Chapter 4

ASSESSING ADHERENCE AND ITS DETERMINANTS AMONG TB PATIENTS

The weariness, the fever, and the fret
Here, where men sit and hear each other groan;
Where palsy shakes a few, sad, last gray hairs,
Where youth grows pale, and spectre-thin, and dies;
Where but to think is to be full of sorrow
And leadem-eyed despairs,
Where beauty cannot keep her lustrous eyes,
Or new love pine at them beyond tomorrow.

John Keats
Ode to a Nightingale
INTRODUCTION
Despite different connotations, the terms "compliance" and "adherence" are used interchangeably. Though "adherence" is considered to be a less pejorative term and perhaps the more accurate term in that it indicates patient's choice in medication taking. Adherence is defined as the extent to which a patient's health-related behaviors correspond to the medical advice. Adherence encompasses many aspects of patient behavior which range from follow-up with medical referrals from another provider or a screening program, keeping regular appointments, taking prescribed drugs, and abide by health-related advice (Broers, 1994; Aversa, 1996; Paper, 1997; Crespo-Fierro, 1997; Catz S, 1999). Measuring adherence among TB patients serve a cornerstone of any successful TB control program. Greater emphasis is placed on assessing TB control program in terms of achieving higher levels of adherence among registered patients which in other words mean high cure rates, less resistance and complications and effective eradication. Adherence with medication is the immediate concern of most clinicians while prescribing chemotherapy; failure to keep medical appointments may be a harbinger of difficulty in adhering with a regimen. Non-adherence is believed to delay sputum conversion to smear negative, increase the relapse rates 5-6 times, and help the emergence of resistant mutant strains (Combs DI et al., 1987; Peronne C, 1995; WHO, 1997).

Measuring the degree of non-adherence is crucial due to its clinical outcomes and fatal consequences. For example it can lead to hospitalisation, facilitate new opportunistic infections, transmission of infections to others and ultimately disabilities and death. The impact of non-adherence on clinical outcome is dependent on the effectiveness of therapy, the seriousness of untreated disease, the pharmacokinetics of the drug, and resistance. Chemotherapeutic agents like isoniazid, rifampicine and regimen containing combination like thiocetazone may be poorly tolerated or have short half-lives and exert enormous selective pressure favoring drug-resistant strains unless therapeutic levels are maintained continuously. If a patient takes very little or no drug, the likelihood of resistance is relatively low because there is little or no pressure to select a resistant mutant. In theory, if adherence is complete (100%) with potent combination therapy, bacterial replication will most likely be halted and resistant bacterial mutants are unlikely. Patients who intermittently or irregularly take drugs, (the majority of patients in clinical practice), the likelihood of selection of mutants that are resistant to the drug(s) increases, a consequence of both continuing bacterial replication and selective auto-microbial pressure. Thus, such regimen may be among the most unforgiving of prescribed medications as their continuous therapeutic coverage is needed. Extensive research on infectious diseases including TB have demonstrated that 1) adherence to drug regimens is poor across populations; 2) health care providers are not able to predict who will or will not adhere to drug regimens; and 3) providers consistently overestimate patients' adherence to the recommended drug regimens. Clearly, the degree of adherence to therapy affects treatment outcome; low adherence reduces both efficacy and toxicity. Combination of drug therapy is highly effective in TB but is difficult to adhere.

Effective therapy requires a treatment regimen with a regular and daily intake with proper timing, dietary restrictions and multiple doses per day and a great deal of devotion. It requires maintaining continuous therapeutic levels in order to be effective and to cure TB effectively. It may cause severe side effects and make the consequences of non-adherence to combination
drug therapy more fatal. Most important and threatening aspects of non-adherence are 1) drug resistance develops rapidly with non-adherence to the prescribed dosing regimens, 2) a high level of cross-resistance to other medications and associated conditions like HIV/AIDS may develop and result in limited treatment options, 3) increase in mycobacterium load, 4) decline in health status and susceptibility to other infections, 5) rapid disease progression and 6) transmission of a resistant strain of the virus. In spite of high annual infection rates and immigration influx, TB control in marginalized Pakistani population has been very less focused in the research. The study was undertaken in a community, which comprises alarming number of TB patients in the country. Study population included patients from the largest infection pool inside Pakistan (sample size of 621 TB cases). This part of the study examines specifically, the level of adherence and factors determining non-adherence to TB medications in the light of information-motivation-behavioural skills model in order to explore the basic tenets relevant to Pakistani setting. With respect to socio-economic, demographic, quality of TB care, patient's awareness and perceptions and behavioural attitudes towards medical treatment, all essentials were thoroughly studied. This chapter provides full account of the focus and responsiveness of TB control program to the adherence issue.

COMMUNITY CHARACTERISTICS

Pakistan is located in Southern Asia, bordering the Arabian Sea, between India on the east and Iran and Afghanistan on the west and China in the north. Country's total population is 154 million and total area is 803,940 square kilometer. With an area of 74,500 km and 20 million of population, NWFP is one of the four provinces in Pakistan and has a 2500 km long border with Afghanistan. Literacy rate in NWFP is 21%. The annual caseload is more than 554/100,000 (1998). The geographical location of NWFP, (see Figure 3) has played a significant role in the current magnitude of TB infection. The prevalence of tuberculous infection is higher in aboriginal communities but also Afghans living in Pakistan. The likelihood that TB infection will prevail in these communities in the foreseeable future. With the annual rate of TB infection of 1.7 %, large number of unstable and refugee population poses a huge threat to the infectious disease control (WHO, 1997; Arshad J, 1997; De Myneck, 2001). More than three million of Afghan refugees are currently residing in Pakistan. 80 % of population in NWFP is rural.

Despite some economic growth, health and educational indicators have remained unchanged in the past. The province is divided into 24 districts. Peshawar is the capital of NWFP. Health services are predominantly public but private sector is rapidly emerging and contributing in the health provision. There exist remarkable inequalities and disparities in the distribution, availability and quality of care between rural and urban areas (Sirageldin I al et., 1976; Karim MS, 1993; Bhutta Z.A., 1997). (see chapter 3) Similarly less than 30 percent of the population uses primary health care facilities (PHC). The same PHC serves as the backbone of NTP for the delivery of TB control services (Karim MS, 1993). The tendency of paying out of pocket to private practitioner is very high. Almost every second patient visits a traditional healer or local private practitioner prior to visiting the public health facility. The health indicators are worse in rural areas due to lack of access to health facilities. In Pakistan only 23% of health facilities are available to more than 80 million of population (Akbar Zaidi S, 1985; Karim MS, 1993). Major segment of the population in the NWFP receives TB coverage through the local Government.
of NWFP that is heavily funded and supported by an Italian NGO called Italian Cooperation for development. They are considered the pioneers in the TB control in the area.

An agreement was made between the Government of NWFP and Italian NGO to intensify TB control activities and pledged to introduce DOTS in 1995. Implementation started in 1997 but the progress could not proceed due to a handful of financial and manpower resources allocated to DOTS in the community. Cases detected and under DOTS treatment were included in the sample along with that of non-DOTS due to less differentially and small number. As far as TB control is concerned till 1998 DOTS coverage was 20% in the NWFP, which was primarily achieved by the mutual contributions of international NGOs and provincial Government (ICD 1997; Arshad J 1997). There are 188 hospitals, 4 medical colleges, 87 RHCs, 988 BHUs, 25 TBC units and one sanatorium in NWFP (see chapter 3, page ). Huge gap exists between the rural and urban communities especially in NWFP in terms of the distribution of health personal and health facilities.

CONCEPTUAL UNDERPINNINGS OF ADHERENCE
The term adherence is not as simple as it appears and implies a conscious co-operation and approbation rather than a submission to medical orders (Mehta, 997; Salicrù, 1997). According to Williams (1999) it is the behaviour of taking medication according to treatment dosage and schedule, while taking into account food intake requirements. Non-adherence occurs when the actual treatment the patient receives is different from the intended treatment. Assessing adherence and non-adherence involves a comparison of the number of doses taken properly with the number of doses prescribed (e.g., Chesney & Ickovics, 1999). As far as adherence in the infectious diseases is concerned Friedland (2000) illustrates the conceptual framework and mechanism of action drugs and channels to eradicate mycobacterium. The model presented the role of adherence in the TB therapeutics (see Figure 30) is unique in several aspects. It not
only provides an in-depth understanding of therapeutic phenomenon lying behind adherence but also elaborates the key adherence levels and vicious steps till it achieves the clinical outcome.

To understand the phenomenon of adherence with the TB treatment, it is essential to understand the process through which TB-drugs pass and reach the blood level. Figure 30 therefore provides an illustration of the pharmacokinetics from macro to the micro level. The pathways shown in the diagram clarify not only the significance of adherence with the prescribed regimen but also shows the key nodes where non-adherence can occur or induce effects depending upon the node and time of interrupting treatment. Whenever a drug is taken it passes through multiple stages before it reaches the blood level and achieves its targeted aim. Once an adherent dose is taken by the patient, it achieves its desired level by absorption from the gastro-intestinal tract passes through effective metabolism and transported through systemic circulation till it attaches the desired target of mycobacterium. The elimination of mycobacterium starts once a sufficient level of concentration is attained in the blood inside the host. The process is reversible and the elimination mycobacterium is directly related to the drug intake and serum concentration. In order to overcome the bacterial resistance the drug must be taken for standard time period in a standardised regimen form. In other words the process is entirely dependent on the degree of adherence of the patient. The higher the adherence faster will be the load reduction of mycobacterium and likewise rapid will be the sputum conversion from positive and negative.

**Fig 30 The Role of Adherence in TB Therapeutics**

THE INFORMATION-MOTIVATION-BEHAVIOURAL SKILLS MODEL

The Information-Motivation-behavioural skills model of adherence was selected to guide the approach and design adopted in the study. The model assumes (Figure 31) that people comply with treatment under specific set of conditions. Patient undergoing therapy must have a minimal level of health knowledge (information), motivation and skills to decide and cope with the disease and relevant consequences accordingly. Patient must be assured of the fact that the effort is going to bring a rapid and positive clinical outcome. But they should also be aware of the possible consequences of non-adherence with the therapy. The effectiveness of model is widely proved and is considered an appropriate tool to design or to improve the adherence of patients. While assessing adherence among the TB patients, special attention was given to the following integral components of the model.

First Component
This component includes adherence information about the regimen e.g., how (specific food & fluid requirements) and when (timing) to take pills; procedures for dealing with missed doses. Also information about adequate adherence e.g., knowledge of the effects of missed dosages; the consequences and costs of non-adherence and benefits of adherence as well as information about potential drug-drug interactions & side effects, prescription of non-essential or supplemental drugs.

Second Component
As motivation (psychosocial factors) is directly related to the degree of adherence there the model addresses the issue of motivation among patients very aggressively. It assesses attitudes towards medications; to non-adherence (e.g., taking non-prescribed drug holidays); to the perceived benefits of taking medications; to the perceived costs of not taking medications; to the perceived obstacles to taking medications; to the individual's drug regimen in particular; personal significance of adherence with regimen; trust in provider; Social Support; social network support for taking medication; support from provider; quality of patient-provider interaction

Third Component
This component comprises of adherence behavioral skills and combine objective skills and self-efficacy in managing treatment like the ability to self-administer medications. It ranges from obtaining, refilling, intake and appropriately storing medications. Incorporating adherence into the ecology of daily life (e.g., creating cues for pill taking times, maintaining confidentiality at work, problem-solving difficult adherence-related situations), enhancing coping skills with the side effects. Encouraging patients in obtaining further information as needed for proper adherence. Besides moderating factors, which include living situation of a person under treatment (e.g., homeless), access to medication/services (e.g., transportation, insurance), other supportive resources necessary to take pills (e.g., support network, home health aid), proper drug storage etc. Health outcome measurement is an important end point where the objectives are achieved mainly curing the disease, eradicating infection (reduced bacterial load, decreased bacterial mutations, psychological variables (e.g., overall well being), improving the quality of life, other health indicators and associated conditions. In the following section the mechanism and conceptual pathways of adherence is given in figure 31, which depict various level of adherence interventions.
ADHERENCE ASSESSMENT PLAN
The adherence assessment plan designed for the study consisted of three exclusive steps and divided in this chapter into parts. Part first mainly aimed at: 1) Preliminary quantitative assessment of TB cases by identifying adherent and non-adherent TB cases from the pool of registered infected patients (smear positive); and checking their medical records in the facility and that of patient’s TB cards, 2) Examining adherence by the sequence of attendance/visits to the TB facility for periodic follow up, 3) As adherence is more subjective and can be biased if relies only on patient’s statement, therefore to consolidate the verbal adherence of the TB patients with that of physical evidence, urine examination was scheduled to confirm oral intake by checking the possible traces of urine metabolites and urine discoloration of two key anti-TB drugs i.e., isoniazid and rifampicine, 4) Evaluation of adherence by checking chemotherapeutic regimens among adherent and non-adherent cases of the registered TB patients in the facility. For this purpose TB center in District Sawabi was selected due to the following reasons, 1) high TB caseload among native as well as Afghan refugee population, 2) a high annual rate of TB infections i.e., 1.7% in the area. Part two adherence assessment plan focuses on patients selected already in part one. Based on the criteria of inclusion given later in the chapter, patients (n=621) were selected and subjected to an in-depth interview either at home or at the TB facility. The aim was to identify various determinants leading to non-adherence in this particular area. Multivariate analysis was performed with SPSS on the data collected from the TB patients. The statistical association for non-adherence and the level of satisfaction were examined for various designated determinants.

Figure 31 The Information-Motivation-Behavioural Skills Model of Adherence
Part three adherence assessment plan is mainly aimed at generating qualitative knowledge and in-depth insights into the issue by performing focused group discussions. Exploring the underlying attitudes, perceptions and behavioral aspects conducive to non-adherence and also to identify barriers in care seeking among defaulted TB patients were thoroughly discussed. Focused Group Discussions (FGDs) were conducted at the TB facility in the NWFP. It is believed that the proposed design for adherence assessment will ensure the representativeness and validity of the study and will substitute the conventional shortcomings of merely quantitative approaches and will also avert the reductionism or abstracted empiricism, which is the peculiarity of exclusive quantitative methods. The components selected in the study design also gave an account of the reasons as well as the social characteristics of patients who do not comply with tuberculosis treatment. This can guide the control program towards higher risk groups of treatment failure and consequently prevent the probability of transmitting infection to others by enhancing and promoting adherence and arresting TB infection in the bud.

The study was guided by the basic theoretical framework of information-Motivation-Behavioral Skills model of adherence (see Figure 31). The model is based on components, which explore factors conducive to adherence. In accordance with the theory, it was predicted that adherence information, motivation and behavioral skills influence medical adherence to a large extent and clinical outcome of the chemotherapy. Lack of these fundamentals in any control program impedes the intended health action for example to seek treatment regularly and reinforcing factors, which contribute to the persistence of the particular behavior. Besides, the model has proven to be a useful tool for examining sick role behaviors such as adherence (Allan EL el at., 1992; Dube CE el at., 2000; Kalichman SC 200; Jeffrey DF, 2000).

