

***Strategic Plan for  
Centre for Environmental and  
Population Health  
2013 - 2015***

**AN INTEGRATED ENVIRONMENT,  
POPULATION AND HEALTH  
APPROACH IN SUPPORT OF  
CROSS-SECTORIAL  
COLLABORATIVE RESEARCH**

**AN INTEGRATED ENVIRONMENT,  
POPULATION AND HEALTH  
APPROACH IN SUPPORT OF CROSS-  
SECTORIAL COLLABORATIVE  
RESEARCH:**

*Centre for Environmental and Population Health*



# Contents

1	<b>Directors' Message</b>	4
2	<b>The Centre for Environmental and Population Health</b> Vision and Mission	5
3	<b>Executive Summary</b> Overview of the Environmental and Population Health Research (EPHR) Strategic Plan	6
4	<b>Themes for Environmental and Population Health Research</b>	7
5	<b>Focus Areas for Environmental and Population Health Research</b>	22



## Director's Message



I am pleased to share with you the 2013-2015 Strategic Plan for the Centre of Environmental and Population Health (EPHR). An integrated approach which translates fundamental knowledge and research competency on environmental and population health will be established for local and global community needs and environmental sustainability. The more we know about environmental exposures and hazards to health, the better we can manage the risks in our efforts to promote human health and disease prevention activities. The purposes of having this strategic plan are to communicate the identified prioritized focus areas to all stakeholders for successful implementation and to align these strategic themes/goals with IRDI's strategies.

Environment, population and health are interrelated entities. Urbanization and increased populations have directly or indirectly contributed to drastic changes in the global environment including air, water and soil contaminations, greenhouse effects, global warming and climate change. These environmental threats will eventually affect human health at different life stages e.g. prenatal, pregnancy, and old age. The incidence of disease and mortality in susceptible populations may increase due to emergence and re-emergence of communicable diseases, vector-borne diseases, nutritional diseases due to food insufficiency, respiratory diseases, non-communicable diseases, physiological and neurological disorders. Measures should be taken immediately to reduce the adverse health impacts of these environmental risk factors.

These strategic themes and goals are also formulated to target and strengthen the early disease detection and prevention in addition to assessment and control of the environmental factors. Providing appropriate interventions and treatments in a timely manner will create a better health-support environment for the population. Successful implementation of these strategies will largely depend on how best the proposed activities can be consolidated within the institution and with other national and international academic and industrial entities.

**Professor Dr Mak Joon Wah**

*IMU, Vice President (Research)*

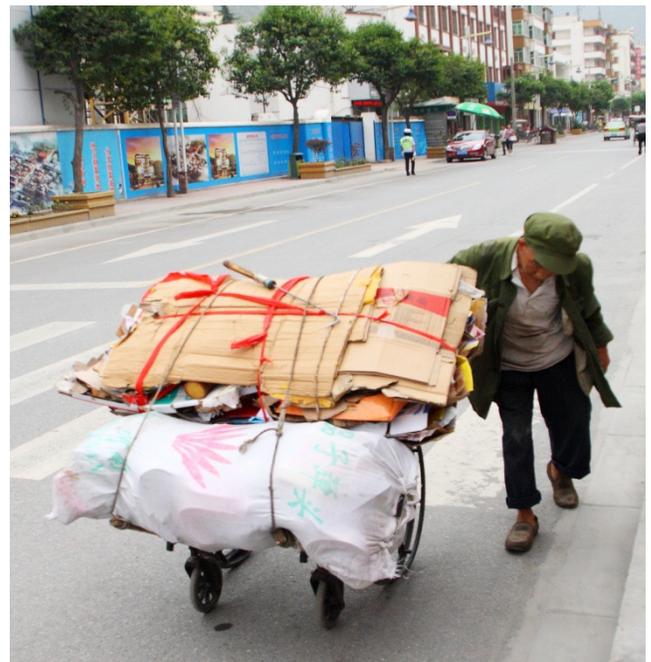
*Institute of Research, Development, and Innovation (IRDI), Director*

*School of Postgraduate Studies and Research, Dean*

## Centre for Environmental and Population Health



In order to align with the IRDI's mission to be a leading private research institute in Asia that creates value through integrating education, healthcare and research, the Centre for EPHR will embark on an integrated approach to transform fundamental knowledge and research competence on environmental and population health so as to reduce healthcare cost with improved health status and environmental sustainability.



# Executive Summary

## Overview of the EPHR Strategic Plan

An Integrated Population, Health and Environmental Approach which supports Cross-sectorial Collaborative Research will be the target for the next 3 years for EPHR. Global health is continuously challenged by human activities such as rapid urbanization and development. Climate change is a product of human actions that affects human well-being. The global population is faced with floods, droughts, heat waves, earthquakes and volcano eruptions that have immense impact on many nations resulting in food shortage and ill health. Rapid urbanization and development also results in adverse health effects due to poor nutrition, polluted and inadequate water supplies, poor air quality and poor sanitation. Changing environments also result in emergence of new diseases or re-emergence of old diseases and creation of new vectors and hosts. As one of the research arms of the IMU Institute of Research, Development and Innovation (IRDI), the Centre for EPHR will address these associated risks on human health and related impacts on disease burden by conducting long-term, high-priority basic laboratory and field researches in environmental and population health and translating promising findings into novel therapeutics and preventive measures which promote population health and quality of life with minimal impacts on surrounding environments.

The Centre will have a blend of clinicians, basic scientists and field researchers in its team and it will endeavor to work with local and international agencies to spearhead research in important areas of global health. Hence, it is imperative that the Centre of EPHR identifies and shares its top priority objectives through its Strategic Plan by steering and aligning the current research on the identified themes: epidemiology, causes and mechanism of infection, effective disease prevention and surveillance, detection, diagnosis and treatment approaches, and health promotion. These strategies could be strengthened by currently available tools and emerging fields in nanotechnology, genomics, proteomics and metabolomics.

## Themes for EPHR - Background

The EPHR Strategic Plan reflects the current state of environmental and population health research and is based on the National Strategic Plan for Environmental Health of Malaysia (Ministry of Health, 2009) and World Health Organization identified needs. In 2010, 52.8 million deaths were reported in 21 regions globally (Lozano *et al.*, 2012). At the most aggregate level, communicable, maternal, neonatal, and nutritional causes were 24.9% of total deaths worldwide in 2010. The global mortality for female and male individuals aged 15-49 years was highest for HIV/AIDS (14.4% of 3.5 millions) and cardiovascular diseases (12.8% of 5.7 millions) respectively.

