

The Emerging Epidemiological Paradigm of Population Health and Disease

La emergencia del paradigma epidemiológico de salud-enfermedad de la población

"A large number of people at a small risk may give rise to more cases of disease than the small number who are at a high risk."

GEORGE ROSE, 1985

INTRODUCTION

After the Second World War, epidemiologists, especially in Great Britain, started to thoroughly look out for the course of "risk factors" leading to chronic diseases. Led by Austin Bradford Hill and Richard Doll with the development of new epidemiological designs (case-control design, cohort follow-up and randomized clinical trials) they elegantly arrived to the bold proposal of associating the growing lung cancer epidemic with cigarette smoking. They quickly realized they were looking for unknown causes that could have multiple "risk factors" to trigger chronic diseases, the new threat of public health.

Risk factor epidemiology could be characterized as the causal search of multiple factors at the individual level, not at a micro inferior level (organs, tissues, cells or molecules), and neither at a macro superior level (collectivity or society), with the guiding concept that these different factors could be analyzed using the new multivariate regression statistics, and could produce and even prevent chronic disease. This type of analysis is represented with the metaphor of the "black box", whose validity is exclusive of the analysis at the individual level. (1)

This surge of epidemiology clarified our understanding of research designs, helped with the proposal of simple large clinical studies encouraged by the group of Oxford led by Richard Peto, and tried to solve the problem of causal inference in a multicausal world, enabling us to develop the power provided by the emergence of computers to dominate the complex analysis of multiple variables.

Despite these irrefutable achievements, the epidemic of chronic non-communicable diseases could not be solved in the world, including developed countries (the vast majority). We must then ask ourselves the question that science poses at certain times: how are we going to choose the concept of our study? Why raise this question? Because it is known that the concept of disease, that we accept unconsciously, rules the

causes we are going to search. It is based on the theory of the dominant paradigm and the scientific revolutions developed by Thomas Kuhn almost 50 years ago. (2) A Kuhnian paradigm is the conceptual framework governing the search for truth of most scientists at a certain time, which is finally discarded and replaced in the scientific revolutions.

Let us then analyze the development of epidemiology, showing which are the paradigms for the concept of disease in each era, and when the discoveries that contradict the paradigm have changed the common shared understanding giving rise to a new concept of epidemiological reality.

HISTORICAL DEVELOPMENT OF THE PARADIGMS OF DISEASE ETIOLOGY

The era of the "miasma" paradigm and of sanitary statistics epidemiology

The "miasma" theory, where the environmental context produces diseases by means of fetid emanations from corrupting organic substances which contaminate the air, prevailed since the XVIII century and throughout a great part of the XIX century. No new biological discovery explained its adoption, but it fitted to the needs of a new social time, with the rise of primitive capitalist accumulation in England, producing the private hedging and appropriation of common lands from the farmers and their displacement to the cities, which led to massive and chaotic urbanization with industrialization in huge manufacturing cities as Manchester.

This led to significant sanitary discoveries with the studies on contaminated water, food pollution and the risks of the different jobs. Rudolph Virchow was the emblematic character and hero of this period, (3) who at the beginning of 1848 was commissioned to investigate the typhus epidemic in Upper Silesia (a Prussian province with mostly Polish population). At the end of 1848 his written report associated the epidemic to poverty and lack of education of Polish peasants, originated by the political oppression of bureaucracy and the economical oppression of the local aristocracy, and as he stated the solution "can be resumed in three words, complete and unlimited democracy". (4)

A few days after his return from Silesia he par-

ticipated in the March revolution in Berlin, defending the barricade in the intersection of Friedrich and Tauben streets. The Prussians, angry with his report, removed him from the Charité Hospital in Berlin in March 1849. After spending years in exile from the Würzburg chair of anatomical pathology, where he developed his ideas about cellular pathology, due to his great prestige throughout Europe he was brought back in 1856 to a new Institute, created at his request, at the Charité Hospital. In 1859 he became a member of the Municipal Council of Berlin, where he remained until his death. There, he fought for and was the main participant to provide Berlin with drinking water and a public sewage system to collect the waste products from the houses.