DETECTING NON-ADHERENCE AMONG PATIENTS
Since there is no gold standard for detecting non-adherence, a combination of methods is applied to yield the desired information. Self-report(open-ended questionnaire/interviews/diary) about medication-taking behavior will detect some non-adherence. Pill counts have been used extensively but are not believed to be accurate; patients may empty the pill box, or take all of the remaining pills before their clinic visit. Accurately recording the date and number of refills in the medical record can make it easier to determine whether prescriptions last longer than they should. The accuracy of drug assays depends in part on the half-life of the drug; longer-acting indicators have been used, but testing will show only past ingestion and not frequency or dosing interval. Biologic markers can also provide useful information. In case of chemotherapy urine samples are also used to check traces of individual drugs. The Medication Event Monitoring System (MEMS) provides a computer chip in the cap of the medicinal bottle; information is recorded each time the bottle is opened (Paterson D, 1999).

Clinical manifestations and level of improvement in physical condition add also to the assessment or detection of adherence with the therapy. Similarly, increasing bacterial load in the sputum smear examination after the initiation of an aggressive regimen might be due to non-adherence with the chemotherapy. Although some of the methods checking adherence among under treatment patients are beyond the cost and reach of developing countries like Pakistan but their use have improved adherence significantly in other settings. Data from the MEMS allows calculation of 1) the adherence rate, or percentage of pills taken; 2) prescribed
frequency; and 3) prescribed interval. Measures of the following possible determinants were included in the assessment battery: contextual factors (e.g., ethnicity, family composition and functioning, behavior, family health, service utilization), motivational factors (e.g., intentions, self-efficacy, health beliefs), capabilities (e.g., knowledge of illness and medical treatment), social interactions (e.g., family communication, social support, parenting), social interdependence (e.g., provider treatment decisions). Outcome was measured in terms of adherence to the prescribed chemotherapy as well as to the health care appointments.
PART ONE

This part mainly consists of preliminary quantitative assessment of registered TB cases by identifying adherent and non-adherent TB cases from the pool of infected patients (sputum smear positive). Checking the medical records in the facility and possibly that of patient's TB cards notified or registered cases in the last four to six months (July-August 2000). After this the selected cohort of TB cases labeled as adherent (non-interrupters) and non-adherent (interrupters) were subjected to urine examination. Urine examination and the rapid scrutiny of previous medical records identify and trace out the true chronic defaulters and treatment interrupters (non-adherent cases for more than three weeks) among the registered TB cases. Medical records of 711 TB patients in the district TB units (SAWABI), who started their treatment (sputum smear positive) were retrieved and reviewed. Default is defined as failure to attend the weekly TB clinic, for a period of more three weeks. The frequency of visits paid to the TB facility was also determined. The treatment outcome was also simultaneously checked during this part of the study. Simple, reliable, and relatively inexpensive direct tests were performed for demonstrating the presence of various metabolites of anti-TB drugs in the urine of patient. In order to verify verbal adherence of patients, cross examination was performed by performing urine tests. Such methods have been frequently applied by various researchers (Eidus & Ling, 1969; Burkhardt KR, 1980; Kirsten el al., 1980; Ellard el al., 1977; Henderson, 1986; CDC 1994) where mostly urine is tested for the presence of isoniazid (H), pyrazinamide (P), rifampin and their respective metabolites, and ethambutol (E).

In our study isoniazid (H) and rifampin (R) were mainly focused as they are the key drugs widely prescribed locally by the physicians. The only limitation to these tests is that they show only recent ingestion of medication (within the past 24 to 48 hours). To avoid any doubt about the status of chronic interrupter or defaulter patient's records were meticulously checked for the history of previous such episodes and were duly matched with the results of urine examination for accuracy. Kilburn [1972] described a procedure for detecting the isoniazid (H) metabolite isonicotinic acid in urine by using a reagent-impregnated paper test strip. The dipstick test, which is convenient in such setting, was applied to measure the presence of the most widely used TB medication (see instructions in the appendix). The isoniazid (H) test strips are shown to be 99% sensitive (very few false-negatives) and 100% specific (no false-positives) for one group of patients when urine was collected in 20 to 24 hours after pills were ingested, and it is believed that for most patients the test is reliable when conducted at any time within 24 hours after pills are ingested (CDC, 1994).

However, the normal rate of isoniazid (H) metabolism differs in various patient populations, and the average time required for clearance of isoniazid (H) from the urine can be less than 4 hours. In addition to normal differences between patients, which are constant over time, temporary factors such as fluid intake, illness, or dehydration may affect INH clearance and can lead to false test results. The method facilitated monitoring the intake of isoniazid by TB patients and the use of isoniazid as a marker for assessing the regularity with which other drugs prescribed for self-administration are actually ingested. Excluding other conditions which can counteract tests for the presence of rifampin (R) or its metabolites was examined by the color of the urine. In most patients, rifampin (R) turns urine, saliva, sweat, and tears to an orange-red color (CDC 1994). A quick glance at a urine specimen reveals whether the patient has recently taken this medication. Patients were interrogated accordingly and urine sample
investigated for the signs of discoloration. For adherence profiling all 711 patients were grouped according to the degree of adherence. 621 (87%) out of 711 total number of patients were classified into two groups of adherent and non-adherent cases and whose urine was examined. Ninety cases were not included in the analysis as fifty one (8%) refused participation and 31 (6%) did not appear at the day of analysis and were assumed as lost and excluded from the study. All cases who fulfilled the set criteria of defaulters or interrupter were selected for the urine examination.

RESULTS
Urine analysis was performed in two successive phases. The preliminary quantitative assessment of part one identified a significant number (n=621) of TB cases from the pool of detected TB cases. (See figure 32) Based on the clinical assessment and medical reports all cases were categorized depending upon the status of their treatment and sputum smear profile. Surprisingly, the major proportion (82%, n=507) of cases interrupted treatment more than once either partially or completely, while merely 18% (n=114) remained truly adhered to the treatment prescribed. The group of chronic interrupters were the focus of attention for the rest of analysis. DST, sputum microscopy and the review of records was performed for all the defaulters and chronic interrupters and the details turned out to be as following, 60% of the cases were newly detected sputum smear positive cases, 20% relapse, 19% resistant and 1% were failure cases (see appendix for definitions). In spite of ongoing chemotherapy all cases, which had interrupted treatment more than three times and had three consecutive positive sputum smear reports in addition to the deterioration in clinical condition, were labeled as chronic interrupters and the rest as non-interrupters (adherent).
Coupled with the review of medical records, the urine check up confirmed the status of their chronic interruption (non-adherence) to the prescribed therapy. The possibility of performing culture sensitivity testing is very limited in the public TB facilities and only private laboratories offer such tests on high costs. Physician rely mostly on their clinical skills and on x-rays and sputum smear examination where available. Due to passive detection and monitoring system chronic interrupters were not necessarily traced and urge given to the treatment completion. The results of urine and physical examination are given in Figure 33 that illustrates the proportion of true interrupters and non-interrupters among the pool of patient. Adherent patients showed more frequent change in color and urine metabolites for rifampicine and isoniazid respectively, likewise the manifestations of regular intake or side effects related to the daily use of these drugs were observed among these patients. Studies showing similar trends were found in Sind Province and Balochistan Provices by Sloan JP in 1981.

Patients with negative sputum smear profile who remained adhered to the treatment seemed to have less associated conditions/ complications and side effects than those with positive. Major proportion of the interrupter category was still sputum positive although treatment duration was more than four months and were treated initially in the rural TB centers or health centers. On the contrary most of the non-interrupters were sputum negative and treated in city hospital or district head quarter hospitals. This obviously reflects the quality of services in providing effective care, case management and more importantly the periodic follow up in the
rural and district TB or health units. The results of naked eye examination and chemical tests of the first adherence assessment plan are shown in figure 33. Urine examination showed marked variations between the interrupters and non-interrupters. Urine discoloration due to rifampicine and isoniazid metabolites were traced more among those who did not interrupt the treatment.

The evidence of non-adherence among patients was more evident in the urine examination for isoniazid and rifampicine in terms of discoloration and usual side effects and in the sputum conversion. Coupled with the assessment of periodic visits the manifestation of commonly observed side effects of chemotherapy and urine examination confirm the degree of non-adherence with the prescribed treatment. In the second part of the adherence assessment plan the sequence of the periodic visits/ attendants were examined. The trend in visits paid to the unit for follow up and drugs collection during the treatment is given in Figure 34 that further explains the gradual decline that was observed between the first and second months. Compared to the abrupt downfall in the number of visits in the fourth and fifth months the downward trend continued in the consecutive months to almost less than half of the total number in the last six months.

Since the Madras study [1959] in India (Liefooghe R 1999-2001) and the advent of ambulatory chemotherapy, failure to attend clinics for follow-up, and non-adherence with the treatment have become a challenge to the control of tuberculosis in the developing countries. The problem is a complex one in this region. The motivating factors, which bear upon a patient and cause him to return to clinic for follow-up, and urge him/her to continue taking
medication, vary from culture to culture (Styblo, 1988). However one of the main motivating factors is how ill a patient feels (Suchmann, 1966). The analysis provided an ample evidence that non-adherence increases the time passes. The reasons leading to such dramatic change in behavior or attitude will be thoroughly investigated in the coming sections. The general impression was that as soon as the patient specially those with the pulmonary TB turns rapidly from positive to negative sputum smear or physically they feel healthy/ recovered that lead to the cessation of therapy. Non-adherence with essential TB drugs (Kasl et al., 1976; Almeida, 1962; Ansari et al. 1988) has long been noticed. However, the local TB control program is non-vigilant in responding to this critical issue.

In the observed cases the preferences of chemotherapeutic agents in the physician’s prescriptions were more towards Isoniazid (99.5%), Rifampicin (96%), Pyrazinamid (94%), Ethambutol (48%) for pulmonary TB (first initial two months) followed by four-month Part of rifampicine (R) and isoniazid (H). Streptomycin (69%) was added in the case of extra-pulmonary TB. Physician’s preference was more for Isoniazid, Rifampicin, and Pyrazinamid respectively because of their practicality and availability in the markets. But on the other side poor adherence was noticed with prolonged regimen containing Isoniazid, Rifampicin, Pyrazinamid and Streptomycin, which are the most commonly prescribed drugs. (See appendix for regimens) Majority of non-adherent patients (especially pulmonary TB) had observed marked side effects and therapy induced complications related to Isoniazid, Ethambutol, Ethambutol and to streptomycin respectively (table 24). With respect to the side effects induced by the chemotherapy the experiences of patients differed. Side effects and non-adherence were predominantly more in cases, where Isoniazid was taken. Isoniazid and streptomycin were the most frequently disrupting chemotherapeutic agents among patients.

<table>
<thead>
<tr>
<th>Chemotherapeutic Agent</th>
<th>Side effects &amp; complications</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid (H)</td>
<td>Jaundice, skin rash(es), edema</td>
<td>18</td>
</tr>
<tr>
<td>Rifampicine (R)</td>
<td>Hepatitis, diarrhea</td>
<td>1</td>
</tr>
<tr>
<td>Ethambutol (E)</td>
<td>Skin rash(es)</td>
<td>4</td>
</tr>
<tr>
<td>Pyrazinamid (Z)</td>
<td>Skin rash(es)</td>
<td>2</td>
</tr>
<tr>
<td>Streptomycine (S)</td>
<td>Nausea, vomiting, hot flashes</td>
<td>1</td>
</tr>
<tr>
<td>Thioacetazone (T)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Patients bear greater concerns about the side effects and complications related to anti-TB regimen used. Perception of the TB treatment prevailing among patients is opposite to what is given in the scientific literature. In many cases the perception of the TB treatment among patients not only makes them hesitate to initiate treatment but also leads to an early cessation of the therapy which creates a complex situation both for the patient as well as for the HCP. Patients may attribute worsening symptoms to medication effect and be less likely to continue medication (Baekeland F, 1973). Conversely, improvement of symptoms is one of the main reasons given for non-adherence (Caldwell, 1970; Hemminki, 1975) as patients no longer feel the need for medication or no longer have symptoms that remind them to take it. Side effects
of medications have been as strongly associated with adherence as might be expected. However, side effects that patients perceive to be related to medication may play a stronger role in adherence behavior. Patient perception of medication effects has been cited as a frequent reason for not taking medication as prescribed (Eldred, 1997). 19% (n=117) of resistant cases (Figure 32) were also included among the chronic interrupters. In addition to the repeated three consecutive sputum smear positive results since the start of the treatment, their status were confirmed by the drug sensitivity tests. The drug sensitivity reports revealed all cases to be resistant to multiple anti-TB drugs. 75% of this group were resistant to the most commonly applied regimen of isoniazid and rifampicine. The rest were resistant to more than two drugs which included ethambutol, pyrazinamide and streptomycin.

Table 27 Types of TB Cases

<table>
<thead>
<tr>
<th>Type of TB</th>
<th>Interrupters</th>
<th>Non-Interrupters</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>%</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>385</td>
<td>82</td>
</tr>
<tr>
<td>EP; Abdominal or intestinal TB</td>
<td>44</td>
<td>82</td>
</tr>
<tr>
<td>EP; TB lymph nodes</td>
<td>24</td>
<td>57</td>
</tr>
<tr>
<td>Cases with mixed manifestations</td>
<td>6</td>
<td>100</td>
</tr>
<tr>
<td>EP; plural effusion</td>
<td>48</td>
<td>100</td>
</tr>
</tbody>
</table>

*EP-extra pulmonary

Category wise analysis showed that high number of non-adherent cases belonged to (see Table 27) pulmonary TB followed by the category of tuberculous pleural effusion in the extra-pulmonary TB. The duration of regimen given to the cases with pulmonary TB was unnecessarily prolonged which showed allegedly an important predictor of poor-adherence among patients with side effects (see table 28, & 27).
Diagnosis of pulmonary tuberculosis was usually delayed in most cases and likewise therapy later started. Awareness and health information profile was also poor which partly played a role in delayed induction and follow up. It signifies further the responsiveness of TB care to the patient related factors. However manifestations profiling care seeking among patients were mainly related to the pulmonary tuberculosis. 88% (n=447) of the interrupters sought care due to manifestations similar to chest infection or pulmonary TB for example, cough, chest pain, fever, bloody vomiting. This pattern had some local and cultural aspects. Patients usually considered chest infection non-malignant and use variety of home based remedies and seek care only when it interrupts or disable them in any respect. 4% (n=21) among the non-interrupters manifested abdominal pain, diarrhea, and weight loss. 8% were the combination of the above-mentioned categories.

