BCG coverage and the association between selected factors and the immunization coverage among children under the age of two years in rural and semi-rural Lhasa District, Tibet

by

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ABBREVIATION

Tuberculosis	TB
Bacille Calmette–Guérin	BCG
Oral Polio vaccine	OPV
Diphtheria Pertussis Tetanus vaccine	DPT
Measles vaccine	MV
Hepatitis B vaccine	HBV
Diphtheria Tetanus vaccine	DT
Expanded Programme on Immunization	EPI
Tibet Autonomous Regions	TAR

ABSTRACT

Aim: Tuberculosis (TB) is a worldwide pandemic. The BCG vaccine still remains the standard for TB prevention in most countries because of its efficacy in preventing life-threatening forms of TB in infants and young children, and BCG is the only vaccine available. To achieve a high BCG coverage, it is important to investigate the BCG coverage in populations and the factors which affect the immunization status. Thus giving us clues for improving the coverage. Few such studies have been conducted in Tibet. The aim of the present study is to estimate the BCG immunization coverage and to investigate the association between the BCG coverage and the selected factors in children less than two years of age in semi-rural and rural areas of Lhasa District.

Methods: The present cross-sectional study was carried out among children less than two years of age in Quxu County (N=484) and in Damxung County (N=496) of Lhasa District, Tibet. In Quxu County we selected all the children less than two years of age and in Damxung County we used multi- stage sampling method to select the sample. The questionnaire consists of core question regarding socio-demographic characteristic of household, the knowledge and belief of mothers related to the immunization and TB, accessibility of health services and the BCG immunization history of children. BCG vaccination scar were checked on the children's shoulder and recorded.

Results: The BCG coverage in the semi-rural area Quxu County was 77%, and that of rural-area Damxung County was 61%. In Quxu County the high BCG coverage was significantly associated with short walking time from home to nearest health facility (OR=3.1; CI, 2.0-4.8), ever vaccinated in health facility (OR=2.5 ; CI, 1.6-4.0), receiving outreaching services (OR=12.0; CI, 7.0-20.6), frequency of outreaching services once per month (OR=7.4; CI 3.7-14.9) or once per two to four months (OR=6.3; CI 2.8-14.5), knowing the time of next outreaching services (OR=2.0; CI, 1.1-3.6), hospital delivery (OR=1.8 ; CI, 1.1-2.7), type of delivery assistance (health worker) (OR=2.0; CI 1.3-3.1), and. In terms of cost of transportation, high BCG coverage were associated with inexpensive cost of transportation (OR=4.6; CI, 1.8-11.6). In Damxung County, the factors significantly associated with high BCG coverage of children were receiving outreaching services (OR=3.8; CI, 2.0-7.2), and knowing the time of next outreaching services (OR=2.7; CI, 1.6-4.5). There was a clear relation between high BCG coverage and frequency of outreaching services, compared to

services once or twice per year the odds were as follows once per two to four months (OR=2.7; CI, 1.6-4.5), and monthly (OR=5.7; CI, 3.0 -11.0).

***Conclusions*:** BCG coverage was significantly higher in semi-rural area Quxu County (77%) than in the rural-area of Damxung County (61%). In order to increase the immunization coverage in the rural and semi-rural area of Tibet, the frequency of the outreaching services should be increased, as well as more polite information about the time of such services should be given. To establish more health facilities to reduce the travel distance for the mothers or to set up transportation free of charge or to a low cost would be helpful. To encourage the mothers to give birth at hospitals would also increase immunization coverage. However, for many families in Tibet, this will be too expensive. At the same time, birth at hospitals would help in decreasing the mother and child mortality in Tibet.

CHAPTER I

INTRODUCTION / BACKGROUND

Introduction /Background

Tuberculosis (TB) is a worldwide pandemic. It is estimated that 8 million new cases of TB occur worldwide annually (1). Half of the new cases are in six Asia countries (Bangladesh, China, India, Indonesia, Pakistan and The Philippines). TB is curable but kills 5000 people every day (2). Bacille Calmette–Guérin (BCG) vaccination is accepted as one of the most important measures to prevent primary TB in children.

1. Definitions

1.1 TB

TB is caused by the bacillus *Mycobacterium tuberculosis.* It spreads through the air. By far, the most important source of human infection is an already infected person (3). When infectious people cough, sneeze, talk or spit, they propel TB germs into the air. A person needs only to inhale a small number of these to be infected (4). Primary infections can occur at any age, but children are most often affected in areas of high incidence and high population density. Even after recovery, the disease can be reactivated and again spread. Agents that supress the immune system, such as corticosteroid therapy or HIV infection, facilitate reactivation. Primary infection may be asymptomatic and often resolves spontaneously. However, it may progress by local spread in the lungs to cause pleurisy or bronchopneumonia. If the infection spreads through the bloodstream, it can affect many organs, including the meninges, the bones, or the internal organs. The disease can be accompanied by TB lymphadenopathy, or this manifestation can occur in the absence of other features (3).

Left untreated, each person with active TB disease will infect on average between 10 and 15 people every year. Some will be infected with TB bacilli every second (4). It is estimated that one third of humanity (approximately two billion people) is infected with TB. Amongst those carrying the pathogen, around 8 million persons present with clinical disease every year; and out of these, about 1.6 million die, not counting TB-related deaths in TB-HIV co-infected individuals. More than 1.5 million new TB cases per year occur in sub-Saharan Africa, nearly three million in South-East Asia and over a quarter of a million in Eastern Europe (5). Ninety-

eight persent of TB deaths occure in the developing world, affecting mostly young adults in their most productive years. TB especially affects the most vulnerable groups such as the poorest and the malnourished (2). In 1993, WHO declared TB as a global emergency, reflecting the magnitude of the concern about the TB epidemic. It is estimated that between 2000 and 2020, nearly one billion people will be newly infected, 200 million will get sick, and 35 million will die from TB – if control measures are not significantly improved (5).

1.2 BCG

By culturing a *M. bovis* isolate from a cow, after a period of 13 years and a total of 231 passages, Calmette, a physician, and Guérin, a veterinarian, created an attenuated variant of *M. bovis*, BCG. In 1921 BCG was first tested in infants as an oral vaccine. New methods of administration were later introduced, such as intradermal, multiple puncture, and scarification (5). Since 1974, BCG vaccination has been included in the WHO Expanded Programme on Immunization (EPI), resulting in more than four billion doses injected worldwide approximately 100 million doses in children each year (6). As recently shown by sequencing, the original BCG strain lost the Regional Delusion 1 region of the *M.* TB genome in the course of the selection process. Major BCG vaccine strains in use today differ even further from the original BCG strain and from each other, with "stronger" strains (Pasteur 1173 P2, Danish 1331) being more reactogenic and, presumably, more immunogenic, than "weaker" strains (Glaxo 1077, Tokyo 172) (5).

No other widely used vaccine is as controversial as BCG. Its effects in large randomized, controlled, and case–control studies have been widely disparate, from excellent protection against TB to no protection. Most studies have demonstrated that BCG vaccines give a higher degree of protection against severe forms of TB, such as meningitis and disseminated TB, than against moderate forms of the disease (7;8). The efficacy of neonatal BCG vaccination also wanes with age, dropping in one study from 82% in children <15 years of age to 67% in 15–24-years-old, and to 20% only in persons > 24 years of age (9). Studies of evaluation of meningitis or miliary TB demonstrated that BCG can provide good protection against these serious forms of TB in young children, with reported efficacy ranges from 46–100% (5). A meta-analysis of five randomized controlled trials and eight case control studies indicated an average protection against meningitis or miliary TB of approximately 80% (10). One study showed that BCG vaccine efficacy persisted for 50 to 60 years (11). In contrast, efficacy

against pulmonary TB, which is more prevalent in adolescents and adults, range from 0–80% (5).

Efficacy of BCG vaccination also appears to vary with geographic latitude – the farther from the equator, the more efficacious the vaccine. Presumably, exposure to non-pathogenic mycobacterium, which is more intense in warm climates, induces a degree of protective immunity in an exposed population, masking potential protection from BCG (5).

Vaccination with BCG still remains the standard for TB prevention in most countries because of its efficacy in preventing life-threatening forms of TB in infants and young children, and also because it is the only vaccine available against TB. It is inexpensive (5), safe (3) and requires only one encounter with the baby (5). Thousands of lives have thus been saved through BCG vaccination over the years. Despite its shortcomings, BCG vaccination is considered a life-saving and important part of standard TB control measures in most endemic countries (12). There is also evidence that BCG provides some protection against leprosy, Four controlled trials and approximately ten observational studies have all shown some protection against leprosy, ranging from 20 to 80% (6). The randomized trial carried out in Malawi (13), cohort analyses in Venezuela (14), and case control studies in Myanmar (15) have all shown an appreciable increase in protection against leprosy with increasing numbers of doses of BCG (or BCG vaccine scars).

