The modern scientific physician: 3. Scientific diagnosis

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Central to the practice of medicine is, of course, diagnosis. In the process of pursuing diagnosis, facts about the situation are secured. At any given stage of the process, the available facts define the corresponding *diagnostic profile*. In this, the facts fall in two conceptually distinct categories. Some of them have to do with *manifestations* of the underlying illness (unknown, pathologically defined); and for any given potential manifestation considered, the available fact is either 'positive' or 'negative' (to one extent or another). The other facts concern determinants of the patient's 'risk' — *propensity* — now to have whatever particular underlying illness whose presence is consistent with the known pattern of manifestations. Part of the propensity profile may refer to the rate of occurrence of the illness at issue, or to determinants of this, in the person's environment in the etiologic period of time. The profile as a whole is consistent with each of a particular, knowable set of possible underlying illnesses, constituting the *differential-diagnostic set* at that stage of the diagnostic process.

It is now well-established that, when focussing on any given illness in the differential-diagnostic set, the proper concern is to arrive at an appropriate *probability* of its presence (as an explanation of the manifestation profile, notably of the positive elements in it). But, how to go about this rationally, as is required in scientific diagnosis?

Learned diagnosticians know what has been written about the principles of this probability-setting. The seminal paper on this, they know, was published by a dentist together with a radiologist in 1959.[1] It introduced the idea that the proper theoretical framework for setting diagnostic probabilities is Bayes' theorem, with 'prior probability' (based on the propensity profile) and the manifestation profile's 'likelihood ratio' as inputs to the calculation of the probability. They also know that 'clinical epidemiologists,' while committed to this basic idea, have relaxed the theoretical assumptions and, on this basis, adopted a simplified modification of it: applying Bayes' theorem sequentially across the entire diagnostic profile.[2] If uncritical, they believe and take for granted the basic idea and the putative justifiability of the modification.

A genuinely scientific diagnostician, however, not only knows prevailing ideas but also reflects critically on them. In the mental habit of all scholars, (s)he begins with critical examination of the *concepts* involved. Central among these is likelihood: the probability of, or probability density at, the manifestational profile, conditional on the presence/absence of the illness at issue. How can this be known, (s)he wonders, as scientific study of it would require assembling a series (large, representative) of cases of that illness, and also of its differential-diagnostic alternatives, *independently* of the profiles which in reality bring the cases to clinical attention? Doesn't the likelihood vary among subtypes of the illness, by severity for example? Isn't the number of possible profiles too large to meaningfully learn about? (S)he comes to realize that serious problems abound.[3]

(S)he thus finds it necessary, as indeed scholars in general do in situations like this, to ask the fundamental question: what really is the *principal concept* at issue — here that of the diagnostic probability to be quantified, notably the concept of the *correct* diagnostic probability of the presence of the particular illness being considered? For, (s)he knows that scientific answers tend naturally to 'flow' from conceptually appropriate questions.[4] And, if able to clear the mind of rote learning, (s)he readily comes to a simple realization: if I knew the *proportion* in which the illness is present in instances like this (ones with this propensity and manifestation profile) in general (in the abstract) — its *prevalence* in this sense — then I would take that proportion to be the correct diagnostic probability in this particular instance of the profile.

This realization leads the diagnostician to ask the *correct*

question — that prevalence question — pertaining to the correct diagnostic probability in the context of the profile at hand. And as for the theoretical framework beyond this critical point of departure, the principles indeed flow from the prevalence concept of correct probability. The obvious concern is to know, for a suitably defined diagnostic domain (broadly by range of age and generic type of main complaint, say), that prevalence as a *joint function* of the set of *diagnostic indicators* involved (pertaining to actual age, particulars of the main complaint, etc.), and to evaluate this function at the diagnostic profile. With this outlook, together with modern statistical theory, the proper theoretical framework is understood to be that of *logistic regression* models for defined domains. For example, a truly modern scientific radiologist, when concerned to set the probability of the presence of pulmonary embolism (PE) in the context of the result from the ventilation-perfusion test, thinks in terms of a suitable logistic regression model expressing the prevalence of PE as a joint function of the relevant descriptors of the obtained image, this in an appropriate domain of suspicion of PE's presence; and (s)he deploys a fitted model of this type,[5] evaluating it at the facts from the image at hand.

The most specifically diagnosis-oriented specialty in clinical medicine is, at present, radiology; and this specialty indeed has been at the forefront of the development of the theoretical framework for diagnosis. Largely from radiology came, as I noted, the idea (mistaken) that Bayes' theorem is the necessary theoretical framework. More recently, leading radiologists have advanced another, even more misguided idea: that diagnostic imaging — they still focus on their own genre of diagnostics in this — actually is *intervention*; and from the adoption of this malformed concept they naturally have taken to flow the idea that imaging actually is supposed to have health-improving efficacy or effectiveness[6] — to be assessed by a comparative study, ideally a randomized controlled trial.[7]

One leader of today's radiology recently posited the precept that "tomorrow's radiologists need to be critical thinkers, learning to read books and journals and to listen to 'experts' more sceptically".[8] How true of colleagues in this specialty when reading their own leaders' writings on the concepts and principles of scientific diagnosis and on the theory of research toward its knowledge base, and equally of whatever specialists studying internists' and others' writings on 'clinical epidemiology.' A pre-eminent leader in everything scholarly, much earlier, advised all of us to "Read not to contradict and confute; nor to believe and take for granted; nor to find talk and discourse; but to weigh and consider."[9]

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