Figure 35 shows 89% patients (n=444) of selected initially allopathic treatment, 2% took homeopathic treatment, 5% took mixed therapy and 3% had no preferred choice in taking treatment. The duration of the chemotherapeutic regimen used was longer than the recommended regimens in both categories. (See table 27) Frequent interrupters were observed predominantly in pulmonary TB cases with the average duration of 10 months followed by the cases of extra-pulmonary with the 11-month duration. Patient’s expressed unwillingness for the use of anti-TB drug namely streptomycin due to its side effects and difficult route of administration. Acquired drug resistance emerging to multiple anti-TB drugs is increasingly reported from all over the country (Sloan JP, 1981; Ansari G, 1988; Khan J, 1993; Arshad J, 1997; Karamat KA, 1999; De Muynck, 2001). A high number of rapidly emerging resistant cases was also discovered during the course of the study. Shown in table 7 & figure 37 (chapter 2) the profile of the resistant cases in the region. The numbers can be interpreted as alarming. Out of 19% of cases traced during the study, 12% were of acquired resistance to multiple drugs while 7% were primary resistance to primary anti-TB drugs (see appendix for definitions). The status of adherence with the prescribed regimens was assessed by classifying cases into three groups. Poor adherence category patients were the ones who missed more than three follow up appointments and drug collections. Fair was the second category of patients denoting when one or two assessments of the health care provider HCP/physician were unfavorable and similarly consecutive appointments were missed accordingly. Good was the last and the least category including patients whose status were confirmed by the assessment of HCP where all clinic appointments were regularly maintained and followed the instructions given.

Table 28 Adherence Profile of 621 (81% non-adherent +19% adherent)

<table>
<thead>
<tr>
<th>Treatment regimen used in initial &amp; Continuation Phase</th>
<th>Average Duration (months)</th>
<th>Adherence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRZE &amp; HR (Pulmonary)</td>
<td>9</td>
<td>Good 4 Fair 13 Poor 49</td>
</tr>
<tr>
<td>HRZES &amp; HT (Extra-Pulmonary)</td>
<td>11</td>
<td>Good 0 Fair 2 Poor 32</td>
</tr>
</tbody>
</table>

Rifampicine (R), Isoniazid (H), Ethambutol (E), Pyrazinamide (Z), Streptomycine (S), Thioacetazone (T)
The adherence was poor for 49% of cases, fair for 13% with the prescribed regimen including HRZE in case of pulmonary TB was alarming as compared to that of 32% in regimen HRZES of extra-pulmonary TB cases. (Table 28) Comparing both regimen with that of recommended regimen specified by National TB control guidelines gave the impression that repeated interruptions unnecessarily prolonged the course of treatment and complicated the expected clinical outcome. Table 29 classify TB patients on the basis of subjective perceptions about their health status since the start of treatment. The physical perception of good health and improvement was more among the non-interrupters than the interrupters.

<table>
<thead>
<tr>
<th>Health Status</th>
<th>Interrupters %</th>
<th>Non-interrupter %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>0.4 (3)</td>
<td>1.4 (9)</td>
</tr>
<tr>
<td>Good</td>
<td>14 (90)</td>
<td>3 (20)</td>
</tr>
<tr>
<td>Fair</td>
<td>25 (154)</td>
<td>9 (58)</td>
</tr>
<tr>
<td>Poor</td>
<td>42 (260)</td>
<td>4 (27)</td>
</tr>
</tbody>
</table>

Additionally patients between both groups were asked about their health condition since they started treatment. The results are given in table 4. Over 42% of the interrupters responded that their health status is poor with compared to 4% of the non-interrupters. The perception of overwhelming majority of interrupters raises several questions about the validity of their response as patients might manipulate or represent their status different than in reality or in order to get the maximum attention and support of the health care providers.

![Figure 36 Sputum Conversion (positive to Negative) among TB Patients](image)
Figure 36 documents the results of their sputum conversion and changes in the trend occurred of patient cohort in both categories of the interrupters and non-interrupters. Observations have shown that sputum conversion (from positive to negative) was twice faster the time among the non-interrupter than in the interrupters. The sputum conversion graph shows almost a linear fashion for sputum conversions in case of adherent cases. More than 50% of the cases had turned sputum smear negative in their third month after the commencement of the chemotherapy. In the sixth month almost 93% of the non-interrupters (adherent cases) were turned to negative than those of interrupters. Sputum conversion was extremely tardiest among the interrupters. Poor adherence delays sputum conversion and complicate clinical outcome. An increasing number of research has shown that chronic interruption not only delay the elimination of mycobacterium but also increases the chances of developing resistance to the drugs (Liefooghe,1995,1999, Khan,2000, Khan, 2002).
PART TWO
ADHERENCE ANALYSIS

As described earlier, patients traced, selected (n=621) for the first phase of adherence analysis, were subjected to the in-depth interviews in the second phase. In the selection of TB cases a revised procedure was adopted by approaching consecutive patient and was asked if they would be willing/prepared for an interview either at home or at the TB unit. This process was continued until a list of 621 patients per site had been created, each of whom had consented to our survey team. Their status were confirmed by referring back to their previous medical profile and sputum smear profile at the TB facility. A predetermined questionnaire with open ended questions that explore all facets of patient's life of TB patients. A cross design synthesis was therefore adopted which comprised socio-epidemiological, personal and medical history and ethno-anthropological components conducive to accomplish the research goals as well as components adherence. In order to obtain a representative and rich sample of TB patients, TB control center in the District of Sawabi, NWFP was selected. The survey team comprised a senior male sociologist and two female public health researchers and two national health workers and two laboratory technicians trained in conducting tests infectious diseases. The instrument was field-tested before the survey and modified where necessary. Responses to open questions were reviewed by the senior team member. Themes were collated manually from transcripts of interviews. Multivariate, logistic regression analysis has been increasingly applied in medical research and the field of public health. It was therefore considered an ideal tool to analyze the phenomenon of adherence among patients. The logistic regression presents an independent association and gives the advantage of determining the effects of each factor while holding the effect of other factors constant. It tests not only for the relationships between variables (dependent) controlling for the effects of other variables (independent) but also a significant association in a multivariate, analysis signifies that a particular independent variable is still significantly associated with a dependent variable when the effects of many other independent variables (e.g., such as ethnicity, age, income, etc.) are controlled for in a statistical test or model involving one dependent variable and more than one independent variable. (See appendix)

Analysis was carried out using SPSS statistical software (Norusis MA, 1995). Based on the model of multivariate regression the test of significance was applied and odds ratio (95% confidence interval) was estimated and multivariate logistic regression analysis was performed to obtain the adjusted estimates of the effect on adherence of all significantly associated variables found in the analysis. (See appendix) The criterion to categorize patients as interrupter or non-adherent was his/her failure to take anti-TB drugs for more than three weeks. Taking into consideration the practicality and feasibility of the administrative procedure, which served the base of the definition adherence. Outcome of the patient's treatment was labeled 0 if patient was adherent non-interrupter, 1 if patient failed to show adherence with the treatment and was used an dependent variable.

Thirty various variables were made and included in the study focusing on socio-demographic variables concerning gender, marital status, age, type and size of the family were included as independent variables. Among other independent variables socio-economic variables were also included in the analysis. Information and data about the income of the family and head of the
ADHERENCE ANALYSIS
Chapter 4

family, environmental hygiene, housing (e.g., rooms per persons available, toilet, sanitation and source of drinking water, area of residence and local practices like pets) and schooling, occupational status, religion, and nationality were gathered and analysed. With excellent response to questionnaire data were collected in two parts (five to six months duration) held partly in the TB facility and partly in patient's houses in a face-to-face manner. The interviewers not only understood the local language called Pashtoo (commonly spoken by the locals in Pakistan and Aghanis) but were also acquainted with the local socio-culture standards. Several interviewees were questioned when they came to the TB facility for their follow up or contacted at the home of the informants. Special attention was given to the local cultural norms and social setting. No interview was held privately and study team was welcomed wherever the setting was launched in the vicinity. The internal consistency and quality of the content interviews the discussions were audio taped and checked twice by the team with that of the written version. All participants were assured the intentions and potential benefit behind the intended research. For the integrity of women special arrangement was made to contain their cultural norms, as they were mostly veiled and wished to keep the discussions confidential.

RESULTS
The study population mainly composed of two categories of TB patients i.e., non-adherent who interrupted the treatment and those who remained adherent and completed the treatment. The study group consisted of total sample of 621 in which 82% (n=507) cases were interrupter (non-adherent) and 18% (n=114) non-interrupter (adherent) respectively. (See figure 37) Efforts were given to reach the proposed equal sample size from both categories but the category of adherent patient remained significantly less than other. Overrepresentation of female (ratio 2:1) was due to the fact that majority of females are confined to home due to their family obligations like households, raising children and cultural obligations. As the study team consisted of females that helped to attract large number of women to participate in the study. The uniqueness of the study is that it represented the opinions of largest number of TB patients and specially that of female for the first time. Contact with them was easier while men go out and stay long outside home to earn their daily living. According to the local interpretation, the odds of the females suffering from TB was more than men.

The fact can be easily teased out by the fact of far less support and accessibility of women to effective care. Overcrowding facilitates the transmission of infection. With the understanding that most patients remain undetected in this community although the risk of contracting infection in a joint family system (where parents and grandparents live along with their children in one house) is more than elsewhere (Spinaci, 1989) no attention is given to the timely detection and treatment. 95% of the participants belonged to joint families and 5% were living as a single family. Similarly family size ranged from 1-15 persons per family with 68% were above 5 and 32% were below 5 persons per family. In the same surrounding 53% had either a close or a relative who was diagnosed with TB. Mean age of the subjects was 27 years (ranging from 3-75 years). 399 cases (64%) were female and 222 (36%) male. 327 (53%) were married (housewives) while (47%) 294 were single. According to the professional profile 55% were housewives (whose spouses earned their daily wages through farming or agriculture or working as low cost laborer), 19% children, 15% skilled were workers and employed, 6% unskilled workers and 5% were pensioners. 64% were from rural areas and 36% from urban
slums where housing and environmental hygiene are extremely poor. 91% had a common indoor toilet for the entire family and 9% utilized outdoor toilets.

53% had no permanent source of drinking water and water from ponds; streams and remote wells was used. 47% had a water pipe connection from the municipal committee. Raising cattle is an important component of household in the rural community. Cattle are kept and looked after by females and children in the family. Local interpretation behind raising cattle is merely economic. Cattle are considered an ideal source of diary products and an alternative for cash money in case family face economic crisis. Besides, they have an important role in farming. The majority of the TB stricken community was from low socio-economic strata. In 495 cases family income was below 2000 Pakistani Rupees (33 $US) while for 126 individuals it was between 2000-3000 (50 $US). 68% of the respondent had no formal education and were illiterate, 25% attended only primary school (6th class) that could hardly write and read, 6% high school (8-10th class) and 0.5% college education. 97% of the total sample comprised of Pakistani nationals and only 3% were Afghans refugees having Islam as religion. Majority of the participants belonged to the nearby villages within the radius of approximately 30 km in the district. In order to distinguish between socio-economic and demographic variables which determines non-adherence among TB patients, eleven risk factors were traced to have significant and likewise are discussed here in the following analysis.

THE ASSOCIATION OF DESIGNATED DETERMINANTS

Given in the figure 37 the detail breakdown of the group of non-interrupters (adherent) as well as non-adherent TB cases. According to the parameters described in the IUATLD, non-adherent TB cases were categorized into three groups, patients who interrupted treatment more than twice for more than a month with positive sputum smear status were called chronic interrupters (61%), patients interrupted treatment with positive sputum smear status once in a month were called moderately interrupters (17%), and those who interrupted treatment only once with negative sputum smear status were called slightly interrupters (4%). (see appendix for definitions) Table 30 summarizes the results of multivariate analysis among the selected variables. Among the thirty designated variables, sex, age (group between 21-49 years), family size (>5 members per family), not income raiser (having no job), illiteracy and lack of access to proper sanitation were shown to have a significant association with the non-adherence or interruption in the treatment.
Based on descriptive analysis of the selected sample of patients, sense of local trends and culture and literature review only eleven factors out of thirty were showed to have some kind of significance and were included in the multivariate analysis. Table 30 shows the results of multivariate (logistic regression model) analysis for a set of proposed eleven determinants of interruption of TB treatment. The analysis showed that six factors were significantly and independently associated with the interruption of the treatment. These were female sex, age group between 21-49 years, family size, having job or being not income raiser, being illiterate, lack of sanitation and raising cattle.

DETERMINANTS OF NON-ADHERENCE

The analysis determined that being female in the society serves as a risk factor for disrupting the treatment and care seeking. The proportion of the non-interrupters were small i.e., 18% of the total sample. The assumption was that being a female, marital status, age and family size might be a risk factor for the interruption of the treatment. For example, as explained in Table 30 the proportion of interrupting TB treatment was 1.8 times higher among females than males. Odds ratio for interrupting treatment among females was 1.8 (p value 0.05) for which the 95% CI lies between 1 and 3.2. This association should be taken cautiously. The logistic regression analysis showed family size above five members per family a strong risk factor as a strong association with the interruption of the treatment was found. With the 95% CI (1.9-4.8), the odds ratio was 3.1 (p-value 0.001) for this correlation. In NWFP the socio-cultural set up makes women more vulnerable to disease, death, disabilities and destitute. Female not only have family obligations and responsibilities but also face countless socio-cultural restrictions. Shown in Figure 37 out of 82% interrupter, 67% (n=340) were females where majority were housewives with joint family system. With respect to the culture elsewhere, women in Pakistan have fairly less access to health care, education. They have profoundly less conjugal powers and their role in decisions making is very limited. In NWFP traditions usually confine women and young girls to home. Outdoor visits are usually not allowed unless permission is granted. Women are not only the prime victims of tuberculosis in many developing nations including Pakistan and India. Studies have shown that the vulnerability index of women are extremely
high. A negligible amount of money from the household income is spent on women’s health (Tinka, 1998). In such communities withstanding the high cost of diagnostics and treatment put tremendous economic pressure on the already overburden families with large numbers. In most cases as here this becomes the main cause of treatment cessation or disrupting the cycle of the treatment and thus leading eventually to non-adherence. This has also been observed that monetary values are more taken into consideration when it comes to obtaining health care among women and children.