In the newspaper, *The Medical Reform*, of which he was cofounder, he wrote that “physicians are the natural attorneys of the poor” and that “medicine is a social science, and politics is nothing else but medicine on a large scale”. He also had a clear idea of the reason behind the development of epidemics, which is still of high value; he stated “if disease is the expression of the individual life under unfavorable conditions, epidemics must be indicative of important perturbations in the lives of the masses”... “Are we unable to see that epidemics always point to the deficiencies of society?” he asked “One can point out the atmospheric conditions, the general cosmic changes and similar phenomena, but none can cause epidemics by itself. These are produced only due to the social situation generated by the abnormal conditions people have lived in for a long time.”

In 1861, with scarcely 40 years, he was elected member of the Prussian parliament, where he challenged the “iron chancellor” Otto von Bismarck. He was doubtless a physician involved with his time, the scientist who discovered the mechanism of thrombosis and cellular pathology and introduced the microscope in the schools of medicine. He was a superb and indefatigable anthropologist, excited by prehistory he was also an archeologist, assisting Schliemann in Egypt and Troy and performing excavations in Germany and the Caucasus.

The era of the germ paradigm and of infectious disease epidemiology

A scientific revolution, in the manner of a change in the paradigm of the causal concept of disease, finally occurred during the last part of the XIX century when the specific cause of infectious diseases was discovered giving rise to the Germ Theory. This theory is introduced after the works of Henle, Koch and Pasteur who showed the presence of specific bacteria, consequently establishing that there is a single cause for each different disease. The bacterial cause and the disease are related and the disease could be eradicated if the germ producing it was eliminated. (5)

The theory was successful for the etiology and control of many infectious diseases, and was reinforced

when the causal agent of metabolic diseases (vitamins, calcium for rickets, etc.) and endocrinological diseases (insulin to regulate diabetes, the thyroid hormone, etc) was found. This success lasted until the middle of the XX century, when it fails to find a single, simple etiology for the explosion of chronic non-communicable diseases, which displace infectious diseases as the main cause of population mortality.

The era of the “black box” paradigm and chronic disease epidemiology

A revolution of thought is produced with the construction of the underlying idea of the multiplicity of causes for a single organic disorder of the individual. The theory emerged when the mystery of new chronic disease epidemics was acknowledged. Over time, this theory of the multiplicity of causes evolved as the current “risk factor” epidemiology.

The “black box” model is a metaphor to represent phenomena that have hidden internal mechanisms which are unknown for the observer. (6) It postulates multi-causality as a network for each pathological process, where the causal effect of each factor depends on its proximity with the presumed effect, and eventually allows breaking the causal chain operating on one risk factor.

This type of epidemiological investigation has identified a large number of non-infectious disease risk factors associated with individual susceptibility in a population, especially related with cancer or coronary heart disease. However, although it answers why an individual is at greater risk or is more susceptible to the disease compared with the least susceptible or at lower risk (relative risk or probability of acquiring the disease) in the population, it does not answer why the incidence of disease is different in time or compared with other populations with different incidences, that also have the same relative risk within their populations, but where the absolute incidence in each of them is very different.

The era of the “china box” paradigm and multilevel epidemiology

During the nineties it began to become apparent that the exclusive approach at the “individual level” could not even stop the worldwide tobacco dissemination and even less the new HIV and hepatitis “B” and “C” epidemics. Thus, the classical epidemiology at the “individual level” started to include the inferior or micro level, which in our times implies molecular biology, and the superior or macro level, which implies the population, the collectivity and society.

In this framework, Mervin Susser (1) puts forward an epidemiological theory unifying diverse phenomena at different levels, from social causes (superior level) through the person (individual level) reaching the disease at the molecular level (inferior level). Disease is conceived as a population phenomenon occurring at multiple, interconnected and hierarchical levels. He

thus postulates that collective health phenomena occur similarly to a set of “china boxes”, so that a system contains another of an inferior level. In this way, the relationships at each level, from molecular to social, are valid only to explain their level; that is, they cannot be generalized to other levels. The proposal was termed by Susser “eco-epidemiology”.

