DEPRESSION IN PRIMARY CARE: CLINICAL EPIDEMIOLOGY & CLINICAL DECISION ANALYSIS — AN ANALYTICAL REVIEW

Haider Ali Naqvi

ABSTRACT

A clinical decision analysis (CDA) is a mathematical tool designed to facilitate complex clinical decisions in which many variables should be considered simultaneously. CDA is a feasible tool for multifaceted problem of management of depression in primary health care. It provides a systematic frame work for organizing all data relevant to the decision on recognition and management of depression. Clinical epidemiological perspective is used for assessing the validity of screening instrument. A decision matrix based on reported probabilities is also constructed. Chance nodes and decisions pertinent to co-morbidities, illness severity and treatment options for depression are also presented.

Key words: Clinical epidemiology, Clinical decision Analysis, Depressive disorder, primary care, Pakistan.

INTRODUCTION

New millennium has witnessed an epidemiological transition with rise in burden of non-communicable diseases. According to 1993 World Bank Report Neuropsychiatric diseases (including self-inflicted injuries) contribute 8.1% to the Global Burden of Diseases (GBD). Subsequently this contribution to GBD has been reanalyzed and found to be 10.5%. This is projected to increase to 15% by the year 2020. The "behavior related problems" contribute an additional 34% to GBD[1].

Prevalence of common mental disorders is estimated to be 30 % to 50% in primary care settings of Pakistan. Most patients with mental disorders initially consult their general physicians (GP)[2]. Although CMD have been diagnosed in third of primary care attendees in developing Asian countries, primary care staff is generally reported to recognize only 10 % of the cases. Studies have shown that a substantial proportion of mental disorders in primary care are inadequately managed by the GPs[3]. There are many facets to this complex problem. Some issues are related to the physicians while other to the patients. Lack of time, awareness and general stigma related to mental illness poses a major problem for GPs[4].

Patients presenting in primary care are much different from psychiatric settings. Generally they have concurrent medical illness, which remains the major focus of management. Another common reason for this under recognition is somatisation, i.e., presentation of psychological distress as somatic symptoms, and poor awareness of this in health professionals[5].

A clinical decision analysis (CDA) appears to be a feasible tool for this multifaceted problem. CDA is a mathematical tool designed to facilitate complex clinical decisions in which many variables should be considered simultaneously. It provides a systematic frame work for organizing all data relevant to the decision. It also assigns a numerical value to various courses of actions, simplifying comparison among them[6].

This is particularly relevant in the context of Pakistan, a South East Asian developing country. With the dearth of mental health professionals, management of common mental disorders is increasingly integrated in to primary health care. Complex clinical decisions are either delegated to clinical nurses or lady health workers. With explicit decision analysis, there is greater likelihood of adequate management of common mental disorders (depression and anxiety) in primary health care. CDA will also serve to promote informed consent as patients input can be taken in to account in evaluating outcomes.

Clinical Decision Analysis and Management of Depressive Disorder in Primary Health Care:

Major depression is a disorder characterized by persistent and pervasive low mood, anhedonia, impaired concentration, disturbed sleep, appetite and morbid death wishes. The point prevalence of major depression from community based studies is estimated to be between 25-66 % for females and 10-44% for males[7,8]. The prevalence estimates for MDD in primary care set-

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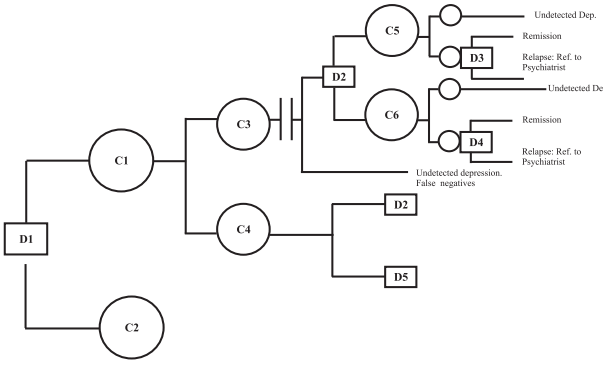
tings of Pakistan is estimated to be approximately 30 % to 50 %[2]. These are many times higher when compared with western countries. Additional problem is dearth of trained mental health professionals and scarcity of allocated resource.

