Biomarkers for proactive health care: A vision of clinical care - should public health cooperate

Proactive protein monitoring is a vision for improving the management of frequently occurring non-communicable diseases (NCDs) in clinical settings (1). With the already advanced public health cooperation between primary health care and clinical practice in countries like Thailand, this vision could be extended to public health as well.

The concept

The basic idea is to switch from reactive to proactive management of health and disease through continuous monitoring. Presently, reactive management begins after the onset of symptoms. The disease must be diagnosed, a treatment scheme must be launched, and the development must be monitored. The treatment is either successful, or the further progression of the illness has to be managed. For the proactive management of selected vulnerable groups at risk of certain diseases, continuous monitoring enables early intervention, attempting to prevent the onset of disease symptoms. In case prevention doesn't work, the traditional reactive approach takes over (1). Such an approach would need the inclusion of sophisticated laboratory methods.

Advancement in laboratory methodologies

The expensive but relatively easy methods for measuring proteins have sparked renewed interest in continuous protein monitoring (1). Methods for sophisticated analysis, not so long ago, the thin-layer chromatography (TLC) was widely applied (2). This is now replaced by clinical laboratory apparatuses that, for instance, use electrochemiluminescence (ECL) techniques (3).

Use of biomarkers in the clinical setting and public health

In the clinical setting, biomarkers are used for what is called 'precision medicine.' This is particularly useful for cancer patients, as demonstrated by a Thai group for lung cancer (4). Public Health might join in for NCDs with a high prevalence in the community. That has already been done with a collection of factors combined in what is known as metabolic syndrome, where risk factors for hypertension, cardiovascular disease, renal dysfunction, and stroke are combined (5). For instance, the results of an investigation in the northeast of Thailand could be translated into a strategy for prevention in the field of nutrition. Sticky rice, as a staple food, is associated with high triglyceride levels and overnutrition, whereas a mixture of traditional and more Western diets is inversely related to abdominal obesity (6). The conclusion was that the traditional diet is linked to T2DM and cardiovascular diseases, while a mixed diet reduces abdominal obesity.

In this context, improved control of NCDs requires being aware of important developments, for instance, in human metabolism, genetics, epigenetics, and gerontology. Public health researchers, usually not equipped with sophisticated research tools, should follow up on what happens in molecular epidemiology and search for biomarkers meaningful for primary and secondary prevention in collaboration with the clinical sector (7, 8). Such as screening for T2DM using glycated hemoglobin (HbA1c) as a clinical reference in the rural area of the Northeast of Thailand was validated (9).

Short overview of the development of health care in Thailand

That public health, particularly in Thailand, could be suitable for a mutual cooperation with the clinical sector is encouraged by the developments of health care in the country.

A benchmark of Public Health policy goes back to the Alma-Ata conference in 1978 (2521 BE). The World Health Organization (WHO) and the United Nations International Children's Emergency Fund (UNICEF) meeting took place in Kazakhstan, at that time integrated into the Soviet Union. With the slogan 'health for all by the year 2000', the main issue evolved as primary health care with rural local health workers (10).

Somehow objected by high-income countries, the need to include NCDs in public health, besides high-income, also into the agenda of low and middle-income countries, was pushed forward by a UN high-level meeting in 2011 (2554 BE). The understanding of politicians, especially in Western countries, centered on infectious diseases as the major public health problem in tropical areas, where the so-called developing countries were mainly situated. Another WHO conference in 2014 (2557 BE) included NCDs as issue 3.4 into the Sustainable Development Goals (SDGs). The main NCD diseases were outlined as cardiovascular diseases, diabetes, chronic obstructive pulmonary disease, and cancer. As 'best buy' strategies for NCDs prevention, smoking, unhealthy diets, harmful use of alcohol, and physical inactivity were defined as major risk factors (7).

Cooperation between clinical and primary health care

Thailand quite early realized that, besides infectious diseases like malaria, NCDs became a very serious health problem, caused by a rapid change in lifestyle patterns and food intake (11). Since working to prevent NCDs is more challenging than focusing on the control of infectious diseases, cooperation between medical personnel within the ambulance and hospital settings and the community-based Public Health is required.

That such cooperation works effectively in the rural Northeast of Thailand was revealed through small talk with the caddy over a nine-hole golf course recently. The blood pressure of the caddy, suffering from hypertension, is regularly measured by the village health volunteer, and she sees the doctor at the district hospital regularly, every three months in her village.

Not only hypertension but also type 2 diabetes mellitus (T2DM) are highly prevalent among the population. Not only in Thailand but elsewhere too, the biomarker blood glucose for diabetic patients brought laboratory investigations to the periphery of health care (9). Though not yet through wearable electrochemical glucose sensors as suggested for the US (12). Such sensors might be too sophisticated to be considered applicable in public health services in countries like Thailand. Yet, making advances in medicine available to the broader fraction of the population should be kept in mind.