In the neonates, preterm birth complications contributed to the highest mortality in 2010 (Lozano *et al.*, 2012) followed by neonatal encephalopathy and sepsis. Lower respiratory infections, diarrheal diseases and malaria are the top killers of post-neonatal children below one-year-old. At ages 1-4 years, neglected tropical diseases and malaria were the major contributors of global mortality.

The global disease burden (loss of disability-adjusted life years) analysis in 2010 for 21 worldwide regions revealed high blood pressure, tobacco smoking and household air pollution from solid fuels as the top three risk factors (Lim *et al.*, 2012). In Southeast Asia, high blood pressure was ranked the highest amongst the risk factors identified (Lim *et al.*, 2012).

The total estimated deaths in Malaysia in 2008 were 124,857, of which 72,202 (57.8%) were males (Yusoff *et al.*, 2013). The life expectancy for Malaysian males and females were 70.2 and 74.8 years respectively. The total years of life lost (YLL) for the Malaysian population in 2008 was 1.51 million in which 0.92 million (60.7%) was males. Approximately three quarter (68%) of deaths resulted from non-communicable diseases, followed by communicable diseases (20%) and injury (12%). By the disease category, the leading cause of YLL in Malaysia is caused by cardiovascular and circulatory diseases (35%), followed by malignant neoplasm (20%), infectious disease (15%), unintentional diseases (14%) and respiratory diseases (6%).

Among the top three leading causes of YLL were ischemic heart disease (17.1%), stroke (9.6%) and road traffic injuries (8.3%). The estimated disability adjusted life years (DALYs) per 1000 capita was reported by WHO at 27 for Malaysia in year 2004 with a total deaths of 28500. Cardiovascular disease, diarrhoea, road traffic injuries and other unintentional injuries were the top four disease categories with highest rates.

Lozano *et al.* Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; 380: 2095–128.

Yusoff *et al.* Burden of premature mortality in Malaysia. *Int J Public Health Res* 2013; 3 (1): 249-56.

Country profile of environmental burden of disease: public health and environment Geneva 2009. World Health Organization.

Lim *et al.* A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *The Lancet*. 2012; 380 (9859): 2224-60.

# Themes for EPHR

1

## Understand the epidemiology, biology and complex interactions between environmental agents and population health

We will conduct and support fundamental research to investigate the basic biological processes on how the human body responds to various environmental stressors, and how exposure to environmental agents contribute to the development of disease conditions in susceptible populations. We will develop capacities at appropriate levels to monitor environmental exposures and to analyze baseline data for impact evaluation.

2

## Improve Early Detection and Diagnosis

We will support the development of new sensor and detection tools, remote detection of exposures, more sensitive analytical methods and high throughput predictive markers or models for the early detection and diagnosis of diseases which impact on population health subsequent to environmental exposures.

## Accelerate Progress in Disease Prevention and Surveillance, and Health Promotion

We will accelerate the discovery, development, and delivery of disease prevention interventions by investing in research focused on systems biology, behaviour modifications, environmental, medical and nutritional approaches.

3

## Develop Effective and Efficient Treatments

We will support the development and dissemination of interventions to treat diseases arising subsequently to climate change and environmental influence.

4



## Understand the epidemiology, biology and complex interactions between environmental agents and population health

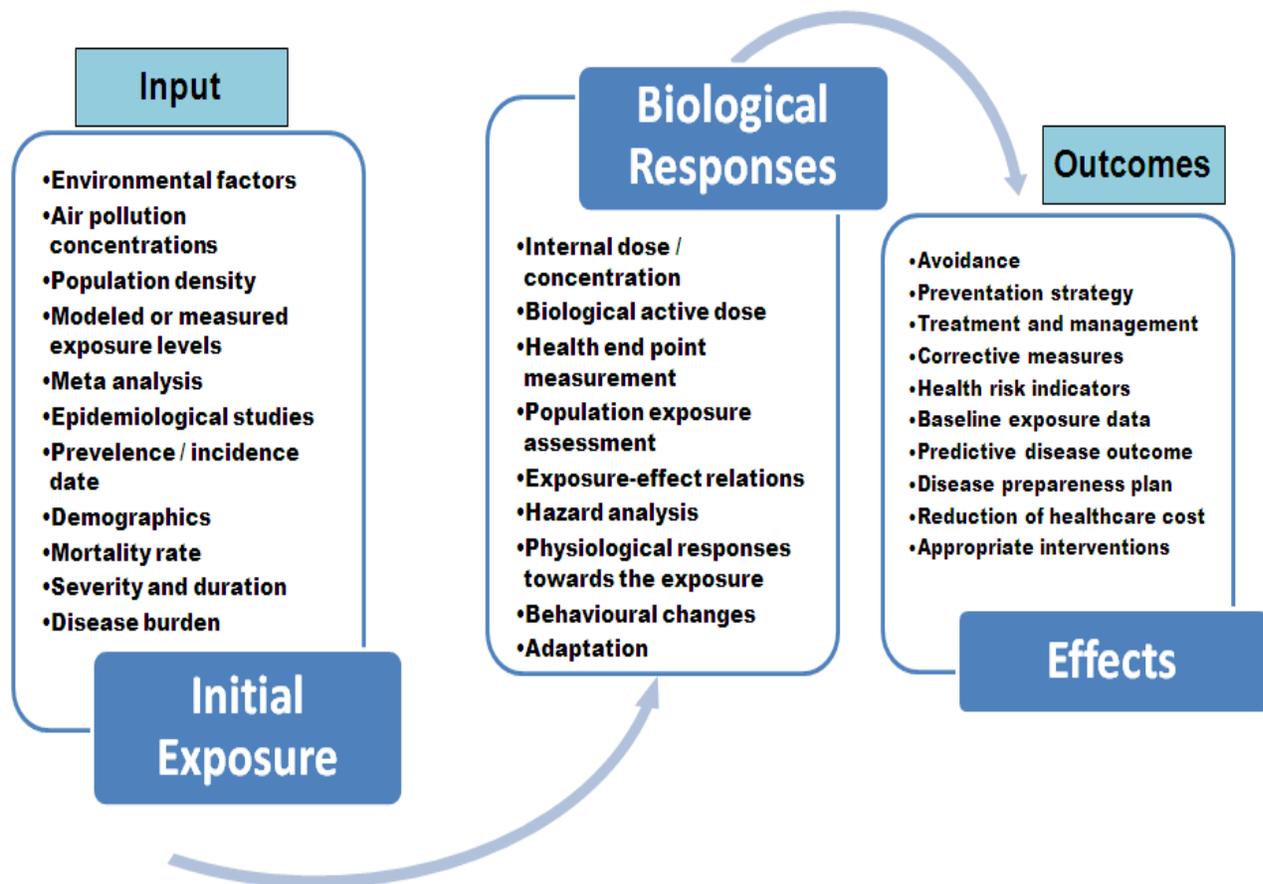
Urbanization, mechanization and globalization are changing the patterns of living, communicating and moving, and also the global natural environment. The changing global climatic patterns have diverse consequences on human health and is receiving worldwide attention. Climate change and variability have been associated with various health outcomes including vector-borne diseases, extreme weather events (heat waves, floods), respiratory infections, malnutrition due to food insufficiency, adverse mental health and many other infectious diseases. Countries in Southeast Asia and Africa will experience the greatest impacts especially for the young, elderly and poor vulnerable groups. Currently, the understanding of the mechanism and roles of environmental exposures in disease pathogenesis is rather lacking and needs to be strengthened.

