Palliative Care Data Analysis – Round 1/Baseline – Results

Context

This study is round 1 of a 4-round cohort study, comparing the effect of HIV palliative care programs between two HIV clinics, Van Don (intervention / case site) and Cam Pha (comparison / control site). The intervention is made between round 2 and 3, therefore, round 1 and 2 are baseline data.

Study introduction
The study evaluates the outcomes and processes of implementing palliative care policies at the district level for people living with HIV in Quang Ninh, Vietnam. The research is designed by FHI, jointly undertaken by FHI and RTCCD. Its implementation has the involvement of two OPCs Van Don and Cam Pha, Quang Ninh province.

Primary objectives:

- To measure changes in three primary palliative care outcomes: 1) pain; 2) depression and anxiety; 3) social support.
- To identify facilitators and barriers to implementing palliative care services at the district HIV care level.

Ethical consideration
In Vietnam, the protocol was reviewed and approved by ethical committee organized by the Vietnam Medical Association in the Decision No.75/THYH dated 5th September 2008.

The total number of participants enrolled in the study, the number of participants who completed the study, all changes in the research activity, and all unanticipated problems involving risks to study participants or others have been reported to the Principal Investigators at the finish of the data collection.

The written informed consent has obtained from each study participant prior to enrollment. In cases of limitted understanding of clients even throughly reading of the writtten consent. The content of informed consent which includes ethical review, risks, benefits, confidentiality, incentives, and participants protection has been provided using verbal presentation made by field researchers. Participants have been provided with a copy of their signed informed consent forms.

Screening and enrollment
These methods were used to approach the PLHIV for screening:

- Attending the group meeting of PLHIV.
- Staying at OPCs full-time to directly invite the PLHIV who came to the clinics to receive treatment to participate in screening interviews.
- OPC involved the home-based care groups in informing PLWHIV who do not receive ARV to come to the OPC earlier than pre-booking appointment to participate in the screening interviews.
- Snowballing introduction to unenrolled clients from enrolled.

After 8 weeks of screening, the numbers of eligible/uneligible participants enrolled for the study are shown at the table 1.

Table 1. Enrollment

Study site	Eligible	Ineligible	Total
Van Don	**353**	**30**	**383**
Cam Pha	**531**	**33**	**564**
Total	**884**	**63**	**947**

Interview

As initiated, the study sample size will include 850 patients (475 for comparison site, and 375 for intervention site). Based on the factual quantity of HIV patients controlled by the Van Don OPC, the 375 is unable to reach. The status of unable-to-interview participants has been reported to the FHI IRB following the SAE form.

The summary of number of interviewed participants is presented at the table 2.

Table 2. Interview

Study site	Enrolled	Interviewed	*Unable to interview*
Van Don	**353**	**345**	***8***
Cam Pha	**531**	**477**	***54***
Total	**884**	**822**	***62***

Aim of this analysis

The main task of the analysis of round 1 is to compare the two clinics in terms of the characteristics of their patients. For this purpose, we can categorize the patient's characteristics into two types: outcome, and non-outcome. Outcome characteristics are key variables including pain and symptoms frequency and severity, anxiety, depression, and social support quality (SSL). Non-outcome variables are other characters such as age, gender, drug use, which may be used as predictors for the outcome variables.

Eventually, the main goal of this study is to compare the treatment and the control clinics on the outcome variables. Therefore, non-outcome variables which:

- Correlate with an outcome variable, AND
- Is significantly different between the two clinics

should be viewed as potential confounders for the main study goal, and should be adjusted either physically (re-distributing the patients amongst the two clinics), or statistically (using propensity score matching, for instance).

If a non-outcome variable does **not** fit in **either** of the above criteria, then it is **not** a confounding factor, and does not require adjustment between the two clinics.

Therefore, the aims in analyzing this round 1 dataset are:

1. To note any significant difference in non-outcome variables between the two clinics
2. To note any significant difference in outcome variables between the two clinics
3. To explore (using regression) the relationship between the non-outcome (as predictor variables) and the outcome variables.

4. To note any confounding factors for the main study goal, and propose appropriate adjustments.

List of outcome variables

This list is based on the file "Palliative care data analysis plan – round 1.doc", sent by Kimberley Green in February 2009.

The outcome variables for this study are

- *Pain and other symptoms*: these are categorical measures of the patient's frequency, severity and pain perception on particular symptoms. These variables are based on 137 symptoms recorded in questions 3.101 to 3.137 of the questionnaire.