A clinical decision analysis and algorithm appears feasible in order to address the above needs and rectify potential problems in the management of depression in primary health care. A rough guide and skeleton of the decision analysis is presented in Figures 1 and 2. Probability estimates of certain outcomes and potential multidimensional utility is presented when and where objective literature on the subject was available.

Fig. 1: Clinical decision Analysis: Management of Depression in Primary care.

CLINICAL DECISION ANALYSIS



D1: Decision Node 1; multiple somatic symptoms of Unknown origin.

C1: Chance node 1; Chance of Functional depressive illness (Pr 0.64)

C2: Chance node 2; Chance of Depression secondary to Co morbid medical condition (Pr 0.36)

C3: Chance node 3; Chances of no Thyroid abnormality (Pr 0.95).

C4: Chance node 4; Chance of Sub clinical Thyroid abnormality (Pr 0.05).

D2: Decision Node 2: Decision on severity of illness.

C5: Chance node 5; Chance of mild-to-moderate depression (Pr 0.86; Detection rate 18.4%).

C6: Chance node 6; Chance of severe depression (Pr .13; detection rate 73%)

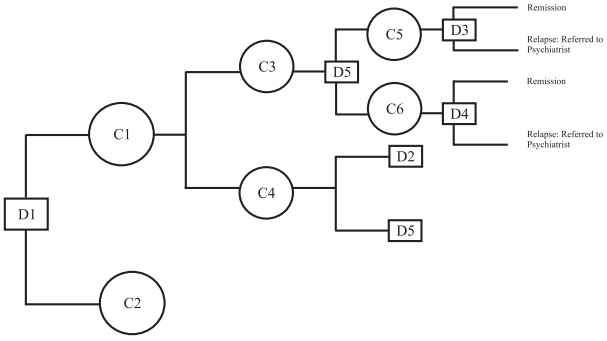
D3: Decision on Psychotherapy based on the severity (mild-to-moderate) and patient's preference.

D4: Decision on Antidepressants Medication based on severity.

D5: Decision to treat the underlying medical illness.

Figure 2: Clinical decision Analysis: Management of Depression in Primary care (Final model after pruning the figure 1)

CLINICAL DECISION ANALYSIS



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Somatic symptoms and high index of suspicion for depression (Node – D-1):

In primary care setting the most common presentation of patients' with depression is with multiple somatic symptoms. This premise is based on the comparative studies carried out by Mumford et al looking specifically at the somatic manifestation of psychological symptoms in the context of Pakistan. The sample population was group of people in Lahore, Pakistan and Leeds, U.K[9,10]. The decision node D-1 pertains to maintaining high index of suspicion for depression when patients' present with multiple somatic symptoms of unexplained nature. There is no study from Pakistan looking specifically at the characteristics or out come of this atypical presentation in Primary care.

The chance node C-1 pertains to the probability of somatic symptoms, given that the patient has underlying depressive illness (Pr 0.64). The chance node C-2 pertains to having somatic symptoms given that patient has underlying medical co morbidity.

According to studies carried out in the west, significant depressive symptoms are seen in 36% of medically ill patients[11]. Those with dementia, diabetes, stroke, hypercortisolism, asthma and renal impairment have especially high rates of co- morbid depression. Conditions like fibromyalgia and chronic fatigue syndrome, exists at the interface of medicine and psychiatry and are associated with major depressive disorder[12,13].

Depression is also associated with use of medications. 3% of patients on high dose steroids report significant symptoms of depression. Calcium channel blockers, beta-blockers and digoxin are known to cause depression. Caffeine use may be associated with increased side effects and failure of some symptoms to improve (for e.g. anxiety and insomnia). Co morbid alcohol use and withdrawal from alcohol and stimulants are associated with depression[14-16]. Co morbid depression will require a similar treatment strategy as functional depression, besides the concurrent medical management.

