**Title: Whither Evidence Based Diagnosis In India?**

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**ABSTRACT**

Providing the best available diagnostic tests and medical care is in line with respecting the right to health. However,diagnostic procedures used on patients often fall short of the ideal, leading to erroneous or delayed identification of problems, which cause medical, social and financial burden on the patients. A variety of factors is responsible for this conundrum in diagnosis, and includes commercial interests and at times frank malpractice.Yet, a lack of understanding of several factors related to the tests,the physicians, the patients, as well as policy level issues, is not well appreciated. Thesefactors need to be identified and dealt with, for which there is a need to create awareness among patients, doctors and policy makers that all is not well in the world of diagnostic testing. This paper tries to explore the pitfalls in diagnosis that ultimately interfere with the practice of evidence based medicine. Until evidence based diagnosis becomes a reality, evidence based medicine and the highest attainable standard of health will remain a distant dream.

**Background**

The Constitution of the World Health Organisation recognises good health as a human right stating “highest attainable standard of health is one of the fundamental rights of every human being”.[1] This health is attainable only if the people get the best available medical care that includes timely and accurate diagnosis and the best treatment. As a corollary, it follows that denial of the best diagnostic tests and treatment, is a violation of human rights. The question that will arise is that is this violation an exception or is it a rule in India? Unfortunately,considerable evidence points towards the fact that evidence based diagnosis and consequently treatment are both grossly lacking in the country.

Evidence based medicine (EBM) is the integration of best research evidence with clinical expertise and patient values.It entails an evidence‑based approach in making clinical decisions.Though being firmly established in the West, EBM is yet to gain a foothold in India, with even attempts at developing standard treatment protocols being tardy and sporadic.[2]

Although it is an accepted fact that evidence based diagnosis preceding rational treatment, is central to the practice ofEBM, this in reality does not seem to be happening with regularity.Diagnostic testing, which includes laboratory tests, imaging and other investigations have a critical role in the diagnosis, monitoring and screening for disease in medical practice, and consequently in medical decision making.[3]

Variation in the practice of medicine that is commonly seen often extends to recommendations for laboratory and imaging tests.[4] One of the important questions that begs an answer is whether diagnostic tests and their interpretation are based on evidence. It is essential to examine the factors that drive the recommendation of particular diagnostic tests, and how their results are interpreted. Cultural differences are known to influence the type of tests that are acceptabe to patients.[5]Add to this the perceived superiority of one type of test to another and you have a situation that defies logical explanation.[6]

Tests may be ordered in series (sequence of tests ordered is based on the results of prior test) or in parallel (several tests ordered during one visit) depending on the urgency of making a diagnosis and the perceived risk (medical or legal) in a clinical situation.[7]Tests can be helpful for screening, i.e. to identify risk factors for disease and to detect occult disease in asymptomatic persons, for diagnosis, i.e. to help establish or exclude the presence of disease in symptomatic persons, and also in patient management.[8] When used appropriately, diagnostic tests can be of great assistance to the clinician.

The number of available tests has risen rapidly in recent decades. For instance, a prominent chain of laboratories in India claims to haveover3,500 diagnostic tests in its repertoire[9] while another claims 4,500.[10]The use of laboratory and imaging tests is increasing in many countries. While much of this increase may be appropriate for aiding the clinicians in their decision making, a growing body of evidence suggests that over-testing is a significant problem. Its futility has been demonstrated in some conditions, notably acute kidney injury. [11]It has been found in a study that diagnostic testing is more common in teaching hospitals compared to non-teaching ones, though this needs corroboration in Indian settings.[12]

The incidence of missed diagnosis and diagnostic errors is significant and is reponsible for moderate to severe harm to patients.[13] It was observed in the US that over a 25 year period, diagnostic errors were found to be most commonly associated with death and led to the largest chunk of malpractice claims.[14]

There is an increasing clamour in India against doctors recommending unnecessary tests. A common belief underlying such concerns is that this is due to profiteering by the doctors, which has so graphically been pointed out by Gadre and Shukla, and which includes the now rampant system of cuts or commissions.[15]Another factor that is important is the rapid rise of the medical diagnostic industry in the country, and the accompanying aggressive marketing.[16]

However, besides the corrupt practices, there are other important factors that have been implicated in the excessive mechanisation of the practice of medicine, such as fear of litigation. In the US and many western countries, litigation has become a way of life, with everyone searching for an opportunity to sue someone for their misfortune!Physicians in the past were mindful of the expenditure of their patients, but today they seem to be more involved in protecting themselves against real or imagined malpractice, so that concern for patients has taken a backseat. Apart from these,there are several other factors that would need to be addressed to establish evidence based diagnosis in India. For the purpose of discussion, it is useful to classify these factors in the following categories.