List of non-outcome variables

Clearly, any variable not listed above can be considered as a non-outcome variable. However, to minimize false discovery rate, we are only interested in non-outcome variables which:

- Are essential descriptive characteristics (such as gender, age), OR
- May be correlated with an outcome variable **in an explainable way**

Correlations between two variables with no apparent reasons (such as place of birth with pain severity) are most likely a false discovery (a result of the data's randomness), and therefore we should not bother testing in the first place.

Under these criteria, we have the following non-outcome variables:

- *Essential descriptive characteristics*
    a. Age
    b. Gender
    c. Education
    d. Marital status
    e. Number of children
    f. Employment status
- *Drug usage*
    a. Drug usage in the last 6 months
    b. Alcohol usage (frequency)
    c. Smoking (frequency)
- *Physical health status*
    a. CD4 count
    b. Clinical stage
    c. Hepatitis B and/or Hepatitis C
    d. If experiencing any side effect from CD4
    e. Date when initiated ART
    f. *Health functionality (HF)*: a numerical measure of the patient's reported health interference with functionality. Higher values indicate **better** health (less interference). This variable is defined as a score ranging from 0 to 63,

based on question 2.11 of the questionnaire. The detailed definition can be found in the appendix.

- *Mental health status:*
    a. Level of discrimination experienced
    b. Number of people patient can rely on for social support
    c. Anxiety and/or depression (if experiencing any)
    d. Use of counseling services, such as CHBC, PLHIV
    e. *Social support quality (SSQ)*: a numerical measure of the patient's social support quality. Higher values indicate **more** social support. This variable is defined as a score ranging from 0 to 3, based on questions 5.103 to 5.109 of the questionnaire. The detailed definition can be found in the appendix.

Results

Result 1: Significant differences amongst the two clinics in non-outcome variables

Significant differences (at 99% confidence level, after adjusted for multiple testing) are found in the following non-outcome variables:

Essential descriptive characteristics

- Education level
- Marital status

Although the age distribution at both clinics are the same, the data indicate that Van Don clinic has a higher portion of patients with lower educational level, and higher percentage of married patients.

Drug usage

- None

There are no significant differences in drug usage (including inject drugs, alcohol consumption and smoking frequency) amongst the two clinics.

Physical health status

- Clinical stage
- Hepatitis C
- Date when initiated ART

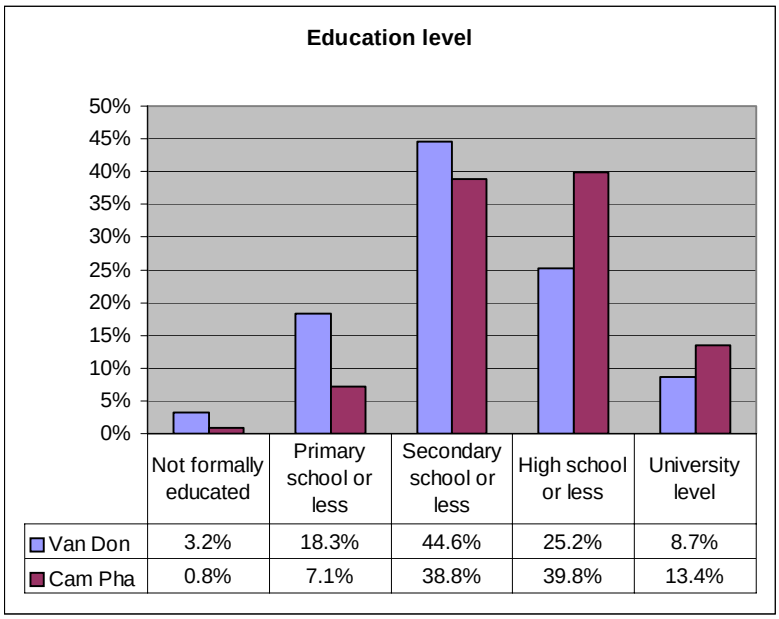
Van Don has more patients in the later stages, with 80% of patients at Van Don at clinical stage 3, while this number is only 40% at Cam Pha. 22% more patients at Van Don have hepatitis C, and a large portion of patients at this clinic started ARV in 2006, while at Cam Pha there are more patients started their ARV in 2007 and 2008. However, in terms of health functionality or CD4 count, there are no significant differences between the two clinics. Therefore, although patients at Van Don clinic are in the later clinical stages, their physical health status are comparable to those at Cam Pha.

Mental health status:

- Number of people patient can rely on for social support
- Use of counseling services, such as CHBC, PLHIV

Patients at Van Don clinic seem to have better social support, with 16% more patients having 5 or more supporters to rely on. Those at Van Don also received more types of supports in the outpatient clinic in the last 3 months, and a higher percentage of patients at Van Don received PLHIV and CHBC support than at Cam Pha.