THE EMERGENCE OF THE POPULATION HEALTH CONCEPT

The notion that the population health as a whole may be sick, at a level superior to the disease of the individual persons, was promoted by the studies of Geoffrey Rose (professor of epidemiology at the “London School of Hygiene and Tropical Medicine”), in his seminal essay published in 1985 “Sick individuals and sick populations (7) and which due to its conceptual importance was published again in the same journal (International Journal of Epidemiology), (8) 26 years later, with several editorial comments.

According to Rose, his main ideas were inspired by George Pickering (an expert in blood pressure) who stated that hypertension was not a binary dichotomic phenomenon of yes or no, but was present as a continuum, and by Ancel Keys (principal investigator of the study for 7 countries) who showed that the complete risk distribution can be displaced in a population when compared with another one, suggesting that the entire population may be sick.

Based upon his studies, he postulated the fundamental concept that there is clearly something that can be called “population health”, and that therefore, the causes of disease incidence at a population level can be different from the causes of cases at an individual level. Thus, a massive population approach for disease prevention is better than treating persons individually; however, this approach suffers what he called “the prevention paradox”, since although the total population benefit may be high, it can be small for each person. Thus, the individual treatment is complementary in people constituting the visible level of the high risk iceberg, while the global epidemic does not disappear. We will follow Rose’s clear and elegant reasoning in his 1985 article. He focuses his observation on the fact that the dominant epidemiological research strategy studies the differences within a certain population, comparing the higher or lower individual risk according to its risk factors. To achieve this, he performs cohort studies with and without exposure to certain risk factors to identify whether the individuals are at greater risk of developing the disease (new disease incidence), or case-control studies where persons with or without the disease are compared to detect whether sick individuals have been more exposed to certain risk factors.

The determinants of individual cases

As stated by Rose: “Applied to etiology, the individual-centered approach leads to the use of relative risk as the basic representation of the etiological force: that

is, ‘the risk in exposed individuals relative to risk in non-exposed individuals’. Clearly, the concept of relative risk has almost excluded any other approach to quantify causal importance. It may generally be the best measure of etiological force, but it is not the measure of all etiological outcomes or of public health significance.

“Unfortunately, this approach to identify the causes and the measurement of its power has to assume the heterogeneity of exposure within the study population”.

And he proceeds with a demolishing hypothesis: “If everyone smoked 20 cigarettes a day, then clinical, case-control and cohort studies alike would lead us to the conclusion that lung cancer was a genetic disease; and in one sense that would be true, since if everyone is exposed to the necessary agent, then the distribution of cases is wholly determined by individual susceptibility.

Further on, he declares that the causal hypothesis of cigarette smoking could be confirmed in the seminal studies of Bradford Hill and Doll, because fortunately at that time the proportion of smokers and non-smokers was equally distributed.

“... But we should not forget that the more widespread a particular cause is, the less it explains the distribution of cases. The hardest cause to identify is the one that is universally present, for then it has no influence on the distribution of disease”, he wrote later.

The determinants of population incidence rate

He distinguishes two types of etiological question according to the level where it is produced: “The first seeks the causes of cases, and the second the causes of incidence. ‘Why do some individuals have hypertension?’ is quite a different question from ‘Why do some populations have a lot of hypertension, whilst in others it is rare?’ The questions require different kinds of study, and they have different answers.”

He then uses the example of blood pressure distribution in the nomad population of Kenya and in London civil servants, which overlap slightly. “The familiar question: ‘Why do some individuals have higher blood pressure than others?’ could be equally asked in either of these settings, since in each the individual blood pressures vary (proportionately) to about the same extent, according to the same variables (risk factors), in each instance... We might achieve a complete understanding of why individuals vary, and yet quite miss the most important public health issue, namely ‘Why is hypertension absent in the Kenyans and common in London?’ The answer has to do with the determinants of the mean population. What distinguishes the two groups has nothing to do with the characteristics of individuals; it is rather a shift of the whole distribution, a huge influence acting on the population as a whole. To find the determinants of prevalence and incidence rates, we need to study the

characteristics of populations, not the characteristics of individuals.

