

## **Caminante no hay camino, se hace camino al andar**

Rodolfo Saracci

*IFC- National Research Council, Pisa, Italy*

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“Wayfarer, there is no path; in going the path is made”. There is no path automatically open in the future of epidemiology: paths will be, as in Antonio Machado’s verses, the result of choices of ends and means, scientific as much as political. Power has indeed to be taken into account as melancholically suggests the closing quotation of Professor Miettinen’s paper (Epidemiology: *Qua vadis*, this issue, pp. 713–718).

### **Epidemiology from World War II to the present**

For more than half a century epidemiology, as an aggregate of knowledge with a methodological core, has expanded in a multiplicity of directions, penetrating in a capillary way the whole field of medicine and public health. This could have been expected for public health given its ancient and intimate connection with epidemiology. Less expected, and a better gauge of the deep impact of epidemiology, is how a contemporary textbook of medicine [1] embodies epidemiological concepts and notions derived primarily from epidemiological studies, including phase three clinical trials (a broad but legitimate inclusion). Disease descriptions carry sections on epidemiology, and risk charts and decision trees to guide the individualization of diagnostic and treatment procedures are systematically used. A whole chain of books, continuously updated, of “evidence based” medicine, health care as well as of website documents is now available, directly based on the epidemiological approach to health and disease, which in essence blends three key ingredients: “population, probabilities, unbiased comparisons”. All these developments rest on the sound foundation of methodology, to which professor Miettinen has contributed key conceptualizations. The first textbook, of an introductory nature, appeared in 1960 [2] while we have today several dozens, at various levels of sophistication, general or devoted to special topics.

Skeptics have argued since at least a decade [3] that “so far so good”, but what epidemiology had to contribute has reached its limits and the future will be one of declining and unexciting scientific activity. Most of the skepticism flows from a single but crucial point, namely the real difficulty, and alleged impossibility, of confidently establishing the causal nature of weak observed associations through observational

studies. As factors entailing high relative risks, like tobacco smoke or cholesterol blood levels, have already been discovered only weak associations (so runs the argument) remain to be identified: as a consequence false positive results become more frequent, are amplified by the media and induce in the public waves of unjustified panic for, typically, environmental hazards or false hopes, say in healthy foods. The media amplification is not unique to epidemiological information but is a separate issue. The evidence from epidemiology itself only marginally supports the skeptics’ arguments, provided one never takes the results of a single study in isolation from other relevant evidence (or if the study is the first, refraining from hasty conclusions). Some recent examples illustrate the point.

First it is not generally true that today one is dealing only with weak associations. Choosing sensitive and specific markers of exposure to several strains of human papilloma viruses has allowed to establish that the virus is not a bystander boarding cancerous cells but a major cause in the carcinogenesis process leading to cervical cancer [4]. Relative risks of the order of 10, 100 and more were consistently observed in several case-control and prospective studies, the size of the risk being one element supportive of the causal nature of the observed association. Second, when weak associations are concerned the consistency of findings in repeated studies and with other pertinent evidence becomes even more decisive. A typical case in point is the association of environmental tobacco smoke with lung cancer, whose causal nature is confidently established on the aggregate evidence for more than 50 studies combined with the knowledge of the effects of (active) tobacco smoking [5].

These are recent and important contributions of epidemiology: and last year “Science” mentioned as “breakthrough of the year” the containment of the epidemic of Severe Acute Respiratory Syndrome (SARS) largely due to the initial alert by the field epidemiologist Carlo Urbani, who first diagnosed the new disease at the cost of his own life, followed by the activation of an effective epidemiological surveillance system at national and international level [6].

Methodology is also moving on several fronts, of which I will mention by way of example the three I have been recently in touch: statistical design and