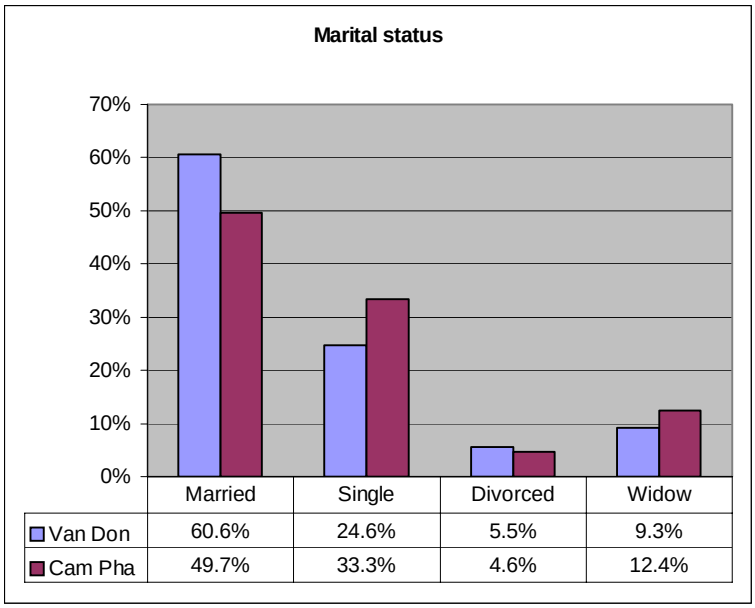
Educational Level



	Not formally educated	Primary school or less	Secondary school or less	High school or less	University level
Van Don	3.2%	18.3%	44.6%	25.2%	8.7%
Cam Pha	0.8%	7.1%	38.8%	39.8%	13.4%

The graph indicates that patients at Cam Pha clinic tend to have higher educational level, with 14% more studied in high school, and 6% more studied at university compared to Van Don. The p-value of the chi-squared test is less than 0.001, indicating that this is a strong difference.

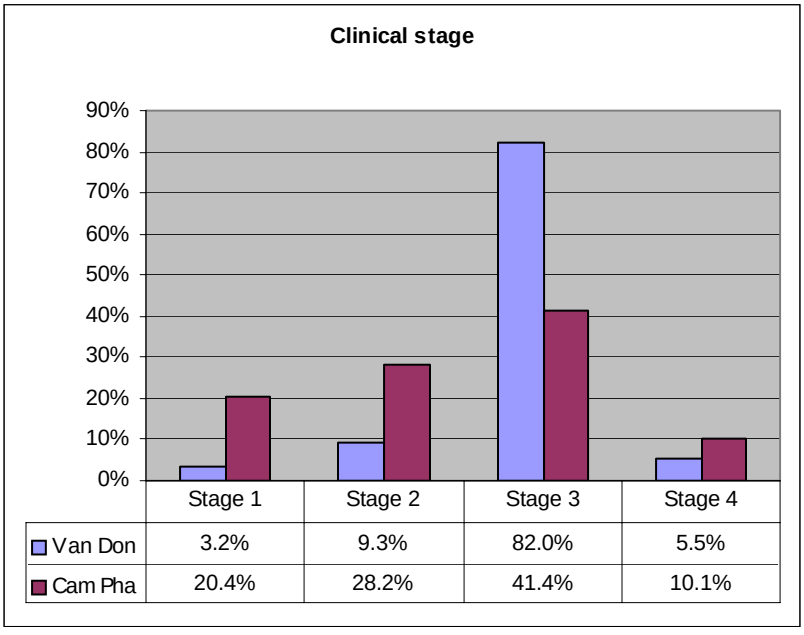
Marital status



	Married	Single	Divorced	Widow
Van Don	60.6%	24.6%	5.5%	9.3%
Cam Pha	49.7%	33.3%	4.6%	12.4%

The graph illustrates that Van Don has more patients with a partner, with 10% more married as compared to Cam Pha. However, the divorce rate of Van Don is around 1% higher than Cam Pha. Comparing with Van Don, 9% more of Cam Pha's patients are single. The p-value of the chi-squared test is 0.009, indicating that this is a weak difference[1].