There is no convincing evidence that boosters are effective in preventing TB. The only controlled trial evaluating the efficacy of a BCG booster in protection of TB was carried out in Malawi, and found no evidence for protection (13). On the basis of such data the WHO has not encouraged revaccination

Most current BCG vaccines are given by the intradermal route, generally by injection with a 25 or 26 gauge needle, in the deltoid insertion region of the upper arm. Some countries (e.g. Japan, South Africa) have employed percutaneous administration with special multipuncture devices (6).

1.3 Adverse effects of BCG vaccine:

Local site lesions:

BCG is the only commonly used vaccine which induces a local ulcer. The local lesion begins as a papule. Two to four weeks after vaccination it proceeds to ulceration, and heals after several months. A scar (typically round and slightly depressed) remains in most vaccination site. Local injection site abscesses may occur, typically as a result of improper injection technique when the vaccine is given into the subcutaneous layer of the skin (6).

Keloid: Keloid formation on the scar site appears to be more common in some - e.g. African and Asian - populations than in others (6).

Local gland involvement: Axillary or cervical lymphadenitis (6).

Rare severe complications: Rare complications include lupus vulgaris, erythema nodosum, iritis, osteomyelitis and generalized BCGitis (6).

1.4 BCG vaccination scar:

BCG scar :

The scar is in the left shoulder, just below the insertion of the deltoid muscle on shoulder, normally the scar is round and 4-7 millimetres wide, but it may be up to 10 mm. It is most often slightly depressed with slightly irregular edges and smooth surface texture (16).

BCG keloid scar:

The scar is in the typical site. The scar tissue balloons upward as a mushroom-like growth with overhanging margin (16).

BCG subcutaneous nodule:

The nodule is at the injection site of BCG. It seems to appear when the BCG vaccine is wrong administrated in the subcutaneous tissue or muscles on the shoulder. Most of them are invisible on the skin, and perceptible only by palpation. Some of them are slightly outstanding or depressed from the skin. It is hard and unmovable. The size of it can not be accurately measured since it is in the subcutaneous tissue or muscles but through estimation by palpation, most of them are approximately 4-10 mm wide (personal communication with Professor Gunnar Bjune, University of Oslo).

1.5 EPI

EPI was established in 1974 with the objective of expanding immunization services beyond smallpox, with emphasis on providing these services for children in developing countries. Six vaccine-preventable diseases have been included in the EPI since its beginning: diphtheria, measles, pertussis, polio, tetanus, and TB. To protect newborns against neonatal tetanus, tetanus toxoid is administered to the mothers either during her pregnancy or prior to pregnancy during the childbearing years. Two more vaccine preventable-diseases have been addressed by the EPI during the 1990s. The World Health Assembly has set the target of including yellow fever vaccine in the EPI by 1993 in countries where this disease poses a risk. Hepatitis B vaccine is being added gradually, with the target date of 1997 for incorporation of this vaccine in the immunization programme in all countries (17). " Expanded" also mean increased coverage (18).

Considerable achievements have been made through EPI, preventing an estimated 3 million deaths per year, globally. However, there are still 3 million deaths occurring annually that could be prevented if immunization could reach every child. The Polio Eradication Initiative (PEI) continues to make progress, with polio eliminated from all but seven countries, and for most cases just in three (India, Nigeria and Pakistan). Globally, in 2002, a total of 43 countries achieved 80% coverage in all districts and 141 countries had introduced hepatitis B vaccine, with 68 countries achieving coverage of at least 80% for three doses of hepatitis B vaccine (19).

1.6 Immunization coverage

Coverage of immunization measures the proportion of the population that has received immunization service, regardless of whether this service results in a biologically effective immune status or not. There are two main methods of measuring immunization coverage worldwide. These are country-generated statistics (service data) and general community-based surveys (20).

2. The problems of immunization coverage

2.1 Varied immunization coverage

Immunization coverage of BCG is often used to reflect the proportion of children who are protected against the severe forms of TB during the first year of life, and also as an indicator of access to health services (21). The estimated immunization coverage of BCG at birth varies from less than 50% to higher than 90% from country to country in 2005 (21). Low levels of immunization can also be seen within a country, with a lower coverage in rural than urban areas.

2.2 The validity of the officially reported vaccination coverage

In terms of the validity of reported vaccination coverage (country-generated statistics), some studies show that officially reported immunization coverage was higher than that reported from population based surveys. The size of the difference increase with the reported coverage rate (22;23).

In calculation of immunization coverage based on service data the denominator is often unknown, and often set to low, leading to a false high coverage. A study from Mozambique showed uncertainties in population data because the service data which was used by province level and district level was different (24). The problem related to service data may also exist in China, where the target number of children reported (10.5-11.3 million) through the immunization system was significantly lower than the birth cohort estimated by the Chinese National Statistical Bureau (25). Thus, the immunization coverage may be overestimated.

3. The factors of importance for the immunization coverage

3.1 Accessibility to a health facility

Accessibility to a health facility for child immunization can be measured in terms of distance, time spent to reach the facility and the cost of immunization. In a study form the Philippine, it was found that the immunization coverage decreased when the distance to the immunization site was more than 0.5 km (26). In a study conducted in US it was reported that the vaccination coverage was lower for children in Detroit if parents reported problems in accessing the health care system, duo to lack of transportation as compared with those who

did not report such problems (27). However, a study from Nigeria, in an area with difficult travelling conditions, the coverage was higher than in the area with better transport facilities (28). In terms of outreaching services, it reduces the travelling distance for the mother from home to the site where the immunization services were given, and increase the accessibility of the immunization services. In many remote village the access to immunization services is difficult due to lack of outreaching services, which often affecting minorities (29).

The cost of immunization comprises many components, such as the out-of-pocket costs, transportation costs, and time costs. The time cost is lower for caregivers (usually mothers) who have fewer wage-earning opportunities. A recent cross-sectional study in a 12-county area of China provides suggestive evidence that access variables such as fee for immunization is significantly related to immunization coverage (30).

3.2 Socioeconomic status.

Socioeconomic indicators have been associated with immunization coverage. Income and wealth are important due to the fact that the service fee may impose a burden on low-income families while it could be easily afforded by high-income families. Conflicting priorities arises for working families that must meet daily survival needs. Families living in deprived socioeconomic areas may have less access to, and are less likely to pursue immunization (31).

Anther commonly used socioeconomic indicators such as education affect not only income, but can also affect attitudes and beliefs about both the efficacy of vaccines and their side effects. Low socioeconomic status and low education level have been associated with low vaccination coverage (29;32;33). However, a study from Philippine showed that there is no association between immunization coverage and educational level of mother (26).

3.3 Knowledge related to immunization and communicable disease

A significant barrier to immunization may be the family's lack of knowledge or inaccurate perception about the importance of vaccines and the seriousness of the diseases prevented by the vaccines. For example, in the US a 1993 poll showed that 47% of parents of children under five did not know that polio was contagious, 36% did not know that measles could be fatal, and 44% did not know that *H. influenza* type b was the leading cause of potentially fatal childhood meningitis (31). There are also some other studies which showed that the

community members lack knowledge about communicable diseases (34), or are afraid of side effects and of vaccine (35).

3.4 Birth order and size of family

The higher the number of offspring in a family, the greater the probability that the youngest will not be vaccinated (32;35). When the family increases in number, successive children are less likely to be vaccinated as the increasing family responsibilities demand more and more time and detract from health care decisions (31). Single parent families are especially at risk since the increased demands of family support and maintenance may impede health care decisions for the single parent who has no partner to share the responsibilities with (31).

3.5 The site of delivery

A child delivered in a hospital or clinic is more likely to be vaccinated than a child delivered at home (36;37).

4. Local conditions in Tibet Autonomous Regions (TAR)

4.1 Background on Tibet

Geography

Tibet is situated in the south-western border area of the People's Republic of China, and the south-western part of the Qinghai-Tibet Plateau. Lying at 78°25'- 99°06'E and 26°44'-36°32'N, it abuts the Xinjiang Uygur Autonomous Region in the north, Qinghai Province in the northeast, Sichuan Province in the east, and Yunnan Province in the southeast. Tibet has a 4,000 km border with the neighbouring countries of Myanmar, India, Nepal, Bhutan and Sikkim and Kashmir. Tibet has an average elevation of more than 4,000 meters. It has an area of 1.22 million square kilometres (38). Mt. Everest (Qomolangma) on the border between Tibet and Nepal is 8,850 meters high, and is the highest peak in the world

Population

By the end of 2001, the Tibet had a population of 2.63 million, of which 92.2 percent were Tibetans, 5.9 percent were Han people, while other ethnic peoples accounted for 1.9 percent (39).