analysis in genetic epidemiology, probably the most rapidly and extensively advancing [7, 8]; error of measurements in exposure and outcome variables, their impact and their statistical control via calibration procedures in multicentric observational studies [9]; evidence assessment and weighting of observational versus randomized studies, crucial to clinical epidemiology, health services research and prevention research: in this area examples of great practical relevance are emerging in which the results of observational studies clash with contrary evidence from randomized trials [10, 11]. Although the randomized trial is the golden instrument, actions (including no action) need often be based on less than golden evidence as not all issues will ever be investigated using this tool. In addition it will never be possible to obtain even observational epidemiological evidence for instance on the health effects of thousands of chemical agents spread in our environment [12] and preventive actions need to be guided by evidence from laboratory studies and a precautionary attitude. Morris stated it [13] in a definitive way forty years ago: "The epidemiological method is the only way of asking some questions in medicine, one way of asking others, and no way at all to ask many": if the words "in medicine" are replaced by the words "on health" this statement describes even more accurately the permanent role and the limits of epidemiology, out of transient excitements or depressions. To any young people wishing pursue science before scoop epidemiology offers today an intellectual challenge and a potential to contribute to health improvement not much different than decades ago, although the fascination of entering a wide and almost virgin area of chronic disease epidemiology (and the prospect of a straight career therein) has obviously gone.

### A critical digression on economics

Today the real reason of concern, which I wish to discuss to some extent, is not the internal dynamics of epidemiology but its context, both scientific and societal, as deriving from a number of current "-omics". Epidemiology can develop a balanced relationship with genomics, transcriptomics and proteomics. It is true that in these fields research is accumulating new knowledge at exponential rate, changing the picture of the diseases and the way they can be meaningfully investigated epidemiologically: but is equally true that these results are often erratic and falsely positive (more than the weak associations in traditional epidemiology) calling for rigorous validation through a sound epidemiological approach [14]. A fruitful interaction can develop with these scientific fields in the same way that it has developed with clinical medicine or pharmacology.

I have instead serious concerns about another "-omics", namely economics. It stems from the way

economics at its present stage of scientific advancement (and of severe limitations) has been and is widely used, in its standard theoretical version and its derived "vulgate" versions, as the inflexible guide, and the effective expropriator, of political actions in all societal areas, including research and health. I have recently pointed out [15] that in the European Union (EU) the 6th Framework Programme of research (FP6), started in 2003, population based research is a hardly visible priority. This is particularly serious in itself, as the EU funds represent a minor but significant resource capable of mobilizing much bigger matching funds from national sources, and because the EU programme may end by becoming an authoritative blueprint in those EU countries which do not have a strong autonomous research policy. The FP6 appears affected by a blind spot obscuring the fundamental fact that in order to deliver "health" to the European citizens such programmes as "Genomics and biotechnology for health" and "Food quality and safety" need extensive additional research at the population level, of which weak traces are present in the initial formulation of the programme, which reflects biological, pathophysiological, pharmacological or technonological viewpoints, not primarily an epidemiological research perspective. Hopefully the successive rounds of calls within FP6 will at least partially correct this orientation, which stems from two main factors: the disproportionate weight that administrative and political elements have in the definition of the research policy and the dominant economical bearing of the EU politics itself. This has its roots in the history of the EU, built on the communality of economic interests of the nations setting aside as far as feasible diverging political views: as a result the EU has become dominated by an economic orthodoxy (stigmatized even by mainstream economists [16]) within which research programmes leading to products by European industries competitive on free markets are regarded as high priority and epidemiological research programmes as a lower one. Yet such programmes, for instance in the health services research area would be advantageously conducted investigating the differences between European health systems (health services and other societal features influencing health). They would provide indispensable information to guide rational adaptations of such systems to the challenge of changing demography, technological advances and increasing people' expectations on health. Instead one keeps hearing the refrain of "the unbearable costs of health services" (whatever their level) and observes the drive, as in all other areas of economic interest, towards increasing privatization of the health services production or of the payment and insurance systems, or both. This all purpose recipe ultimately rests on the shaky assumption that it establishes the conditions enabling *homo economicus* to act rationally towards (in the words of Amartya