**Diagnostic test related factors**

From a diagnostic perspective, tests are ordered to modify the pretest probability of disease, to rule in or rule out disease, or to refer for further evaluation.[17]In primary care, tests are more commonly used to rule out a condition, to help the doctor to make a decision about referral, or provide further information on the patient to a secondary care specialist. Examples which come to mind include PAP screening and mammography in women.[18,19]In contrast, in secondary care, tests are more often used to reach a definite diagnosis.[20]

Diagnostic screening is commonly done as part of health check-ups in apparently healthy individuals.[21]An optimal screening test should meet the criteria related to population, the disease and the test itself.For instance, higher the prevalence of a disease in the population, higher the probability of it being picked up by an appropriate diagnostic test.[22]

Among the disease characteristics, the screening should lead to an improved outcome from early treatment. However, this may not happen with certainty. For instance, it was noted in the US in the case of five cancers (thyroid cancer, melanoma, kidney cancer, prostate cancer, and breast cancer), that over a period of two decades, there was a substantial increase in the detection rates, though the mortality rates remained more or less constant.[23]

Most tests used in the field of medicine have two attributes, sensitivity and specificity. The sensitivity of a test refers to the ability of the test to correctly identify those patients with the disease, i.e. the true positive rate, whereas specificity of a test is the ability of the test to correctly identify those without the disease, i.e. the true negative rate.

A high sensitivity is important where the test is used to identify a serious but treatable disease (e.g. cervical cancer). Screening the female population by cervical smear testing is a sensitive test. However, it is not very specific and a high proportion of women with a positive cervical smear who go on to have a colposcopy are ultimately found to have no underlying pathology.[24]

It is also important for the physician to understand the positive predictive value (PPV) and negative predictive value (NPV) of the test. The PPV of a test answers the question: ‘How likely is it that this patient has the disease given that the test result is positive?’, whereas the NPV of a test answers the question: ‘How likely is it that this patient does not have the disease given that the test result is negative?’

A related term is the likelihood ratio, which is defined as how much more likely is it that a patient who tests positive has the disease compared with one who tests negative.

PPV and NPV emphasise the clinical acumen of the physician, who has to match the results of the test to the history and clinical features of the patient in order to come to the proper diagnosis.

Screening tests are increasingly being used as part of health check-ups in the apparently healthy individuals. Periodic check-ups do make sense and are based on the old logic of “prevention is better than cure”, though the involvement of hospitals in this activity is questionable. The principal role of a hospital is to offer treatment to sick individuals, and sparing of resources to screen apparently healthy individuals may hamper their duty to the sick.

General health check-ups are commonly available in the private health sector, with one of the hospitals in Chennai reportedly having a separate building for the same.[25] Not to be left behind, even the public health sector in Tamil Nadu is offering various packages for health check-ups for the citizens.[26] New companies are being set up whose sole business is to offer health check-ups for corporate and private individuals.[27]Executive health checkups include a battery of tests, with a direct correlation observed with the seniority of the executive in the corporate hierarchy and the number of tests offered.

It should be noted that the Cochrane Collaboration has concluded that general health checks were unlikely to be beneficial as they did not reduce morbidity or mortality, neither overall nor for cardiovascular or cancer causes. However, the number of new diagnoses was increased. Important harmful outcomes, such as the number of follow-up diagnostic procedures or short term psychological effects, were often not studied or reported.[28]

There is also uncertainty involving the value of certain tests. For instance, serum 25-hydroxyvitamin D testing is becoming popular in India, prescribed for many orthopaedic cases, and also part of many corporate health check-ups. The dramatic increase in 25-hydroxyvitamin D testing in many developed nations, with its attendant costs, is well acknowledged.[29]However, the guidelines acknowledge that there is not sufficient evidence to recommend screening individuals who are not at risk for deficiency, advocating the measurement of serum 25-hydroxyvitamin D level by a reliable assay as the initial diagnostic test only in patients at risk for deficiency.[30]

* **Physicianrelated factors**

Most of the factors influencing test ordering relate to doctors, which is not surprising given that the decision to order a test in an individual patient ultimately rests with the individual doctor. Over the last two decades, the growth of diagnostic imaging has been higher than that of any other medical service.[31]