Map of Tibet (40)

.

Health services

Tibet has close to 11,000 health workers, which is a relatively high proportion compared with the rest of China, and roughly equal to 10% of all government employees in Tibet, according to Tibet officials. Tibet has three large hospitals. In addition, each prefecture has at least one hospital and one Tibetan traditional medicine-based medical center. Some 80% of townships have small clinics, and the region has 3,600 "barefoot doctors" to reach out into the hinterlands, although authorities admit that it is difficult to arrange for training and salaries for the personnel in some sparsely populated areas, meaning that many of them exist in name only (41).

Because of the improvement in socioeconomic conditions and the educational status, many of the local diseases, epidemics and fatal diseases, which used to be serious threats, have declined. However, mortality at all ages in Tibet was much higher than the national average. There is a wide gap between urban and rural population in the death rates, higher in rural area. The infant mortality rate is very high in Tibet, 35.3 per 1,000 live birth by the year 2000 (42).

4.2 EPI in Tibet

EPI programme work began in the 1980s. Since 1986 children throughout the region have received Oral Polio vaccine (OPV), Diphtheria Pertussis Tetanus vaccine (DPT), BCG and Measles vaccine (MV). Since 2003 the government has added the hepatitis B vaccine (HBV) into the EPI programme (43). At the end of 2003, more than 81 sanitation and anti-epidemic stations were localized in Tibet (44). Table 1 shows the recommended childhood immunization schedule in China.

Table 1 Recommended childhood immunization schedule in China (45)

	Age										
	Birth	**1 M**	**2 M**	**3 M**	**4 M**	**5 M**	**6 M**	**8 M**	**18–24 M**	**4 Years**	**7 Years**
HBV [1]	Dose 1	Dose 2				Dose 3					
BCG [2]	Dose 1										
OPV [3]			Dose 1	Dose 2	Dose 3					Booster	
DTP [4]				Dose 1	Dose 2	Dose 3			Booster		
DT [5]											Booster
MV [6]								Dose 1			Booster

1. Hepatitis B vaccine;
2. Bacille Calmette–Guérin;
3. Oral Polio vaccine;
4. Diphtheria Pertussis Tetanus vaccine;
5. Diphtheria Tetanus vaccine;
6. Measles vaccine.

4.3 Local conditions which may affect the immunization coverage

Low educational level in rural area

According to the 1990 and 2000 censuses, the education structure of Tibet's population have changed, with an increase in the number of people with higher education and a decrease in the number of illiterates and semi-illiterates. However, there is a striking gender difference in education levels, as well as between urban and rural areas in Tibet. Women and those living in rural area being the more unfavourable (42). In year 2000, the illiteracy rate was 38% higher than the national average of 9.1%. The illiteracy rate was 40.8% in the age group 15-49 years (29.5% for male) and 53% among child bearing age women (46).

Low income

There has been a fast development in economy of the Tibet recent years (47). However, Tibet is still one of the poorest areas in China. The per capita net income of rural households in 2006 was 3587 Yuan/year in China (1 NOK ≈ 1. 2 Yuan), and 2435 Yuan /year in Tibet (48;49). It is estimated that 450,000 people in Tibet living in poverty in 2005 (50).

Geographic spread

Because of the highly decentralized population and the centralized health services, there may be a challenge for the people of Tibet to access to all kinds of health services including immunization services. A report from the U.S. Embassy Beijing in 2000 which said that one of the key difficulties for Tibet's health authorities is that Tibet's 2.51 million residents are widely scattered through 74 counties, with much of the population still very difficult to reach (41). The population density is less than 2.1 people per square kilometre (38).

High proportion of home delivery

A high number of Tibetan women give births at home. This could be due to culture/ tradition, difficult access or lack of transportation means and long distance to hospitals and health centres. There are104 hospitals in the Tibet, and all the seven prefectures and cities host mother and child health clinic. Such a health network covers all townships. However, In 2001, only 22.7 percent of childbearing women in the farming and pastoral areas gave births in hospitals (39).

5 Research question

Before the present study was planned, the idea was to find the BCG immunization coverage in the rural and semi-rural areas of Tibet. Further more to find factors which are associated with high BCG coverage. We formulated the following research question: What is the BCG immunization coverage and which factors contribute to the BCG coverage in a semi-rural and rural area of Lhasa District?

6 Objective

The objective of the present study is to estimate the BCG immunization coverage and to investigate the association between the BCG coverage and the selected factors in children less than two years of age in semi-rural and rural area of Lhasa District.

CHAPTER II

Methodology

1. Research design

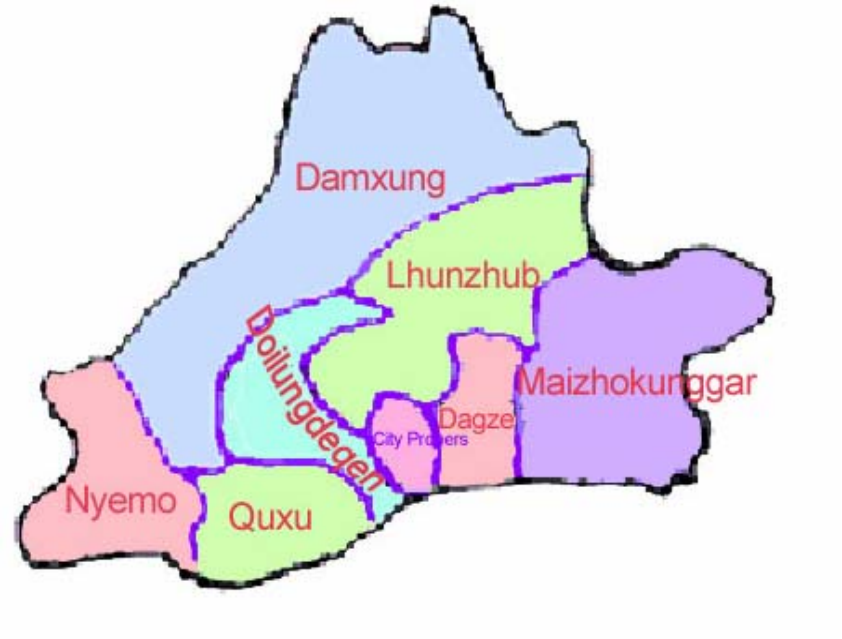
This is a population based cross sectional study.

2. Study area

The study has been conducted in the semi-rural Quxu County and the rural Damxung County of Lhasa District of Tibet.

Lhasa, the capital of Tibet, has a history of more than 1,300 years. It is the political, economic, cultural and transport centre of the region. Lhasa District covers an area of close to 30,000 square km. It has a city centre of 544 square km and a population of 400,000; approximately 140,000 live in the city. Located at the bottom of a small basin surrounded by mountains, Lhasa has an elevation of 3,650 meters (51). Lhasa District is located in the middle part of Tibet.

Map of Lhasa District (51)



Damxung County

Damxung means "selected pasture" in Tibetan language. Damxung County is located in the northwest of Lhasa District and close to the Lhamo Namco Holy Lake. It covers an area of 10,036 square kilometres with an average altitude of 4,200 meters. Damxung County is an

mountainous area with two major mountain chains Gangdise Mountains and Nyainqentanglha Mountain. The Nyainqentanglha Mountain crosses through the whole county (52). It is the most remote county in Lhasa District. There is a distance of 170 kilometres from Lhasa city to the county. The county consists of six *xiang* (area) and two towns with a total population of 41,918. Each *xiang* consists of several villages and each village also consists of several groups. There is a total of 29 villages in the whole county (53;54). Animal husbandry is booming in the area. Most people in this county are herdsman. They raise yaks, sheep, goats and horses (52).

Quxu County

Quxu means "water stream" in Tibetan language. Quxu County is located southwest of Lhasa District and at the lower reaches of the Lhasa River. There is a distance of 60 kilometres from Lhasa city to the county. Quxu County is closer to Lhasa city than Damxung County (55). It covers an area of 1623 square kilometres. It consists of five *xiang* and one town with a total population of 29,690.There is a total of 17 villages in the five *xiang* and one town (56). Agriculture is the main activity in the county. Most of people in this county are farmers.