### Table 30 Results of Multivariate Analysis

<table>
<thead>
<tr>
<th>Designated Determinants</th>
<th>Interrupter</th>
<th>Non-interrupter</th>
<th>Odds Ratio</th>
<th>95% CI limits for OR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No (%)</td>
<td>No (%)</td>
<td></td>
<td>Lower</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>340 67.1</td>
<td>59 51.8</td>
<td>1.8*</td>
<td>1.0</td>
</tr>
<tr>
<td>Age (21-49) years</td>
<td>229 45.2</td>
<td>47 41.2</td>
<td>1.7*</td>
<td>1.1</td>
</tr>
<tr>
<td>Marital status (married)</td>
<td>236 46.5</td>
<td>58 50.9</td>
<td>0.7</td>
<td>0.4</td>
</tr>
<tr>
<td>Family size (&gt;5)</td>
<td>366 72.2</td>
<td>54 47.4</td>
<td>3.1***</td>
<td>1.9</td>
</tr>
<tr>
<td>Job(not income raiser)</td>
<td>393 77.5</td>
<td>66 57.9</td>
<td>1.8*</td>
<td>1.0</td>
</tr>
<tr>
<td>Family Income (&lt;2000)</td>
<td>141 27.8</td>
<td>20 17.5</td>
<td>1.3</td>
<td>0.7</td>
</tr>
<tr>
<td>Illiteracy</td>
<td>363 71.6</td>
<td>60 52.6</td>
<td>1.9*</td>
<td>1.1</td>
</tr>
<tr>
<td>Lack of access to water</td>
<td>273 53.8</td>
<td>57 50.0</td>
<td>0.7</td>
<td>0.4</td>
</tr>
<tr>
<td>Lack of Sanitation</td>
<td>317 62.5</td>
<td>55 48.2</td>
<td>1.8**</td>
<td>1.1</td>
</tr>
<tr>
<td>&gt; 2 persons per room</td>
<td>241 47.5</td>
<td>50 43.9</td>
<td>0.9</td>
<td>0.6</td>
</tr>
<tr>
<td>Raising Cattle in house</td>
<td>307 60.6</td>
<td>50 43.9</td>
<td>1.7*</td>
<td>1.0</td>
</tr>
</tbody>
</table>

*P < 0.05; **P < 0.01; ***P < 0.001.

The analysis revealed that the age group between 21-49 years (n=229) is a risk factor as disruption of treatment occurred in the 45% of people. This age group is considered the most productive period both economically and medically. Men and women urge to earn their wages and fulfill their family obligations or ignorance due to households, which in their view are more crucial than going to seek or continue treatment. Similarly being married was a determinant for non-adherence with treatment as 47% (n=236) were married. 76% (n=393) of people were not income raisers who disrupted allegedly the treatment. Not having a job is an obvious determinant of poverty and in other words the inability to sustain treatment and was proved to have high significance for non-adherence. Individuals who were dependent on family income had fewer opportunities to continue treatment and to bear the cost of the diagnostics. Undergoing TB treatment entails an expensive task, which embraces the costs of travel to the TB units and also loss of wages. Time of travel and cost of travel to the TB facility is also one of the interacting factors, which lead to discontinue treatment among patients.
Literacy is strongly linked to a good health and healthy care seeking behavior. The analysis has proved that illiteracy has link to the non-adherence with treatment and care. Illiteracy was highly prevalent among the majority of the TB patients and 71% (n=363) of the interrupter (non-adherent) cases were illiterate. Education and health awareness have strong repercussions for the sustainability of TB care. It plays a decisive role in keeping patient informed enough to keep them adhered with treatment. This aspect was adequately evident in the collective response of patients towards the query of recognition of the conventional TB signs and symptoms and possible awareness and health education. The response of 84% (n=522) to the question was negative and stated no knowledge of how to identify the disease. None of them could understand what are the most typical manifestations and causes of TB and above all their disbelief that TB is curable. Only 16% (n=99) could recognize one of the conventional manifestations of TB. As majority of the participants were illiterate, living in a community where health awareness and patient's knowledge about the disease was very limited. Hence patients perceived the treatment to induce irreversible side effects even if they are normal associated manifestations. These opinions and perceptions circulate and prevail among the community and cause significant damage to the people's faith in TB drugs. Pharmacologically side effects are the normal manifestation experienced by the patients once the intake is regular. It was observed that in many instances patients usually who are unaware of the facts associated with the chemotherapy do not consult their care providers for such complaints and usually abandon the treatment.

<table>
<thead>
<tr>
<th>Adherence check</th>
<th>Chronic interrupters</th>
<th>Moderately interrupters</th>
<th>Slightly interrupters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pills usually forget</td>
<td>****</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Pills some time forget</td>
<td>-</td>
<td>**</td>
<td>-</td>
</tr>
<tr>
<td>Pills rarely forget</td>
<td>-</td>
<td>-</td>
<td>*</td>
</tr>
<tr>
<td>Don’t know what to do when a dose is missed</td>
<td>**</td>
<td>***</td>
<td>-</td>
</tr>
<tr>
<td>Took the missed pills next day</td>
<td>-</td>
<td>-</td>
<td>***</td>
</tr>
<tr>
<td>Did not take the missed pills at all</td>
<td>-</td>
<td>-</td>
<td>*</td>
</tr>
</tbody>
</table>

* = <10%, ** = <30%, *** = <60%, **** = <70%, ***** = <100%

To verify and testify their skills in managing missed doses and medication this aspect of the adherence was subjectively asked from the patients. Information showing motivation and skills of interrupters in taking medication is given in table 31. Chronic interrupters frequently forget the regular intake of pills and had limited knowledge and skills of treatment compensation. Less than 10% of the interrupters repeated the missed pills next day. Lack of safe drinking water is a major problem in the surveyed community but the analysis could not prove the statistical association or high significance to the treatment interruption. Sanitation means formulation and application of measures designed to the disposal of sewage and protect public health. As a matter of fact majority of the TB patients were from the rural slums where the facility of sanitation was almost non-existent. 63% (n=317) of the non-adherent or interrupter category were reported to come from areas lacking proper sanitation.

The analysis proved the fact that non-adherence or treatment interruption was more among the patients with the large family size. The statistical association proved this peculiar
relationship (see table 30) between the larger number of family members and the higher degree of non-adherence among TB patients. It has a very reason in this community as pashthoons belonged to joint family system. Larger family set up is a common tradition in Northern Pakistan and 72% of the \((n=366)\) interrupters were from such families, which composed of more than five persons. Larger family entails more expenditure on household, less saving, and less money for the costs of health care and specially TB treatment. Greater tendency towards treatment interruption is evident from the fact that less per capita income and larger families make poverty stricken individual reluctant and less motivated for paying the costs of the treatment. In addition to the larger family size in the surveyed community, style of housing and indoor over crowdedness and especially the relationship between non-adherence and cattle in the housing was worth noticing. Multivariate analysis showed that raising cattle in the house was significant associated with the treatment interruption among TB patients.

A striking and a unique fact revealed by the study was that the majority 54% \((N=273)\) of the interrupters had a close or distant relative with TB in their family compared to 46% of the interrupters who had no contact source in the family. The attitude of disrupting treatment among this group was mainly related to their previous experience, poor moral and low confidence in the treatment. In addition to that fears of side effects that urge patients either not to seek care or interrupt the treatment. Some cases reported that they reduced the dosages of the drugs in order to lessen the side effects or unwanted reactions of the chemotherapeutic regimens. Raising cattle is an essential component of rural community and are widely used in farming, occasionally for transportation and also sold when cash money is needed. The association proved the assumption that raising cattle have a stronger role in the disrupting the sequence and cycle of the treatment. The cost of the treatment is almost paid by the TB units depending upon the type of facility they visit. In spite of this, majority of patients face severe financial constraints.

They have to pay, in most cases, the cost of their additional associated diagnostics and antibiotics for which neither the facility nor the patient have enough capability. Thus patients are trapped in the vicious circle of poverty which in many cases leads to no other option rather than to disrupt the treatment. The analysis showed that majority of the patients sought care from the medical (89%) either from the peripheral TB units (81%) or from the district hospitals (8%), however 61% paid also from their own pockets (see figure 35). The analysis did prove the relationship of those individuals who were not raising income which means more dependency on already single or poor income sources of the family. Similarly highly significant was the association of large families to the issue of non-adherence in the analysis. It reflects the unavailability of financial resources for those infected with TB in large families. Response of patients to the query about the cost of the treatment, majority declared the reason of interruption followed by side effects of the chemotherapy. In the order of highly significant determinants in the analysis , interruption can be categorized 1) sex (female); 2) family size >5; 3) not income raiser (joblessness); 4) illiteracy; 5) lack of sanitation; and 6) raising cattle in house.
TB CONTROL & DETERMINANTS OF SATISFACTION
As satisfaction is a crucial element-underlying adherence, the same set of data were subjected to second stage of multivariate analysis. To provide broader vision the data were slightly modified and variables with odds ratio less than one were redefined to assess the level of satisfaction among the TB patients. Figure 38 & table 32 illustrate the stratified form of satisfaction profile in which 46% cases were satisfied while 54% were dissatisfied. More precisely, the profile of dissatisfied patients is further shows that 9% were slightly dissatisfied, 16% moderately dissatisfied, and 29% strongly dissatisfied. Eleven designated determinants were extracted from the multivariate regression analysis to have significant relationship. Shown in the following figure, factors that lead to the dissatisfaction complicate further the adherence of patients with the treatment. Looking at the issue of satisfaction with the patient's perspectives as far as the TB treatment offered in the facilities concerned, the multivariate analysis presented an interesting association which is given in table 32. Reviewing the profile given in the Table 32 the probability of being satisfied from the quality of treatment was high among patients whose family size was smaller than five. The odds ratio was 2 (p-value 0.001; CI 1.4-2.9). In the order of determinants of satisfaction 1) family size <5; 2) monthly income (having a job); 3) literacy; 4) lack of sanitation; and 5) not having or raising cattle in house. As CI always show the association with the figure of the odds ratio. In other words, the higher the figure of the odds ratio the narrower the CI will be. The narrower CI means the more precise the obtained relationship or association will be. Among the designated determinants given in table 32 family size; monthly income; education level; lack of access to water and sanitation; and having no cattle were significantly associated with level of satisfaction.

It is believed that those without access to sanitation had lower expectations from the health care providers. This might explain why they were shown to be more satisfied than those without sanitation. This might hold true even if they were handled differently. While the results suggest in general that well-off patients were more satisfied than their poorer counterparts, it is believed that access to sanitation indicates the threshold of satisfaction.
rather more than the socioeconomic status. On one hand the majority of families without access to sanitation are in fact poor and have, therefore, lower satisfaction threshold. On the other hand, not all families with access to sanitation were well-off families. The same argument explains the relationship between the level of dissatisfaction and family size of five or less persons per family.

Table 32 Results of Multivariate Analysis

| DESIGNATED DETERMINANTS | Satisfied | | Not-satisfied | | | Odds Ratio | | 95% CI limits for OR | |
|-------------------------|-----------|---|----------------|---|---|-------------|---|---------------------|
|                          | No        | % | No              | % | |             | |                      |
| Sex (male)               | 113       | 39.2 | 109          | 32.7 | | 1.2        | | 0.7 - 1.8          |
| Age (21 - 49 Year old)   | 129       | 44.7 | 147          | 44.1 | | 0.8        | | 0.6 - 1.2          |
| Marital status (married) | 138       | 47.9 | 156          | 46.8 | | 1.2        | | 0.8 - 1.8          |
| Family Size (<5)         | 116       | 40.2 | 85           | 25.5 | | 2.0***     | | 1.4 - 2.9          |
| Occupation (unemployed)  | 195       | 67.7 | 264          | 79.2 | | 0.8        | | 0.5 - 1.3          |
| Monthly income (>2000)   | 239       | 82.9 | 221          | 66.3 | | 2.1**      | | 1.3 - 3.2          |
| Education (literate)     | 113       | 39.2 | 85           | 25.5 | | 1.8**      | | 1.2 - 2.7          |
| Access to Water (no)     | 148       | 51.3 | 182          | 54.6 | | 1.1        | | 0.7 - 1.8          |
| Sanitation (absent)      | 175       | 60.7 | 197          | 59.1 | | 2.0**      | | 1.3 - 3.1          |
| Crowding (> 2 per room)  | 133       | 46.1 | 158          | 47.4 | | 1.2        | | 0.8 - 1.6          |
| Cattle (no)              | 159       | 55.2 | 105          | 31.5 | | 3.1***     | | 2.0 - 4.7          |

*P < 0.05; **P < 0.01; ***P < 0.001

Having no cattle signifies less resources and less purchasing power for the family. As in the rural community, people usually lack cash money and cattle provide a source of income in the time of need. The analysis showed the absence of cattle highly significant for being dissatisfied and also proved its strong association with the level of satisfaction among the adhered TB patients. This also pertain how strong the level of satisfaction is related to the phenomenon of adherence among patients. Poverty is a risk factor but it is not defined in monetary term or in financial terms in the society. Usually family income does not explain the real economic status of the family. It is mainly attributed to problems in reporting, as 1) nobody report family income in precise manner; 2) the unwillingness to report or even if there is a willingness still many patients usually women do not exactly know about the exact income of their income raiser ;3) the sources of income are so unstable and varying from months to month. There are several theories about the definition of poverty. This has also been noticed very frequently that patient's income is low but have production assets for example, cattle used in agriculture, tractor or farms. Moreover social network in the society play a crucial role. There also exist entitlement issues or differentials to the services which make it clear that family income or monetary income does not reflect the income status of the family. For instance if a patient comes from a family having a doctor, or any family member who have personal relations, will get better treatment or attention or priority at the facility than the others.
Why is more income a determinant of satisfaction? The answer to this question is straightforward i.e., more cash money and more informal payments within the health system. Male sex was designated as a determinant of satisfaction in this round of analysis. It is believed to be because of the discriminating nature of the system in which females are handled differently than men. Males appeared to be more satisfied than female but this may also be due the way they are treated. But the adherence analysis showed that females disrupted the treatment more because of various domestic and economic reasons shown in table 33. Family size less than five is expected to be more satisfied and likewise more compliant. On the other side family size of above five members is expected to be dissatisfied and interrupt more. The association of having no cattle with the state of being satisfied was of particular attention here. Coupled with heavy household routine work in the fields and that of raising cattle it is usually considered a demanding job which requires a great deal of attention and priority over other issues including that of health and treatment from the owner or raiser. In this context having no cattle means no additional responsibilities and no extra time spending. This further signifies more time for self care and for the state of being satisfied with the overall situation. This might have also some psychological component which need further assessment and extensive research.
PART THREE
ASSESSMENT OF BEHAVIORAL & CARE SEEKING PATTERN

INTRODUCTION
In Pakistan, socio-cultural disparities widely exist between urban and rural women which not only limit the power of decisions in making personal and independent choices and but also greatly restrict their movement in the society (Jafarey SN, 1995; Tinker A, 2000; Hunte, 1992; Rubel AJ, 1992; Liefooghe R, 1995). More important the financial inability playing a crucial role in care seeking and continuing treatment among women (Brown L, 1992; Karim MS, 1992). They are the part of highly marginalized society and majority of them are reported not even aware of their fundamental rights. No satisfactory and anecdotic answer is available to, firstly why the reservoir of TB infection and its complications are particularly increased among women, secondly why utilization rates have been declined, thirdly why women in specific tend to interrupt TB treatment and delay care seeking in Pakistan. Efforts of NTP to minimize the time from the symptoms onset to the initiation of therapy, known, as diagnostic delay is very crucial for any successful program, are unfortunately lacking. The epidemiological facts signify the need why is it so important to assess attitudes and behavior towards the currently available TB treatment in Pakistan. To fine-tune NTP of Pakistan towards the legitimate expectations and local needs this part of the research is believed to provide qualitative vision and insight to the community perceptions. To acquire the aims focused group discussions were exclusively held among 60 women in the district Mardan (31 rural and 29 urban with history of chronic treatment interruption)

This part of the qualitative research is directed to explore the fundamental tenets of care seeking and behavioral assessment towards TB treatment with reference to Northern women in Pakistan. Due to low literacy profile and unfamiliarity of the target population with the in-depth interview, the instrument to analyze adherence was particularly tailored and an informal verbal component of the focused group discussion (FGDs) was therefore included in the study design. Discussions were held with chronic interrupters and resistant TB patients. Patient's knowledge regarding etiology, manifestation, detection, prevention and treatment of tuberculosis was assessed and their attitudes towards the locally provided services were noticed. The output of this component provided a multidimensional vision of the believes, behaviors, perception of the treatment and stigma attached to tuberculosis in the Pakistani cultural. Barriers, which overtly limit their access to the TB care, were also discussed.