Clinical stage



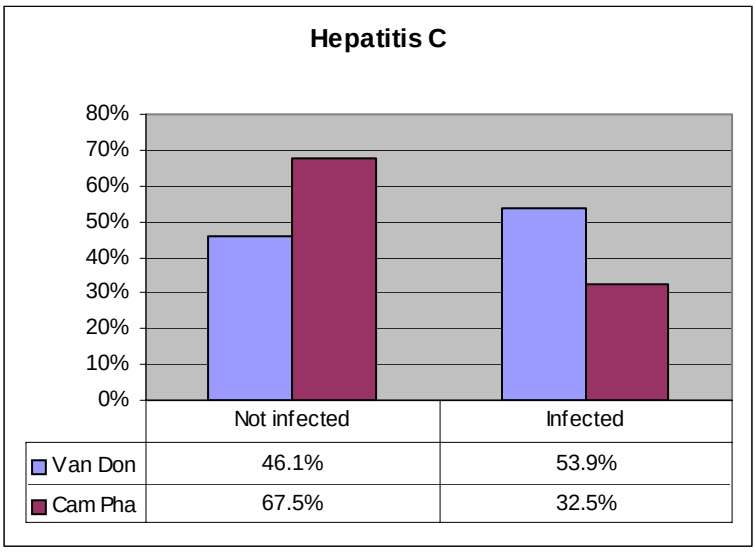
	Stage 1	Stage 2	Stage 3	Stage 4
Van Don	3.2%	9.3%	82.0%	5.5%
Cam Pha	20.4%	28.2%	41.4%	10.1%

The graph indicates a drastic difference in clinical stage 3 of Van Don and Cam Pha's patients. The number of patients in stage 3 of Van Don is double the amount of patients in Cam Pa. On the other hand, Cam Pha' has double the amount of patients of Van Don

[1] Since we have to adjust the alpha level for multiple testing, results are considered strong only if their p-value is less than 0.001

who are in stage 4. The number of patients of Cam Pha is more concentrated in stage 1 and 2 as compared to Van Don. The p-value of the chi-squared test is less than 0.001, indicating that this is a strong difference.

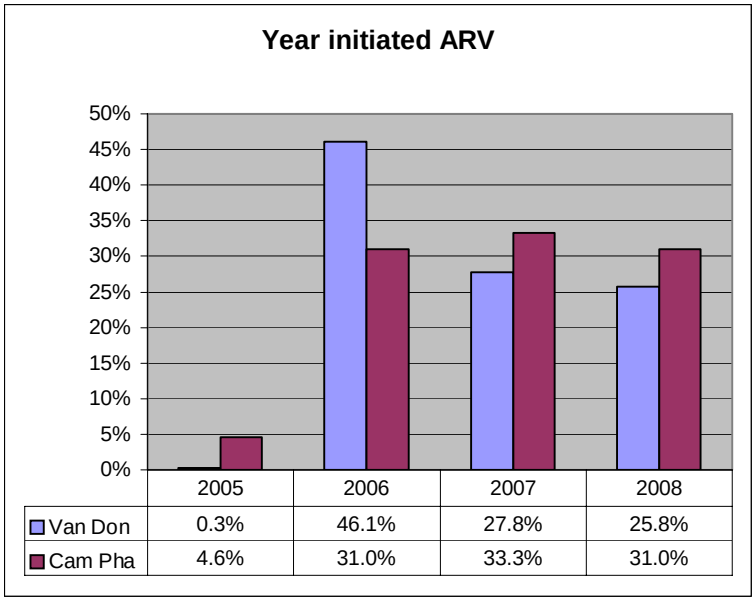
Hepatitis C



	Not infected	Infected
Van Don	46.1%	53.9%
Cam Pha	67.5%	32.5%

The graph demonstrates that more patients in Cam Pha are not infected with Hepatitis C comparing with Van Don. 22% more patients in Van Don are infected with Hepatitis C than patients in Cam Pha. The p-value of the chi-squared test is less than 0.001, indicating that this is a strong difference.