How do the causes of cases relate to the causes of incidence?

"Most non-infectious diseases are still of largely unknown cause. If you take a textbook of medicine and look at the list of contents you will still find, despite all our etiological research, that most are still of basically unknown etiology."

"We know quite a lot about the personal characteristics of individuals who are susceptible to them; but for a remarkable large number of our major non-infectious diseases we still do not know the determinants of the incidence rate."

He then proceeds: "There is hardly a disease whose incidence rate does not vary widely, either over time or between populations at the same time. This means that these causes of incidence rate, unknown though they are, are not inevitable. It is possible to live without them... The clues must be sought from the differences between the populations or from changes within the populations over time."

Prevention

These two approaches to etiology -the individual and the population-based- have their counterpart in prevention: "high risk" strategy and "population" strategy.

The "high risk" strategy

This is the traditional medical approach to prevention aiming to identify susceptible individuals at high risk and offer them some individual protection. The physician accepts responsibility for sick patients and for individuals who are not sick today but may be sick tomorrow; the fact of receiving medications legitimizes his definition as a patient before society.

Advantages: The "high risk" strategy has some significant and clear advantages; first of all it leads to appropriate interventions for the individual and adequate to subjects advised to adopt them. For example, in case of high serum cholesterol the advice is on changes in the diet or statin prescription; then, that intervention is appropriate to that particular individual who has a metabolic problem, and as a second advantage it facilitates the subject's motivation. For similar reasons, the third advantage of the "high risk" approach leads to physician motivation, who feels comforted that there is a proper and special justification for preventive intervention.

In turn, it produces a cost-effective use of limited resources, and as an ultimate benefit it provides a favorable risk-benefit ratio, because if the intervention has an adverse effect, the higher the risk, the more favorable the benefits.

But the "high risk" strategy has also some disadvantages and serious limitations.

Disadvantages: The first disadvantage is focused on the difficulties and cost of screening. If we propose

a screening for high cholesterol, questions would immediately arise: What do we call high levels?, at what age do we start?, during childhood?, with what frequency?, at what intervals?

As Rose states: "The second disadvantage of the "high-risk" strategy is that it is palliative and temporary, not radical. It does not seek to alter the underlying causes of the disease but to identify individuals who are particularly susceptible to those causes. Presumably, in every generation there will be such susceptible individuals; and if prevention and control efforts were confined to these high-risk individuals, then that approach would need to be sustained year after year and generation after generation. It does not deal with the root of the problem".

The third disadvantage of the "high risk" strategy is that the focus has a limited potential both for the individual as for the population, since our power to predict future cardiovascular disease with risk scores is quite limited and weak and most of those who are affected and die are in the rest of the population considered as low risk. (9) As he definitely points out: "A large number of people at a small risk may give rise to more cases of disease than the small number who are at a high risk".

"A further disadvantage of the 'high risk' strategy is that it is behaviorally inappropriate. Eating, smoking, exercising and all our other lifestyle characteristics are constrained by social norms. If we try to eat differently from our friends it will not only be inconvenient, but we risk being regarded as cranks or hypochondriacs. If man's working environment encourages heavy drinking, then the advice that he is damaging his liver is unlikely to have any effect. No one who has attempted any sort of health education in individuals needs to be told that it is difficult for such people to step out of line with their peers. This is what the 'high risk' preventive strategy requires them to do".

The Population Strategy

On this point, Rose expressed: "This is the attempt to control the determinants of incidence, to lower the mean level of risk factors, to shift the whole distribution of exposure in a favorable direction. In its traditional "public health" form it has involved mass environmental control methods; in its modern form it is attempting (less successfully) to alter some of society's norms of behavior".

Advantages: "The first major advantage is that it is radical, because it attempts to eliminate the underlying causes that make the disease common, implying an epidemic."

Studies of different cohorts show that 10 mmHg decrease in systolic blood pressure, corresponds to about 30% reduction in the total attributable mortality. Thus, it emerges as a great potential for the population, when focused collectively.