Among these patients work up for thyroid abnormality should be carried out in order to rule out psychological symptoms secondary to thyroid abnormality (Node C-3). Thyroid abnormality typically mimics symptoms of depression and should be exclusively ruled out in the context of primary care. There are no studies from Pakistan on prevalence of abnormal thyroid hormones in the setting of primary care. However in clinical population (PC) from western countries it is estimated to be around 5 % (Node C4). In psychiatric subset with chronic treatment resistant depression, the prevalence of subthreshold thyroid abnormality is estimated to be much higher (around 50%)[12].

After ruling out secondary and co morbid depression it is pertinent to establish the diagnosis of depression. Use of screening test/instrument is particularly relevant in the context primary care, where constraints of time and resources demands rapid assessment. It should be considered that any screening test, however robust it may be has its limitations. Result of screening instrument should be checked against a gold standard, measure of assessment. A brief discussion on the definition, process and limitations of screening is particularly relevant here, followed by issues pertaining to screening for depression in primary care setting.

Clinical decision analysis and disease screening:

Screening has been defined as "*presumptive* identification of *unrecognized* disease or defect by the application of test, examination, or procedure which can be applied *rapidly* to sort out apparently well person who *probably* have a disease from those who *probably do not*. A screening test is *not* intended to be diagnostic" (commission on chronic illness; italics added for emphasis).

The whole process of screening appears to be quite simple but there are several underlying complexities, alike the subject of clinical epidemiology. There are concerns regarding the cost of screening which may be apparent or hidden. Cost can be related to screening process/instrument or treatment of additional cases however, identification of these subjects in the pre-clinical stage by astute screening instrument does make the early intervention possible. Thus screening can facilitate primary and secondary prevention.

Suitable disease & screening:

A variation among natural history of the diseases has an impact on the utility of early detection and treatment. A disease with long pre-clinical phase, like carcinoma of cervix, will definitely require early detection and screening, in order to modify its course. Besides the long latency period, severity of the illness also merits consideration while designing a screening program. A screening program for detection of upper respiratory tract infection will be less cost effective than screening program for breast cancer, solely based on the disease morbidity and mortality. In order to have effective screening program the disease under consideration should be an important health problem. The disease should be progressive with serious health consequences. An effective treatment at an earlier stage should be able to modify the natural history and course of illness[17].

Major depressive disorder does full fill all these criteria. It is prevalent in community and primary health care setting, if undetected leads to progressive worsening with tragic loss of life by suicide. Long term vulnerability factors like loss of parent/s during child hood by death or separation and current non confiding spousal relations does lead to sub threshold symptoms. Thus detection of this preclinical phase of illness by screening test helps in early intervention and subsequent modification in its natural history.

Suitable test & instruments

There are certain consideration regarding the choice of screening test and instrument. Screening test should be inexpensive, easy to administer with minimal discomfort to the clients. Colonoscopy might be very effective in early detection of carcinoma of colon, but it has limited acceptability in routine use for apparently healthy subjects. Another important characteristic of good screening instrument is its ability to separate people with and without disease. A robust screening instrument should have high validity and reliability.

Validity & Reliability (Precision)

Simply stated, a test is said to be valid when it does what it is suppose to do. This is usually measured through its sensitivity and specificity. Sensitivity can be described as the ability of the test to identify correctly those who

have the disease. In conditional probability notation, sensitivity is written P (T+/D+). Specificity of the test is its ability to identify correctly those who do not have the disease. In conditional probability notation, specificity is written P (T-/D-). Sensitivity and specificity determined by comparing the result with a definitive diagnosis. It is important to note that sensitivity and specificity are reciprocal in nature[18].

Consistency and reproducibility of the test is said to be its reliability. It depends upon variation inherent in the method. The variation can be inter-observer or intra-observer. A same individual can rate the same observation differently on different occasions. Alternatively there can be a natural variation among two raters. In rounding off some raters have preference for higher values while others for lower values.