Physician related factors may be divided into non-modifiable and modifiable factors.The non-modifiable factors includeage and sex, practice location, practice setting, specialisation of the physician, etc.For instance, in a review it was foundthat a greater degree of specialisation was associated with more test ordering. Thus, gastroenterologists, cardiologists, orthopaedic surgeons, vascular surgeons and infectious disease specialists, all ordered more diagnostic tests or ordered tests earlier in the patient’s illness than internal medicine physicians.6

The modifiable variables included physician experience and knowledge, belief systems, fear of malpractice lawsuit and physician regret, financial incentives, awareness of the cost of testing, and education and feedback.Physician experience and knowledge did not appear to consistently affect test ordering.However, their personal beliefs that were not entirely evidence based did affect the frequency of test ordering. Fear of malpractice and financial incentives increased test ordering, whileawareness of the cost of testing decreased test ordering in most cases. For instance, in one study, knowledge about the cost of diagnostic tests was shown to reduce the number of tests ordered.[32]Provision of education or feedback or both considerably reduced the number of tests ordered.

Often, obsolete tests continue to be performed, simply because physicians loathe moving on. Finn observes that it is often more difficult to sunset an obsolete clinical laboratory test than to onboard a new test.[33]

When receiving information from screening tests, the answer expected from the result should be a “yes” or a “no.” Receiving an inconclusive result amounts to a “don’t know”; i.e. a level of uncertainty regarding the diagnosis similar to that of not conducting the test at all. This psychological uncertainty experienced after an inconclusive test result can lead to investigation momentum, i.e. additional, and potentially excessive, diagnostic testing. In contrast, not conducting the unreliable test would result in no further action.[34]

Finn though argues that the most astute medical practitioners treat laboratory results not as yes-or-no diagnostic switches, but as ways to either increase or decrease the probability of a given disease relative to the probability that existed before the results were received. He frets over the culture in medicine that resists the principle that a laboratory test is a means by which to hone pre-test probability, rather than the magic answer to a given medical question.[35]

This requires in the physicians a basic competence in statistics. However, statisticsas such is a derided subject by medical students in India.Indeed, lack of a functional knowledge of statistics has been documented in several studies in the West.

For instance, in a study that investigated whether primary care physicians in the US understand which statistics provide evidence about whether screening saves lives, the results were unflattering. About 47% of the physicians incorrectly said that finding more cases of cancer in screened as opposed to unscreened populations “proves that screening saves lives.”[36]

Another study that included pregnant women, their companions, midwives and obstetricians as participants, estimated the probability that a positive screening test result meant that a baby actually had Down’s syndrome on the basis of all the relevant information, which was presented in a scenario. It was found that 86% responses were incorrect. While it is understandable that only 9% of the pregnant women gave correct answers, only 34% obstetricians could respond correctly. Worse, most of them were confident in their incorrect responses.[37]

One more commonly encountered issue is the shotgun approach to testing, where again statistical illiteracy can influence the ordering of tests and their interpretation. A common feature of modern medical practice is the panel of laboratory tests ordered together. For many biochemical tests, the normal range is simply defined as two standard deviations from the mean of a healthy population. By definition, therefore, about 5% of results on each test from normal persons will be mislabelled as abnormal.

**Table 1: Probability that a healthy person will have abnormal results in biochemical tests**

|  |  |
| --- | --- |
| *Number of tests* | *Probability of at least one abnormal test (%)* |
| 1 | 5 |
| 6 | 26 |
| 12 | 46 |
| 20 | 64 |
| 100 | 99.4 |

*[Adapted from: Deyo RA, 2002.]*

The table shows the probability that at least one test will be abnormal for various numbers of tests performed. For instance, for a panel of 12 tests, commonly ordered in modern practice, there is a 46% chance that at least one test will be abnormal even in completely healthy persons. This has led to the cynical aphorism that “the only normal person is someone who hasn’t had enough tests!”[38]

Unfortunately, both patients and naive physicians may fail to appreciate the statistical basis for the normal ranges of chemical tests, underestimate the likelihood of false-positive results and fail to recognise that many abnormalities will not represent disease.

