

## CHAPTER IV

### DATA EXERCISE

#### 4.1 Introduction

The impact of HIV on TB has been most marked in upper northern Thailand. In Chiang Rai province, despite the recent decline in HIV incidence and prevalence, HIV epidemic still has long –term impacts as reflected by the increase of TB. The incidence rates of new TB case per 100,000 population were 63 in 1987 and 50 in 1990 and increase to 117 in 1998 and 140 in 1999. Among TB patients in 1999, 43% were HIV-positive, 32% HIV-negative and 25% unknown [Saisorn et al., 2000]. This burden of HIV and TB co-infections requires an urgent need for interventions, including possible implementation of tuberculosis preventive therapy for tuberculosis among HIV-infected individual. [Msamanga, 1997]

In response to the dual epidemic, there are 10 out of 16 district hospital in Chiang Rai which have established INH prophylaxis therapy program(IPT), but, without strong policy support and supervision from provincial health office. Also, there are differences in the implementation of IPT programs in each hospital.

It is widely recognized, that poor adherence or non-adherence to therapy is the major obstacle to tuberculosis control. This also may be true for administering tuberculosis preventive therapy to asymptomatic HIV-infected persons because they are

not clinically ill and may not be motivated to undergo treatment. Non-adherence occurs commonly in all steps of the treatment process.

Determinants of adherence to treatment of TB and LTBI are not well understood [Sumartojo, 1993]. Therefore, this study was conducted to determine the effectiveness of program in term of completion rate and reasons associated with default to the INH preventive therapy (IPT) among HIV-infected persons in 4 district hospitals in Chiang Rai province. The lessons learned from this data exercise will be used to improve further data collection technique and also gathering the basic information about INH preventive therapy in order to improve a proposal for prospective clinical trial of TB preventive therapy.

## **4.2 Objectives**

### **4.2.1 General objective of data exercise**

Develop skill and gain experience in conducting a analysis of secondary data and qualitative method in order to apply the information from data exercise for prospective clinical trial of treatment of LTBI.

### **4.2.2 Specific objectives**

1. To assess the effectiveness of TB preventive therapy in term of the treatment outcomes of 9-month INH preventive therapy against tuberculosis in HIV infected persons in 4 district hospitals, Chiang Rai province.

2. To identify common factors affecting default of INH preventive therapy(IPT) against tuberculosis in HIV infected persons in 4 district hospitals, Chiang Rai province.

## **4.3 Method of the study**

### **4.3.1 Study design**

This study was a retrospective secondary data.

### **4.3.2 Study population**

HIV infected persons who received INH preventive therapy in Chiang Rai province.

### **4.3.3 Study site:**

Four hospitals which had enough number of HIV infected persons (More than 100) who received INH were selected for site visit.

1. Pan 809 cases
2. Mae Chan 428 cases
3. Chiang Khong 202 cases
4. Mae Sai 103 cases

#### **4.3.4 Study duration:**

Retrospective secondary data were collected from four hospitals and semi-structured interviews with health staff who were responsible for the IPT program from January to March, 2002.

#### **4.3.5 Data collection**

##### **Review of secondary data**

Data of Isoniazid (INH) preventive therapy were collected from Pan, Mae Chan, Mae Sai and Chiang Khong Hospital. Secondary data were available from registration and follow-up logbooks of INH preventive therapy and Day Care Center. With support from staff at TB/HIV research project-Chiang Rai, IPT and Day Care center's data were transcribed on a record form and entered into computer databases using Epi Info version 6.02. Data were then validated for transcription and other errors. Some data (variables) were not available due to incomplete documentation of the registration book.

##### **Semi-structured interview**

1 Doctors or nurses from each hospital who were responsible for in the program were interviewed using four probing questions with Semi-structure interviews as following:

- How to screen PLWA for enrollment in the IPT?
- What is the follow-up system like?

- Who is responsible for the IPT?
- Why are there high default rates of the IPT in this hospital?

#### 4.3.6 Data analysis

There are 2 parts for analysis of data exercise.

##### 1. To analyze the treatment outcomes of IPT.

Treatment outcomes were classified as completed, defaulted, death, TB disease and others (stop due to side effect, , migration, etc.)

*Definition of treatment outcome of IPT program*

**Completed :** Continued taking medication for TB prevention until completion at month 9 without default.

**No complete:** (stopped taking medication before 9 months) due to..

**Default :** failure to take medication for 60 consecutive days without a known reason to the program during the scheduled 9 months duration. Cases who died more than 60 days after the last contact with the program were classified as default rather than death.