### Strategic Goal 1.1

#### To identify, monitor and evaluate the environmental risks on population health

1. To describe the 'baseline' relations between different environmental or climatic conditions and health outcomes
2. To investigate, monitor and evaluate the environmental hazards and the associated health risks
3. To determine the factors that determine individual susceptibility to acute/chronic diseases resulting from environmental stressors across the life span
4. To understand the individual genetic susceptibility to various environmental stressors

# Conceptual Framework to Assess Environmental Exposures



Adapted from sources:

1. van Kamp I, Babisch W and Brown AL. Environmental noise and health. *In Environmental Health.*
2. Shendell DG. Human exposure assessment. *In Environmental Health.*

## Strategic Goal 1.2

### To Identify and understand fundamental biological mechanisms subsequent to environmental exposures

1. To investigate the effects of the environmental factors (diet, stress, prenatal nutrition, chemical exposures) on individual genome structure and function, epigenetic regulation of biological and pathological processes
2. To determine the mechanism that regulates resistance and susceptibility to environmental stressors
3. To identify environmental factors that contribute to altered human development, maturation, reproduction, biological processes and aging
4. To investigate the roles of the human microbiome and its influence on environmental and population health
5. To investigate the interactions of infectious agents and environmental exposures
6. To understand the impacts of environmental factors on initiation, promotion and progression of various disease conditions
7. To identify environmental factors that influence epigenetics of various diseases, the vectors and the microorganisms which cause infections
8. To use relevant *in vitro* and *in vivo* experimental models to further investigate the effects of environmental stressors on biological processes, epigenomes/genomes and proteomes of the host.
9. To apply gene silencing and knockout technologies to investigate the mechanism of disease pathogenesis and progression

## Strategic Theme **2**

### Improve Early Detection and Diagnosis

Early detection and diagnosis of environmental hazard exposures on human health can dramatically reduce healthcare costs, improve treatment efficiency and survival which eventually reduce the mortality rates. Well-designed epidemiologic studies rely on inference of associations between environmental exposures and diseases or response variables. However, the greatest limitation or uncertainty for these studies is the lack of accurate, reliable, high-throughput and cost effective approaches to measure early changes in biological processes particularly at the molecular level. The measurement of responses normally reflect the late stage in the disease process such as morbidity, mortality, tissue pathology or tumor development. Defining the risk at a late stage for a particular disease process will hinder the management and intervention of the disease. It will be best if the disease process can be identified at the early biological stages by measuring reliable predictive markers of exposure, early changes or susceptibility in the overall exposure-disease continuum.

#### Strategic Goal 2.1

##### **To identify new technologies and methods for assessing environmental exposure and disease pathogenesis**

1. To develop sensing devices which are able to measure environmental agents (biological and chemical agents) accurately and reliably
2. To identify new predictive markers of biological processes subsequent to environmental exposure
3. To support the development and evaluation of high-throughput, cost-effective technologies that permit rapid and accurate patient diagnosis
4. To support training related to technology development, and support for developing and validating technologies for early detection and diagnosis
5. To establish collaborative research in environmental and population health through regional and international networks

## Strategic Theme **3**

### Accelerate Progress in Disease Prevention and Surveillance, and Health Promotion

By examining the aggregate disease burden attributed to key environmental risks globally and regionally, appropriate preventive measures can be taken to reduce the morbidity and mortality, and also healthcare costs. Better understanding of the disease endpoint and how diseases are impacted by environmental influences will enable the development and implementation of more effective preventive approaches. Preventive strategies can be classified as primary, secondary or tertiary prevention (McMichael *et al.*, 1996). Primary prevention refers to avoidance or removal of the hazardous exposure. Secondary prevention involves the early detection of a subclinical health disorder and subsequent intervention to avert progression to overt disease. Tertiary prevention refers to treatment and attempts to minimize the adverse effects of disease. Certain diseases can be reduced by modifying the exposure to environmental factors such as diarrhoea (unsafe drinking water, poor sanitation and hygiene), lower respiratory tract infections (indoor and outdoor air pollution due to cigarette smoking, emission from motor vehicles, household solid fuel usage), malaria (policies on land use and deforestation, water resource management, improved drainage) etc. Other environmental health interventions that can be implemented may include phasing out of leaded gasoline (which causes mental retardation), reducing extreme poverty and hunger, removal and ban usage of hazardous agricultural pesticides.

#### Strategic Goal 3.1

##### **To promote and accelerate translation of basic research findings into applied intervention and prevention methods and strategies**

1. To identify approaches to change the environment conditions that will reduce the vector and/or host habitats, and will produce unfavorable conditions for vector propagation
2. To identify and manipulate human behavior and habitation which reduce the contact between human and vectors or environmental risk factors
3. To develop/implement new prevention strategies or policies with more advanced technologies and better preventive and public health measures