Another prominent issue is the practice of defensive medicine by doctors. Defensive medicine is the ordering of treatments, tests and procedures primarily to help protect the physician from liability rather than to substantially further the patient’s diagnosis or treatment. While perhaps not “unnecessary” care, defensive medicine is meant more to offer economic and psychological benefit to the physician than to the patient.[39]

A study in physicians observed that 91% physicians ordered more tests and procedures than needed to protect themselves from malpractice suits.[40]Another study involving orthopaedicians noted 96% having practiced defensive medicine, and that on average, 24% of all ordered tests were for defensive reasons.[41]

It has been estimated that the average American family pays an additional $1,700 to $2,000 per year in healthcare costs simply to cover the costs of defensive medicine.[42]

Avoidance of litigation and the psychology of regret is an obvious driver as professionals can be punished for missing the early signs of disease, yet don’t generally face sanctions for overdiagnosing.[43]

While the dimensions of defensive medicine are not known in India, with the Consumer Protection Act-1986 covering doctors’ liability, there is reason to believe that doctors would be recommending substantial number of investigations to guard themselves against claims from patients.[44]

* **Patient related factors**

Factors related to the patient can influence test ordering in a variety of ways. Patient preference, either to undergo or not undergo testing or for one test over another, can influence test ordering.16

Test ordering is related to patient demographics. For instance, older patients or female patients are likely to receive a disproportionate number of tests.

Doctors may decide to order a test to reassure the patient that he or she is not suffering from a more severe condition. For instance, ordering a scan in a patient with headache to reassure him or her that he or she does not have a brain tumour.

Patients too often request particular tests “just to be sure”. This may especially happen when patients rely on “internet diagnosis”.

Patients frequently express strong preferences for medical tests of their own choosing, even when physicians believe that they are not beneficial. Physicians may grant such requests,acompelling reason for which is to avoid confrontation.Patient-physician relationships flourish in an atmosphere of trust and goodwill, and physicians rightly worry that disagreement will threaten those relationships.[45]

Meanwhile, the increasing availability of direct-to-consumer screening tests is undermining physician efforts to provide high-quality, cost-conscious screening services to patients through shared decision making.[46]

Purveyors of these services have sprouted up all over the country, selling “packages” of screening tests at “discounted” prices. Tests are offered at various locations, often with a local hospital, academic medical centre, or physician group as an advertising sponsor.Anyone can purchase these tests, regardless of age or risk factors for disease or whether testing is truly indicated.

However, because of a lack of counselling by the companies about the potential risks of an “abnormal” test result, the consumer is initially unaware that this may open a Pandora’s Box of referrals, and additional testing to monitor or treat these abnormal findings. That most of these tests are not indicated in the first place is left undisclosed, nor is there a discussion of potential adverse consequences or additional costs.

Promoting and selling non-beneficial testing violates the ethical principles of beneficence and non-maleficence.While patients’ autonomy to make their own medical decisions should be respected, the choices should be informed by evidence, not advertising claims.

Consumers are generally unaware of the potential harms of screening vis-à-vis the intended benefits. The enthusiasm of the public for cancer detection, documented by Schwartz et al, offers a good example. In their study, 87% of respondents believed that routine cancer screening is almost always a good idea. Most had a strong desire to know about the presence of cancer regardless of its implications, with 66% saying they would want to be tested even if nothing could be done.[47]

It is important to consider the consequences of test results on the patient. An accurate positive test result may also have negative effects such as increased anxiety, increased insurance premiums and workplace discrimination.

The consequences of inaccurate test results should also be considered.A false positive diagnosis of a condition may result in unnecessary further tests and treatments, needless anxiety and psychological distress and increased expenditure.A false negative result may mean that patients continue to experience unexplained symptoms, causing anxiety because they do not know what is wrong with them, or failure to get timely and appropriate treatment which may have adverse effects on their prognosis. For instance, failure to diagnose and surgically correct a prolapsed vertebral disk may lead to urinary or faecal incontinence.

In a systematic review and meta-analysis, it was found that diagnostic tests for symptoms with a low risk of serious illness do little to reassure patients, decrease their anxiety, or resolve their symptoms. This finding is inconsistent with beliefs expressed by physicians. A small reduction in subsequent primary care visits after diagnostic testing was observed, but this reduction required several patients to undergo testing to prevent one visit.[48]

* **Policy and organisational factors**

It is imperative to weigh the potential benefits and harms of screening prior to initiating a programme at the community level. Test characteristics too assume significance in such a situation.For instance, if a test with 90% sensitivity and 96% specificity is used to screen for a condition with a prevalence of 0.6% (as with some cancers), 88% of abnormal results will be erroneous; for every 1,000 patients screened, only six will have the condition,but 40 will have false-positive results. This may be acceptable if the benefits obtained by the six patients with true disease outweigh the harms incurred by the 1,000 patients who undergo screening.Butwhat if there is little evidence that early detection improves their prognosis? If only oneor two of the six patients obtain benefit, is it ethical to subject the entire population to screening?[49]