Hence, new dimensions of independent variables were operationalized by concrete variables, which were directly and strongly relevant to patient and his/her life style. The weakness of this approach lies in the fact that the instrument was curtailed to fit local situation, which creates difficulties in comparison with the study of others. The study reflects the perceptions and concerns of only those individuals who sought care and not necessarily of those who remained undetected which is attributed to the limitations of the research. Discussions were held in a local language called Pashtoo (see appendix), which is widely spoken both in Afghanistan as well as in Northern Pakistan. Ten women in rural and five in urban group were Afghans settled in Mardan. Relevant responses and opinions of patients were categorized according to the subject. Their opinions regarding the sequential experiences, visits, preferences, domestic and
external events through which they came across in the urge of care seeking, were carefully recorded and scored.

PARTICIPANTS PROFILE
Average age of both groups was 28.5 years with a very low literacy profile. A single woman from the rural group could only write and read her name while nine women from the urban group had a complete primary school education. Eight Afghans and five Pakistani women from the rural group were hospitalized previously for the respiratory illnesses. Eighteen women out of forty were diagnosed extra pulmonary TB and the rest were initially diagnosed as pulmonary TB. Almost half of the participants in both groups had a close family member/relative with the history of TB. The average number of children were comparatively higher in rural than in urban i.e., 6 and 4 respectively. One in the rural and two in the urban group were unmarried. All questions were standardized and checked for their sensitivity and specificity before the discussion. The questions were explained to them by a trained female health worker. Strict compliance to the issue was maintained during the discussion. Their statements regarding perceived barriers and frequently commented preferences were scored according the relative degree of importance. The discussions continued for two hours each in two consecutive days. The facilitator through a common starting point of general interest to build up their confidence and encourage them in their expressions initiated the discussion.

MAJOR CONCERNS WOMEN CONFRONTED WITH TB
Key points of the discussion are summarized here in the following. Women's perceptions of TB as a disease and treatment and commonly followed trends in the FGD greatly differed between the urban and rural. Women access to care is complicated by multi-factors that play role in molding their attitude and motivation. Close family members, socioeconomic status, traditions practices and community have a marked influence. Their opinions about the quality of care are worth noticing. Women in both groups expressed their concerns about the limited freedom in making choices and in most cases including that of being sick they have to depend especially on men's will and permission, income and other family obligations. Young girls and women are expected to observe strict Purdah [a curtain, screen, or veil shielding women from the sight of men or strangers in Muslim communities]. A male member of the family must always accompany. Women's perception of TB as a disease lays in the physical power which she endowed as women from the nature and weighs her lesser in every aspect than man. Table 1. outlined patient's perspectives on the currently available TB care.

Majority of women (56%) expressed their concerns about the insufficient time and attention given by the health care provider for listening their chief medical complaints and concerns whenever they come in contact with the health personnel. Lack of privacy in the TB facility was the most annoying factor for women. Large crowds of mixed patients (male and female) in the facility made several good and adhered TB cases to search for other alternatives. Women try to keep their disease and treatment course undisclosed, as they fear of stigmatization and being abandoned by the family or community. Medical inquiry rarely preserves their identity and confidentiality of the treatment. Several women are examined in one room simultaneously. Diagnostic facilities are usually out of order. X-rays and other laboratory tests are performed outside the facility on their private costs. 90% of the patients were given no instructions
related to the treatment and preventive health education and prophylactic treatment for their close contacts although most of women had children who were not put on any treatment.

**EXPRESSIONS/COMMENTS ON THE AVAILABLE CARE:**

"Women are weak and the process of bearing children weakens them. Men are not infected mainly because they are physically strong by nature. My mother said that much contact with animal’s garbage also triggers the chances of getting TB" [Rural Afghan].

"Since I am diagnosed the whole family members and my close friends turned me off. I am abandoned from almost every one in the society. I can’t even go to attend any wedding ceremony because the people look at me as I am no more a human being" [Rural Pakistani].

"TB drugs are full of complications and specially the tablets are so big and unpleasant while swallowing. One of my relative told me not to take all the drugs together because it induces Yarqan [Jaundice]. But I took it for two to three weeks. I stopped it because I got severe loose motions and my health got worse afterwards" [Urban, Pakistani].

"I don’t know much about TB but elder people say that you can never get rid of it once you get it" [Rural Pakistani].

"My 55 year old uncle died of it although he got treatment in a city hospital. My father is a local healer and he says that nobody can cure it except God. Doctors just sell their drugs. They don’t care about whether they help or not? They have many bad side effects which makes you more sick" [Rural Afghan].

**COST OF THE TREATMENT AND TRAVEL:**

"My man simply can’t afford travel to the center as he is jobless. My man does farming for the landlord. We all live together in a joint family and at least ten individuals are dependent on him. We survive mainly what he earns from his farming. My man sold his cow due to the hospital expenses when my son got sick last year. For my illness he borrowed some money from the landlord. In such circumstances weekly even monthly visits are not possible and I can’t force him because I know his situation[Rural, Pakistani].

"My father sold our stored wheat just to be able to take me to the TB center and to bear the costs of treatment. I can’t ask him for the visit" [Rural Pakistani].

"My husband says that we will try to find some other better, cheaper and shorter treatment. H e says that there is Peer [a man who perform religious rituals] in the remote mountains in Swat valley where you serve him for a few days in the shrine and you are relieved from your sins and all evil eyes as well Jinn. We can’t afford to come here every time" [Rural Afghan and Pakistani].

**SOCIO CULTURAL RESTRICTIONS:**

"We are Pathans [see appendix] and we are not supposed to go out alone as long as the male member of the family is not accompanied. To tell you the truth there is no arrangement for woman’s privacy in the TB center or hospitals. Women and children have to struggle in the crowd to get in. Women are checked without any privacy and in a very panic way while the doctor talk to others in the same room" [Rural, Afghan].
"We never prefer to go to such places alone. We have to wait outside the clinics for many hours in mix gatherings" [Rural, Pakistani].

"My man said women are molested and harassed when they go alone outside their homes. I consider myself unsafe when I am alone in the street. When any women goes alone it is considered equal to family insulting or humiliation in the public". The same statement were given by one of urban Pakistani [Rural, Afghani].

**PERMISSION FROM THE MALE MEMBER OR HUSBAND:**

"My husband works in Karachi and pays us a visit once in two months. We can't go out for any reason in the village and we must have to wait till he comes back as there is no other male member in the family. He strongly advised my mother in-law not to permit anybody [females] for any purpose out side home. Furthermore nobody is allowed to visit us even females. Therefore it is very difficult to go out. In his absence my mother in law have the authority to use money and make decisions" [Rural, Pakistani].

"We are almost locked from outside when my man leaves home. I can't ask him for a visit or to collect drugs from the center since I got sick. He remains outside the home, comes late at nights and rarely listens to my problems" [Rural, Afghani].

"My man doesn't allow me to travel alone to the TB center" [Rural Pakistani].

"I can't go out without asking him [my husband] even for treatment. My man says why don't they give you all the treatment in one visit. Who will take care of my family" [Urban Pakistani].

"I can't go out without the permission of my father or brother. It is important to have them while traveling and visiting a doctor. They can get easily through the large crowds and get the OPD ticket in the TB center. My father always travels with me whenever I go. Traveling in a bus without him is totally impossible for me. All the seats are occupied by men" [Urban, Pakistani].

**FAMILY SUPPORT AND RESPONSIBILITIES:**

"My husband works at the bus station. He always turns deaf ear to my problems including those even related to my health. He takes only kids to hospitals for treatment when they are sick. I lost my TB card and I was afraid to tell him. I have fever and cough for the last two months and have used varieties of syrups because my cough was so annoying. He brought me once a homeopathic medicine after my repeated requests. He brought me here today because you will pay for this travel" [Urban, Pakistani].

"It is not feasible for me to pay weekly visit. I have four children and every time I come here I have to leave my kids with my neighbor" [Rural Pakistani].

"My man stays mostly outside home to earn money and has no time for such visits" [Rural Pakistani].

"I am responsible for the whole household, children and Gham Khadi (community affairs). Hospital staff usually prescribe to expensive medicines to purchase on our own cost. Only once I got free drugs and the second time he told me that drugstore is over. Besides, the costs of private laboratory investigations are beyond our reach to which I am often referred too" [Rural Afghani].
TB STIGMATIZES WOMEN:

"Although my two young daughters have TB but I can't bring them to the center every week. If anybody in the community watches them coming here they will come to know that they have TB. This will close all their marriage proposals in the community. I usually come to collect drugs for them. My youngest daughter hasn't recovered yet because we live in a remote area away from the health center and it is not possible for us to reach here. Her father strongly resisted whenever I insisted for a visit. Nobody from the TB center came to visit us till now" [Rural, Pakistani].

"I can't describe my feelings when I was told that I have TB. I was very upset" [Urban Pakistani].

"Once I couldn't go to the hospital for check up to collect the drugs. I sent my husband with my prescriptions to do it. He returned home with a totally new face of being so strange to me and brought other drugs instead of my own. He started keeping my kids away from me and started criticizing me. People say that everything is possible in this advance era but why don't they search for a shorter and easy treatment "[Rural Pakistani].

ADHERANCE:

"I got my treatment from private rural practitioner (Shafakhana) in Afghanistan and then we migrated to the city Peshawar in Northern Pakistan where we stayed for a month. My husband had some conflict there and left to another village (Sawabi refugee camp). We were foreign over there and did not know any TB center and therefore I couldn't get any treatment further. I don't know where our next destination will be. It is our family disease and one of my sister died of it when we were in Afghanistan. I want to start the treatment no matter how it is because I am losing all my power to work now" [Urban, Afghani].

"My treatment was very long and my relative told me to use herbal treatment for my symptoms. It is so easy that I can even make it myself at home. My cough is better now but my body is getting weaker" [Rural, Pakistani].

TRENDS OF TRADITIONAL MEDICINE:

"The treatment advised to me for the first time was intolerable. I felt myself weak enough after using it. There was extreme weakness in my limbs after I started. My man told me not to take all the anti-TB drugs regularly as they are very "Garam" giving hotness to the body" [Rural Pakistani].

"Allopathic drugs carry inevitable side effects. I had always experienced severe headache, diarrhea or heartburn whenever I started it. I couldn't mentioned it to any body because of the fears that they will turn to another stronger therapy" [Urban, Pakistani].

"I am a widow and live with four children in my mother's residence in a city area. I got the treatment for more than one month but it had no effect on my health. I changed the drugs and started homeopathic treatment to balance the harmful effects. I was very scared about the reactions of the drugs" [Rural Pakistani].

"In the mean time I used other recipes from Hakeem (local healer) in order to buffer the strong effect allopathic medicine. I used always many expensive medicine before this but they were not effective" [Urban, Pakistani].

"To get rid of TB soon I tried to use Unani recipe for TB along with the allopathic regimens" A llopathic drugs are Garam [hotness giving to the body], which make blood hot enough and worsen the condition further" [Rural Afghani].
TB CENTER RELATED FACTORS; WAITING HOURS:
"I came twice with my brother all the way from high mountains to get treatment and went home without any consultation in spite of waiting the whole day in a huge crowd for my number" [Rural, Pakistan].

"We are refugees here and they are very harsh to us. They usually send us to wait outside and never call for check up" [Rural Afghan].

"X rays machine is always defective and laboratory personal send us to do tests privately. I am an Afghan woman how can I go out every time to another strange man to do my x-rays and check me up" [Rural Afghan].

"My brother always inquires first whether the doctor is a male or female. We never go to a male doctor or nurse when we are sick" [Rural, Pakistani].

"I don't know what should I do with my children. I have to stay for long hours in extremely hot summer with other strange men as there is no separate waiting room for women in the TB center" [Rural, Afghan].

STAFF'S ATTITUDE:
"When I told the doctor that the medicine didn't help me he said, come to my private clinic so that I do some special investigations for you and tell you how to go ahead with treatment. He gave me his private address but I couldn't go there due to high charges" [Urban, Pakistani].

"Here they have no time for us but if we go privately and pay them fee then they are very gentle and kind" [Urban, Pakistani].

"The staff behavior is not good at all. There exists extreme nepotism they never try to understand our financial situation and the sufferings we faced all the way to reach here. They never tell us how to use medicine and what to do in case some complication occurs. The doctor told me that we should tolerate all whatever occurs in the fight against TB" [Rural, Pakistani].

"I lost my first TB card on the way and could not find it although I searched it all over. I wanted to visit the doctor and tell him my story. One of the staff person said either pay double fee for this or turn back home. My husband jolted me and said that he will never allow me to come again for the treatment here" [Rural, Pakistani].

TREATMENT INSTRUCTIONS AND AWARENESS:
"I was given medicine without any explanation and the cautions about it. I am very keen to know how should I use it and what should I do when there is any side effect. Go to the paramedical staff who will tell you about it, I have to examine other patient as well-the doctor said" [Urban, Pakistani].
"I have the habit of forgetting things so I told the drug distributor to tell my son who will remind me about it. He didn’t listen to him and said it is written on the package which none of us could read or understand" [Rural, Pakistani].

"I was prescribed some TB drugs by the doctor to purchase from the pharmacy outside the center and was asked to visit again after a few days for collection. I live far away. Their attention is usually unjustified and more towards those patients who visited them in their private clinics and pay them high fees. Therefore they are given priority in the center to be examined first [Rural Pakistani and Afghani].