3. Population

The total population of Damxung County is 41,918 in and that of the Quxu County.is 29,690 The birth rate was 17.4 per1000 in Tibet 2004 (57). The number of newborns during one year is estimated to be 716 in Dumxung County and 516 in Quxu County. Thus, the total number of children less than two years of age will be approximately 1432 in Damxung County and 1032 in Quxu County.

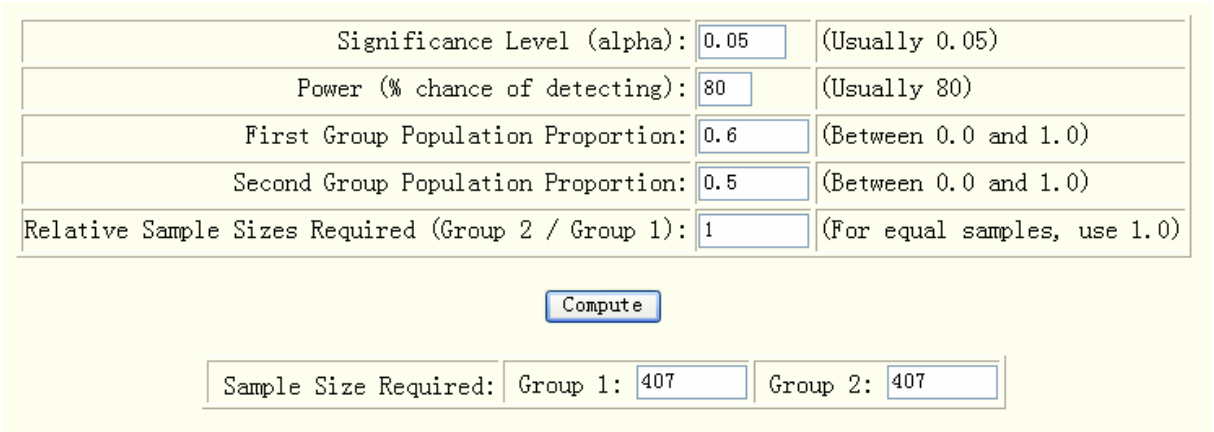
4. Inclusion criteria

1. The study population consists of children who were less than two years of age at the time of data collection.
2. The children must have been born in Lhasa District and residing in Quxu County or Damxung County.

5. Sample size calculation

When we planned the study, we wanted to detect a difference in BCG immunization coverage between the rural and semi-rural areas with a power of 0.80 (beta) and a significance level of 0.05 (alpha). Our assumption was that around 50% were vaccinated and approximately 10% higher in the semi-rural area than in the rural. Due to unexpected differences between the two areas in health service factors and socio-demographic factors, we had to do separate analysis for the two areas. Thus, we have lost power to detect differences when we split the two samples, with a risk of type II error, failure to detect a real difference/association. We planned to include 500 individuals in each of the two counties separately. Higher than calculated (407). Thus, giving some room for refusals and sub-group analysis.

Original sample size calculation (JavaStat user) (58).



6. Sampling method

Quxu County (semi-rural area)

It was difficult to find 500 children in Quxu County. Therefore we selected all the children less than two years of age. A total number of 484 children were therefore invited from Quxu County. Thirty-two children were not in their home when we did the household survey and were therefore not included.

Damxung County (rural area)

In the Damxung County we use the multi-stage sampling method. The following five stages sampling procure was preformed.

1. We made a list of name of villages and towns and randomly selected four *xiangs* and two towns out of six *xiangs* and two towns. Since the Gongtang Xiang and Dangqu town have been looked upon as one unit in the local area, we included them as one area. Thus we selected five areas and aimed at selecting 100 children in each.
2. We made a list of group names and randomly selected ten groups in each of the five selected *xiang* or town. Thus the ten children were selected in each of the ten groups in five *xiang* or town. We went to the centre of each of the ten selected groups in each *xiang* or town, spun a coke bottle and randomly selected one direction to walk for start recruiting children.
3. Then we randomly selected one out of all houses in that direction as the first house to visit. The second house is the one closest to the front door of the first household, until ten children less than two years of age were found. When we couldn't get adequate number of children in one direction. We went to centre again and randomly select another direction by spinning the bottle, until we got ten children from the group.
4. In every *xiang* we did not manage to get the sufficient number of children from ten groups. Therefore we randomly select several other groups according to the lacking number of children and did the same procedure as before. Until we achieved 100 children within one selected town or *xiang*. Finally 69 groups were included in our study. A total of 63 children were not in their home when we visited.
5. When we finished the study and checked the children's birthday by solar calendar from the information we got using lunar calendar from mother, we found that four of the children were several days preponderate older than 24 months, so we excluded them from the sample. Thus, 496 children less than two years of age were included from Damxung County.

7. Data collection

7.1 Recruitment of the field workers

Two field workers were recruited from the staff at Tibet University of Medical College. They were all men, able to speak and write the Tibetan and Chinese Languages and had a medical

background. They were all trained to conduct the data collection, in particular to understand the meaning of each of the questions in the questionnaire.

7.2 The data collection instruments

7.2.1 Questionnaire (enclosed see appendix)

We used an interviewer-administered structured questionnaire with a few open-ended questions. Four groups of questions were addressed:

A) Variables related to the socio-demographic characteristic of household.

B) Variables related to the knowledge and belief of mothers related to the immunization and TB.

C) Variables related to the health services.

D) Immunization history.

Twenty days before data collection, a pre-test of questionnaire was carried out in a group of 10 mothers with children less than two years of age in three different groups of Quxu County. The respondents were asked to report if any of the questions were unclear. Based on the results of the pre-test, changes were made on the structure of the questionnaire before data collection began.

The questionnaire was also checked by experienced health workers in immunization from the county EPI centre to check for clarity, its applicability and acceptability in the local context. Some local authorities were also asked to comment on the questions about socio-demographic characteristic of household in local contexts, thereafter variable comments were incorporated.

7.2.2 Immunization card:

The children's immunization card was checked and recorded afterwards the mother recalled the children's immunization history. The information on the immunization card was not included and analysed in this thesis.

7.2.3 Clinical examination of scars:

Data from the clinical examination was used for determing the BCG coverage and the association between coverage and selected health services factors. The BCG vaccination scar

was checked by the field worker after finishing the interview and after checking the immunization card. The BCG scar was checked in both right and left shoulder since the local health worker injected the BCG mainly in left but sometimes right side. The biggest scar was measured and recorded when there were more than one scar. When there were both the BCG keloid scar and BCG scar, the first one was measured. When there was neither BCG keloid scar nor BCG scar, the both shoulders were checked for BCG subcutaneous nodule at the injection site.

7.3 Data collection procedures:

The survey was carried out between 7th of September to 11th of December of 2006.

Data collection was not done continuously; we went to Quxu County twice and once to Damxung County. The first time we went to Quxu County for data collection, most of the farmers were busy in harvesting. At that time we collected data on some children, and then of the end of November, two month later, we went again to collect the remaining data.

Practical approach:

(1) The leader of a Xiang Clinic was contacted in advance. One of the health workers from the Xiang Clinic or a government worker of the village who was familiar with local area lead the way and helped us to find the centre of each group to spin a coke bottle. Three times only it was difficult to count the numbers of house in one direction to randomly select the first household. When we came to each selected household the local helper introduced us to the family.

(2) The key informants for our research were the mother of children. Before we started to ask the questions, we informed them briefly about the aim of the study and asked them if they were willing of participate. Fortunately, no one refused.

(3) The children's BCG status was recorded through recalling the children's immunization history from the mother at first, and than by checking the immunization card, and at the end checking the BCG vaccination scar of children.

(4) Completed questionnaires were reviewed each evening by the researchers.

8. Data analysis and statistical methods

The questionnaires were coded and data entered to laptop computer and analysed using the SPSS 12.0 version.

Univariate analyses were used to describe the study population and to estimate immunization coverage. Bevariate analysis were used for identify factors associated with BCG coverage. Logistic regression was used in order to control for possible confounding factors in associations between the risk factors and immunization status. Level of significance was set to $P \leq 0.05$ and/ or 95% confidence interval.

9. Ethical considerations

Official permission to start this study was granted by the Ministry of Health of TAR. The researcher (Cirenyangzong) was in charge of carrying out the data collection and field work according to local standards and legislation. Two researcher assistants were trained and assisted through the data collection. Before asking the questions to mothers, the aims and objectives of the study were explained to the invited mothers. They were reassured about the confidentiality of data and informed about our research objectives and that they could refuse to participate and withdraw from the study at any time without any consequences for themselves. The Norwegian Ethical Committee for Medical Research also approved the study.