Clinical practice guidelines have been advising us to screen earlier to detect occult disease,though certain changes can be discerned over a period of time. For instance, McGregor and Martin note that in British Columbia in the 1990s,the guideline for measuring lipid profiles in otherwise healthy people was 45 years of age for men and 55 for women. In 2008, the guideline was revised to start screening in men older than 40 years and women older than 50 years. Applied to the population of the province, this change potentially added an additional 343,400 cholesterol screening tests. Among the individuals screened with these tests, there would be an estimated 17% of healthy men and 13% of healthy women whose results will be reported as elevated,leading to multiple follow-up cholesterol tests to track progression or resolution over time.[50]

They note that the guideline committees that make recommendations do not appear to consider cost-effectiveness, opportunity costs and the potential harms of decisions to broaden screening guidelines.

Many definitions of diseases, particularly non-communicable diseases, have shifted in the past few years. They note the previous definition of diabetes was a fastingblood glucose level higher than 7.8 mmol/L, which changed to a fastingblood glucose level of higher than 7.0 mmol/L in British Columbia. They fear this has created an epidemic of new patients with diabetes. They also point out that the guidelines recommend that all patients with diabetesundergo twice-yearly measurement of haemoglobin A1clevels, and annual measurements of urine protein oralbumin-creatinine ratio, creatinine levels and lipid profile, thus considerably increasing the laboratory testing for those who are diagnosed with diabetes.

Welch et al estimate that expanding the diagnosis of “high” cholesterol from 6.2 mmol/L to 5.2 mmol/L can result in an 82% increase in individuals with a “diagnosis” of dyslipidaemia, which works out to more than 4.3 million people in the United States.[51]

In this context, Moynihan flags the conflicted panels producing expanded disease definitions and writing guidelines. He takes up the example of prehypertension, a diagnostic category created in 2003, and points out that among the 12 members of the panel that created the category, 11 received money from drug companies and half of those people declared extensive ties to more than 10 companies each.[52]

It has also been observed that payment by salaries is associated with lower test ordering than a fee for service approach where doctors are reimbursed for each test performed.[53]

Prevention is no doubt a part of health care delivery, but what ratio of resources should be devoted to health screening and treatment of the sick is a matter of debate. Currently, India spends only 1.3% of its GDP on healthcare.[54] Most patients have no option but to seek the private sector for treatment, where with low rates of insurance coverage, out of pocket health expenditure as a proportion of private expenditure on health is very high (89.2% vis-à-vis the world average of 45.5%).[55] Besides, India also ranks very low in terms of health personnel (0.7 doctors per 1,000 population vis-à-vis 1.5 for the world average).[56]The impact of diversion of resources to screening apparent healthy individuals could be limited in countries with adequate medical facilities, but could be disastrous in countries like India where medical facilities are already strained.

In the West, conscious efforts are being taken to address the issue of unnecessary testing. For instance, in the US, the Choosing Wisely campaign is working since 2012 with the goal of advancing a national dialogue on avoiding wasteful or unnecessary medical tests, treatments and procedures.[57] One of its significant contributions is the comprehensive lists created by the national medical specialty societies, representing specific, evidence-based recommendations. Each list provides information on when tests and procedures may be appropriate, for the clinicians and patients to discuss and decide.

In India, no such organised effort is visible. On the contrary, we have a situation where repeat testing to increase profits of testing laboratories is common when testing laboratories belong to the hospital. Many hospitals also force patients to repeat all tests, stating that testing at another centre is not reliable.The load of this testing on the patient leads to a financial burden, and to their dissatisfaction with the medical care offered,acontributory factor for the deterioration of doctor-patient relationships.

To dissuade the practice of recommending a diagnostic test for the commission earned, the Medical Council of India, in its Code of Medical Ethics Regulations (2002), makes a special mention forbidding it (see Section 6.4).[58] Its enforcement though remains a moot question.

**Conclusion**

When conducting clinical research, so much attention is paid to the rights of participants, it is unfortunate that there is so little consideration for the rights of patients who are not in trials. Patients also increasingly feel that they are being made scapegoats in the commercialisation of medicine, a situation that benefits none.

Ina country like India, with a struggling public health sector and burgeoning private health sector, where a majority is uninsured and have to pay out of their pocket, policy recommendations for testing assume a lot of significance. Educating the physicians for prudent decision making is essential to make good of the very limited resources available. Evolving a framework for evidence based diagnosis is thus the need of the hour.

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