Diseases suitable for proactive protein monitoring

Not all diseases suggested as suitable for proactive continuous monitoring within the clinical setting might be suitable for a public health approach, even if the collaboration with the ambulatory sector of hospitals close to public health initiatives could be assured. This could depend on the policy towards public health in a given country, the frequency of the disease, and the capacity of the health care system. Neurological diseases, i.e. Parkinson's and Alzheimer's, as well as sepsis, for the time being, should be reserved solely for the clinic. Among the metabolic diseases, T2DM has more or less already made its way into public health in Thailand, whereas heart failure and autoimmune diseases might have a promising potential to be observed on a population basis with the help of biomarkers.

Cardiological disease and B-type natriuretic peptide (BNP)

Quite some time ago, a neurohormone, named B-type natriuretic peptide (BNP), was discovered. The secretion of the protein through the cardiac ventricles is intensified in response to an increase in blood volume, due to a malfunction of the heart and subsequent expansion of the ventricles. The patient's symptom is shortness of breath, called dyspnea by the physician (13, 14). More recently, BPN was advocated as a promising, valuable prognostic test (15). It might be particularly useful for congestive heart failure (CHF) and left ventricular dysfunction in cases of cardiovascular diseases (1, 16). At the final stage of heart failure, the right ventricular dysfunction might also be indicated by BPN.

Women and NCDs

Features of diseases differ for women and men (17). This is also true for heart diseases, especially given the still neglected drastic change in the overall metabolism for women during and after menopause (18). Long-term indicators of women's cardiovascular health would be highly beneficial, including highly sensitive C-reactive protein (hsCRP), low-density lipoprotein cholesterol (LDL-C), and lipoprotein (a). These biomarkers are suggested for longer periods, enabling early-life intervention for women starting from the onset of menopause (19).

Women and autoimmune diseases

Mankind consists of two biological sexes. Men and women not only differ in the features of one and the same disease, but some diseases are more prone to occur in one sex more often than the other. This is true for most of the common autoimmune diseases (20). The rapid demise of 'western ideology' from biological facts resulted in neglect of women's health, particularly in biochemical research, including pharmacology (17). Corresponding to what public health is due to women, therefore, autoimmune diseases should be of higher interest in public health (21).

Advances in the etiology and therapy of autoimmune diseases

This claim additionally is justified through recent research results, which shed light on the higher risks for women to suffer from this group of diseases, attributed to the different arrangement of the female sex chromosomes compared to men (20), and the Nobel Price for physiology and medicine 2025 was given to three scientists, which opened the improved expectation to come up with a more effective treatment, compared to the present more symptomatic one (22).

Epidemiological data on the burden of autoimmune diseases throughout Thailand are missing. However, recent publications shed light on the two important diseases in this group, i.e., systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) (23, 24). As expected, both diseases are more prevalent among women compared to men. The female-to-male ratio accounts for 9.61:1 for SLE, and the prevalence of RA in women in the year 2020 was 78.3%. It is important to know that the main age group for SLE, with 40 to 49 years, differs from RA, in that elderly women aged 60 to 69 years are predisposed to RA. Both diseases are especially prevalent in southern Thailand, and the number of cases by all means justifies public health attention. The cases of SLE in 2017 accounted for 55.956 with a point prevalence of 85.8/100.000, and for RA in 2020, 64,849 at 99.2/100.000. For RA, no biomarker has been identified yet; serum C3 and C4 have been mentioned but seem to require further investigation over the course of the disease (25).

Conclusion

The US authors of the underlying main publication, probably overwhelmed by the rapid and striking advances in biochemistry, particularly genomics, have spread out their vision to encompass proactive protein monitoring from the perspective of specialized clinical and laboratory medicine (1). Yet they are well aware of the down-to-earth background needed to implement such a scheme.

They resort to the various stages of 'preventive care', working within the triangle of patient, physician, and electronic health record (HER) (see Fig.4 (1)). How this will work within the given overall health care of the US remains to be sorted out.

It seems Thailand is in a good position to try out for selected diseases, such a demanding project. The vision of primary health care was not lost in Thailand, even throughout the

challenging occurrence of NCD, and devastating periods with AIDS and the coronavirus calamity. With the Ministry of Public Health's guidance, a trial program could be launched in a particular area. From public health, epidemiology, statistics, risk-factor measurements, and screening technologies could be offered. Last but not least, a further benefit would be to expand research on NCDs to generate valuable research questions for biochemistry and metabolism as well.

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Frank P. Schelp is responsible for the manuscript's content, and the points of view expressed might not reflect the stance and policy of the Faculty of Public Health, Khon Kaen University, Thailand.
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Grammarly software was used to improve English, but the AI function was disabled.