Also "The approach is behaviorally appropriate. If non-smoking eventually becomes 'normal', then

it will be much less necessary to keep on persuading individuals. Once a social norm of behavior has been accepted and (as in the case of diet) once the supply industries have adapted themselves to the new pattern, then the maintenance of that situation no longer requires effort from individuals. The health education phase aimed at changing individuals is, we hope, a temporary necessity pending changes in the norms of what is socially acceptable".

But, unfortunately, the population strategy of prevention has also some drawbacks.

Disadvantages: "It offers only a small benefit to each individual, since most of them were going to be all right, anyway, at least for many years. This leads to the prevention paradox: (10) A preventive measure which brings much benefit to the population offers little to each participating individual". This has been the history of public health: of immunization, the wearing of seat belts and now the attempt to change various lifestyle characteristics. Of enormous potential importance for the population as a whole, these measures offer very little -especially in the short term- to each individual; and thus there is poor motivation of the subject ... Much more powerful as motivators for health education are the social rewards of enhanced self-esteem and social approval".

In the population approach there is also a remarkable lack of doctor motivation, as many become disheartened because no more than 5% to 10% of their patients stop smoking, resulting in a decrease in their professional esteem for the absence of those behavioral skills.

"In mass prevention the risk-benefit ratio is worrying, since usually the expectation of benefit for the person is small and therefore it could be outweighed by any possible risk, even not very significant. So it is important to distinguish two approaches. The first is the restoration of biological normality by the removal of an abnormal exposure, as stopping smoking, moderating relatively recent deviations from the diet, or controlling the growing danger of air pollution or global warming, as there could be a presumption of safety. The other approach leaves intact the underlying causes of the incidence and seeks to introduce some new supposedly protective interventions (jogging) or drugs, (immunization, statins, etc.). It is essential to know that the benefits far outweigh the possible risks.

Next, the full conclusions of Geoffrey Rose are quoted:

"Case-centered epidemiology identifies individual susceptibility, but it may fail to identify the underlying causes of incidence. The 'high risk' strategy of prevention is an interim expedient, needed in order to protect susceptible individuals, but only for so long as the underlying causes of incidence remain unknown or uncontrollable; if causes can be removed, susceptibility ceases to matter."

"Realistically, many diseases will long continue to call for both approaches, and fortunately competition

between them is usually unnecessary. Nevertheless, the priority of concern should always be the discovery and control of the causes of incidence".

DOES CONCERN FOR INDIVIDUAL LEVEL RISK FACTORS MAKES US "PRISONERS OF THE PROXIMATE"?

The relationship of the parts with the whole

Priority was given to the specific characteristics, either biomedical, defining the pathophysiology of diseases, or behavioral and of other causes that are 'close' to the disease because they can be quickly examined with "individual" clinical data and manipulated in the context of the laboratory, and are easily identified in the comparison of individuals within the population. Therefore, priority was due to the greater scientific certainty on the role of disease etiology, which was more difficult to establish with the more "distal" causes, as social or population ones.

However Rose gave priority to the more "distal" or upstream causes -which will be identified characteristically in the comparison between populations-, since they are more important for offering greater potential for prevention strategies. They are defined as "exposures" characteristic of groups or populations and not characteristic of the individuals, which are therefore invariable within the group. (11)

In the relationship between the "whole" (groups and populations) and the "parts" (individuals within populations), Geoffrey Rose invokes a perspective similar to that of Durkheim, when he declares that although populations are formed by individuals, they have characteristics that are different from the simple sum (average) of the characteristics of individuals within the population. (12) The characteristics of the population may be influenced by the characteristics of individuals, but the characteristic and behavior of individuals are also shaped by the characteristics of the population.

Durkheim (13) states: "Whenever any elements combine and by the very fact of their combination produce new phenomena, it is evident that these phenomena are not given in the elements but in the totality formed by their union." That is to say, he proclaims that what we call "emergence" of new attributes in the whole, that is not in the simple sum of the parts; as he says, "it is in the whole, not in the parts" and exemplifies, "the hardness of bronze is not in the copper, nor in the tin, nor the lead which served to create it and which are soft and malleable bodies; it is in their mixture.". He continues later. "Let us apply this principle to sociology. If, as granted, this sui generis synthesis which every society constitutes yields new phenomena, different from those which take place in the individual consciousness, we must admit that these specific facts reside exclusively in the very society which produces them, and not in its parts, that is to say, in its members".