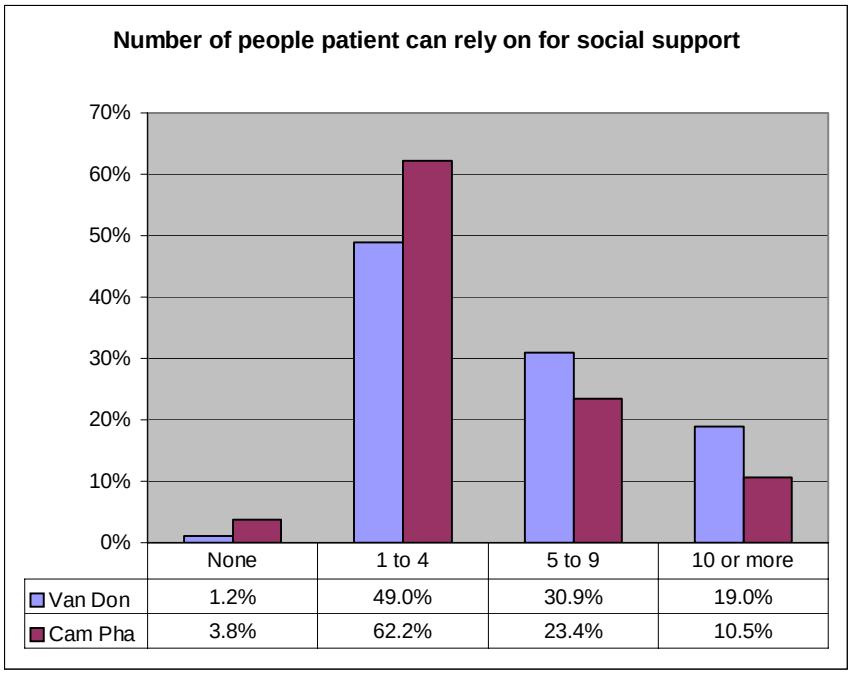
Year initiated ART



	2005	2006	2007	2008
Van Don	0.3%	46.1%	27.8%	25.8%
Cam Pha	4.6%	31.0%	33.3%	31.0%

The graph indicates that patients in Van Don tend to initiate ARV earlier; with 15% more of them initiated ARV in the year of 2006 as compared to Cam Pha. Patients in Cam Pha tend to initiate ARV later. The p-value of the chi-squared test is less than 0.001, indicating that this is a strong difference.

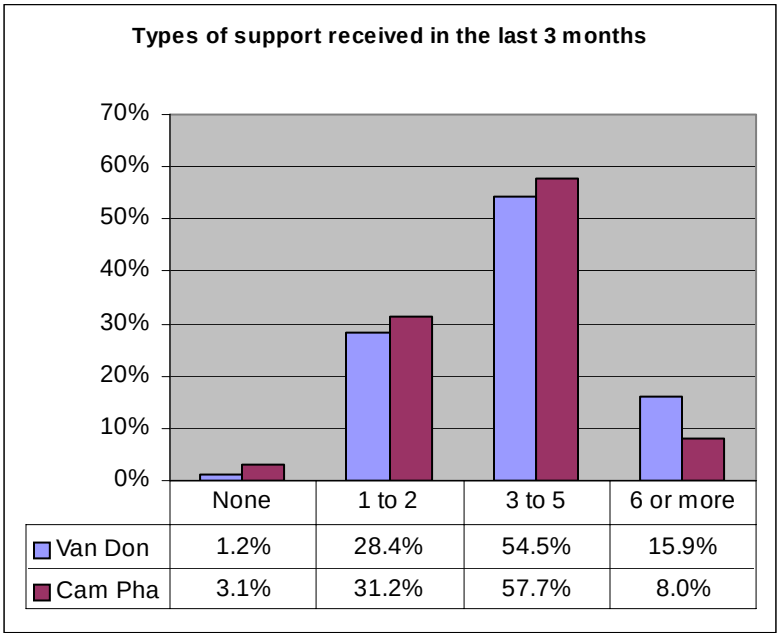
Number of people patient can rely on for social support



	None	1 to 4	5 to 9	10 or more
Van Don	1.2%	49.0%	30.9%	19.0%
Cam Pha	3.8%	62.2%	23.4%	10.5%

The graph demonstrates that more patients in Van Don rely on social support. In the category of 10 or more patients who relied on for social support, Van Don's patients almost doubled the amount of Cam Pha's patients. The p-value of the chi-squared test is less than 0.001, indicating that this is a strong difference.

Use of counseling services

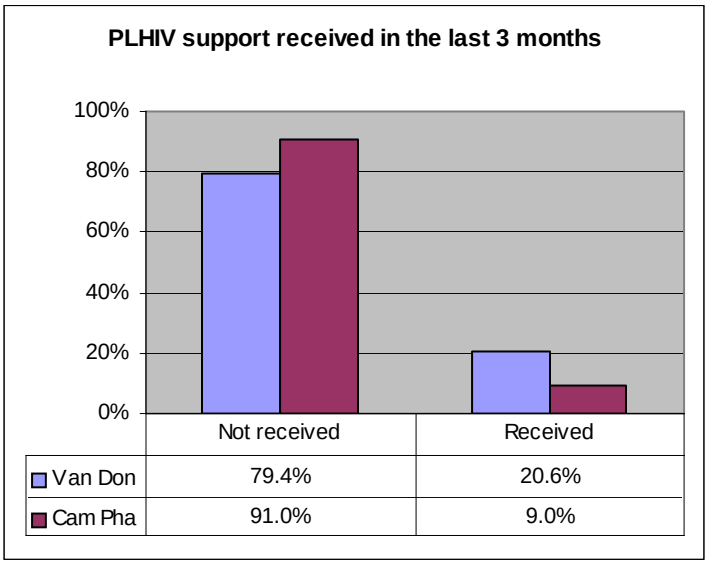


	None	1 to 2	3 to 5	6 or more
Van Don	1.2%	28.4%	54.5%	15.9%
Cam Pha	3.1%	31.2%	57.7%	8.0%