Determining performance of screening instrument (AKUADS) and assigning probabilities:

While the specificity and sensitivity remain an important issue in considering the use of instrument for diagnostic and screening purposes, the psychometric measurement becomes an additional issue when an instrument is applied in a cultural setting which is different from the one in which it was originally developed. EMIC-instruments and questionnaires with cultural sensitive explanatory models are reported to be preferable over ETIC-instruments (instruments developed in another cultural setting). But research findings of studies using EMIC-instruments only, without established cross cultural validity are open to question.

Aga Khan University Hospital Anxiety & Depression Scale (AKUADS) is a 25 item screening instrument, developed indigenously in the primary health care and psychiatric setting of Pakistan, for screening depression and anxiety disorder. It incorporates culturally pertinent somatic metaphors of depressive disorder. It has an advantage over ETIC instruments, in assessing locally relevant idioms of distress in the primary health care settings in Pakistan. To assess the performance of a screening instrument i.e., AKUADS, we take a hypothetical population of 10000 and calculate the sensitivity, specificity based on the sensitivity and specificity found in the literature.

Table 1

Sensitivity & Specificity of Aga Khan University Anxiety and depression scale (AKUADS) as a screening instrument*

		Disease status		
		+	–	Total
Test Results	+	2070	1470	3540
	–	930	5530	6460
Total		3,000	7,000	10,000

Summary of test performance characteristics (as stated in the published reports)[4]

1. P (D+)= P (Major Depressive disorder)= .30
2. P (T+/D+)= sensitivity = True positive rate = .66
3. P (T -/D+)= 1- sensitivity = False negative rate= .34
4. P (T-/D-)= specificity = true negative rate = .79
5. P (T+/D-) = 1- specificity= false positive rate= .21.

These test characteristics can be used to generate 2 x 2 tables, or decision matrix, using an arbitrary sample size of 10000 patients (table 1). This can be used to assign probabilities to the branch node C-2, thus an accurate estimate of how the screening instrument is functioning.

1. P (D+/T+) = 2070/3540= 0.58.
2. P (D-/T+) = 1470/3540= 0.41
3. P (D+/T-) = 930/6460= 0.14
4. P (D-/T-) = 5530/6460= 0.85.

Bayes' rule is a mathematical formula that can also be used to calculate unknown conditional probability, such as predictive value positive [P (D+ /T+)] directly from the reported values for sensitivity [P (T+/D+) = 0.66], specificity [P (T-/D-) =0.79] and prior probability of major depressive disorder [prevalence, P (D+) = 0.30][19]. Thus,

$$P(D+T+) = \frac{P(D+T+)\,P(D+)}{P(D+T+)\,P(D+) + P(T+D-)\,P(D-)}$$

$$= \frac{(0.66)\,(0.30)}{(0.66)\,(0.30) + (1-.79)\,(0.70)} = 0.5739.\text{ or } 0.58$$

In above example 1-sensitivity will be interpreted as probability of test results as negative given the disease status to be positive. For any screening instrument false negative rate is a major concern. This is particularly so in the context of primary health care in Pakistan. FNR of 0.34 means that quarter of a patients attending primary health care will be misclassified, therefore, losing valuable opportunity of early recognition and intervention.

In this circumstances use of another screening instrument simultaneously or sequentially can serve to rectify this potential problem. Use of two screening instruments simultaneously will serve to increase the sensitivity while sequential use will increase specificity. The choice for either mode of screening depends upon the purpose of screening.

With a population to psychiatrist ratio of 1: 100,000, primary care in Pakistan serves as the sole care provider, unlike its filtering role in western countries[20]. Therefore high specificity is desirable in the contest of Pakistan. Thus sequential screening using AKUADS followed by another instrument/tool might be more desirable. Diagnostic confirmation based on DSM-IV diagnostic criteria described by Reza H et al can be used sequentially with AKUADS, in the context of primary health setting in Pakistan[21].

Depression sub-typing: differences in primary care and psychiatry (Node D-2):

There are number of factors mentioned in literature regarding "type" of depressive disorder seen in primary care and psychiatry. Patients seen in the two settings may be quite different. Depression seen in primary care is less severe and less impairing. Evidence of this comes from Michigan Depression Project (MDP), a long-term study of depression in primary care that has provided valuable data regarding the similarities and differences between depressed patients in primary care and psychiatry and whether the same treatment is appropriate in both settings.