**Death :** dead during 9 months

**Develop to TB disease** : during 9 months, PLWA developed a TB disease, so IPT had to be stopped and replaced by a proper medication for treatment TB disease.

**Other:** side effects, migration, transfer out , etc.

## **2. To analyze the factors associated with default of IPT program.**

Relative risks (RR) with their associated 95% confidence intervals (CI) and Chi-square were performed using SPSS 10 to determine the strength of association between baseline predictors and treatment outcomes(default)

## **4.4 Result**

**Table 4.1 : Treatment outcome of INH preventive therapy against tuberculosis and factors affecting follow-up status in Phan Hostipal, 1995-2001**

Factors	N	Default (%)	Complete (%)	Active TB (%)	Death (%)	Change diagnosis (%)	Side effect or transfer out (%)	Relative Risk to be default (95%CI)
<b>Start Year</b>								
1995	63	46.0	39.7	0.0	11.1	0.0	3.2	Ref.
1996	260	58.8	30.0	0.8	7.7	0.0	2.7	1.28 (0.96 <RR< 1.70)
1997	175	58.9	29.1	0.0	12.0	0.0	0.0	1.28 (0.95 <RR< 1.72)
1998	175	54.3	27.4	0.6	15.4	0.0	2.3	1.18 (0.87 <RR< 1.59)
1999	102	50.0	24.5	1.0	22.5	0.0	2.0	1.09 (0.78 <RR< 1.51)
2000	26	50.0	34.6	0.0	7.7	0.0	7.7	1.09 (0.68 <RR< 1.73)
2001	8	87.5	12.5	0.0	0.0	0.0	0.0	1.90 (1.31 <RR< 2.76)
<b>Over all</b>	809	55.8	29.3	0.5	12.3	0.0	2.0	
<b>Sex</b>								
Female	439	57.4	33.9	0.5	5.0	0.0	3.2	Ref.
Male	368	53.5	23.9	0.5	21.2	0.0	0.8	0.93 (0.82 <RR< 1.06)
Missing	2	100.0	0.0	0.0	0.0	0.0	0.0	1.74 (1.61 <RR< 1.89)
<b>Day Care registration</b>								
Yes	110	48.2	36.4	0.9	14.5	0.0	0.0	Ref.
No	699	56.9	28.2	0.4	12.0	0.0	2.4	1.18 (0.96 <RR< 1.45)



### **Phan hospital**

There were 63, 206, 175, 175, 102, 26 and 8 PLWHA enrolled in the IPT program in 1995, 1996, 1997, 1998, 1999, 2000 and 2001 respectively as shown in table 4.1 Out of 809 cases enrolled, 29.3% completed, 55.8% defaulted, 12.3% died, 0.5 stopped due to the development of active TB and 2.0% stopped due to other reasons (migration, transfer out, and side effect). The defaults were still high in each year. Year of enrollment, gender, and day care membership were found NOT to be associated with default. However, information from interviews with the staffs who were responsible for the IPT programme found that many other factors were related to default as following:

- The government started Antiretroviral therapy, therefore, some PLWA stopped INH in order to take antiretrovirus, believing that it could improve the immunity and thus there is no need to undergo IPT.
- Some symptomatic HIV-infected persons were included. The symptoms (Such as oral candiditis, weakness) reduce their ability and toleration to self-care including taking medications.
- PLWA who did not have any symptoms or were not ill tended to fail to comply with and complete the treatment believing that it is not necessary.
- Workload, nurses had to take responsibility for both tuberculosis and HIV/AIDS, and IPT was not a priority in these hospitals. They had a plan to stop IPT programme.



**Table 4.2 : Treatment outcome of INH preventive therapy against tuberculosis and factors affecting follow-up status in Mae Chan Hospital, 1995-2001**