## Strategic Theme **4**

### Develop Effective and Efficient Treatments

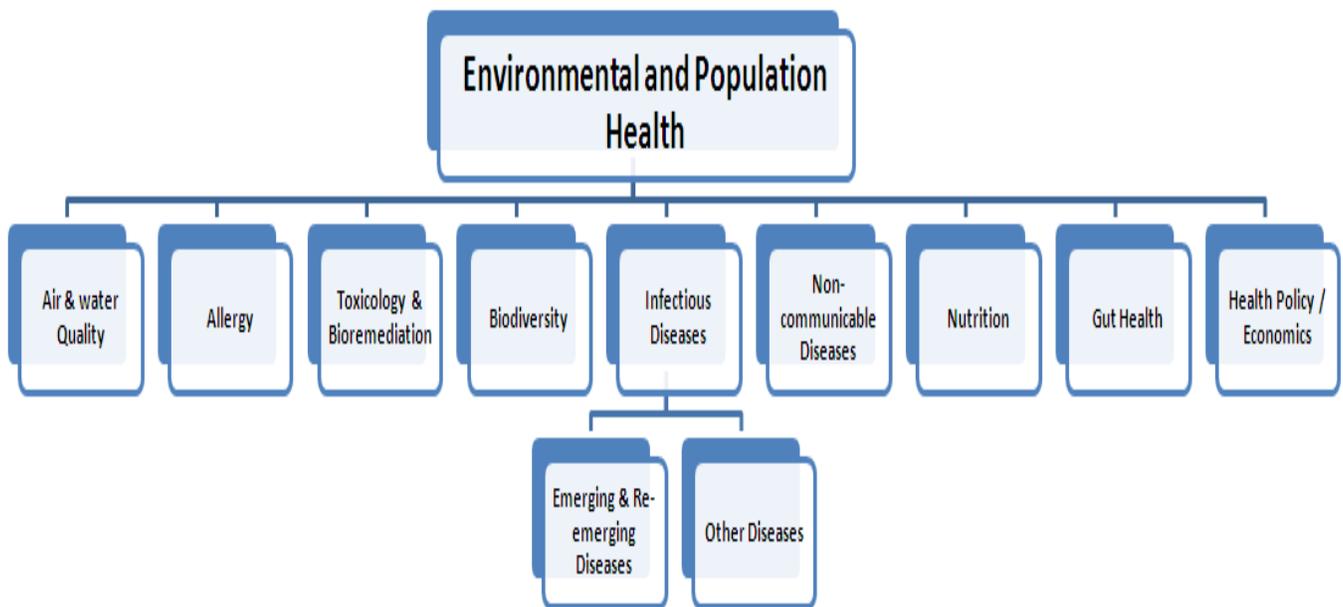
Providing early efficient and effective treatments and management to the vulnerable populations will improve their well-being and quality of life. Understanding of the fundamental mechanisms leading to disease pathogenesis subsequent to environmental risk factors exposure will enable the identification of key biological processes in the disease condition as targets for treatment. Different interventions or approaches such as dietary modification, medication, behavioral changes can be applied. Accelerating target validation and the development of new treatment modalities will be possible through recent advances in biomedical technologies such as genomics, proteomics, metabolomics, nanotechnology, and imaging. Rapid translation from development to delivery will ensure that promising therapeutics move safely and efficiently from preclinical development through late-stage clinical trials and into clinical practice.

#### Strategic Goal 4.1

##### **To support the discovery and development of novel treatment and management approaches**

1. To study the vector and/or host ecology and its management
2. To identify and implement interventions in reducing the adverse impacts and enhancing health impacts
3. To maintain and strengthen emergency management and disaster preparedness plan including stockpile vaccines and other control measures for any anticipated disease outbreak
4. To develop new vaccines and/or drugs for the elimination of diseases associated with environmental factors
5. To promote multidisciplinary interactions and collaboration among basic scientists, clinicians and behavioral and social scientists in managing environmental hazards

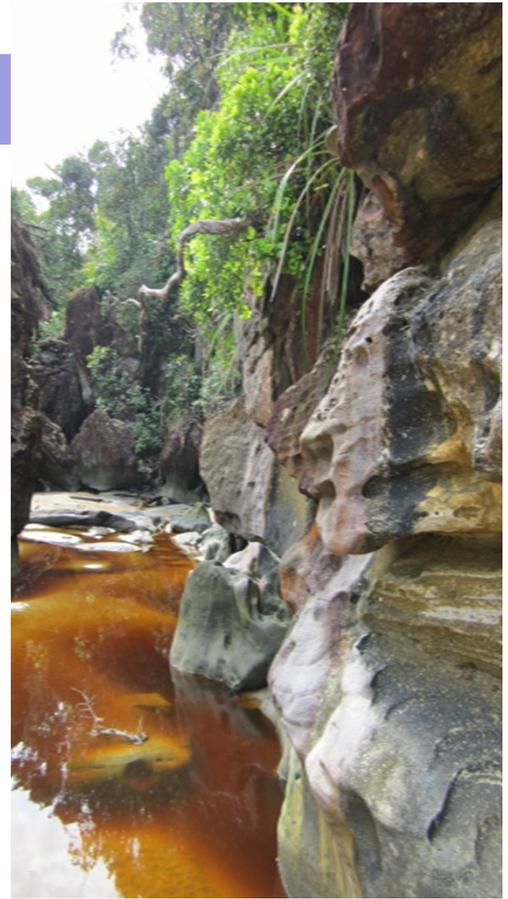
# Focus Areas of EPHR



## Air & Water Quality

Air pollution, both indoor and outdoor, has been reported as one of the risk factors for various respiratory diseases, allergic diseases and cardio-pulmonary conditions. The sources of indoor pollution may include cigarette smoke, chemicals contained in household paints and cleaning materials, dust mites and cockroaches, fungal spores, emissions from building materials and furniture. The outdoor air pollutants may include but are not limited to particles from vehicle exhaust, industrial emissions, toxic gases e.g. carbon monoxide.

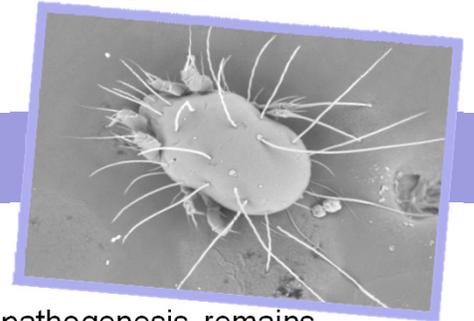
Access to clean drinking water is essential for health. Safe drinking water is needed for domestic purposes including drinking, food preparation and personal hygiene, and for food and pharmaceutical industries. Consumption of safe drinking water will eliminate or minimize the risks of waterborne diseases especially for infants and young children, elderly and those who are debilitated.