The graph illustrates that majority of Van Don's patients receive lesser support in the last 3 months as compare to Cam Pha's patients. However, there is a minority group of Van Don's patients, ie. almost 8% more than Cam Pha, received 6 or more support in the last

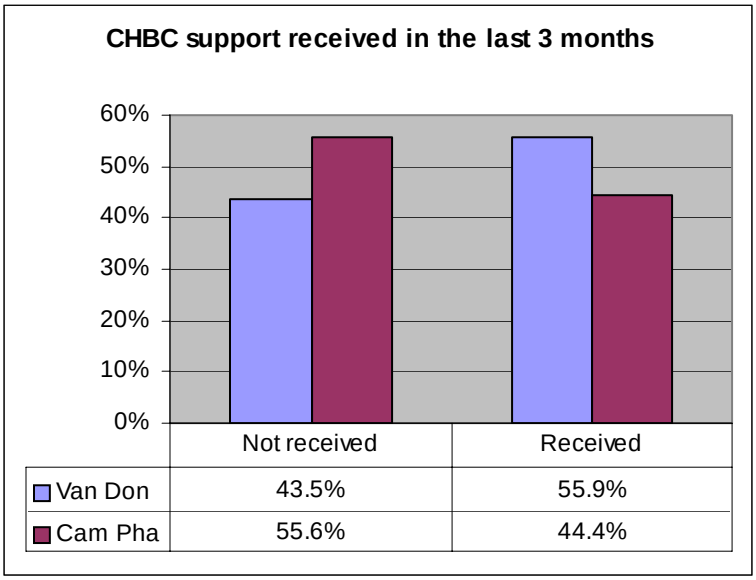
3 months. The p-value of the chi-squared test is 0.001, indicating that this is a strong difference.

PLHIV services received in the last 3 months



The graph demonstrates that 12% more patients in Cam Pha did not received PLHIV support in the last 3 months as compared to Van Don. Only 9% of Van Don's patients received PLHIV support in the last 3 months while 20.6% of patients in Van Don received the support in the last 3 months. The p-value of the chi-squared test is less than 0.001, indicating that this is a strong difference.

CHBC services received in the last 3 months



Similar to the PLHIV graph, this graph shows that 11% more patients at Van Don have received CHBC support in the last 3 months than those at Cam Pha. The p-value of the chi-squared test is 0.001, indicating that this is a strong difference.