The FGDs elicited differences in the attitudes and preferences in the seeking care and in the utilization of TB control facilities specially among women (see table 33). Women depicted TB as potentially disempowering by virtue of its uncontrollability, infectiousness and perceived vulnerability towards TB. Women's construction of TB as a disease and its treatment differ markedly from those given in the scientific texts. Factors which matters are given in the order of their importance and cruciality. Group dynamics helped greatly to provide additional facts about women's perceptions and also served as an opportunity to express their mutual problems and issues of all nature with which they are heavily confronted with as far as TB treatment or control is concerned. For importantly, the discussions revealed expressions about the WHO strategy of DOTS and provided a window of opportunity or possibility to improve it according to the local perceptions. Permission from the husband, male company to the TB center, and the attention of the health care provider were given higher priority by the patients. This played leading role in disrupting care seeking and a strong factor to enforce chronic defaulter.

Table 33 Ranking Preferences of (chronic defaulters) women

<table>
<thead>
<tr>
<th>Category</th>
<th>Very important</th>
<th>Important</th>
<th>Less important</th>
<th>Not important</th>
</tr>
</thead>
<tbody>
<tr>
<td>Permission of the husband or father</td>
<td>****</td>
<td>*</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Family responsibilities, obligations</td>
<td>****</td>
<td>*</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cost of the diagnostics and treatment</td>
<td>****</td>
<td>*</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cost of traveling to the TB center</td>
<td>****</td>
<td>*</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Time per patient given</td>
<td>****</td>
<td>*</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Staff attitude and behavior</td>
<td>****</td>
<td>*</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Willingness for supervised therapy</td>
<td>-</td>
<td>*</td>
<td>*</td>
<td>***</td>
</tr>
<tr>
<td>Drugs availability in the TB center</td>
<td>****</td>
<td>*</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Family back up support for therapy</td>
<td>***</td>
<td>*</td>
<td>-</td>
<td>*</td>
</tr>
<tr>
<td>Regimen with short duration</td>
<td>***</td>
<td>*</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Regimen with less side effects</td>
<td>**</td>
<td>*</td>
<td>*</td>
<td>-</td>
</tr>
<tr>
<td>Additional therapy</td>
<td>**</td>
<td>*</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

* = 20%, ** = 40%, *** = 60%, **** = 80%, ***** = 100%

Analysis of determinants of seeking care among women in similar settings have been explored and have provided some important clues about the association of discrete variables like household characteristics, age, educational level, economic status, occupational, family structure and location of residence. This part of the analysis gives valid clues about the cultural perceptions and psychological factors which play a greater role (Jafarey SN, 1995; Tinker A.
2000; Hunte, 1992; Rubel AJ, 1992; Liefooghe R, 1995. The characteristics like quality of health care, proximity of care provider who practices within the community are more frequently selected for a visit (Sauerborn R, 1989; Litvack JI, 1993; Agyepong IA, 1994; Bastian I, 1999). Prolonged waiting times and disrespect to the privacy and concerns of patient decrease their interest and motivation for the next visit and treatment. The attitude of the staff and skills of communication towards patients are considered crucial for improving utilization and patient-providers interactions and building their confidence. In majority of the cases women's desire to seek care exists but is largely hampered by factors over which she has little control. Contextual factors and differences, which matter to women in both groups whenever they think of a visit to the TB facility, are given in the table 33. Rural women were more dependent on men for their income. The cost of treatment and travel were the most thwarting factors, on which patient usually count mostly. Almost 80% of women (both rural & urban) gave absolute priority to man's permission, consent, and family support for their company to the TB center. The disparities found in the opinions of urban and rural women are given here in the following.

PAKISTANI VS. AFGHANI WOMEN
Perception regarding TB and treatment differs between Afghani and Pakistani women. Compared to Pakistani, Afghani women relate TB more to natural weaknesses and perceives themselves less worth full than man. Women in majority carry unrealistic, unscientific opinions about the TB treatment. The tendency to seek care exists but mainly dominated by traditional and social norms in both groups. The perception about the treatment in Pakistani women is mainly based on local beliefs and trends. Awareness about the transmission of TB and support is lacking more in Afghani than in Pakistani. Afghani women suffer more but try little to express herself than Pakistani. The use of additional drugs, tonics are more common in Pakistani than in Afghani women. Afghani women are reluctant to pay daily or weekly visit to TB center.

RURAL VS. URBAN
A rural woman is relatively more dependent on her family, less informed than the urban one and more traditionally oriented. Rural woman is more conservative than urban and more conscious about cultural bonds and social impact. TB stigmatizes more rural women than the urban and more Afghani than the Pakistani women. The tendency to disrupt treatment is more in Afghani as well as in the rural than urban Pakistani women. Access of rural women to TB control facilities is limited than urban women. Inability to pay for the cost of treatment was more marked in the rural than urban group resulting in compromised adherence and care seeking. Rural women pay fewer visits to the TB center than urban. Older women are bold, more likely to interrupt treatment, delay care and search for non-medical treatment alternatives. Younger women are shy to express themselves and more conservative than older one.

TRADITIONAL VS. NON-TRADITIONAL THERAPY
Rural women rely more on cheaper, simpler traditional and homeopathic drugs than the urban women. Overall educational level was poor in both groups but comparatively higher in urban groups. However little change has been witnessed in their health beliefs, awareness and approach in seeking care and completing treatment. Educated women are committed to seek
care than the non-educated. Women were reluctant to ask their husbands to accompany them to the TB center due to several reasons. Firstly they have to earn their wages and stay mostly out. Secondly in most cases men usually lack the understanding towards women's problems and sharing in that. Family obligations were fulfilled first before they intended to go for treatment and were also labeled among the major reasons of interruption as well as delaying care. Women expressed their concerns that TB treatment is very long and expensive for their monthly income. Majority (80%) of women reported associated diseases like diabetes, rheumatoid arthritis, diarrhea, malnutrition, pleural effusion etc. for which they were under treatment. Male companionship is considered an important condition among rural women for visiting the TB facility. The trend of using additional therapies of various types was also very common in both groups. Women bear fairly strong fears in their minds about the side effects of TB drugs. Women in Northern Pakistan are not oblivious to their health but uses alternatives, which suit them. Women in both groups were prone to go for traditional healers and others spiritual remedies. They argued by saying that they are easy to access, take and follow up, quick in action and less or no side effects.
DISCUSSION
The attempt crystallized the fact that an overwhelming majority of TB patients was non-adherent. This poses a greatest challenge for the TB control program in the area. The unique findings of the study generated significant vision about the contextual factors that lead to the disruption of the treatment among patients and their ability to sustain chemotherapy. It partly generated the valuable knowledge about the available TB care and its responsiveness to the patient's alleged desires and expectations. Knowing the context of adherence in every society is a complex issue and needs thorough understanding of the entire system. Despite life threatening consequences of non-adherence to the TB patients tend to interrupt TB medications. A wide array of factors have been identified to come into play which are closely related to the quality of health care, personal choices and social environment. Physicians cannot accurately identify noncompliant patients, and it has been reported that patients commonly conceal this behaviour from their physician. The results of the study are in line with that reported by Mousa et al. who found that 41% of smear-positive TB patients in Alexandria in 1993 were non-adherent (Mousa I, 1995). Similarly in China, TB treatment was completed by 73.1% of patients within 9 months, while 26.9% failed to complete their regimen (Lee SK, 1995). Management of tuberculosis in NWFP generally is weak and directed only at curing the sputum positive patients with unnecessary prolonged regimes through home-based therapy.

The escape of such large number of interrupters and resistant cases from the detection and tracing system of TB control program not only undermines the impact of NTP in the long term but also increases the risk of exposure to the rest of population. In addition to the results the increasing number of chronic interrupters and resistant cases show, un-standardized regimens, poor adherence and programmatic mismanagement (Sloan JP, 1981; Ansari G, 1988; Khan J, 1993; Arshad J, 1997; WHO, 1997; Karamat KA, 1999; De Muynck, 2001). Based on the theoretical underpinning of the model selected for the analysis, information, motivation and adherence skills were widely lacking among the interrupters. Patient's knowledge was found deficient in many aspects. Their complex perceptions, enormous traditional barriers and psycho-social conditions greatly interfere with the sustainability of the treatment. Informed consent (Freeman, et al. 1996) and clear explanations, incentive, reassurance, explanations, feedback and systematic follow-up by the health care provider is reported to dramatically increase adherence of the patient (Williams, 1999; Reynolds, 1999). Kleinman, et al. observation showed that effective treatment also needs an understanding of patient's ethnic and personal conception of illness and to develop a link of openness to their own explanatory model of health related problems. Provided with accurate medication knowledge patient might be encouraged to resist the pressure of neglecting his/ her health needs in favor of many other competing motives such as work, traveling, festivities that interfere with patient's intention to comply with the treatment (Becker, 1979; Caplan, 1976).

Care in the most of the TB control facility embarks upon prescribing treatment which differs in regimen and pays far less attention to the patient's socio-economic and cultural and personal factors. 82% of the patients interrupted the treatment due to variety of reasons. The reasons, which lead to the alleged disruption, were not thoroughly taken into consideration once patient visit the facility after a long delay. Treatment with the frequent monitoring of the regimen's effectiveness, sputum conversion and the supportive activities are not performed. Most of the
patients coming from rural areas were not approached. In tuberculosis control the 'on-and-off-treatment' is a well-known phenomenon (Mankodi et al., 1984).

Patients ask for medicine if severely hindered by the disease and drop out of treatment if they feel better. Symptoms experienced by the patients can be regarded as internal reminders and hence as 'cue to action' (DiMatteo, 1982). For Patients who live under harsh conditions, it is very difficult to continue chemotherapy when bodily perceived 'cues' are omitted. The lesser physical health of the interrupters (non-adherent individuals) at the time of interviewing is illustrative in this context. If internal reminders disappear after some time, it seems plausible to replace them by external reminders such as home visits or postcards to aid memory. Chaulet recommended making a list of patient's potential addresses, including those of family, friends and place of work from the very first day. Married women (housewives) were more unlikely to adhere to the TB regimens. Patients who reported undetectable of sputum smear positive status were less likely to report being non-adherent to their chemotherapy. Good general health was positively associated with adherence to chemotherapy. The confrontation with side effects to treatments was significantly associated with interruption (non-adherence) in the chemotherapy. In addition to the unavailability of essential drugs and diagnostics, poor attention to patient's factor for example, to increase their motivation, information and skills of the patients to cope with the therapy allegedly contributed to the poor adherence. Studies on the association of demographic characteristics of patients with adherence to anti-tuberculosis medication give inconsistent results. The present work revealed that these factors (age, sex, work, income, education and more resources) were associated significantly with adherence.

Increased delay leads to more fatal clinical outcomes by the time patient presents and also increases the risk of exposure to other non-infected individuals in the community (Lawn SD, 1997; Gibson N, 1998). Research on care seeking pattern and behavioral assessment has revealed several thwarting factors, which contributed to influence behavioral pathways of adherence with the prescribed TB treatment. Delay in care seeking, seeking care from inappropriate sources and underutilization of available facilities in women is largely reported (Siann G, 1984; Omordion FI, 1992; Agyepong IA, 1994; Bastian I, 1999; Barnhoorn F, 1992; Agboatwalla M, 1997). More importantly the phenomena of care seeking and tendency to use medical care differ from man to woman and also among women of different socioeconomic and ethnic origins (Sauerborn R, 1989; Nougtara A, 1989; Omordion FI, 1993; Agyepong IA, 1994; Weller SC, 1997). Similarly perceptions of health also vary from culture to culture. Needless to say that women differ in their likelihood of vulnerability and approach towards the health care alternatives. Women's health is greatly impaired through an intricate web of physiological and behavioral interrelationships and synergies between traditionally determined roles (Hunte, 1992; Liefooghe R, 1995-99; Khan A, 2000; Rabbani F, 2000). The impact of TB on woman's life is far reaching as compared to man. They not only affect women themselves but also their children, families and society in general. More surprisingly research on adherence with the TB treatment has shown that the number of TB resistant strains, failure and relapse cases is largely increased among women than men (Liefooghe R, 1995-99; Khan A, 2000; De Muynck A, 2001).

The study reveals that adherence with anti-tuberculosis therapy was significantly higher among those who were well informed about TB and were treated in urban areas than in rural
communities. Clinical outcome and adherence with shorter regimen was effective. It has also been documented that when patients usually do not know about the natural history of TB, its complications and the importance of complying with drug therapy, their adherence to the prescribed regimen is improved. In a similar study in India in 1992, the authors found that there was an association between the adherence behaviour of patients and their knowledge of specific aspects of the disease. Patients who perceive their illness to be more serious and who believe that treatment will alleviate the condition are more likely to be compliant (O’Hanrahan M, 1981). Features of the disease are potential determinants of compliance. Patients with active disease and those with symptoms are more compliant (Haynes RB, 1979).

Patient’s records were followed from four to six months, which in fact may confound the findings, since adherence decreased over time (Styblo k, 1988). Another limitation was, that the interviewer knew whether an interviewee had completed treatment or not. For these reasons, the results of the study should be interpreted with caution. Not all anti-tuberculosis drugs and diagnostics are given free of charge, additional costs such as the fare of transport or the loss of daily wages can become insurmountable for patients. In District Mardan, TB drugs are delivered twice or once a month and patients are supposed to collect drugs by showing their physical appearance. This is one of the biggest barriers for female in the male dominant and strict socio-cultural settings where they have to fulfil huge obligations. DOTS prospects in the area are already threatened due to the same reasons. With out significant modification the supervised component of DOTS opposes local tradition and cultural framework especially in case of women.

Communicable diseases like TB, in general, take its biggest toll on the poor, while rich and poor can become sick with a communicable disease, the poor are the most likely to die and their livelihoods most compromised when they contract a communicable disease. There exists an inextricable relationship between TB and social development where ever TB is prevalent. Where TB flourishes, social and economic development progress is compromised, and where the development of health and education system, national economies and national security are weak or failing, TB thrives (WHO, 1998). Given the unique nature of tuberculosis, to remain latent for years after infection, and in many cases for entire lives, TB is a unique barometer of social development. It robs people of opportunities, limits their choices, and ultimately, slows national development. TB traps people in a vicious cycle of poverty and disease. It exacts serious psychological and social costs, particularly in country like Pakistan where poverty is prevalent and people and families with TB face discrimination, including loss of jobs, education opportunities and marriage prospects (WHO, 1998). As the dynamics of infection show that TB waits for the opportunity to convert into full blown contagious disease when the immune system weakens due to factors like TB, malnourishment, or poverty. In other words, TB affects most severely disadvantaged groups both in native and immigrant communities in NWFP, Pakistan who are already the most vulnerable to disease and death.