EPHR is targeting:-

1. To identify and explore suitable air and water quality management strategies for Malaysia
2. To identify and explore appropriate air pollution management policies for adoption into the Malaysian context
3. To explore and identify reduction strategies for air pollution emissions that will be appropriate for the Malaysian context
4. To initiate or develop better control and prevention guidelines/strategies for environmental factors (early warning systems), legal requirements, engineering factors (contaminant characteristics), economic factors (capital cost etc.)
5. To identify and explore appropriate clean drinking water management policies for adoption into the Malaysian context
6. To implement restoration strategies: (a) long-term plan for achieving water quality goals; (b) improving water quality – storm water treatment areas

# Allergy



Allergy cases reported are increasing worldwide but the pathogenesis remains poorly understood. The severity of allergies ranges from minor localized irritation on skin to systemic life-threatening anaphylaxis. Allergies arise from aberrant innate and adaptive immune responses and are result of the complex interactions between genetic and environmental stimuli including pollen and dust mites. Genetic predisposition and environmental stimuli may determine the involvement of different immune cells and the expression of specific cytokine profiles. The immunological pathogenesis of allergy involves an imbalance in helper T cells -  $T_H1$  and  $T_H2$ .  $T_H2$  cells secrete a panel of cytokines upon stimulation by allergens including IL-4, IL-5, IL-13 and GM-CSF which mediate the differentiation of  $T_H2$  subpopulation and eosinophils, the proliferation of B lymphocytes and IgE switching (Robinson *et al.*, 1992; Pukelsheim *et al.*, 2010' Bodey *et al.*, 1999). Without the allergen stimulation, a panel of  $T_H1$  cytokines (IFN $\gamma$ , IL-12) is produced. Decreased secretion of  $T_H1$  cytokines and increased  $T_H2$  cytokine secretion are reported to be associated with increased production of IgE which subsequently lead to degranulation of mast cells and eosinophils and causing airway hyper-reactivity (Yazdanbakhsh *et al.*, 2002).

EPHR aims:-

1. To investigate the prevalence of various allergic diseases and their association with genomic and epigenetic changes subsequent to environmental allergens exposure
2. To identify environmental factors that contribute to the development of various allergies
3. To determine the mechanism that regulates allergic responses subsequent to environmental allergens exposure
4. To investigate the gene-environment interactions in allergy and asthma
5. To identify new or to improve existing diagnostic and therapeutic measures for allergy and asthma
6. To improve the management and surveillance of allergies in Malaysia

Robinson *et al.* Predominant TH2-like bronchoalveolar T-lymphocyte population in atopic asthma. *N Engl J Med* 1992; 326 (5): 298-304.

Pukelsheim *et al.* Cytokine profiles in asthma families depend on age and phenotype. *PLoS One* 2010; 5 (12): e14299.

Bodey *et al.* Cytokine profiles of BAL T cells and T-cell clones obtained from human asthmatic airways after local allergen challenge. *Allergy* 1999; 54 (10): 1083-93.

Yazdanbakhsh *et al.* Allergy, parasites, and the hygiene hypothesis. *Science* 2002; 296 (5567): 490-4.

## Toxicology & Bioremediation

Environmental toxins are derived from either natural (animal venom, microbial and plant toxins) or synthetic and anthropogenic pollutants (e.g. heavy metals, pesticides, fertilizers and pharmaceuticals). Environmental health toxicology involves the study of the adverse effects of environmental toxicants on human health. Environmental chemicals or toxicants can be degraded via abiotic and biotic processes. Abiotic processes involve the degradation under the influences of ultraviolet light (photolysis) and water (hydrolysis). Degradation of environmental contaminants through the enzymatic actions of microorganisms (mainly bacteria and fungi) is referred as biotic degradation or bioremediation. The ultimate goal of remediation is to convert the toxic organic contaminants to simple, less toxic end or intermediate compounds (Kumar et al., 2011). Currently, the effectiveness of bioremediation in removing the contaminants has not been addressed fully. Limited attempts have been put in place to determine the toxicity of the end or intermediate bio-remediated products compared with the parental compounds.

EPHR aims:-

1. To develop effective and innovative bioremediation processes for environmental toxicants
2. To investigate the effects of remediation of environmental chemicals on potential toxicity to mammalian organisms
3. To develop bioassays for evaluating the biological responses to environmental contaminants before and after remediation
4. To develop bioassays for assessing the effectiveness of remediation

## Biodiversity

Biodiversity refers to all the biota in the ecosystem. Disturbances to the ecosystems may lead to adverse undesirable or unintended consequences to human health. Biodiversity contributes vastly as natural resources for new drug discovery e.g. penicillin antibiotic produced by fungi.



Biodiversity is essential for securing food supply for humans. Loss of genetic diversity within crops may lead to susceptibility to diseases and pest infestation, and drought or other natural and man-made disasters. Pollinators including bees are essential to maintain the genetic diversity of agricultural crops. Microbial diversity also affects food security and healthy living of humans (normal flora). Soil microorganisms are required to recycle the organic wastes and to fix the nitrogen from atmosphere for healthy plant growth. Disturbance in growth and distribution of normal flora on the human body will greatly affect human health and eventually result in overgrowth of pathogenic microorganisms and hypersensitivity such as skin allergy, asthma and allergic rhinitis. Disturbance of ecosystems shifts the distribution of plants, animals, human and pathogens which will lead to emergence and re-emergence of infectious diseases. However, many linkages between biodiversity and human health remain unknown. Increasing concerns about the impacts of biodiversity loss and changes to health have attracted the attention of many worldwide agencies.

EPHR intends to focus on:-

1. Capacity building: develop plans to facilitate active learning opportunities for researchers in strategic planning for biodiversity management
2. Biodiversity targets: identify underlying causes of biodiversity loss; promote sustainable use; safeguard ecosystems, species and genetic diversity; enhance the benefits to all from biodiversity and ecosystem services; enhance implementation through participatory planning, knowledge management and capacity building