CHAPTER III

RESULTS

1. Result of BCG

1.1 The BCG coverage

The tree kinds of scar of BCG were clinically checked on the children' shoulders.Table 4 presents the BCG coverage by different types of scars. The prevalence of BCG immunization scar was higher in Quxu County (77%) than in Damxung County (61%) (P<0.01).

Based on reports from mothers, 76% of the children in Quxu County and 56% of the children in Damxung County have been vaccinated with BCG which is slightly lower than based on clinical examination, but not statistically significantly different from each other; Quxu County (P=0.3) and Damxung County (P=0.06). When we treat the clinical examination of BCG vaccination scar as the gold standard, the sensitivity and the specificity of the mothers' reports were 92% (CI, 89%-95%) and 64% (CI, 55%-73%) in Quxu County, 69% (CI, 64%-74%) and 51% (CI, 44%-58%) in Damxung County.

Table 2 Distribution of BCG coverage (clinical examination) and mothers reports in semi-rural (Quxu County) and rural (Damxung County) Tibet

	Mothers reports of BCG vaccination					
	Semi-rural (Quxu County) N(%)			Rural (Damxung County) N(%)		
	Yes	No	Don't know	Yes	No	Don't know
BCG scar	314 (93)	14 (4)	11 (3)	177 (72)	49 (20)	20 (8)
BCG subcutaneous nodule	19 (86)	3 (14)	0 (0)	31 (57)	22 (41)	1 (2)
BCG keloid scar	7 (100)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)
No	38 (33)	74 (64)	4 (3)	67 (34)	99 (51)	29 (15)

1.2 Timing of BCG vaccination (age of the child)

According to the mothers' report, among children who were vaccinated by BCG, 54% and 21% of children in the Quxu County and Damxung County respectively were vaccinated at correct time just after birth. It was significantly more common in Quxu County than in Damxung County to be vaccinated at correct time (p<0.01). Only one and five mothers reported that they did not remember the BCG vaccine time in Quxu County and Damxung County respectively.

1.3 The site of being vaccinated by BCG vaccine

Based on the mothers report significantly more children in Quxu County (56%) than in Damxung County (19%), were vaccinated at the health centre ($P < 0.01$). One of the mother in Quxu County and 12 in Damxung County did not remember where their children were vaccinated.

2. The socio-demographic factors

The characteristics of children

Among the 484 children in Quxu County and 496 children in Danxung County examined, girls constituted 55% and 47% respectively.

The average age of the children from Quxu County was 12 months (SD +/- 6.7), and of 13 months (SD +/- 6.7) in Danxung County. There were only five children from Quxu County and one from Damxung County who were half Tibetan and half Chinese Han. All the others were Tibetan.

The characteristics of mothers

Twenty-six (5%) of the mothers in Quxu County and 23 (5%) of those in Damxung County were less than 20 years old, while 42 (9%) and 70 (14%) respectively were older than 35 years. All were Tibetan.

In terms of the marital status, 86% and 81% of the mothers in Quxu and in Damxung County, respectively were living together with their husband.

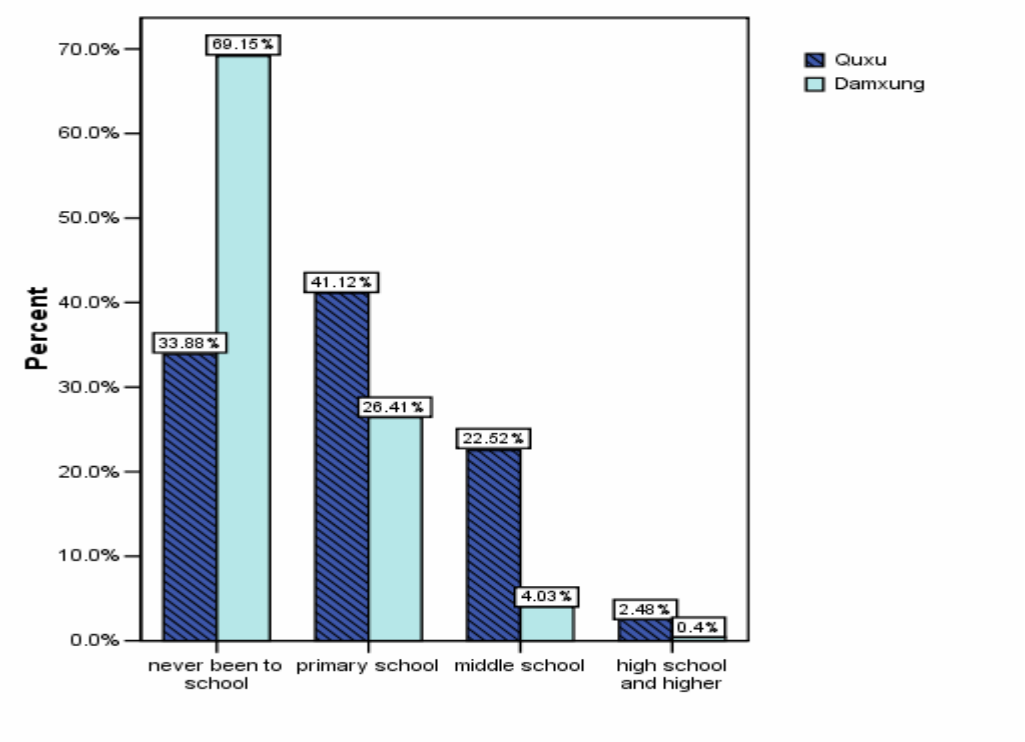
Only seven percent and tree percent of those in Quxu and Damxung County respectively had income themselves (government worker, part time jobs, business). Table 3 present the occupation of the mothers.

Table 3 Mother's occupation in the semi-rural (Quxu County) and rural (Damxung County) Tibet

Mother's present occupation	Quxu county		Damxung county	
	N	%	N	%
Farmer	380	78.5	1	0.2
Herdsman	12	2.5	86	17.3
Housewife	57	11.8	396	79.8
Government employed	10	2.0	1	0.2
Part time job	24	5.0	11	2.3
Business man	1	0.2	1	0.2

Figure 1 shows the educational level of the mothers, indicating that 34% from Quxu County and 69% from Damxung County had never been at school. Forty-one percent and 26% from Quxu and Damxung County respectively had primary school only.

Figure 1 Education level of the mothers in semi-rural (Quxu County) and rural (Damxung County) Tibet



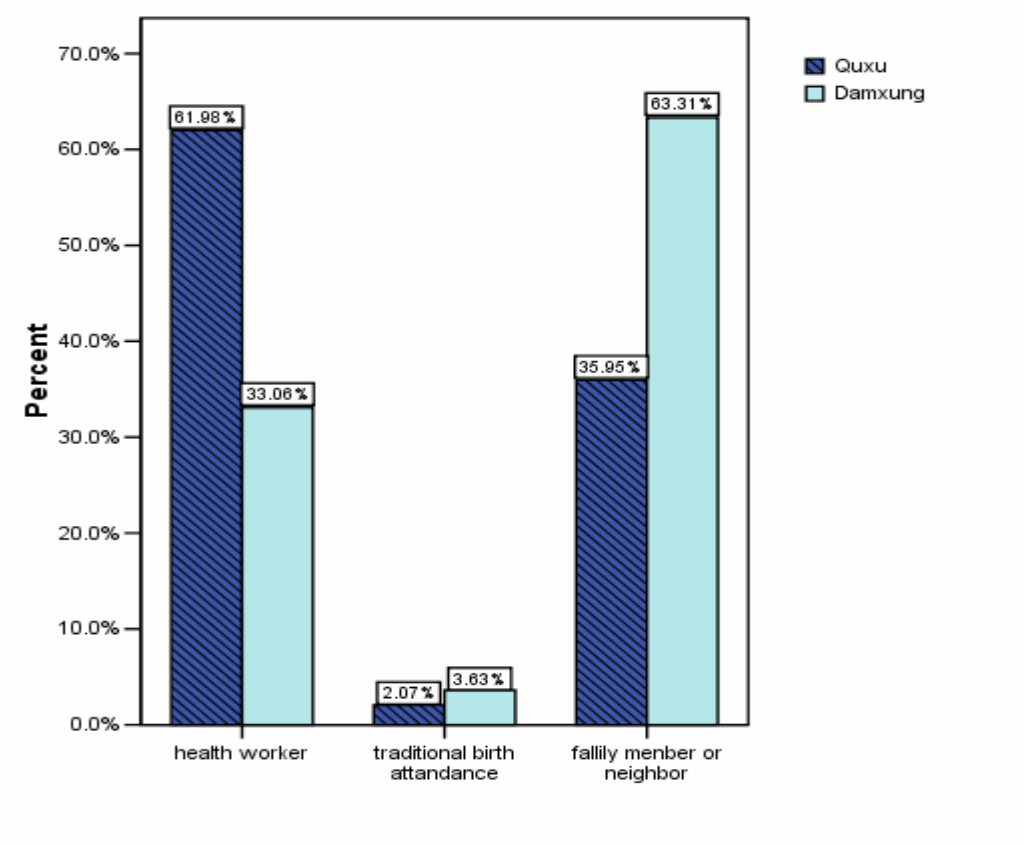
3. Health services factors

Location of delivery and delivery assistance

The home delivery rate was significantly higher in Damxung County (82%) than Quxu County (33%) (P<0.001).