Factors	N	Default (%)	Complete (%)	Active TB (%)	Death (%)	Change diagnosis (%)	Side effect or transfer out (%)	Relative Risk to be default (95%CI)
<b>Start Year</b>								
1995	50	62.0	32.0	0.0	4.0	0.0	2.0	Ref.
1996	100	36.0	49.0	1.0	13.0	0.0	1.0	0.58 (0.41 <RR< 0.82)
1997	103	26.2	60.2	0.0	12.6	0.0	1.0	0.42 (0.29 <RR< 0.62)
1998	68	30.9	54.4	0.0	11.8	1.5	1.5	0.50 (0.33 <RR< 0.76)
1999	87	18.4	54.0	0.0	25.3	0.0	2.3	0.30 (0.18 <RR< 0.49)
2000	15	6.7	86.7	0.0	0.0	0.0	6.7	0.11 (0.02 <RR< 0.72)
2001	5	0.0	100.0	0.0	0.0	0.0	0.0	-
<b>Over all</b>	428	30.8	53.5	0.2	13.6	0.2	1.5	
<b>Sex</b>								
Female	245	25.3	64.9	0.0	7.3	0.4	2.0	Ref.
Male	171	33.9	40.9	0.6	23.4	0.0	1.2	1.34 (0.99 <RR< 1.81)
Missing	12	100.0	0.0	0.0	0.0	0.0	0.0	3.95 (3.19 <RR< 4.90)
<b>Day Care registration</b>								
Yes	333	23.7	59.5	0.3	15.3	0.0	1.2	Ref.
No	95	55.8	32.6	0.0	7.4	1.1	3.2	2.35 (1.81 <RR< 3.06)

### **Mae Chan hospital**

There were 50, 100, 103, 68, 87, 15 and 5 PLWA enrolled in the IPT program in 1995, 1996, 1997, 1998, 1999, 2000 and 2001 respectively as shown in table 4.2. Out of 428 cases enrolled, 53.5 % completed, 30.8% defaulted, 13.6% died, 0.2% stopped due to the development of active TB and 1.5% stopped for other reasons (migration, transfer out, and side effect). The default declined steadily over the study period, i.e. 62.0%, 36.0%, 26.2%, 30.9%, 18.4, 6.7% and no default in 2000. The following factors were found to be associated with default; gender, day care membership and year of enrollment. Male were significantly of default higher than female as 1.34 times with 95% confidence interval 0.99-1.81. PLWA who did not register at Day care center before taking past IPT program were more likely to default from the IPT program 2.35 times than PLWA who registered at Day Care center with 95 % confidence interval 1.81-3.06. However, information from interviews with the staffs who were responsible for the IPT programme found that many factors were related to default as following:

- In the beginning of the programme, default was high because the PLWA were prescribed anonymously. They could not be traced when they were lost from the follow-up.
- There was no well-established system to follow up the patient in case of lost contact. The latter years saw a decrease in default rate and a higher completion rate after the programme was implemented by the Day care center.

**Table 4.3 : Treatment outcome of INH preventive therapy against tuberculosis and factors affecting follow-up status in Chiang Khong Hospital, 1995-2001**

Factors	N	Default (%)	Complete (%)	Active TB (%)	Death (%)	Change diagnosis (%)	Side effect or transfer out (%)	Relative Risk to be default (95%CI)
<b>Start Year</b>								
1995	7	0.0	100.0	0.0	0.0	0.0	0.0	-
1996	43	23.3	76.7	0.0	0.0	0.0	0.0	Ref.
1997	40	40.0	60.0	0.0	0.0	0.0	0.0	1.72 (0.89 <RR< 3.34)
1998	17	17.6	82.4	0.0	0.0	0.0	0.0	0.76 (0.24 <RR< 2.42)
1999	32	31.3	65.6	0.0	0.0	0.0	3.1	1.34 (0.64 <RR< 2.84)
2000	38	36.8	52.6	2.6	7.9	0.0	0.0	1.58 (0.80 <RR< 3.14)
2001	25	88.0	0.0	0.0	12.0	0.0	0.0	3.78 (2.16 <RR< 6.64)
<b>Over all</b>	202	37.1	58.9	0.5	2.9	0.0	0.5	
<b>Sex</b>								
Female	140	32.1	63.6	0.0	4.3	0.0	0.0	Ref.
Male	59	47.5	49.2	1.7	0.0	0.0	1.7	1.48 (1.03 <RR< 2.12)
Missing	3	66.7	33.3	0.0	0.0	0.0	0.0	2.07 (0.90 <RR< 4.78)
<b>Day Care registration</b>								
Yes	92	32.6	59.8	1.1	6.5	0.0	0.0	Ref.
No	110	40.9	58.2	0.0	0.0	0.0	0.9	1.25 (0.87 <RR< 1.82)