This observation might also explain the findings that the rural population, tended to be more interrupters (non-adherent) than patients living in urban areas due to socio-economic reasons. Mull et al. have pointed out in their study on Pakistani leprosy victims that economic and social aid appears to be a valuable tool in reducing the number of treatment defaulters (Mull J. D., 1989). Patients whose disease was brought under control were given an interest-free loan to
help him or her to establish a household and/or a means of earning a livelihood. However, before the obstacles to a treatment regimen can be cleared away, patients have to develop health beliefs and social norms consistent with the model of information, behavior and skills. The data from this study reveal that patients who had an active orientation toward tuberculosis were more likely to be adherent than patients who fostered a more fatalistic approach. The decline in the visits of TB patients once they are registered to the TB facility is of great concern. The trend of non-adherence can be viewed by the figure 00 which reduces dramatically in the second month and more abruptly in the following months. Becker et al. also found that mothers, who had an active view on preventive care, visited clinics more than the mothers who did not have this view (Becker et al., 1974).

Mothers who had a more passive approach visited more frequently the child clinic for treatment of illness or accidents (Becker M. H,1977). Moreover, recent research has suggested that the more the patient is well informed and aware of the clinical consequences and posses coping skills higher is the level of adherence (Chesney, 1997;Friedland, 1997; Reynolds, 1999; Catz et al., 1999). Adherent patients seem to perceive tuberculosis as more severe than non-adherent patients do. This is also true for patients who believe in the benefits of care and the efficacy of the treatment. The regular ingestion of drugs requires a thorough effort for a patient like remembering to take the medication and to maintain routine. The health care provider can help the patient by making the treatment regimen as simple as possible and by structuring the regimen into discrete tasks. Testing the patient's understanding of the particular regimen and tailoring the regimen to the habits, rituals, times and places that are reinforcing in the person's daily life, may enhance compliance. These efforts of the medical practitioner may also increase patient satisfaction with treatment (Chesney & Ickovics, et al.1997). A major conclusion to be drawn from the analysis is that adherence behaviour is associated with previous experiences and also to social support from family and/or other persons as doctor, health worker, and neighbours. Patients who knew that the attitude of their family regarding the regular intake of medicine was positive were more likely to be adherent.

The participatory component of the study added much to the exploration of the underlying causes of the adherence. Discussions with patients, family members, community leaders and paramedical staff revealed valuable facts related to the non-adherence among TB patients. An abundant evidence of knowledge claims that the perceived social support from close contacts in the family and other sources on cooperation with the medical treatment. In Pakistani and Indian culture it is rather more intensively attached to family ties and marital bonds (Cohn, 1971; Liefooghe R, 1999 & 2001). Berenson et al. found that the interaction between having other person to prepare meals and breakfast regularly was one of a small subset of key predictors of self-reported adherence. The habit aspects of these practices appear to affect adherence behavior. A 'significant other' person could be helpful in acquiring routine in taking pills. Patients should be encouraged to continue with the treatment regimen and should be protected from 'backsliding' after engaging in a treatment program.

The practitioner's poor interest in psycho-social issues such as attitudes, beliefs, norms and knowledge fostered by the patient and his or her situational problems reduces the patient's acceptance of the treatment procedure. In particular the health worker's pessimism about the patient's abilities to change, may serve as a barrier in the relationship between health care providers and patients.
providers and patients. This is clearly manifested with patients who are economically poor. Health care providers tend to view poor patients as unlikely to make behavioral changes to enhance their health. Hence, these patients are less likely to be given explanations or information about their treatment (Pratt L, 1970). That patients are indeed willing to change some habits seemed also valid for tuberculosis. Finally, the information from this study provides preliminary evidence that tuberculosis outpatients, who descend from such backward and underprivileged subpopulations as the members of the lower social classes in Mardan District in Pakistan, do hold realistic beliefs and perceptions about their illness and treatment. This finding warrants a plea for further prospective investigations and for the implementation of effective educational and health promotive program targeted at the social and economical emancipation of tuberculosis patients.

Personal and environmental factors that influenced adherence with a prescribed treatment regimen are summarized and depicted in Figure 39. The model is conceptualized on the analogy of the original Information-Motivation-Behaviour Skills and DiMatteo and DiNicola's compliance theory. Further studies are needed to determine whether our approach is applicable to other Third World populations and whether the development of a diagnostic tool concerning adherence offers prospects. Such adherence-oriented guiding principle in discussions with patients should be made a routine part of the usual medical examination process. One in every 4 cases reported is a woman. The attributable factors for such rapid spread of the epidemic across the country today is labour migration and mobility in search of employment from economically backward to more advanced regions, low literacy levels leading to low awareness among the potential high risk groups, together with gender disparity, sexually transmitted infections and reproductive tract Infections among men & women. The social stigma attached to sexually transmitted infections also hold good for TB, even in a much more serious manner. There have been cases of refusal of admission of TB patients in hospitals and nursing homes both in Government and Private sectors. This has compounded the misery of the TB patients.

More often it is mistaken to be a contagious disease and patients are isolated in the ward creating a scare among general patients. In the workplace there are instances of discrimination leading, in some occasions, to loss of employment. The active part played by some non-Governmental organizations in bringing out public interest litigations against such cases of discrimination and judicial pronouncements by courts in support of the rights of such people has helped partly in alleviating the misery of the affected persons. The treatment options are still in the initial stage and are prohibitively expensive. While there is no vaccine in sight, multi-drug anti-retroviral therapy, popularly known as "cocktail therapy", has many adverse effects, if not administered under proper medical supervision besides being prohibitively expensive. There are instances of quacks taking advantage of the situation and claiming cure through so called herbal treatment, and defrauding people who are infected with mycobacterium of large sums of money.

With a high prevalence of TB infection in Pakistan, the problem of TB-HIV co-infection also poses a major challenge. Treatment of TB among the TB-infected persons is a new challenge to the National effort to control tuberculosis. Some of the drugs which are recommended for TB treatment pose complications in case of TB-infected persons and had to be withdrawn in
areas of high TB prevalence. At the same time looking for TB among TB infected persons may also cause the problem of scaring away a large number of TB infected cases in the country from seeking treatment under the DOTS strategy. Clearly, the TB epidemic progresses differently in different situations. It is driven by individual behaviours which put people at risk of infection. Their behaviour may in turn be driven by poverty, by unequal relationship between men and women or between old and young people, or by cultural and religious norms that leaves people with little control over their exposure to the mycobacterium. The social, economic and cultural situation that creates this kind of vulnerability to TB infection have not been adequately studied or explained. Perhaps, there is virtually little information available for different socio-cultural groups in Pakistan on the basic drug-taking behaviours and patterns of TB networking that determine the mycobacterium spread through a population.

Coupled with the results of the study, literature review gives some vivid explanations about the four main domains that are crucial to understand in any highly endemic country. Several factors influence patient's decision to get screened, diagnosed as TB person and remained adherent throughout the course of therapy. Adherence of patient is embedded in an intricate web of physical, social and psychological elements. Behavior which molds patients either to be adherent or non adherent is mainly based upon the essential foundations such as personal health believes and perceptions, the social environment of the patient, obstacles that impede the intended health actions for example to go for treatment regularly and reinforcing factors which contribute to the persistence of the particular behavior (Barthoorn F, 1992). Therefore the development and maintenance of health behavior to keep patient adhered is undeniable complex. Three factors are held firmly true for poor adherence in the case of chemotherapy for most TB patients; the duration of TB treatment is long, treatment is preventive rather than curative, and patients usually get asymptomatic early in the beginning of therapy (WHO, 2000). Due to wide array of variations in the medical and cultural practices on the transnational level it has become extremely difficult to derive a universal outline which better describe the pattern and reasons of non adherence among patients undergoing prolonged therapy for TB and HIV/AIDS. However the review of pertinent literature gives an account of factors which classify adherence into four main axis (Veilleux PC, 1994-5). Planning interventions must understand and consider the following essential domains.

**CHARACTERISTICS OF THE PATIENT**

As far as the dynamics of TB therapy are concerned, a patient should be the central focus. Conditions, circumstances and behavior of the patient have a strong relationship either to be adherent or non-adherent (Corcoran et al., 1986; Nazar et al., 1992). The issue of adherence has become far more important since the epidemic of HIV and TB struck the world's poorest communities. Program launched to eradicate infectious disease in developing countries lately recognized how intervention should be fine tuned in order to build patient's faith and interest in the treatment. The aim of responsiveness of infectious disease control program is not only enough to understand patient related factors but also to make the health care providers conscious and react timely to factors which are conducive to adherence. Socio-demographic factors such as age, race, level of education and income are the predictors of adherence and diseases are specifically associated with increased non-adherence. Young age (Mehta et al., 1997; Chesney, 1997), gender (Mehta et al., 1997), race (Muma et al., 1995; Singh et al., 1996),
low level of education, no medical coverage (Crespo, 1997; Kalichman, 1999) and working outside of home (Chesney et al., 1997) are reported to decrease adherence with the treatment. Research also shows that unemployed, homelessness, victim of a violent crime (Ickivics et al., 1997; Broers et al., 1994) and low social support (Catz et al., 1999; Kalichman, 1999; Williams, 1999; Chesney, 1997; Mehta et al., 1997; O’brien et al., 1996; Rabkin et al., 1998) threaten adherence. Social and behavioral attitude is believed to mold patient willingness to the treatment. In psychological perspectives looking at adherence patients have cardinal features. Type A personality (Competitive, sense of urgency and hostility) have a tendency to feel that the medical regimen hinders on their personal freedom and to react by non-adherence in order to regain a feeling of control (Veilleux PC, 1994-5; Rhodewalt, 1990). Depression, stress and anxiety, emotional disturbance, and personal weakness in adaptation strategies have a vital role in lowering the level of adherence (Wilson et al., 1967; Catz et al., 1999; Tseng, 1998; Crespo-Fierro, 1997; Holzemer, et al., 1999; Mehta et al., 1998; Lyketsos, 1997; Singh, 1996).

Gloominess lowers the degree of confidence towards the treatment (Williams, 1999; Aversa et al., 1996; Freeman et al., 1996; Muma et al., 1995). More in this regard is the increasing support for good comprehension of the goals of the treatment (Stephenson, 1999; Elred et al., 1997;) and of the disease as such (Williams, 1999) can boost the patient's will to remain adherent (Veilleux PC, 1994-5). Similarly feeling of control on one's life - an internal control locus (Elred et al., 1998; Flskerud, 1995) are associated with strong adherence. History of opportunistic infections and perception of disease severity (Singh et al., 1996), adherence in a previous situation (Ickovics et al., 1997) further underpin its role in strongly adherent patient. Cultural beliefs about disease and health (Mehta et al., 1997), type of drug and frequency of use (Halkitis et al., 1999), beliefs and experiences of relations with chemotherapy agents (Williams, 1999; Mehta et al., 1997; Aversa et al., 1996) are though controversial but can influence patient's adherence either positive or negative. Alcoholism, substance abuse (Mushlin et al., 1977; Stephenson, 1999; Williams, 1999; Lerner et al., 1998; Ickovics and Meisler, 1997; Mehta et al., 1997; Crespo-Fierro, 1997; Pablos-Mendez, et al., 1997; Elred et al., 1997; Singh, 1996; Broers et al., 1994) can negatively influence the patient behaviour towards the treatment. To take into account the adaptation mechanisms of the individual in chronic diseases and the characteristics of the medical treatment individuals were observed more active in taking charge of their medical treatment. They were less adherent of their medical treatment when the treatment was at the hospital and more adherent when it was at home. Conversely, with more passive patients, adherence was better at the hospital than at home. (Christensen et al., 1990) Symptoms occurring while taking medication may increase non-adherence.

PATIENT-PHYSICIAN INTERACTION
According to Talcott Parsons patient-physician relationship has a direct and fundamental role in keeping patient adherent to the prescribed treatment (Vanderstraten R, 2000; Waiztkin H, 1979). Health care provider is the primary contact of a patient and can strongly affect the patient's commitment to a correct regimen, particularly by means of clear communication about the regimen (Caplan, 1976; Barnhoorn, 1992). As for as adherence in chronic diseases is concerned physician or health care provider can mold patient's behavior on either side i.e., both negatively and positively depending upon his/ her attitude and flexibility (Kalichman, 1999; Reynolds, 1999; Tseng, 1998; Lerner et al., 1998; Ickovics et al., 1997). The more a patient is satisfied from a physician the higher is the level of adherence (Chesney & Ickovics, et
ADHERENCE ANALYSIS
Chapter 4

Among the other important determinants of adherence in patient-provider relationship trust, consistency, and continued interaction have a leading role. In a study by Altice and colleagues conducted among prison inmates with TB disease, a scale designed to measure trust in physician was used to demonstrate that increased trust was associated with both increased acceptance and adherence to chemotherapy medication. Adherence to medication has multiple overlapping determinants. In terms of patient characteristics, social support is probably the most important factor. The literature on adherence strongly and consistently demonstrates that adherence cannot be predicted based solely on age, race, sex, or educational status. Addressing individual health beliefs, and understanding the individual's risk-benefit equation is a key in influencing adherence.

TREATMENT CHARACTERISTICS & CLINICAL SET UP
Characteristics of the treatment and clinical set up have a profound effect on patient's social, medical and psychological adherence. Patients in general and TB in specific have certain criteria, imaginations and highly personalized way of thinking about the nature and way of induction of the chemotherapy which are deeply related to their socio-ethnic background, level of education and more to culture and traditional practices. In developing countries it is widely observed that TB patients mostly search for health care and remedies which suits not only their socio-economic priorities but must also match their cultural set up, unsuitability and feasibility to the lifestyle. This has been the cause of treatment interruption in several cases (Cohn, 1971; Sloan JP, 1981; Ansari G, 1988; Barnhoorn F, 1992; Catz et al., 1999; Kalichman, 1999; Stephenson, 1999; Khan A, 2000; Liefooghe R, 1999 & 2001). Treatment aspects like proportional to the number of treatments, frequency of posology (The study of the dosages of medicines and drugs), complexity and length of treatment (Reynolds, 1999; Williams, 1999; Crespo-Fierro, 1997; Ickovics et Meisler, 1997), taste and ease of administration of medication (Reynolds, 1999; Bozek et al., 1998; Friedland, 1997), side effects (Reynolds, 1999; Catz et al., 1999; Chesney, 1997) and inconveniences of the regimen (Ickovics and Meisler, 1997) have been abundantly reported to decrease adherence of the patient to the prescribed treatment. Privacy of the clinical set up offered and quality of care which includes time consumed per patient, respect and attention paid to the patient's personal history while maintaining confidentiality of the treatment and sharing the cost of the treatment were documented to have stronger association with confidence building and keeping patients highly complied (WHO 2000). More over cost of treatment (too expensive) (Mehta et al., 1997), dysphoric mood such as fear, anger, apprehension or confusion induced by the treatments (Samet et al., 1992; Veilleux PC, 1994-5; Muma et al., 1995) negatively influence patient's compliance.