## Infectious Diseases

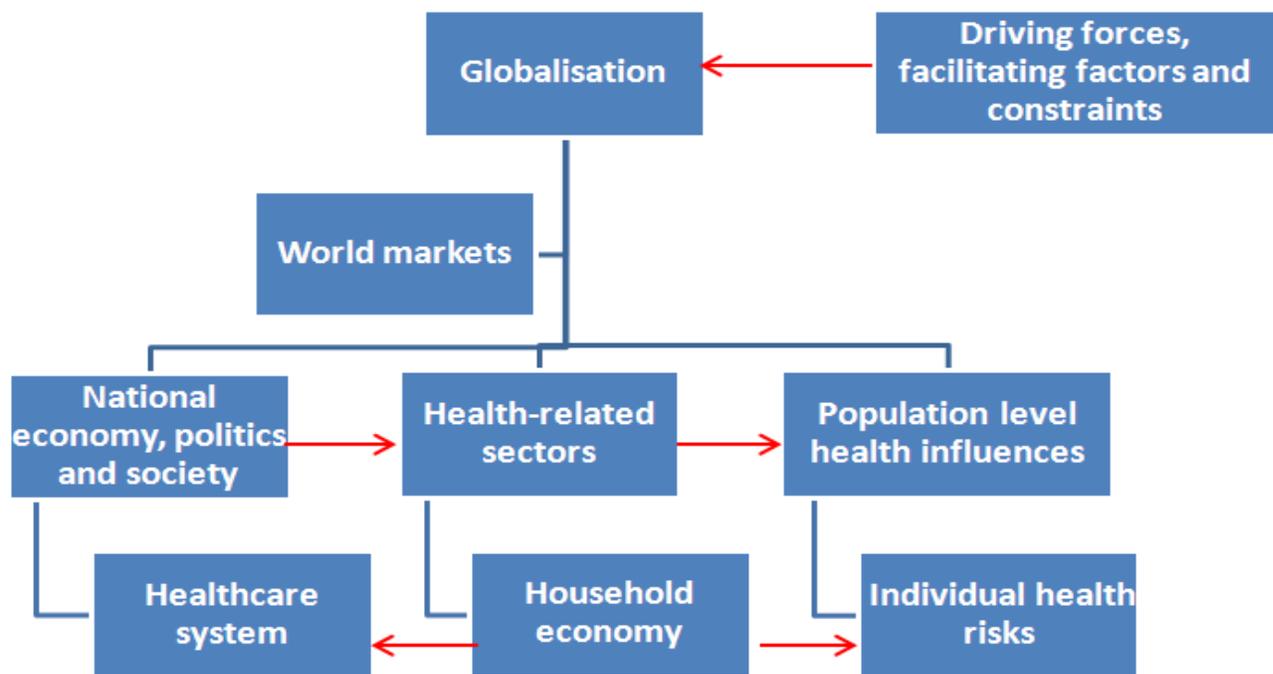
Knowledge that microbes cause infectious diseases has been known since the 19<sup>th</sup> century, with the germ theory introduced by Louis Pasteur in 1857. Over the centuries remarkable advances in medical research have led to breakthroughs in the eradication and treatment of several infectious diseases. Nonetheless, infectious diseases remain among the leading causes of death worldwide. The social and economic costs of infectious diseases are far from negligible for individuals, families and countries. Meanwhile, microbes continue to evolve and adapt to their environment, adding anti-microbial resistance to their evolutionary pathways.

Malaysia in the past decade encountered its share of challenges in dealing with infectious diseases. These include virus outbreaks: Nipah (1999), Tioman (2000), avian influenza virus H5N1 (2004), Melaka (2007), and Kampar (2008). Together with vector-borne diseases, such as dengue (dengue virus) and malaria (*Plasmodium falciparum*), infectious diseases continue to inflict significant human suffering, and escalate economic burden on individuals and families, as well as lead to increased costs of diagnostics and treatment.

In a world of rapid globalization, institutional, economic, social-cultural and environmental factors have become increasingly interconnected and interdependent. The links in the causal chains connecting globalization to health are exemplified in the model of Woodward *et al.* (2001). For example, rapid means of transportation moving large numbers of people across international borders provide opportunities for the spread and establishment of common or novel infectious diseases. The chain effect of disease risks accelerates in an era of dynamic technological and economic transformations, bringing about changes in the population health landscape. Disease and lifestyle patterns have also altered in tandem. Amidst these vicissitudes, knowledge gaps continually surface to challenge public health scientists. How can we leverage on the beneficial effects of globalization on population health status, and minimize the adverse ones?

Woodward *et al.* Globalization and health: a framework for analysis and action. Bulletin of the World Health Organization, 2001, 79: 875–881.

# Conceptual framework linking globalization and health (Woodward *et al.*, 2001)



## Infectious Diseases Continued

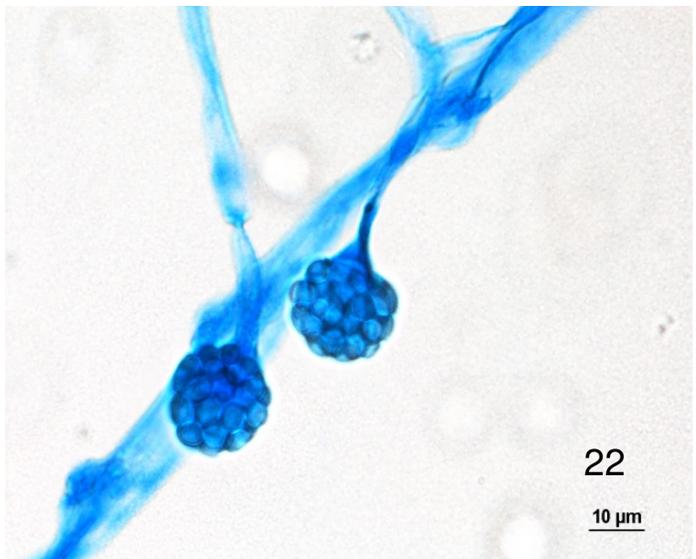
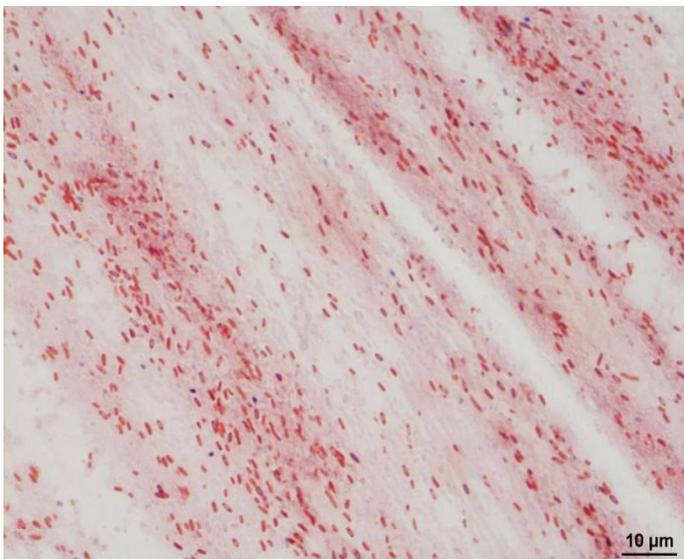
EPHR will target on:-