The social fact, constituted by the combination of individual action, releases a new product. "And as this

synthesis takes place outside each of us (because in it participates a plurality of consciousness), it necessarily has the effect of fixing, instituting outside us certain ways of acting and certain judgments that do not depend on each individual taken separately."

"... Here, then, is a category of facts which present very special characteristics: they consist in the manner of acting, thinking and feeling external to the individual, and which are invested with a coercive power by virtue of which they exercise control over him"; we could say in its own right that they are independent of their individual manifestation.

Social facts include all of the spoken and unspoken (or implied) rules of society, in which individuals were born and educated. We must think that the rules have a history that was prior to the history of the individuals affected by them and that is sustained even though the individuals who comprise the group change. They can be accepted, as most do, or may be rejected, as does a minority, but in both situations they provide constraints on individual behaviors.

Although the causal variable may bear the same name at population or individual level, as for example, "unemployment", the construct validity of its meaning is different and not interchangeable in the two organization levels. At the "individual level" the unemployed is exposed, while the employed is not exposed to that situation. However, the effect of living in an area with a high unemployment rate (high incidence at population level) exposes the whole group, both unemployed and employed, to health consequences in many other ways than the simple increase in the probability that an individual is unemployed at that time; for example, the interactions with unemployed people, worse conditions in the neighborhood, evictions, business closure, difficulty in payments, the stress generated in the group faced with the uncertainty of keeping the job, etc.

We speak of ecological fallacy when population studies are performed, but there may also be ecological fallacy in individual studies. An example that explains this situation is to consider a jury that does not reach an agreement; its characteristic as a group is "indecision" because it cannot decide whether the defendant is guilty or innocent. However, to infer that individual jurors are "undecided" would be absurd. Members of an "undecided" jury are very "decided", so much so that they cannot persuade one another. Therefore, to attribute to the members of this group the characteristics that emerge from the group (indecision) is thus a case of ecological fallacy. A focus on "construct validity" highlights the recognition that ecological fallacy is a problem that is everywhere and can occur with data at the individual level as well as with ecological population data. (14)

While no one argues that the sharp increase, to the top, of death from lung cancer during the twentieth century was due to increased cigarette smoking, this appears as an individual behavior. But as proposed by Rose, the effect of cigarette advertisement by manu-

facturers on the smoking rate of a country, cannot be investigated from a comparative study at an individual level, since this exposition is exercised equally throughout the population. However, comparing the experience with other populations that have advertisement restrictions and banning, it demonstrates the importance that this factor has in reducing population smoking rate. The progressive threefold increase in the price of a pack of cigarettes over a decade demonstrated in the populations of France and South Africa, a 50% decrease in the incidence of smoking during this historical period. Advertisement and price, the two key factors to lower deaths (approximately 6 million people per year worldwide) are detected only in population studies comparing between populations and comparing over time in the same population. It also shows that the "population prevention" strategy of the "distal causes" is extremely effective compared to the poor "individual prevention" performed by the doctor treating the "proximate cause" of the individual smoker's risk behavior.

If we accept that society produces social facts, this implies that the autonomy and choice of individuals is constrained by the social position and physical environment in which he lives. One cannot, as "individual" isolated from its "context" simply "choose" to be healthy or "behave" in a way that increases its health. We all endure social limitations to the choices we face as individuals.

LAY EPIDEMIOLOGY AND THE PREVENTION PARADOX

Frankel, Davidson and Davey Smith (15) described public perceptions of health risks as the result of a process called "lay epidemiology"

"This refers to a scheme in which individuals interpret health risks through the routine observation and discussion of cases of illness and death in personal networks and in the public arena, as well as from formal and informal evidence arising from other sources, such as television and magazines."

