools in Delhi in year 1996-1998, showed that the intervention group was significantly less likely to have been offered, received, experimented with or have intentions to use tobacco in future as compared to control group (Reddy et al, 2002). Project MYTRI is another example to show the effectiveness of HRIDAY’s tobacco prevention intervention model. It was conducted in 16 schools of Delhi (northern India) and 16 schools of Chennai (southern India) among 6th-10th grade students (aged 10-16 years). This multi-component two year intervention program was a group randomized trial involving classroom activities, school posters, parent postcards and peer-led health activism. This model of school – community interactions starts at the individual classroom level, wherein trained Peer Leaders communicate with their classmates on health issues influencing the interpersonal and social-environmental factors. Figure 1. shows the effect of programme components leading to programme goals i.e. prevention and reduction in tobacco use. MYTRI baseline finding indicates that sixth-grade students were using significantly more tobacco than eighth-grade students which required urgent public health intervention. The end line survey results of MYTRI showed that students in the intervention group were significantly less likely than were students in the control group to exhibit increases in cigarette smoking or bidi smoking over the two year study period (Perry et al, 2009).

**Fig. 1 Intervention model for Project MYTRI** (*Mobilising Youth for Tobacco Related Initiatives in India*)

<table>
<thead>
<tr>
<th>Programme components</th>
<th>Classroom curricula</th>
<th>School posters</th>
<th>Parent postcards</th>
<th>Peer-led health activism</th>
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<tr>
<td>Intro-personal factors</td>
<td>Increase Knowledge about health effects of tobacco use</td>
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<td>Increase skills to resist social influences to use tobacco</td>
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<td>Programme objectives</td>
<td>Social-environment factors</td>
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<td>Promote tobacco-free social norms in school, home</td>
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<td>Increase exposure to tobacco-free role models</td>
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<td>Provide support for others to abstain/quit using tobacco</td>
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<td>Provide opportunities to learn about, support and influence policies on tobacco</td>
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<tr>
<td>Programme goals</td>
<td>Prevent/reduce tobacco use among youth in urban India</td>
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</table>
**Research Needs**

1. Collaborative research focusing on developing intervention models to change health behaviours among children and adolescents with the goal of preventing chronic diseases. This can involve both qualitative and quantitative research in this area using innovative health promotion models.

2. Tobacco cessation intervention research among adolescents in India (group randomized trial focusing on non-pharmacologic, community based intervention models).

3. Surveillance studies to track trends in childhood obesity in India - effective and appropriate intervention models to address malnutrition and obesity to be developed and tested for effectiveness.

4. Intervention model for promoting healthy eating and physical activity practices among youth and their families.

**SUGGESTED READING**


Summary and Recommendations

An ICMR – MRC Workshop on Chronic Diseases, held on 4-5 November 2009 in Delhi, was the first initiative under the collaboration efforts between the two agencies in the area of chronic noncommunicable diseases. Experts from both India and the UK spoke to a programme designed to identify research questions on the causes, prevention and treatment of chronic disease and specifically to address:

- The strengths and weaknesses of the current research landscape in both India and the UK – unmet needs and roadblocks
- The capacity/capability of research institutions and ultimately health systems, and other elements of civil society, to respond to these needs and roadblocks
- Potential areas for the development of evidence-based research programmes

The focus of the workshop was 1) cardiovascular disease and diabetes, including the contribution of obesity and early-life under-nutrition in the aetiology of disease, and 2) chronic obstructive lung disease especially the role of smoking and indoor pollution in its development.

It is intended that the outputs of the meeting will provide the basis for the development by ICMR and MRC of a jointly-funded programme, the details of which will be announced in due course.

Having acknowledged the importance of globalisation, economic development, urbanisation and nutrition transition in the development of the global epidemic of chronic disease, the strengths and weaknesses of the research and healthcare environments in India and the UK, relevant to these diseases, were identified. It was agreed that mutually beneficial lessons could be learnt from past experiences of researchers from both countries.

After two days of wide ranging discussions, the following conclusions were reached:

1. The importance of looking at the linkages and common aetiology of the major chronic diseases under consideration, including the development of molecular markers.

2. In the context of the Indian situation, more accurate data was needed on the burden of disease, management measures and outcomes as well as a greater understanding of what legal and fiscal measures were most effective in changing behaviours.

3. The need for more effective surveillance structures in both countries including more robust and objective measures of nutrition, exercise, tobacco use etc – the results obtained from self reporting and questionnaires were often inaccurate and misleading.

4. The importance of regional and cultural differences in both India (especially rural versus urban) and the UK in terms of risk factors (diet – fat, salt, sugar etc, exercise, tobacco consumption) and the ability of health and other public sector services to adapt policy and implement the results of research outputs.

5. The importance of a multidisciplinary approach to chronic disease, building capacity at all levels in disciplines such as social science, health economics, bio-statistics, data management etc as well as public health.

6. The need to build consortia of research groups, using standardised methodologies, avoiding the fragmentation and unnecessary repetition associated with small scale studies.

7. The importance of building on and enhancing studies that are already underway in India and the UK several of which have an international dimension.

8. In the Indian context, further studies on the effectiveness of local community health workers, including ASHAs, were needed, in conjunction with the Ministry of Health and other agencies.