### **Chiang Khong Hospital**

There were 7, 43, 40, 17, 32, 38 and 25 PLWA enrolled in the IPT program in 1995, 1996, 1997, 1998, 1999, 2000 and 2001 respectively as shown in table 4.3 Out of 202 cases enrolled, 58.9% completed, 37.1 % defaulted, 2.9% died, 0.5% stopped due to the development of active TB and 0.5% stopped for other reasons (migration, transfer out, and side effect). The default was still high over the study period, i.e. 23.3%, 40.0%, 17.6%, 31.3%, 36.8% and 88% respectively. The gender only were found to be associated with default, day care membership and year of enrollment were not associated with default. Male were significantly of default higher than female as 1.48 times with 95% confidence interval 1.03-2.12. However, information from interviews with staffs who were responsible for IPT found that many factors were related to default as following:

- Out-migration in search of work. Some cases who underwent the treatment for 1-2 months and were still healthy moved to work in other city.
- Some symptomatic HIV-infected persons were included. The symptoms reduce their ability and toleration to self-care including taking medications.
- No well-established system to follow up in case of lost follow-up.
- Lack of supervision and monitoring from provincial health officers.

**Table 4.4 : Treatment outcome of INH preventive therapy against tuberculosis and factors affecting follow-up status in Mae Sai Hospital, 1995-1999**

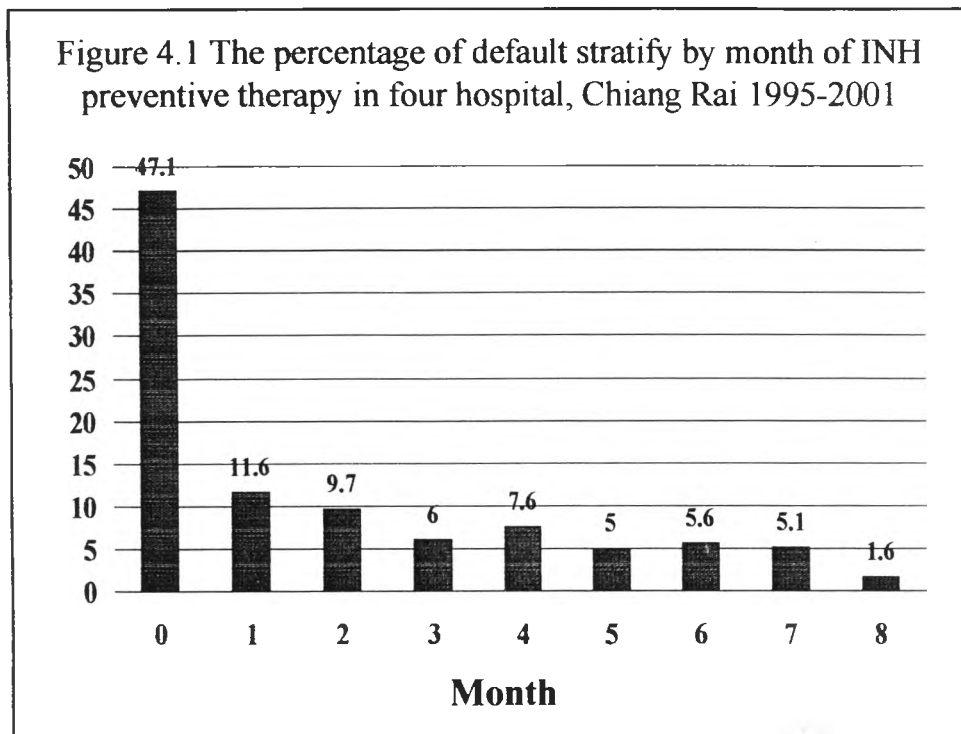
Factors	N	Default (%)	Complete (%)	Active TB (%)	Death (%)	Change diagnosis (%)	Side effect or transfer out (%)	Relative Risk to be default (95%CI)
<b>Start Year</b>								
1995	6	83.3	16.7	0.0	0.0	0.0	0.0	Ref.
1996	56	17.9	76.8	0.0	5.4	0.0	0.0	0.21 (0.11 <RR< 0.42)
1997	33	63.6	30.3	0.0	6.1	0.0	0.0	0.76 (0.49 <RR< 1.19)
1998	7	85.7	14.3	0.0	0.0	0.0	0.0	1.03 (0.64 <RR< 1.64)
1999	1	0.0	0.0	0.0	100.0	0.0	0.0	-
<b>Over all</b>	103	40.8	53.4	0.0	5.8	0.0	0.0	
<b>Sex</b>								
Female	57	35.1	63.2	0.0	1.8	0.0	0.0	Ref.
Male	46	47.8	41.3	0.0	10.9	0.0	0.0	1.36 (0.86 <RR< 2.17)
<b>Day Care registration</b>								
Yes	78	34.6	57.7	0.0	7.7	0.0	0.0	Ref.
No	25	60.0	40.0	0.0	0.0	0.0	0.0	1.73 (1.11 <RR< 2.70)