CHARACTERISTICS OF THE DISEASE
In patients community countless theories are associated with the natural history of tuberculosis. Of particular attention is the perception of TB in the masses. Majority of patients who suffer from TB in developing countries have a unique picture about the disease in their minds. This has not only grave repercussion on their lives but also impacts on their behavior and care-seeking pattern is worth noticing. The fear of losing job, family and marriage break up, being socially abandoned urge them not only to hide their symptoms, TB status, treatment and even going for a regular visit but also markedly affect the level of adherence. Stigma and uncertainty caused by the disease (Crespo Fierro, 1997), asymptomatic state (Tseng, 1998; Munzenberger et al., 1997) and improvement or even a disappearance of symptoms (Tourette-
Turgis, 1999) decrease adherence among patients. Adherence also dwindles with the passage of time by the chronicity of the disease (Chesney & Ickovics, 1997), occurrence of opportunistic infections, prophylactic treatments (Williams, 1999) or in conjunction with other treatment (Ickovics and Meisler, 1997). More advanced stage of the disease can decrease or increase adherence among patients (Freeman et al, 1996; Samet et al., 1992; Singh et al., 1996). Interrupters of TB treatment in the Sawabi District, Pakistan, experienced serious obstacles in achieving set targets. National TB control Program need to respond to the socio-economic conditions, and patients factors who need sound health information, coping skills and treatment which suits their life style. Moreover awareness on social support from family or non relatives and had an awkward relationship with their health care provider, that prevented them from regaining health and attaining the goal of TB eradication. Health promotive investments-social and economic: aid, increased social support, training and supervision-in tuberculosis victims, especially those with high-risk non-adherence features, should stimulate participants to continue with a treatment programme. Prevention of tuberculosis is best accomplished by rapid detection and effective treatment of all cases. This will interrupt the chain of transmission of infection and ensure the cure of the infected ones. Based on the experience of WHO in highly endemic countries, DOTS is considered the ultimate tool to combat TB. The peculiarities due to which DOTS is suggested are will be discussed in the following section.

Dr. Zaheer HAE says,

"Health and culture are so intertwined in Islamic countries that it is impossible to address the one without the other. Improvements in health require sensitivity to culture and religious beliefs. At the same time, health is a requirement for culture to flourish. Islam teaches its followers to "seek medical treatment" because, according to the Prophet, "God has not created a disease without creating a cure for it. If treatment is administered with the right cure, the patient will recover by God's grace." These explicit Islamic teachings clearly endorse medical practice and can help with treatment, particularly TB patients taking daily medication over long periods of time. From this perspective, Islam may be seen as reducing social or cultural obstacles to treatment and adherence to the regimen prescribed by DOTS.

In remote areas where there is poverty and illiteracy, many TB patients happily comply with DOTS because it has become part of their belief system. There are still, however, cultural obstacles to overcome. One of them is the stigma associated with TB, which is still very much alive in Islamic societies and communities. TB is feared, particularly among women, because it can bring ridicule, divorce, abandonment, and death. Once sick with TB, women have little chance of marriage because of TB's powerful label declaring them unfit to be wives and mothers. Migrating groups such as the Bedouins pose other challenges. These groups are particularly vulnerable to diseases like TB. Their itinerant lifestyle makes TB diagnosis and treatment difficult. Integration of the TB control program with communities and primary care centers must be made in order to overcome the cultural obstacles that prevent patients from receiving DOTS. The DOTS strategy allows for flexibility and is adaptable enough to be used in any setting".

EMRO, 1999- DOTS success in Morocco.
Based on the overall results of adherence assessment figure 39 presents a diagrammatic sketch of pathways of various vital components related to the quality of care and society which strongly influence care seeking and shaping behavior in TB patients.

Figure 39 Pathways of Care seeking and Adherence among TB Patients

Moreover the results validate further the conceptual framework of information, behavior and skills model which places strong emphasis on the patient's perception, degree of awareness about the disease, treatment and the capabilities of coping skills. In future DOTS implementation in the area need to be curtailed to the already ignored aspects by the NTP. Fine tuning of TB control interventions to the most widely affected group of the community i.e., women should be the prime aim. Relevant measures should be undertaken particularly to the domains or areas identified by the designed model given in the figure 39. DOTS which is WHO universally applied short treatment strategy for successful eradication of the TB in developing countries. In addition to the doctrine of DOTS modification is desired according to the local setting in NWFP. Using sound technology DOTS focuses on the technical, logistical, operational and political aspects. DOTS works together to ensure its success and applicability in a wide variety of contexts. DOTS is comprised of five key components.

- Government commitment to sustained TB control activities.
- Case detection by sputum smear microscopy among symptomatic patients self-reporting to health services.
- Standardized treatment regimen of six to eight months for at least all sputum smear positive cases, with directly observed therapy (DOT) for at least the initial two months.
- A regular, uninterrupted supply of all essential anti-TB drugs.
- A standardized recording and reporting system that allows assessment of treatment results for each patient and of the TB control program performance overall.
Government commitment to sustained TB control is essential for the other four components
to be implemented and sustained in all health and TB facilities. It is necessary for the
mobilization of resources and the sustainability of TB programs. Sputum smear microscopy is
the most cost-effective method of screening pulmonary TB suspects referring to health
services. It identifies sputum smear positive, highly infectious TB cases. TB is diagnosed using
patient history, clinical examination and diagnostic tests. A sputum sample is submitted to the
laboratory and the results of the microscopic exam are entered into the laboratory register. The
goal is for all suspects to have a sputum smear microscopy exam and for all patients diagnosed
with TB to be registered and treated.

**DOTS WITH DIRECT OBSERVATION OF DRUG INTAKE**

Short-course chemotherapy refers to a process treatment regimen that lasts six to eight months
and uses a combination of powerful anti-TB drugs. Standardized regimens are based on
whether the patient is classified as a new case or a previously treated case. DOTS is essential at
least during the intensive part of treatment (the first two months) to ensure that the drugs are
taken in the right combinations and for the appropriate duration. With direct observation of
treatment, the patient doesn’t bear the sole responsibility of adhering to treatment. Health care
workers, public health officials, governments, and communities must share the responsibility
and provide a range of support services patients need to continue and finish treatment. One of
the aims of effective TB control is to organize TB services which are integral part of health
systems so that the patient has flexibility in where he or she receives treatment, for example in
the home or at the workplace. Treatment observers can be anyone who is willing, trained,
responsible, acceptable to the patient and accountable to the TB control services.

Where DOTS is implemented, an accurate recording and reporting system provides the
information needed to plan and maintain adequate drug stocks. The recording and reporting
system is used to systematically evaluate patient progress and treatment outcome. The system
consists of: a laboratory register that contains a log of all patients who have had a smear test
done; patient treatment cards that detail the regular intake of medication and follow-up
sputum examinations; the TB register, which lists patients starting treatment and monitors
their individual and collective progress towards cure; and reporting forms from districts to the
national level, which allow assessment of control efforts. To fit DOTS more to the Pakistani setting and socio-cultural framework it needs to be modified. The results of our study showed that access to care is denied due to many reasons which range from the costs of the drugs to the cultural barriers. Therefore TB care should be delivered at the doorstep by involving other male members like fathers, brothers in the TB program. Preferably female through female contact is believed to convince women and enhance intimacy and adherence. Closely relative male family members have an important role in their decisions and in the initiation of seeking care (Brown L, 1992; Omorodion FI, 1993; Speizer IS, 1999; Bhatti L, 1999; Winkvist A, 2000; Needham DM, 2001; Callister LC, 2001). To accomplish a culturally competent TB control care the author recommend TB control through men’s motivation with more emphasis on cultural needs and expectations of Pakistani women.

Shown in the pyramid (Figure 40) of adherence enhancement plan for the HCP peer counseling and particularly involving men in the process will facilitate the TB control. Revising the views of women as the natural guardians of their family’s health and also by drawing other family members particularly husbands into their orbit (Brown L, 1992; Omorodion FI, 1993; Speizer IS, 1999; Bhatti L, 1999; Winkvist A, 2000; Needham DM, 2001; Callister LC, 2001). To involve religious groups to use their influence in improving community’s attitudes and creating flexibilities for gender specific TB control measures. With a great deal of commitment and sincere efforts, access to women should be improved through their men as well as women volunteer in the community. Strengthening TB units in PHC and employing more female workers to pay door-to-door visits. Screening TB along with HIV/AIDS, early prophylaxis in pregnant and lactating women and in close contacts (sputum smear positive) need to be done in order to prevent transmission. Coupled with the brief declarative as well as procedural awareness campaign on the disease etiology, natural history and instructions respectively will fortify TB control activities further. Options of increasing acceptance of allopathic alternatives by introducing treatment facilitators, reminders and more patient-centered fortification, combinations of relevant social and economic enablers, arrangement of food, clothing, literature, grants, transportation facilities, and appropriate outreach programs are suggested. Better equipping the rural TB centers to reduce the caseload on the busy centers and providing patients enough time and attention. Impressive gains have been made in the ability of chemotherapy to suppress bacterial replication and delay disease progression in patients with TB. However, given the current recommendations to use highly aggressive combination therapy, drug options remain limited. In order to replicate the findings observed in the study of these combinations, and to maximize the potential of each drug, targeted efforts to increase adherence in the real clinical setting are essential.

Community-based setting offers greater opportunities for individualized attention to deal with adherence issues. Community-based interventions can complement/supplement information provided by medical providers. Mental health services with counseling and psychotherapy can play an important role in the strict adherence to the drug regimen role. Behavior medicine (daily reminders, timers, memory aid), cognitive re-structuration, self-exploration (clarification of personal objectives; motivation and medical treatment; attitude of the patient in adherence with treatment) are the tools additionally to be considered in the TB control interventions. Outline the pros and cons of the various options and make sure that patients understand the commitment required, the consequences of repeated interruption, and the potential benefits of
therapy. Provide written instructions to patients, and inform them of what they can expect when starting medications, including the common side effects and how to manage them. To minimize interruptions in therapy, patients should know whom they can call should serious or unexpected side effects develop. Schedule a follow-up appointment soon after initiating new therapy. Review the importance of remaining on all medications in a combination regimen and the effect of stopping one medication in a combination.

Discuss the procedure for obtaining refills. For example, for patients with busy and unpredictable schedules, the convenience of twice daily dosing may outweigh issues of initial side effects. Patients whose daily schedules are less busy may choose tolerability over convenience of dosing schedule. For patients who require frequent dosing of medication (more than twice daily), options to ensure mid-day dosing, either with medication timers or other reminders should be discussed. Establishing an outreach program for remote and rural areas, which periodically visit patients, especially females who cannot regularly pay visit the TB health facilities and interrupt treatment due to any of the mentioned reasons. Helping such patients plan for taking medication at home and on a visit and in complex situations. Priority should be given to simplify regimens and supervise treatment whenever possible and, if possible, and eliminate medications when patients are overwhelmed by the complexity of their regimens. When non-adherence is suspected, considering regimens that minimize cross-resistance and leave options for future effective chemotherapy combinations. Inquiry about medication-taking behavior at each visit. Relapses in behavior commonly occur long after a behavior is well established. Advances in TB pathogenesis and bacterial dynamics, and the availability of bacterial load assays and potent chemotherapeutic regimens have provided new opportunities to treat patients with TB. Supervised treatment; short course strategy has enormous potential to delay disease progression and death. However, achieving this practically in the local setting involves addressing the complex behavioral issue of adherence.

Improving adherence to chemotherapy therapy is considered one of the most critical determinants of success in clinical therapeutic for TB infection today. In the absence of a curative regimen, current therapeutic strategies (DOTS) are lifelong and involve the use of multiple drugs taken at different times. Less than 95% adherence can lead to the development of drug resistance to available medication and can compromise an individual's health and future treatment options. DOTS, which is widely, proved an effective strategy because of shortest duration, cost-effectiveness and supervised component, which ensure complete eradication, offers an ideal alternative for such situation. However the above mentioned components of DOTS do not entail any significant benefits to women and children in culturally and male dominant societies. The example is evident in the case of mixed population with diverse socio-cultural needs and traditional set up. Previous efforts to implement DOTS in NWFP have failed due to lack of attention to the most widely affected population of women and children (Liefooghe R, 1995; Jadoon M. A, 1999; De Muynck A, 2000; Khan A, 2000). In the light of current research and previous attempts modifying DOTS will enhance case detection, cure rates and increase adherence among patients specially by employing more for female health care provider.

While there is no panacea for non-adherence, several interventions can be effectively and directly applied to improve the use of short chemotherapy. Prepare patients for the use of
combination therapy by discussing the use of these drugs before prescribing them. Other measures include encourage female to female contact, involving husbands, fathers and brothers to endorse treatment and monitor, involving community, launching local TB committees to enhance awareness and local donation collection to finance the treatment cost for those who interrupt frequently. Delivery of the drugs needs to be simplified and tailored to patient's convenience.

**FIGURE 40 MODEL OF ADHERENCE ENHANCEMENT INTERVENTIONS**

Given in Fig 31 the model suggests essential components of the adherence-pyramid for DOTS. It is not easy for physicians to identify non-adherent patients as few socio-demographic characteristics predict non-adherence. Therefore, it must be assumed that all patients have the potential for non-adherence, even those who have been adherent previously. To maximize adherence, health care providers ought to focus more patient's related factors while prescribing DOTS. Starting from a brief counseling and achieving high level of satisfaction to the appropriate selection chemotherapeutic regimen for each case. The regimens chosen must minimize the frequency of daily dosing select the well tolerated (minimum side effects) and tailored it according to a patient's lifestyle, feasibility, practicality and affordability. There are widely emerging beliefs about the coverage and efficacy of the BCG vaccination program that has been put in place. Though the efficacy of BCG (Bacillus Calmette Guerin) has become very controversial in the last decade due to resurgence of infection is spite of extensive use of BCG.
BCG has been very unsuccessful in preventing pulmonary TB. However it is still widely recommended in highly endemic countries like Pakistan for the prevention of tuberculous meningitis. Vaccines are derived from an attenuated isolate of Mycobactium bovis. The original strain was distributed to many laboratories throughout the world where the organism has been propagated under different conditions. BCG vaccine was first used in France in 1921, in Scandinavia in early 1930's and was widely used following WHO's recommendations in 1950's; and over 3 billion doses have since been administered. The rationale for administering BCG to an unvaccinated individual is to enhance the host's cellular immunity to subsequent challenge from virulent tubercle bacilli and to induce tuberculin sensitivity. The effectiveness of BCG is expressed in terms of its efficacy, defined as the percentage reduction in risk of disease among those vaccinated compared with similarly exposed non-vaccinated individuals. The observed efficacy of BCG vaccine in protecting against tuberculosis as estimated in ten such trials conducted in different parts of the world, has varied from zero from south USA and India, to 80% as observed in British MRC trials. The observed variations cannot be explained on one single factor. One explanation being the difference between the BCG strains prepared in different laboratories; second most popular explanation has been that it reflects regional differences in the prevalence of infections with environmental mycobacterium. Other explanations are based on immunological mechanisms or hypothesis of genetic, physiological or geographical differences (WHO 2000).