### A. Emerging and re-emerging infections

1. To determine disease surveillance, epidemiology, mode of transmission and outbreak in Malaysia
2. To study the vector and/or host ecology and its management
3. To improve or develop control and preventive strategies for emerging and re-emerging infectious diseases
4. To improve and accelerate the development and application of diagnostic tools for early detection and monitoring

### B. Antimicrobial resistance

1. To strengthen surveillance, regulate and promote rational use of antibiotics in humans and animal husbandry for combating antibiotic resistance
2. To promote improved healthcare quality in order to minimize the spread of hospital acquired infections and methicillin-resistant *Staphylococcus aureus* in healthcare setting
3. To create public and regulatory awareness on the sale and proper use of antibiotics, and patient compliance to antibiotic treatment



## Non-communicable Diseases

Infectious or communicable diseases were the major causes of mortality worldwide for centuries until about the end of the Second World War. Increasing resources spent on medical research brought about important breakthroughs including the discoveries of vaccines and antibiotics. With increasing life span, improvement in living and work conditions and changes in lifestyles, the disease patterns have also changed concomitantly, shifting towards a dominance of non-communicable diseases (NCDs). Currently 63% of all deaths worldwide stem from NCDs – chiefly cardiovascular diseases (CVDs), cancers, chronic respiratory diseases and diabetes.

The NCDs are responsible not only for deaths, but are also disabling. Degenerative disorders of bones and joints, for example, may cause as much as a quarter of all incapacitating conditions, thus being the single most important common cause of physical disability. Deaths due to NCDs in the developing world account for two-thirds of the world's total, at some 25 million annually. The rapid rise in coronary heart disease (CHD) burden in developing countries is attributed to rapid economic development, increase in life span and acquisition of lifestyle related risk factors. An example is the dietary intake shift over the years from the traditional diet high in grains and vegetables to one dominated by animal sources of fat and protein.

Malaysia is no exception with respect to having to bear a high NCD burden. According to the Ministry of Health (2010), NCDs identified as cardiovascular diseases, diabetes, cancer, mental illness and injury related conditions, constitute the major health burden of the country. Among the NCD risks targeted by MOH in its Strategic Plan 2010-2014 are a reduction in the prevalence of diabetes mellitus and obesity among ages 18 years and above.

In light of the above backdrop, EPHR will focus on the following NCDs and their risk factors, including biologic, behavioural, social-cultural, economic and environmental determinants and their interactions:

- Cardiovascular diseases
- Diabetes
- Chronic respiratory diseases
- Cancers
- Degenerative diseases
- Injury prevention



## Nutrition



Nutrition plays a pivotal role in health and sickness. Macro- or micronutrient deficiencies affecting a crucial life stage can bring about severe enough adverse impairment that may span generations. A case in point is the consequence of serious under-nutrition during pregnancy leading to intrauterine growth retardation (IUGR) and predisposition of the child to an increased risk of chronic diseases in adulthood.

Malnutrition is acknowledged as a primary cause of immunodeficiency worldwide, and while much has been elucidated about the pathogenesis of this interaction, nonetheless, as emerging and re-emerging infections continue to impact high economic costs and human hardship in developing countries, the complex interfaces of nutrition, immune functions and infections deserve contextual research investigations. These initiatives range from epidemiology, immune mechanisms, diagnosis, treatment, to prevention. Such insights into nutrition-immune functions and interactions would provide opportunities to enhance intervention efforts in controlling infectious diseases operative in a teeming tropical environment.

Several micronutrients have been implicated directly or indirectly in the etiology of NCDs, thus providing windows of opportunity for further fundamental and applied studies. Taking vitamin D as an example: there has been an explosion of information on its implications in diseases including CVD, some types of cancer, tuberculosis, multiple sclerosis, diabetes and Alzheimer's disease.

In the broader context of increasing population growth, research attention will continue to be accorded to the interrelationships among agriculture and food production, environmental changes, economic development, nutrition and health. This wide scope of "econutrition" that integrates environmental and population health will arguably be the focus of research for years to come.

In summary, nutrition studies in the Population Health Research Unit will encompass a wide ranging breadth of areas that impinge on health, productivity and quality of life.

## Gut Health

Mammals are hosts to trillions of symbiotic bacteria and fungi, and to a certain extent pathogens. It has been estimated that more than 100 trillion ( $10^{14}$ ) of microbes inhabit in human gut, far exceeding the total number of hosts' cell (Wallace *et al.* 2011). These microbes mainly reside in the large intestine and the caecum, where they contribute to ~60% of the total faecal mass produced.

It is widely acknowledged that the presence of the gut microbiota is a key factor in gut development, structure and function (Tannock, 2005; O'Hara and Shanahan, 2006). Recently the gut microbiota has been reported to vary significantly between obese individuals and normal individuals thus, suggesting that gut microbial metabolism and species variations in the mammalian host is of considerable importance in determining calorific bioavailability to the host (Turnbaugh *et al.*, 2007; Ley *et al.*, 2006; Dave *et al.*, 2012).

Gut microbiota dysbiosis has also been implicated in metabolic disorders such as insulin resistance and children with neurodevelopmental disorders such as autism (Caricilli *et al.*, 2013; Finegold *et al.*, 2002). Owing to the close association with human diseases and metabolic responses, the understanding of gut microbiota dynamics in different populations is key for future personalized drug design and dietary treatment (Finegold *et al.*, 2010). Characterizing and modelling microbial-mammalian metabolic interactions will give new insights into the complex interplay between host genetics, diet and gut microbial variation. Since the microbiota are extremely active, metabolically, and co-metabolize many endogenous and xenobiotic compounds, they clearly have the potential to affect the biochemical composition of the tissues and biofluids of the host.

Wallace *et al.* Human gut microbiota and its relationship to health and disease. *Nutr Rev* 2011; 69: 392-403.

Tannock. Commentary: Remembrance of microbes past. *Int J Epidemiol* 2005; 34: 13-5.

O'Hara and Shanahan. The gut flora as a forgotten organ. *EMBO Rep* 2006; 7: 688-93.

Turnbaugh *et al.* The human microbiome project. *Nature* 2007; 449: 804-10.

Ley *et al.* Ecological and evolutionary forces shaping microbial diversity in the human intestine. *Cell* 2006;124: 837-8.

Dave *et al.* The human gut microbiome: current knowledge, challenges and future directions. *Transl Res* 2012; 60: 246-57.

Caricilli *et al.* The role of gut microbiota on insulin resistance. *Nutrients* 2013; 5: 829-51.

Finegold *et al.* Gastrointestinal microflora studies in late-onset autism. *Clin Inf Dis* 2002; 35 (Suppl 1): S6-16.