### **Mae Sai hospital**

There were 6, 56, 33, 7 and 1 PLWA enrolled in the IPT program in 1995, 1996, 1997, 1998, 1999 and then stopped as shown in table 4.4. Out of 103 cases enrolled, 53.4% completed, 40.8% defaulted, 5.8% died. The defaults were still high over the study period, i.e. 83.3%, 17.9%, 63.6%, 85.7% respectively. The day care member was a factor found to be associated with default; gender, and year of enrollment was not associated with default. PLWA who did not register at Day care center before taking part in the IPT program were more likely to default from the IPT program 1.73 times than PLWA who registered at Day Care center with 95 % confidence interval 1.11-2.70.

However, information from interviews with the staffs who aware responsible for the IPT programme found that many factors related to default as following:

- No well-established system to active follow up in case of lost follow-up.
- Turn-over of staff
- PLWA met physician only once at the start of the IPT.
- Lack of knowledge about TB preventive therapy including standard practice.



From figure 4.1, the most patient loss to follow up in the first month at 47.1% and 11.6 % at second month, 9.7 % at 3<sup>rd</sup> month, 6% at 4<sup>th</sup> month, 7.6% at 5<sup>th</sup> month, 5% at 5<sup>th</sup> month, 5.6% at 6<sup>th</sup> month, 5.1% at 7<sup>th</sup> month and 1.6% at 8<sup>th</sup> month.

#### 4.5 Discussion

In order to improve the effectiveness of program in term of completion rate, there were experiences from Mae Chan hospital and Mae Sai hospital that the integrating IPT into DCC activities might improve the completion rate of programme. However, at Chiang Khong and Phan Hospital, which also having a DCC, default rates at these hospitals were not improved. There were no significant difference for PLWA

who were enrolled and not enrolled in DCC. Anyway, in a DCC of each hospital, there also were differences in activities and packages of care for PLWA. DCC at Mae Chan was recognized as a model of home-based care and community-based AIDS prevention program by WHO and UNAIDS. [Piyawowarong, 2000, Pintatum 2000]

Male tended to default than female as shown in Mae Chan and Chiang Khong hospital. Therefore, to improve the effectiveness in term of completion rate and decrease default, hospitals need to pay more attention to counseling male patients. To set against the WHO requirement that 80% complete rate of the IPT should be obtained and less than 30% of defaults is allowed, the completion rate of the IPT in Chiang Rai is considered low and the default is still high.

#### **4.6 Lessons learned and Recommendation**

There are some points which will be gain experience and useful for improving the proposal and the implementation of the clinical trial project. They are as follows;

1. Interviews: During the interviews, which were conducted in the morning, there were many interruptions which to some degree blocked the flow and reduce the quality of the interviews. Morning hours were usually a busy time for the DCC staff who had to attend the patients who come to the entrée for the services. Interviews should be best arranged in the afternoon where there are less patients and the staff are willing to talk at length about their work. Furthermore, rapport should be built with the staff before the interview in order to get in-dept quality information.



2. Hospital site preparing: Recognizing that staffs turn-over rate is high, skills and knowledge for counseling in tuberculosis preventive therapy are inadequate, and that there are differences in standard to provide tuberculosis preventive therapy in Chiang Rai province, the training is needed for 10 hospital site before starting clinical trial in order to ensure the same standard guideline as practice for tuberculosis preventive therapy.
3. There is a serious problem with workload of staff in some hospitals. DCC nurses have to look after two programmes, i.e., HIV/AIDS and TB programmes. These two jobs receive different priority ( i.e., HIV/AIDS receive higher priority). Before starting a clinical trial project, the researchers have to ensure that the hospitals pay adequate attention to IPT programme.
4. The results of this data exercise suggest that integrating IPT into DCC activities might improve the completion rate of programme. However, the understandings about how DCC function and whether there are critical issues in the successes or failures of the DCC are not well-established and there are difference in each hospital. These understandings are necessary for the identification of opportunities and barriers to maximize the capacity of the DCC before implement the IPT programme.

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