Professional epidemiology establishes the possibility that someone may or may not suffer from heart disease; in turn, lay epidemiology raises the archetypes of those who may or may not have a heart attack. Thus, four different situations in a 2 x 2 condition are established, and for the people there are two concordant situations: those who are "candidates" to have a heart attack and suffer it and those who "are not candidates" and have no coronary disease. Rose's prevention paradox shows the two remaining discordant situations as anomalies in the public perception of those who may or may not have a heart attack. (16)

The first anomaly is the "unwarranted survivor", archetypically a physically inactive person, overweight, heavy smoker with poor diet and low in essential nutrients such as fruits and vegetables. He is the "false positive", in whom a "false alarm" occurs when he is identified as a candidate for a heart attack by prevention, but actually survives to an old age.

The other anomaly, the “last person you would expect to have coronary disease” (16), is archetypically fit, young, active and with a healthy diet, a lifestyle above reproach in all relevant aspects, and who unexpectedly has a heart attack. He is the “false negative” in whom a “false reassurance” occurs when he is pointed out as an ideal candidate to be free of cardiovascular disease. Both situations express the limitations of existing scores to characterize high risk.

Often, the personal experience of these anomalies is expressed in popular sayings as “you get some people who have a dreadful lifestyle but who are very healthy (laughs) and live for years... Others seem to be doing all the right things and still things go wrong, you know that (laughs). I don't suppose there's a hard rule without exception. (16)

In the public perception there are behaviors that are viewed as “bad and toxic”; for example eating contaminated processed foods that produce uremic-hemolytic syndrome in children. In such situations the impact of the disease is immediate, acute, of specific nature and of medical explanation, with a high risk imposed by others and the person is assumed as a victim. However, in behavioral risk factors for chronic diseases, the impact of the disease appears as distant for many years, the causes are varied and non-specific and as they are considered the result of a lifestyle, disease is interpreted as a moral rather than a medical alteration, a self-imposed condition, qualifying the patient as a fool rather than a victim, because they are “bad and undesirable” behaviors.

In the massive message, lifestyle modification was matched rather with disease avoidance than with decreasing risk; so there will be numerous anomalous situations that inevitably violate the archetypal candidate system and undermine the confidence of the population, often invoking notions of capricious appearance or destiny and the “Russian roulette” metaphor.

CONCLUSIONS

The impact of the mean population shift for the different risk factors has been known for over 40 years. The epidemiological cross-sectional study of Japanese emigrants to the United States (California) compared with those who continued to live in Japan, shows a twofold increase in definite coronary heart disease, which correlates with increased levels of blood pressure, serum cholesterol, blood sugar and smoking in the population. (17)

In turn, the cohort study on the effect of total cholesterol made in China, published 25 years ago, (18) shows a population with a low coronary heart disease death risk (7%), because the average cholesterol concentration in the population (162 mg/dl) was frankly low for the levels of developed countries. However, it may still be observed that within the population there is a strong positive relationship between cholesterol concentration and death from coronary heart disease

($p < 0.001$) and that from the lowest to the highest quartile the relative risk increased 4 times; moreover, within the usual cholesterol concentration range studied (147-182 mg/dl) there was no threshold evidence.

The case-control study of acute myocardial infarction (INTERHEART) conducted in 52 countries on all continents with almost 30,000 subjects enrolled, (19) showed that 9 risk factors (abnormal lipids, smoking, hypertension, diabetes, abdominal obesity, psychosocial factors, daily consumption of fruits and vegetables, alcohol and regular physical activity) accounted for 90% of the population attributable risk in men and 94% in women of all ages and worldwide.

But in the discussion it is acknowledged that “since ApoB/ApoA1 ratio was the most important risk factor in all geographic regions of our study, *a substantial modification of its distribution in the population is important to reduce myocardial infarction worldwide*. This act will probably need a joint effort, *including both population-based strategies to change the distribution and targeted treatments for people with the greatest abnormalities*.” (Emphasis in italics is added by the author).