In its first phase, MDP screened 1928 adult patients from fifty family physicians practices in southeast Michigan and completed structured diagnostic interviews on 425 distressed primary care patients and 123 depressed psychiatric outpatients using the structured clinical interview for DSM-III-R (SCID). Clinicians were asked independently whether each of the patients was clinically depressed. The full sample received comprehensive assessment of stress, social support, overall health, health care utilization, and depression severity at intake and 4.5 and 9 months after enrollment. Of the 425 depressed primary care patients, 13.5% were diagnosed with Major Depression, but over 40 % of those meeting the criteria for MDD were mildly depressed. Many of the primary care patients with mild or moderate depression were not diagnosed; family physician only diagnosed 35% with MDD and 28% patients with any depressive disorder[22]. However detection rate for severe depressive patients was significantly higher; 73% of severely depressed patients were selected compared with 18.4% of mildly depressed patients.

In case of functional depressive disorder severity of the illness has implication on detection rate (D-2). Detection rate for sever depressive disorder is 73 % while detection rates for mild-to-moderate depression is 18.4%. This is in the context when 80-to-86% of the Depressive disorders is mild-to-moderate in intensity.

In primary health care mild-to-moderate depression is the most common presentation as compared to psychiatric setting[23]. The severity of illness has implications for treatment; as mild to moderate depression is best treated by psychotherapy. Sever depressive disorder will invariably require anti-depressants medication therapy. There are no studies on severity of illness and its subsequent detection rates in primary care setting from Pakistan. This is shown in chance node C-5 and C-6.

Treatment option in primary care (Node D-3):

The third decision (D-3) is related to the available choice of therapies. General Physicians can prescribe short term (8-10 sessions) psychotherapy. Mild-to-Moderate depression is preferably treated with short term psychotherapy/counseling, in the setting of primary health care. However, the option of psychotherapy needs to be discussed with the patient, with clear delineation of utility and outcome.

In a randomized control trial, Ali et al showed the effectiveness of psychotherapy when conducted by minimally trained therapist. Short term counseling was particularly effective in low income group and can be usefully delivered in primary health care setting[23].

Chance nodes on remissions and relapses are given in the decision making tree. Unfortunately there is no literature on the long term outcome of specific treatments for depression from Pakistan. In cases of relapse of the illness it is advisable for the Primary care physician (health worker) to refer the patient to a psychiatrist.

Decision node D-4 pertains to choice of psychotropic medication in cases of depressive disorder with moderate to sever intensity. There are no studies on the long term outcomes of depression in the context of Pakistan. Extrapolating findings from western literature, around 60 % patients with depressive disorder relapse with in a year. This is in the situation of successful response to psychotropic medications. However in the context of primary care setting in Pakistan, any recurrent and relapsing case should be referred to a psychiatrist. There may be complicating psychosocial determinants or co morbid psychiatric problems (personality disorders), that may be safely treatment by mental health physician.

Limitations:

There are certain limitations to this decision analysis. The data on outcomes and utilities is based on western literature; its generalizibility to the culturally unique setting of Pakistan needs to be considered carefully. Prospective data from primary care settings is required, in order to develop any robust model that serves decision making for management of depression in the context of primary care in Pakistan.

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Assuming 30 % prevalence rate of MDD in primary health care, in a hypothetical population size of 10,000

people, screened with AKUADS, with a sensitivity of 66% AKUHADS will correctly identify 2,070 individuals who has the disease. It will however fail to detect 930 individuals who have depressive disorder. Similarly with a specificity of 79 % it will detect their disease free status among 5,530 individuals out of 7,000. However it will misclassify 1470 disease free individuals as disease positive, thereby creating some, albeit transient anxiety among them.