Finegold *et al.* Pyrosequencing study of fecal microflora of autistic and control children. *Anaerobe* 2010; 16: 444-53.

Prakash *et al.* Gut microbiota: next frontier in understanding human health and development of biotherapeutics. *Biologics* 2011; 5: 71-86.

## Health Policy / Economics

Along with economic prosperity come diseases of affluence: obesity, diabetes, drug addictions, and heart disease. Cancers of all kinds are more common among those with these morbidities. As more jobs and lifestyles become sedentary in Malaysia, chronic diseases will increase as they have in other nations. In this sense, Malaysia might learn from the successes and mistakes of other countries in preventing, discouraging, or managing the many lifestyle diseases that emerge along with sedentary lifestyles found in information and manufacturing-based economies.

Prevention is the key. Through education, outreach, and screening, good lifestyle choices can replace poor ones. Reducing the prevalence and impact of NCDs on healthcare systems and national healthcare budgets is a World Health Organization priority. The basic approach to managing NCDs includes screening for manifest disease. Better yet is to screen for risks early enough to intervene at the behavioural level to avoid diseases. Five common indicators of risk observed by clinicians are blood pressure, high cholesterol, tobacco use, alcohol consumption, and obesity or excess BMI.

The worst risk and perhaps the most preventable are smoking and tobacco use. All tobacco use increases risks of life-threatening NCDs, and to the extent preventable, might reduce incidence of many NCDs. Smoking increases odds of cancers of all types, and heart disease. In addition, effects of smoking cause chronic obstructive pulmonary disease (COPD) and compromise circulation by direct and passive inhalation. In the US, for example, it can be considered child abuse to carry a child in the automobile with smokers. Second hand smoke is now recognized as a serious danger. Smoking in public places has been reduced or eliminated by public bans and increasing prices by increasing taxes. Interventions and support can help people quit tobacco, but public policy is the most effective at the population level (Figure 7). Physician initiated intervention is the most effective at the patient level. National smoker quit lines are modestly effective, but are low cost, so for the effectiveness they offer, they end up cost-effective.

After prevalence of each NCD is established, interventions should be theory-based and incrementally implemented, preferably on equivalent samples. This allows program steering, i.e., move, change, or redirect resources according to what works when, for whom, and where. One type of intervention might be effective for one ethnic group or region but not elsewhere, or just not as well elsewhere.

## Figure 7

	Effects of bans on:	Effects of price on:
Prevalence	Public bans associated with 25% prevalence reduction in 18- to 25-year-olds (Repace, 2004). Adults had an 11% drop; total worksite bans account for 6% of the reduction (Levy et al., 2006)	Reduces prevalence by 3.7% in adolescents (Hopkins et al., 2001);
Consumption	Bans associated with 14% lower consumption and 6% lower prevalence in workers (Farrelly et al., 1999)	10% increase in price associated with a 4.1% decrease in consumption (Hopkins et al., 2001)
Smoking prevention	Bans reduce youth participation (Chaloupka & Wechsler, 1997)	Price more effective in discouraging young people (Levy et al., 2006)
Economic impact on entertainment businesses	In studies that found a negative impact on business, the odds of subjective measures were 4 X higher and the odds of not being peer reviewed were 20 X higher; 94% of negative impact studies were sponsored by tobacco companies (Scollo, Lal, Hyland, Glantz, 2003)	Causality too tenuous; no literature on this effect
State tax revenue	Uncertain	Pre-ban hoarding, post-ban drop, and then a new equilibrium emerges.
Reduced exposure to SHS	90% reduction in airborne particulate matter (Repace, Hyde & Brugge, 2006)	Too tenuous of a casual relationship; no literature on this effect
Compliance	Public work and hospitality bans are associated with near 100% compliance within 30 days.	Price increases in one state lead to increased business in cross-border cities (Efrati, 2007 and Farrelly et al., 2003)

Once population behavioural change is effected, support to maintain change is crucial. Tobacco and smoking quit lines are an obvious of example of support for recent “quits” that are tempted amidst their smoking buddies and in familiar social contexts. For chronic degenerative or rare diseases, social support can be a huge quality of life gain. With the Internet, support communities may be formed even for those who are unable to leave their house. Patients with a condition share information as to what works for them outside of the constraints of evidence-based care delivery. Indeed, the “softer” data that comes from living from day-to-day with a chronic and sometimes fatal disease needs to be shared with others suffering from the same condition. Only patients with the condition are credible in knowing and sharing what living with the disease is really like. Such internet conversation threads should be monitored by a medical or healthcare professional to make sure they do not stray into nonsense. PatientsLikeMe.com is one successful website already in the US.

All interventions should be tested for their benefit versus their economic impact. In the USA, economic benefit in terms of treatment or loss of productive lives must be masked as resources losses, since no one wants to admit that costs really are at the centre of many healthcare decisions.

The health care market information asymmetries in the USA resist any changes that jeopardize current fee structures and profitability. When patients have some stake in their healthcare bills, they tend to spend wisely. Also, when physicians need to share the financial risks of patient care, they are less likely to order needless tests, i.e., tests that do not add information to the most likely working diagnosis.

## Health Policy / Economics Continued

Actually, a powerful moderator to medical over-treating and over-testing is the informed patient. An informed patient can influence medical decisions in a patient-centred care scenario. This would especially be important for NCD patients where the visit is for managing symptoms rather than curing disease. The patient needs to state their realistic health goals as shaped by an education about their disease. Physician training shapes their decision-making. With respect to NCDs, physicians may be the least qualified person to offer decisions and solutions. Informed patients, specially trained nurses, or a kind of “health coach” might serve as an intermediary and patient advocate that keeps an eye on the patient’s goals and alternatives to care.

Informed medical decision-making is seen as a solution to many issues in chronic degenerative diseases and chronic pain in the US. Incentivizing patients to take care of themselves can be exasperating. With respect even to acute care, Malaysia should embrace many of the informed medical decision-making initiatives. Finally, all interventions to be seen as economically viable and helpful to the public as they are first tried and tested as models.

Public health scientists are in the early stages of gathering concrete evidence on the effects of globalization on population health. This evidence is required to inform policies and actions to protect and promote the health of the poor. The challenge is to find ways to measure impact and formulate evidence-based national and international policy responses.

Bloom *et al.* The Global Economic Burden of Non-communicable Diseases. Geneva: World Economic Forum. 2011.  
National Strategic Plan for Non-Communicable Disease. MOH Malaysia 2010