Figure 2 shows the different source of help to the mothers during delivery. Sixty-two percent of the mothers were assisted by a health worker in Quxu County, compared to 33% in Danxung County. No one reported that she delivered alone without any kind of assistance.

Figur 2 Distribution of personal assisting at deliveries in semi rural (Quxu County) and rural (Damxung County) Tibet



Accessibility of the health facility with immunization site

Table 4 presents the time needed for walking from the home to the nearest health facility. Most mothers 82% from Damxung County had to walk for more than one hour to reach the nearest health facility compared with 41% in Quxu County (p<0.01). Almost 50% of mothers from Damxung County had to walk more than three hours.

Table 4 Distribution of walking time from home to nearest health facility and the use of vehicle

	Quxu county		Damxung county	
	Walking time N (%)[1]	Ever taking vehicle N (%)[2]	Walking time N (%)[1]	Ever taking vehicle N (%)[2]
Less than half hour	147 (30.4)	22 (15.0)	44 (8.9)	11 (25.0)
Half hour to one hour	140 (28.9)	48 (34.3)	46 (9.3)	28 (60.9)
One hour to three hours	129 (26.7)	61 (47.3)	169 (34.1)	118 (69.8)
More than tree hours	68 (14.0)	64 (94.1)	237 (47.8)	219 (92.4)

[1] The percent is based on all participants in the county;

[2] The percent is based on the participants in the different sub-groups of walking time.

Forty-two percent of the mothers in Quxu County and 76% from Damxung County had ever taken a vehicle from home to the nearest health facility. In terms of the cost of transportation, 18% in Quxu County and 33% percent in Damxung County respectively out of those who had ever taken vehicle from the home to nearest health facility reported that it was expensive.

Twenty percent of mothers in Quxu County and 19% of mothers in Damxung County reported they knew the working hours of nearest health facility. However, Only two percent in Quxu County and five percent in Damxung County did report the same working hours of nearest health facility as health workers.

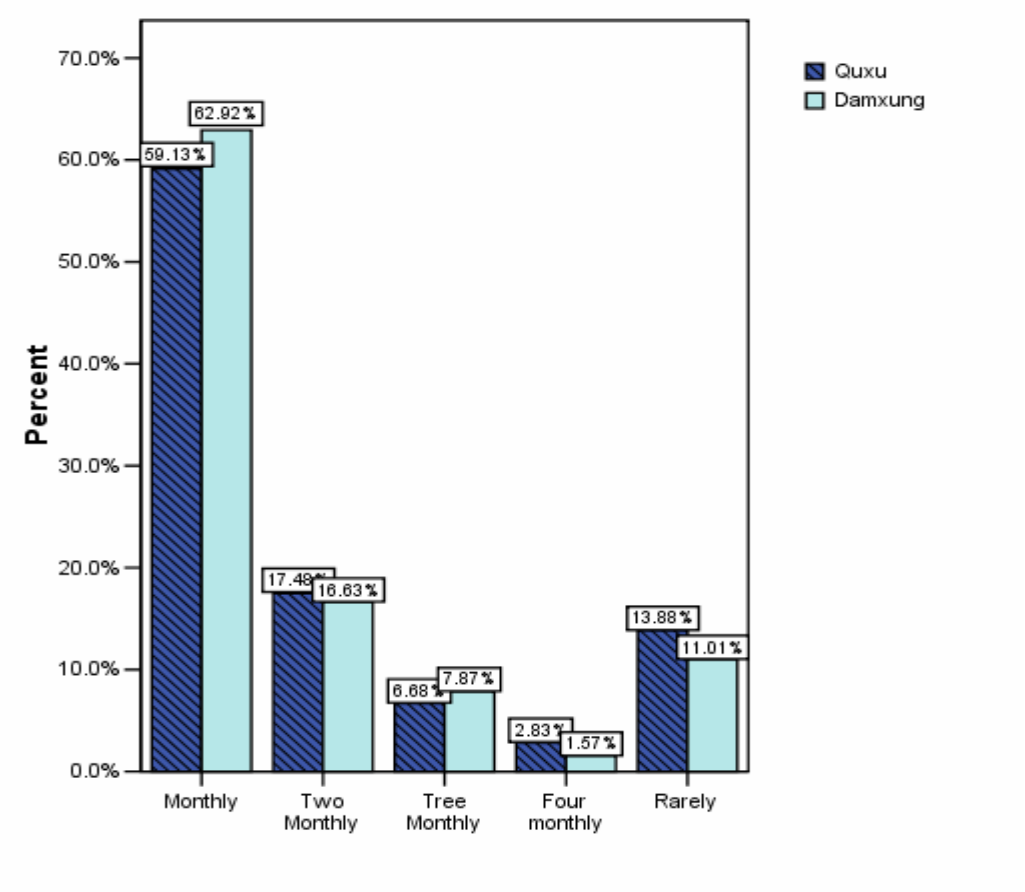
Fifty-nine percent of all mothers from Quxu County and 24% from Damxung County reported that their children had ever been vaccinated in health facility at least once.

Outreaching services

Eighty-one percent of the mothers in Quxu County and 91% in Damxung County reported that there were immunization outreaching services available.

Among the mothers who reported that there were immunization outreaching services available, all except three of the mothers in Quxu County and five in Damxung County did not remember the frequency of the outreaching services. Figure 3 present distribution of frequency of outreaching services reported by mothers respectively in semi-rural (Quxu County) and rural (Damxung County).

Figure 3 Distribution of frequency of outreaching services reported by mothers in semi-rural (Quxu County) and rural (Damxung County) Tibet



4. The association between BCG coverage and selected factors

In the present thesis, a focus is made on the association between selected health services factors and the immunization coverage

Walking time and cost of transportation from home to the health facility

Table 7 shows bivariate associations between walking time, the cost of transportation from home to the nearest health facility and BCG coverage. In Quxu County high BCG coverage was significantly associated with short walking time from home to nearest health facility (OR=3.0; CI, 2.0-4.7). High BCG coverage was associated with inexpensive cost of transportation (OR=5.7; CI, 2.3-13.8). In Damxung County these two factors were not associated with the BCG coverage.

Delivery and birth assistant

Table 8 shows the bivariate associations between location of delivery, type of delivery assistance and BCG coverage. In Quxu County there was a statistically significantly association between high BCG coverage and hospital delivery (OR=1.9; CI, 1.2-2.9), and delivery assistance (health worker) (OR=2.2; CI, 1.4-3.5), However, in Damxung County these two factors were not associated with the BCG coverage.

Services of health facility

Table 5 shows the bivariate associations between services of health facility and BCG coverage. In Quxu County there was a statistically significant association between ever being vaccinated in health facility and high BCG coverage (OR=3.0; CI, 2.0-4.5). Knowing the working hours of health facility was, however, not associated with BCG coverage. In Damxung County none of these two factors were associated with BCG coverage.

Outreaching services

Table 6 shows bivariate associations between outreaching services and BCG coverage. In Quxu County there was a statistically significant association between high BCG coverage and outreaching services (OR=11.2; CI, 6.7-18.8), and knowing the time of the next outreaching services (OR=2.4; CI, 1.4-4.3). The association was significantly regarding high. Similar findings were reported from Damxung County in table 10.

Adjusted associations between BCG coverage and selected factors

Table 9 and Table 10 present adjusted association between BCG coverage and health service factors in Quxu County and Damxung County. Only those factors which were significantly in bivariate analysis were included in multivariate analysis. In Quxu County we adjusted the association between the walking time from home to nearest health facility and the BCG coverage for education level and marital status. For the other analysis in table 9, we additional adjusted for the walking time from home to nearest health facility. In Damxung County we adjusted all analysis for education level and marital status (table 10). In adjusted analysis, none of the variables lost their statistically significance, and the point estimate remained more or less, as compared with bivariate analysis.