Result 2: Significant differences amongst the two clinics in outcome variables

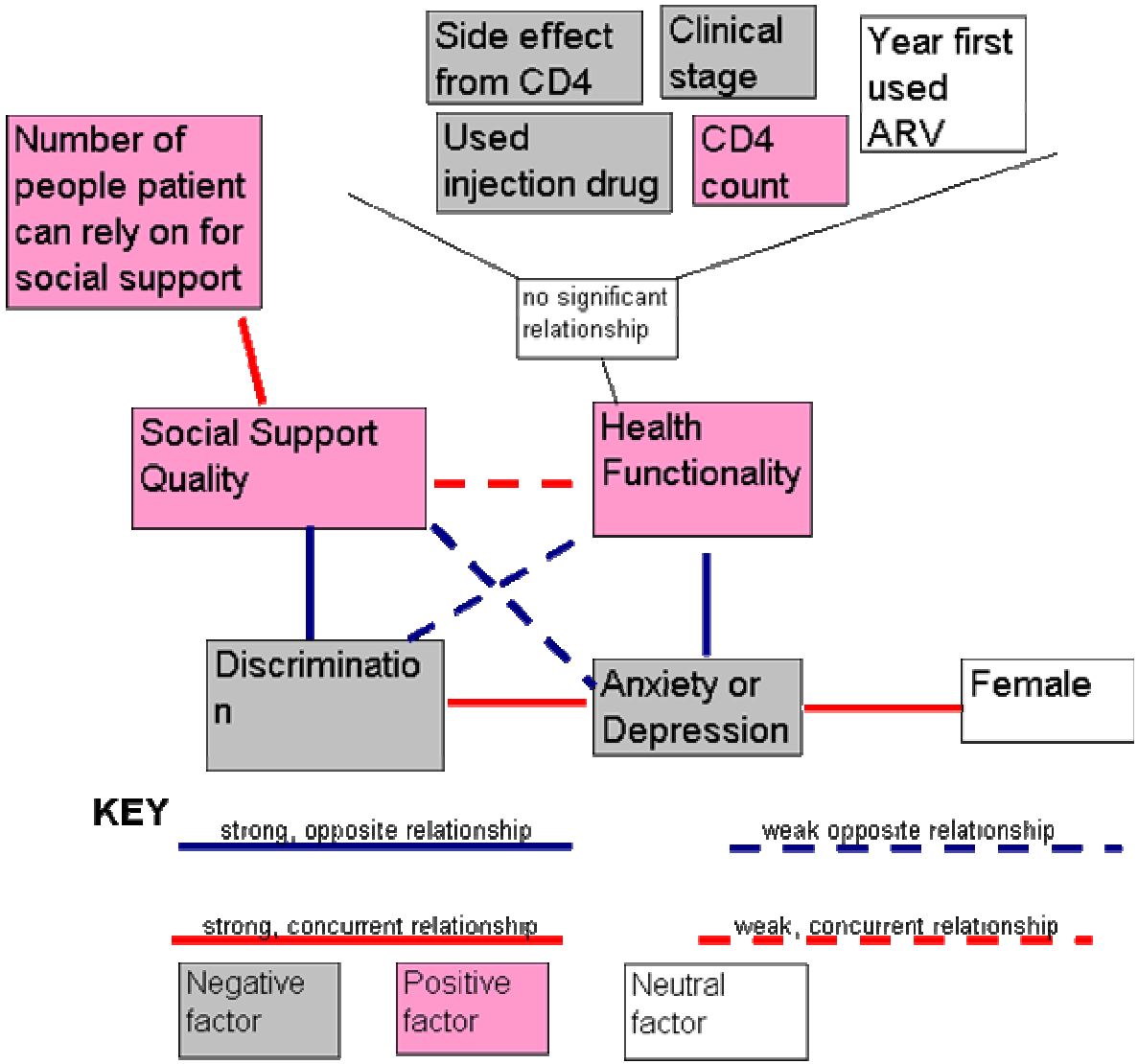
Out of 548 variables tested, there are only 3 variables with p-value < 0.01, but not less than 0.001. Upon closer inspection, it is clear that these results are false positives. In other words, there are **no** significant differences in any of the key variables between the two clinics.

Result 3: Regression results and interpretations

For each symptom, a logistic stepwise regression model was used to explore the relationship between the symptom variable and the non-outcome factors. It should also be noted that several non-outcome factors display high correlation, and therefore regression and ordinal logistic regression models are used to explore the relationship amongst the key non-outcome factors.

Relationships amongst non-outcome variables

Logistic and multivariate regression models showed that the relationship amongst non-outcome variables are complicated, and is best represented in the graph below.


Side effect from CD4
Clinical stage
Year first used ARV
Number of people patient can rely on for social support
Used injection drug
CD4 count
no significant relationship
Social Support Quality
Health Functionality
Discriminatio n
Anxiety or Depression
Female
KEY
strong, opposite relationship
weak opposite relationship
strong, concurrent relationship
weak, concurrent relationship
Negative factor
Positive factor
Neutral factor

In the above graph, red lines indicate concurrent relationship, while blue lines indicate opposing relationship. For instance, we see that higher discrimination is associated with higher anxiety or depression, less social support quality score and less health functionality. Dotted lines indicate a weak relationship (p-value > 0.01 but < 0.05), while continuous lines indicate a strong relationship (p-value < 0.01). The boxes are color-coded into pink, gray and white depending on whether they are positive, negative or neutral factors. An increase in positive factors in patients indicates better health, while an increase in negative factors indicates worsening health.

The graph highlights the link between mental health and physical health: the variable health functionality, which is a measure of physical health status, **does not correlate** with physical health factors such as CD4 count, clinical stage, year started ARV, but **does correlate** with the three mental health indicators: discrimination level, anxiety or depression, and social support quality.

The results also indicate that female patients are more vulnerable to anxiety and depression than males, which is an important fact for counseling programs.

Relationships between non-outcome and outcome variables

Given that there are 137 symptoms, each with 4 questions encompassing prevalence, frequency, severity and pain tolerance, over 500 logistic regression models were built. In order to adjust for false positive discoveries, significant relationships are defined as those where at least 2 out of 4 models related to this symptom have R-squared > 7.5%. Under these criteria, the five symptoms identified below have significant correlation with key non-outcome variables.