9. The role of “polypharmacy” in the prevention and treatment of CVD, diabetes and stroke, addressing issues of pricing, acceptability and adherence.

10. The involvement of the private sector – healthcare, pharma and IT – would be important in the acquisition and implementation of research findings.

Taking account of these conclusions a more specific research agenda for undertaking collaborative research will be developed by ICMR and MRC.
ICMR-MRC Workshop on Chronic Diseases, New Delhi, INDIA  
Dates: 4-5 November 2009  
Objective: Building Indo-UK Collaboration in Chronic Diseases Research

### Programme

#### Introduction and Welcome

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<tr>
<td>Dr Bela Shah (ICMR)</td>
<td>08.45</td>
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<td>Dr Wendy Ewart (MRC)</td>
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#### SESSION 1 – Burden of Chronic Disease in India and the UK

**Chair:** Prof Prem Pais, St. John’s Medical College, Bangalore

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<tr>
<td>Cardiovascular Disease</td>
<td>Dr Rajeev Gupta (Fortis Escorts Hospital, Jaipur)</td>
<td>09.00</td>
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<td>Prof Nishi Chaturvedi (Imperial College London)</td>
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<td>Diabetes</td>
<td>Dr Nikhil Tandon (All India Institute of Medical Sciences)</td>
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<td>Prof David Matthews (University of Oxford)</td>
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<td>Chronic Obstructive Pulmonary Disease</td>
<td>Dr Randeep Guleria (All India Institute of Medical Sciences)</td>
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<td>Prof Peter Barnes (Imperial College London)</td>
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<td>Mental Health</td>
<td>Dr Nimesh Desai (Institute of Human Behaviour and Allied Sciences, Delhi)</td>
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<td>Chronic diseases to chronic conditions:</td>
<td>Dr Vikram Patel (London School of Hygiene and Tropical Medicine;</td>
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<td>health care research</td>
<td>Sangath Centre, Goa)</td>
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<td>Questions and discussion</td>
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### SESSION 2 – Update on current research activity in chronic disease
Chair: Prof Salim Yusuf, McMaster University

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<td>ICMR chronic diseases research initiative</td>
<td>Dr Bela Shah (Indian Council of Medical Research)</td>
<td>11.30</td>
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<tr>
<td>Aetiology and prevention of type 2 diabetes: current and future research needs</td>
<td>Dr Nick Wareham (MRC Epidemiology Unit, Cambridge)</td>
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<td>Obesity and undernutrition</td>
<td>Dr Chittaranjan Yajnik (King Edward Memorial Hospital, Pune)</td>
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<td>Dr Sanjay Kinra (London School of Hygiene and Tropical Medicine)</td>
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<td>Life-course influences on chronic disease</td>
<td>Prof George Davey-Smith (University of Bristol)</td>
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<td>National Institutes of Health National Heart Lung and Blood Institute/Ovations Programmes</td>
<td>Dr K M Venkat Narayanan (Emory University, Atlanta)</td>
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<td>Translating gene identification into biological insights and clinical advances</td>
<td>Prof Mark McCarthy (University of Oxford)</td>
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<td>South Asian Network for Chronic Diseases</td>
<td>Prof Shah Ebrahim (London School of Hygiene and Tropical Medicine/Public Health Foundation of India, New Delhi)</td>
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# SESSION 3 – Experience from Interventions and programmes

**Chair:** Prof Anoop Misra, Fortis Group of Hospitals, New Delhi

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| **Government Programme on Prevention and Control of Diabetes, CVD and Stroke (and the role of National Rural Health Mission)** | Dr Sudir Gupta  
(Ministry of Health and Family Welfare)                                                                 | 15.00 |
| **Indian Government Tobacco Policies**                                | Prof K Srinath Reddy  
(Public Health Foundation of India)                                                            | 15.15 |
| **CVD Prevention and the workplace**                                  | Dr Dorairaj Prabhakaran  
(Centre for Chronic Disease Control, New Delhi)                                                | 16.00 |
| **Polypill (TIPS) and CVD prevention in developing economies**         | Dr Denis Xavier  
(St. John’s Medical College, Bangalore)                                                        | 16.15 |
| **Chronic Disease Prevention Initiatives in School Setting**           | Monika Arora  
(Health Related Information Dissemination Amongst Youth – Student Health Action Network)    | 16.30 |
| **Questions and discussion**                                           |                                                                                               | 16.45 |
| **Round up and Questions for Panel Discussion**                       | Chair: Prof Mark McCarthy                                                                     | 17.00 |
| **End of Day One discussions**                                        |                                                                                               | 18.00 |
SESSION 3 – Experience from Interventions and programmes
Chair: Prof Anoop Misra, Fortis Group of Hospitals, New Delhi

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Topics of Discussion for Session 4
1. Strengths and weaknesses of current research landscape - unmet needs
2. Capacity to respond to unmet needs in chronic disease research in India. What are the roadblocks and how can they be overcome?
3. Potential areas for developing evidence – based research programmes in India
   a. What are the key research questions that need to be addressed in order to make a significant public health impact?
   b. What should be done – scoping and developing specific research activity?
4. Funder responses – mechanisms for MRC – ICMR collaboration
5. The way forward

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Ontario
ICMR – MRC
Workshop on Chronic Diseases

4-5 November 2009, New Delhi, India

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