Table 5 Bivariate associations between walking time, the cost of transportation from home to nearest health facility and BCG coverage in semi-rural (Quxu County) and rural (Damxung County) Tibet

	Quxu county							Damxung county						
	N	Immunization status				P	OR	N	Immunization status				P	OR
		Yes		No					Yes		No			
		N	%	N	%		(95% CI)		N	%	N	%		(95% CI)
Walking time from home to the health facility														
≤ 1h	287	242	84.3	45	15.7	0.00	3.0 (2.0-4.7)	90	54	60.0	36	40.0	0.91	1.0 (0.6-1.5)
> 1h	197	126	64.0	71	36.0		1	406	247	60.8	159	39.2		1
The cost of transportation														
Free	36	18	50.0	18	50.0	0.40	0.7 (0.3-1.7)	174	107	61.5	67	38.5	0.51	1.2 (0.7-1.9)
Inexpensive	124	111	89.5	13	10.5	0.00	5.7 (2.3-13.8)	79	41	51.9	38	48.1	0.42	0.8 (0.4-1.4)
Expensive	35	21	60.0	14	40.0		1	123	71	57.7	52	42.3		1

Table 6 Bivariate associations between location of delivery, type pf delivery assistance and BCG coverage in semi-rural (Quxu County) and rural (Damxung County), Tibet

	Quxu county							Damxung county						
	Immunization status							Immunization status						
	N	Yes		No		P	OR	N	Yes		No		P	OR
		N	%	N	%		(95% CI)		N	%	N	%		(95% CI)
Delivery assistance														
Health worker	300	245	81.7	55	18.3	0.00	2.2 (1.4-3.5)	164	107	65.2	57	34.8	0.17	1.0 (0.6-1.5)
Others	184	123	66.8	61	33.2		1	332	194	58.4	138	41.6		1
Location of delivery														
Hospital	275	223	81.1	52	18.9	0.00	1.9 (1.2-2.9)	91	53	58.2	38	41.8	0.63	0.9 (0.6-1.4)
Home	209	145	69.4	64	30.6		1	405	248	61.2	157	38.8		1

Table 7 Bivariate associations between services of health facility and BCG coverage in semi-rural (Quxu County) and rural (Damxung County) Tibet

	Quxu county							Damxung county						
	Immunization status							Immunization status						
	N	Yes		No		P	OR	N	Yes		No		P	OR
		N	%	N	%		(95% CI)		N	%	N	%		(95% CI)
Ever vaccinated in health facility														
Yes	284	239	84.2	45	15.8	0.00	3.0 (2.0-4.5)	121	76	62.8	45	37.2	0.60	1.1 (0.7-1.7)
No	200	129	64.5	71	35.5		1	375	225	60.0	150	40.0		1
Knowing working hours of health facility														
Yes	95	72	75.8	23	24.2	1.00	1.0 (0.6-1.7)	93	53	57.0	40	43.0	0.48	0.8 (0.5-1.3)
No	389	296	76.1	93	23.9		1	403	248	61.5	155	38.5		1

Table 8 Bivariate associations between outreaching services and BCG coverage in semi-rural (Quxu County) and rural (Damxung County) Tibet

	Quxu county							Damxung county						
	Immunization status							Immunization status						
	N	Yes		No		P	OR	N	Yes		No		P	OR
		N	%	N	%		(95% CI)		N	%	N	%		(95% CI)
Outreaching services														
Yes	392	336	85.7	56	14.3	0.00	11.2 (6.7-18.8)	450	286	63.6	164	36.4	0.00	3.6 (1.9-6.9)
No	92	32	34.8	60	65.2		1	46	15	32,6	31	67.4		1
Frequency of outreaching services														
Monthly	230	209	90.9	21	9.1	0.00	7.4 (3.7-14.9)	280	203	72.5	77	27.5	0.00	5.4 (2.8-10.4)
Once per two-four months	105	94	89.5	11	10.5	0.00	6.3 (2.8-14.5)	116	66	56.9	50	43.1	0.00	2.7 (1.4-5.5)
Rarely	54	31	57.4	23	42.6		1	49	16	32.7	33	67.3		1
Knowing the time of next outreaching services														
Yes	119	103	86.6	16	13.4	0.00	2.4 (1.4-4.3)	103	80	77.7	23	22.3	0.00	2.7 (1.6-4.5)
No	365	265	72.6	100	27.4		1	393	221	56.2	172	43.8		1

Table 9 The association between BCG coverage and selected health services factors in Quxu County

	Quxu county	
	High BCG coverage	
	p-value	OR[3] (95% CI)
Walking time from home to the health facility [1]		
≤ 1h	0.00	3.1 (2.0-4.8)
> 1h		1
The cost of transportation [2]		
Free	0.33	0.6 (0.2-1.6)
Inexpensive	0.00	4.6 (1.8-11.6)
Expensive		1
Delivery assistance[2]		
Health worker	0.00	2.0 (1.3-3.1)
Others		1
Location of delivery [2]		
Hospital	0.01	1.8 (1.1-2.7)
Home		1
Ever vaccinated in health facility [2]		
Yes	0.00	2.5 (1.6-4.0)
No		1
Outreaching services [2]		
Yes	0.00	12.0 (7.0-20.6)
No		1
Frequency of outreaching services [2]		
Monthly	0.00	6.2 (3.0-13.1)
Once per two-four months	0.00	5.7 (2.4-13.5)
Rarely		1
Knowing the time of next outreaching services [2]		
Yes	0.03	2.0 (1.1-3.6)
No		1

[1] Adjusted for educational level of mothers and marital status of mothers;

[2] Adjusted for the walking time from home to nearest health facility educational level and marital status of mothers;

[3] Adjusted odds ratios.

Table 10 The association between BCG coverage and selected health services factors in Damxung County

	Quxu county	
	BCG immunization	
	p-value	OR[1] (95% CI)
Outreaching services [2]		
Yes	0.00	3.8 (2.0-7.2)
No		1
Frequency of outreaching services [2]		
Monthly	0.00	5.7 (3.0-11.0)
Once per two-four months	0.00	2.7 (1.3-5.5)
Rarely		1
Knowing the time of next outreaching services [2]		
Yes	0.00	2.7 (1.6-4.5)
No		1

[1] Adjusted odds ratios;

[2] Adjusted for educational level of mother and marital status of mothers.

CHAPTER IV

DISCUSSION AND CONCLUSIONS

This study shows that the BCG coverage is significantly higher in the semi-rural area Quxu County (77%), than in the rural area Damxung County (61%). The study further shows that health service factors including short walking time from home to nearest health facility, low cost of transportation, ever vaccinated in health facility, location of birth (hospitals), type of delivery assistance (health workers), receiving outreaching services and high frequency of it, knowing the time of next outreaching services are associated with high BCG coverage in Quxu County. In Damxung County, however, only receiving outreaching services, high frequency of it and knowing the time of next outreaching services were significantly associated with high BCG coverage.

1 Methodological discussion:

1.1 The sample size and type II error

The sample size calculation was based on analysis of difference in BCG coverage between factors of interested in the whole sample. Because of several differences between the two counties, we decided to do separate analysis. This has certainly reduced the power of detecting statistically significant differences at 95% -level in separate analysis of data from the two counties. It means that we may have done type II errors, it failed to detect real differences.

1.2 Systematic errors

In epidemiological observational studies there are always possibilities for systematic errors. The main errors to consider are: selection problems, information problems and confounding.

Selection problems

Selection is a general problem in observational epidemiological studies, difference between invitees and the target population or that non-responders differ from the responders on risk factors and / or outcomes.

Selection bias could be caused by a skewness in the children who participate in our study and those who did not. However, nobody refuse to participate in the study. The sampling method which we used in our study in Damxung County was multi-stage sampling method. The

selection of *xiangs* and groups (stages) was done randomly. However, when we selected the household from the each group, the only randomly selected household was the first household of each direction; the second household and so on were chosen as we selected them as the closest household (door to door) to that determined in the previous step. The iterations are repeated until the required number of households is surveyed. This method has been used in EPI sampling method and is regarded to give an acceptable accuracy of the true level of the of vaccination coverage in population. The EPI method rarely overestimates the actual proportion and is often within 10% points of true value (60). No designs are perfect. It means by using this sampling method, there could be a small bias in the estimate of the BCG coverage and it will be slightly underestimate. Only 32 children in Quxu County and 63 children in Damxung County were not in their home when we invited them. Most of the children who were not in their own home were sent to their relatives. It is not likely that there were differences between children who were in their home and not. However, if it is so that the children who were sent to relatives have parents who are less able to take care of their children. It is likely that the vaccination coverage is lower in this group. Thus, we may have done a slightly overestimate of the vaccination coverage.