REFERENCES

1. Murray CJ, Lopez AD. The Global Burden of Disease: A comprehensive assessment of Mortality and Disability from Disease, Injury and Risk Factors in 1990 and projected to 2020. Boston: Harvard School of Public Health, WHO and World Bank, 1996.
2. Mirza I, Jenkins R. Risk factors, prevalence, and treatment of anxiety and depressive disorders in Pakistan: systematic review. BMJ 2004; 328: 794-7.
3. Patel V, Pereira J, Mann AH. Somatic and psychological models of common mental disorder in primary care in India. Psychol Med 1998; 28: 135-43.
4. Naqvi H, Khan MM. Depression in Primary care: Difficulties and paradoxes. J Pak Med Assoc 2005; 55: 393-8.
5. Naqvi H, Iqbal R. Prevalence of mental disorder in Pakistan: A need for integrating their management in primary care. Med Today 2003; 1: 107-11.
6. Sackett DL, Hayes RB, Tugwell P. Clinical Epidemiology: A basic science to clinical medicine. Boston: Little Brown, 1985.
7. Mumford DB, Nazir M, Jilani FU, Baig IY. Stress and psychiatric disorder in Hindukush: a community survey of mountain village. Br J Psychiatry 1996; 168: 299-307.
8. Mumford DB, Saeed K, Ahmad I, Latif S, Mubbashar MH. Stress and psychiatric disorder in rural Punjab: a community survey. Br J Psychiatry 1997; 170: 473-8.
9. Mumford DB, Tareen IA, Bajwa MA, Bhatti MR, Karim R. The translation and evaluation of an Urdu version of The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand 1991; 83: 81-5.
10. Husain N, Chaudhry I, Asfar S, Creed F. Psychological distress among patients attending a general medical outpatient clinic in Pakistan. Gen Hosp Psychiatry 2004; 26: 277-81.
11. Frasure-Smith N, Lesperance F, Talajic M. Depression and 18-month prognosis after myocardial infarction. Circulation 1995; 91: 999-1005.
12. Pies R, Rogers D. The recognition and treatment of depression: A review for primary care clinicians. CME/CE [On line] 2005 [cited on October 12, 2005]: Available from : URL: http://www.medscape.com.
13. Walker EA, Peter P, Katon WJ. Irritable bowel syndrome and functional psychiatric illness. Am J Psychiatry 1990; 147: 565-72.
14. Patten SB, Love EJ. Drug induced depression. Psychotherapy and psychosomatics 1997; 66: 63-73.
15. Peroutka SJ, Newman H, Harris H. Subjective effects of 3,4-methylenedioxymethylamphetamine in recreational users. Neuropsychopharmacology 1988; 1: 273-7.
16. Kendler KS, Heath AC, Neale MC, Kessler RC. Alcoholism and major depression in women: a twin study of the causes of the Comorbidity. Arch Gen Psychiatry 1993; 50: 690-8.
17. Gordis L. Assessing the validity and reliability of diagnostic and screening test, In: Epidemiology Philadelphia, Elsevier Saunders 2004.
18. Fletcher RH, Fletcher SW, Wagner EH. Clinical Epidemiology: The essentials. Baltimore: Williams & Wilkins, 1982.
19. Feinstein AR. Clinical biostatistics. Clin Pahrmacol Ther 1979; 25:108-16.
20. Naqvi H, Khan MM. Pathways to psychiatric care in Karachi. J Coll Physicians Surg Pak 2006;16:438-9.
21. Reza H, Khan MM. Depression: Diagnosis and management in general practice in Pakistan. J Pak Med Assoc 2003; 53: 500-5.
22. Spitzer RL, Williams JB, Kroenke K. Utility of a new procedure for diagnosing mental disorder in primary care: the PRIME-MD 1000 study. J Am Med Assoc 1994; 272:1749-56.
23. Schwenk TL, Klinkman MS, Coyne JC. Depression in the family physicians office: what the psychiatrist needs to know: The Michigan depression project. J Clin Psychiatry 1998; 59: 94-100.
24. Ali BS, Bahbar MH, Naeem S, Gul A, Mubeen S, Iqbal A. The effectiveness of counseling on Anxiety and Depression by Minimally Trained counselors: A Randomized Controlled Trial. Am J Psychotherapy 2003; 57: 324-36.