Sen [17]) the “canny maximization of self-interest”. The *homo economicus* postulated and required for the theory validity is in fact a caricature model of human behaviour or, again in Sen’s words [18], a “rational fool”. There is ample evidence [19] against the reality of such a perfect human information processor and single-minded rational calculator, some simply elicited through test problems of the kind I recently gave, for my own curiosity, to a class of thirty public health students. For half of the class, randomly chosen, the problem was “Two public health programmes can reduce the expected deaths (600) in a population: programme A has a 100% probability of saving 200 lives, programme B a 33% probability of saving 600 lives and 67% probability of saving none. Which programme you recommend?”. For the other half of the class the problem was phrased as “Two public health programmes can reduce the expected deaths (600) in a population: programme A has a probability of entailing 400 deaths, programme B a 33% probability of zero deaths and 67% probability of 600 deaths. Which programme you recommend?”. 66% of the students confronted with the first formulation recommended programme A, while 66% of the students confronted with the second formulation recommended programme B; only 10% of each group recognised that the two programmes are equivalent. Results like this, consistent on a micro-scale with those obtained in well designed *ad hoc* studies, undermine the basic assumptions and the scientific status of the prevailing economic theories. In reality as Joan Robinson [20], one of the most distinguished economists of the Cambridge school, wrote “Economics has always been partly a vehicle for the ruling ideology of the period as well as partly a method of scientific investigation (she trenchantly added: “Economics is not only a branch of theology”).

### **Epidemiology, equity and the future**

The “ideology of the period” which provided the seeds and greatest thrust to the development of contemporary epidemiology profoundly differs from the ideology which has gained ground over the last twenty to thirty years and is today dominant. In the period which goes roughly from 1945 to 1975 the ideology reflected the impulse of post-war reconstruction and economic expansion and a dominant, if not universal, sense of solidarity directly issued by the harsh war experiences shared by men and women of all social standing. This climate favoured epidemiology in two ways. First the concept of health as the right of everybody gained for the first time wide acceptance and for this purpose epidemiology, with its focus on populations rather than individuals, prevention rather than late disease events presented as an eminently suitable instrument to be developed and financially supported. Second epidemiologists

could reasonably and comfortably assume that the results of their studies would be translated by decision makers into benefit for the whole population, witness for instance the establishment in many countries of systems of universal health insurance. The assumption may have turned out too optimistic but it had substantial factual support. This ideology, born in the aftermath of World War II (with recognizable germs in the thirties, the “New Deal” time), survives today as a viable but minority view in a context driven by the neoliberal ideas and policies previously discussed. The assumption of an unobstructed continuity between epidemiological results and their translation into benefits for all sections of society is not any more warranted, as an economic barrier may be raised to impede or distort this transfer at any stage. Disturbingly a dissociation becomes patent between two facets implicit in the term “population”. On one side the population is the tool of the epidemiologist’s trade: we typically use populations as tools to investigate disease etiology (and today thanks to the increasing availability of biomarkers even pathogenesis) as other researchers use cell systems or rats. On the other side there is the population with its burden of disease waiting to be reduced, and this may happen only to the extent that epidemiological results are translated into effective interventions.

Here comes the question and the key choice alluded to in the opening paragraph of this article: are we going to use the populations as a tool for science and forget (or pay lip service) about the populations as a target for interventions, as indeed it has more than once happened in developing countries? One answer is “yes, we are only investigators” at various level of sophistication from the simple routine surveillance to the most complex hypothesis testing multinational study. I find this answer inconsistent with the fact that we claim societal support in the name of health benefits for society as a whole, with the added claim that such benefits may be more immediately flowing from direct epidemiological studies in humans than from scientific results obtained in other biological study settings. If the answer should be “no”, as I think it should, two important consequences follow.

First as epidemiologists we should be active in the formulation of both research and health policies. We should participate in decision making as citizens with special technical competence and knowledge making clear that while we strive to be impartial intellectually in our assessment of scientific issues, we cannot be “neutral” morally as our chosen role in society is to take side without ambiguity for health, starting from the health of those more in need (other social actors will legitimately argue for other interests, economic, legal, etc.). Second the health equality (theoretical) and health equity (empirical) issue should be not only one area of study, scientifically interesting in itself,

but a “translation control criterion” attached to any stream of epidemiological research and its results. It verifies the extent to which they translate into actions and health benefits diffused to all segments of society and analyses the determinants favouring or hampering the diffusion. No other investigator than the epidemiologist can competently do this work: in this context and with equity as the overarching reference both new methodology and economic analyses not burdened by implicit and unwarranted assumptions can be developed with economists.

“In going the path is made” by epidemiologists advancing science and ensuring in a socially responsible way that the path effectively transfers science into people’s health.

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*Address for correspondence:* Rodolfo Saracci, IFC-National Research Council, Pisa, Italy  
E-mail: saracci@hotmail.com