Symptom:		Lack concentration				Lack energy				Feeling nervous				Breath shortness				Feeling worried			
		1	*2*	*3*	*4*	*1*	*2*	*3*	*4*	*1*	*2*	*3*	*4*	*1*	*2*	*3*	*4*	*1*	*2*	*3*	*4*
Health functionality		**- 5%**		**-6%**		**-10%**	**-6%**	**-9%**		**-10%**			**- 6%**	**-7%**	**-8.9%**	**-9%**		**-4.5%**			
Social support quality							**-40%**														
Number of supporters	1 - 4 supporter												**-86%**						**-77%**	**-79%**	
	5 - 9 supporter												**-90%**						**-85%**	**-86%**	
	>= 10 supporter							**-58%**					**-88%**						**-87%**	**-86%**	
Discrimination	Rarely																				
	Sometimes																				
	Often																			**+309%**	
	Frequent			**+ 400%**			**+327%**								**+765%**	**+500%**			**+427%**	**+450%**	
Anxiety or depression		**+400%**		**+ 210%**		**+360%**	**+200%**	**+300%**		**+560%**			**+430%**	**+335%**		**+275%**		**+556%**	+290%	**+248%**	
Female gender		**+160%**		**+180%**														**+207%**	**+169%**	**+171%**	

Key: 1 = Has symptom, 2 = Has high frequency, 3 = Has high severity, 4 = Cause much pain to patient

The numbers reported in the table are odd ratios, and should be interpreted as followed: a negative odd ratio indicates a decrease in the risk of the patient getting the symptom, while a positive odd ratio indicates the reverse. For instance, for the symptom "lack concentration":

- For every 1 point increase in health functionality, the risk of the patient getting the symptom is reduced by 5%, and the risk of the patient getting high severity in this symptom is reduced by 6%
- If the patient has anxiety or depression, then the risk of the patient getting this symptom is increased by 400%, or 4 times, as compared to patients of the same condition but without anxiety or depression
- If the patient experiences discrimination at the "frequent" level, then their risk of experiencing high severity in this symptom is increased by 4 times as compared to those who do **not** experience discrimination at all.

We note the following:

- 4 out of 5 symptoms are mental, rather than physical distress. The fact that all of these symptoms have negative correlation with health functionality once again underlines the link between mental and physical health.
- Number of supporters plays an important role in the patient's ability to cope with nervous and worrisome feelings. If patients without supporters are given just 1 supporter, their risk of getting high stress level from nervous feelings is reduced by 86%, and their risk of experiencing frequent worrisome feelings is reduced by 77%.
- Social support quality plays an important role in reducing the patient's feeling of lacking in energy. Those who have 1-point-higher in social support score have 40% less chance of feeling lacking in energy frequently.
- Females are at significantly high risk than males from experiencing lack of concentration and feeling worried. Once again, this strongly indicates the need for special mental care for female patients.
- From the definition of anxiety / depression, it is expected that there is a strong link between having anxiety and depression, and having these symptoms. However, it should be noted that anxiety and depression also correlates with shortness of breath, which is a physical symptom.
- Only 24 patients reported experiencing discrimination at the frequent level. Therefore, the odds ratio for this variable may be more sensitive to variations in the data than other variables. However, the consistently high odds ratios across all symptoms for this variable indicate that discrimination, especially at higher severity level, plays an important role in determining the patient's mental health.

Detailed results including confidence intervals and p-values can be found in the appendix

Results Discussion and Recommendations

The analysis showed that:

1. **There are no variables which acts as confounders to the main study goal**, since there are no significant differences in the patient's symptoms despite some significant differences in the patients' characteristics between the two clinics.
2. **There is a strong link between patient's mental health and physical health**. The study indicates that patients who experience less discrimination, have higher social support quality, and have no anxiety or depression tend to have higher health functionality.
3. **There is a strong link between 5 symptoms and health functionality, social support quality and number of supporters, discrimination, anxiety/depression, and female gender**. As summarized above, the trend across all 5 symptoms are the same: those at lower risk of experiencing these symptoms are those with better health functionality, more supporters, better social support quality, experience less discrimination and have no anxiety/depression.
4. **Females are at higher risk of experiencing anxiety or depression, experiencing lack of concentration and feeling worried more than males**. This indicates the need for healthcare program specifically for female patients to help them overcome these mental stresses.

Appendix A: Descriptive results for all variables, by clinic

Please refer to the word document **Tables_PK_V1.doc**

Appendix B: Regression results for symptom variables

Please refer to the spreadsheet total and details in the file **total.xls**