This clarification is important because the different combination of risk factors and their mean population values in each country would explain the remarkable fourteenfold increase in the standardized mortality rate for ischemic heart disease between Japan and Russia when the INTERHEART study was performed. (20)

In another part of the discussion it addresses the causes of the causes, the high level that explains the risk factors: “these studies, together with InterHeart suggest that one of the major emphases on research should be to understand why presently known risk factors develop in some individuals and populations, and to identify approaches to prevent or reduce their development. For example, understanding the mechanisms by which social factors influence the development of risk factors (urbanization policies, food and tobacco, changes in tasks that consume energy to sedentary tasks and urban structure, etc.) may lead to new approaches to avoid the development of risk factors (primary prevention), which in turn could substantially reduce coronary heart disease”. (19)

As Ezzati and Riboli contrast: (21) “Studying individuals helps to identify and establish risk factors that causally affect non-communicable diseases, and hence points to specific tools for disease prevention. However, it provides little information on how effective each of these tools may be in disease prevention at the population level, because the latter depends on the prevalence of risk factors in the population. Comparison of disease rates across populations or over time, especially when done in relation to risk factor levels in the population, indicates how much of the disease may be prevented and what the most important risk factors are at the population level”.

Therefore, the different patterns of lung cancer

and its risk factors worldwide and over time, show that stopping smoking (90% of the cause in Western countries), and some environmental interventions in specific locations, as in some parts of China, where coal is commonly used for cooking and heating in poorly ventilated homes (lung cancer mortality of people who have never smoked is about 4 to 5 times higher), can reduce lung cancer to very low levels in each population.

This illustrates the important point that the most effective disease prevention strategies are those that take into account prevalent risk factors in the target population and to what degree reducing any combination of these risks may lower disease levels.

Half a century ago, mortality rates from stomach cancer in adults was as high as 150 to 200 per 100,000 among men in Japan, Finland and Chile. These have now declined by almost 4 times, to 50 per 100,000 among Japanese men. In addition to this variation over time, in Japan it is currently 5 to 10 times higher than the approximately 5 per 100,000 in Canada, the United States and some other Western countries.

The discovery that about 75% of the 870,000 annual gastric cancers worldwide are attributable to *Helicobacter pylori* infection, present in the gastrointestinal tract, a risk factor for lesions that are stomach cancer precursors, has created new possibilities for its prevention with antibiotics.

Epidemiological studies have also established salt consumption, smoking, and diets that are low in fruits and vegetables as risk factors for stomach cancer. In the United States, where *H. pylori* prevalence is lower than in most other world regions, these lifestyle and dietary factors together account for about 60% of stomach cancer deaths.

"The impressive declines in stomach cancer began before the epidemiological studies that identified these risk factors. Reductions in salt intake appear to have played an important early role in stomach cancer decline at least in Japan and Finland. Stomach cancer prevention was also facilitated through improvements in hygiene, the living environment, and the use of refrigerators, which reduced the need to use salt for preserving food, improved the storage of fruits and vegetables, and may have also reduced infection rates creating an unintended success in prevention." (20)

Even more than the examples of these cancers, cardiovascular disease has a large number of risk factors and each increases the risk of disease by a relatively small amount. The diversity and the combinations of cardiovascular disease risk factors across individuals and populations create more subtle variations in disease risks and rates, which in turn make it more difficult to identify their independent roles in disease causality and prevention. However, it is empirically clear that reducing a moderate number of risk factors will have large benefits in cardiovascular disease prevention.

Reducing these risk factors in the overall population has contributed to former successes in cardio-

vascular disease reduction in many countries. For example, high-quality surveillance data show that the impressive two-third decline in Finland, from the approximate 1,200 deaths from cardiovascular disease in the 1950s, was due to reduced blood pressure and one of the highest cholesterol levels of the world. Mean systolic blood pressure in men and women was 143 mmHg and 138 mmHg respectively. Since then, it has declined by about 10 mmHg and serum cholesterol levels above 236 mg/dl dropped 39 mg/dl.

There is much to be gained against the cardiovascular disease epidemic with the additional reduction of these risk factors at the population level, especially in low and middle income countries.

These past and future findings confirm Rose's seminal work where he traces the foundations of population-based prevention with the heading premise, that "a large number of people at a small risk may give rise to more cases of disease than the small number who are at a high risk".

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