Information problems

Misclassification is defined as erroneous classification of an individual, a value, or an attribute into a category other than that to which it should be assigned. The probability of misclassification may be similar in all study groups (non-differential misclassification) or may vary between groups (differential misclassification) (61).

Non-differential misclassification occurs when the probability of misclassification of exposure is the same for cases and non-cases (61). Non differential misclassification occurs in most epidemiological studies, but the question is which of the associations under study may have been distorted towards the null value. For example when we analysing the association between ever vaccinated in health facility and BCG coverage, mothers report erroneously that children have ever been vaccinated in health facility, and some report erroneously that have not been vaccinated in health facility, this errors will tend to weakened the association. When errors in the classification of the exposure or outcome are randomly distributed, any prevalence estimates will be correct. But the association measures will, however, be affected. Any association tend to be “washed out”. It usually

biases the association towards the null value of 1. Hence, non-differential misclassification tends to produce "false negative" association (61).

Differential misclassification occurs when the misclassification of exposure is different in diseased and non-diseased persons, or when the misclassification of disease is different in exposed and non-exposed persons. This can bias the observed association either toward or away from the null value (61). In the study the mothers have to recall some information for example the walking time to health facility. It is likely that the recall problems are not different in those who have got the BCG and those who have not. But it may be so that the mothers who have not given their child BCG vaccination may report longer walking time to the health facility (to reduce bad impression). This will lead to a bias away from the null value, it lead too strong association between walking time to health facility and BCG coverage. And in terms of the children's immunization history which recalled from their mothers, current evidence on the quality of data from maternal recall is not straightforward. Some results suggest low accuracy of mothers' recall of vaccinations (62;63).Others, however, indicate high levels of accuracy, with between 83% and 98% of vaccinations recalled correctly by mothers (64;65).

Confounding

A confounding factor is an independent variable that distorts the association between another independent variable and the problem under study. For a variable to be a confounder, it must be associated with the first risk factor and be an independent risk factor for the problem understudy. Thus, the confounding factor is associated with both the independent and dependent variable. On the other hand: a variable, which is merely a link between the risk factor and the outcome, is not a potential confounder. Background variables such as age, education, economic status are notorious confounders, as they are related to many aspects of life (66). In analysis of association between BCG coverage and health services factors, we have treated the marital status and education level of mother and the distance form the home to the nearest health facility as confounding factors in Quxu County, and the first and second in Damxung County. These factors are associated with the other health service factors understudy and are independent risk factors for the low BCG coverage. However, the adjustment did not change the associations.

2 Discussion of results

2.1 BCG coverage

The goal for immunization coverage in China for the year 1995 was set at 85% for the 1:3:3:1 vaccine series (one dose of BCG, three doses of DTP, three doses of OPV and one dose of MV). However, based on data from the 2004 EPI Coverage Survey in China, 10 (32%) provinces, which were among the poorest did not reach the target of national coverage >85 percent with the "four EPI vaccines" including BCG, DPT, OPV, and MV (43). The results from the present study are in line with the previous finding. The BCG immunization coverage in the two poor areas under study is 77% in Quxu County and 61% in Damxung County, which is lower than the goal of 85%.

Wrong administration of the BCG vaccine was apparent in both areas. BCG vaccines should be given by the intradermal route, but we detected several BCG subcutaneous nodules which may be caused by subcutaneous or muscle injection of BCG vaccine. In a cases report of seven children from China of such wrong administration, it was described that 1-7 days after wrong injection of BCG, the injection site was swollen and a subcutaneous nodule appeared about 1.0cm ×1.0cm× 1.0cm. Through anti-tuberculosis chemotherapy it disappeared after 1-4 months (67). But if this kind of result of wrong injection method was not recognized by parents and was not treated, the nodules in subcutaneous tissue or muscles of injection site could be remaining at least for a longer period. Five percent of children from Quxu County and 11% from Damxung County have BCG subcutaneous nodules. This might be an underestimate because we checked the BCG subcutaneous nodule only when there was no BCG scar or BCG keloid scar on the children's shoulder. In addition, some children have got BCG vaccine more than once because there was more than one scar on some children's shoulder. This may increase the likelihood that there are more undetected subcutaneous nodules. Health workers in the village explained that it is often difficult to stop children from moving and crying when the children were given the vaccination, and the injection was set too deep. Thus, the poor injection skill of health workers could be the reason of wrong administration of BCG vaccine. In Damxung and Quxu County, most of the health workers who are responsible for the immunization work have low education level and lack training.

A study conducted in 2004 in children under tree years of age in four district of Tibet excluding Lhasa District, showed the a BCG coverage of 94.58% (68). Also another study

from seven districts of the Tibet including Lhasa District conducted in 2004 in the children who were born between the January 1st 1999, to the June 30th of 2002 showed a BCG coverage of 90.91% (by clinical examination of scar) in Lhasa District (69). These results conflicts with the present findings.

The BCG coverage in the present study is also lower than reports of BCG coverage from some other part of China, Nanning (95%) (70), Beijing (97%) (71). The finding from Damxung County is more similar with the reports from Dongkou County (66.3%) (72) and Hengnan County (65.06%) (73). and with reports from some other developing counties, Philippines (66%) (74), Turkey (50.8%) (75).

2.2 The time and site of being vaccinated by BCG vaccine

Within the children who have got BCG vaccine, 54% and 21% in the Quxu County and Damxung County respectively received BCG at the correct vaccination time just after birth. A study from other provinces of China showed that the delayed injection of vaccine was highest in poor rural and mountainous areas (45). This is in accordance with present results, that the injection rate of BCG at the birth was significantly lower in the most rural and mountainous area Damxung County, as compared with Quxu County only.

Within the children who have received BCG vaccine, 56% and 19% in the Quxu County and Damxung County respectively received it at health centre. This large difference between Quxu County and Damxung County could reflect that outreaching services are important when it is difficult to access or long distance to health facility.

2.3 Health service factors

In the present study we have investigated associations between selected health services factors and BCG coverage.

Walking time and cost of transportation from home to the health facility

The variables which were used to assess the accessibility to the health services are the walking time from home to nearest health facility and the cost of transportation. Forty one percent of mothers from Quxu County and 82% from Damxung County had to walk more

than one hour to reach the nearest health facility. During the data collection some mothers reported that even when they were ill, they seldom went to the health facility to see a doctor because it was too far away, and thus they are not that interested in bringing their children for vaccination. It is previously reported that the immunization coverage decrease with increasing distance to the health facility (26). This is accordance with findings from Quxu County where we found the association between the short walking time and high BCG coverage. The children whose mother had to walk less than one hour had 3.1 times higher odds for being BCG vaccinated than those children whose mother needed to walk more than one hour.

Among those who had ever taken a vehicle from the home to the nearest health facility respectively 18% in Quxu County and 33% in Damxung County thought that the transportation fee was expensive. It is previously reported difficulty of transportation could increase the barriers to the immunization (27). The present results from Quxu County support the previous findings, and shows that the children who had inexpensive transportation had 4.6 times higher odds of being BCG vaccinated than the children who had expensive transportation. However, free transportation was not associate with the high BCG coverage, this is probably because understanding of free transportation is may not be valid. The persons who reported free transportation include those who have a car themselves, or persons who have no money but could get a lift, or the persons who may be sent by the village government by in a car together. The transportation may be regarded as free for all theses groups. In other words, people understand this question differently.

We did not either find an association between BCG coverage and waking time or cost of transportation in Damxung County. It may be because the immunization services in Damxung County mainly depended on the outreaching services

Delivery and birth assistant

Most children from Damxung County were born at home, in contrast to Quxu County almost a third of children were born at home. Two thirds of mothers were assisted by a health worker during delivery in Quxu County, while in Damxung County only one third had such assistance. Home delivery and delivery without health worker assistance decreased the odds for associated being BCG vaccination both in Quxu County. No such association was found in Damxung County. The results from Damxung County was different from previous studies

which have reported that children delivered in a hospital or clinic are more likely to be vaccinated than children delivered at home (36;37).

Services of health facility

Some mothers reported that they knew the working hours of health facility, but most often it did not overlap with the reports from the health workers. Thus, the mothers would need to visit the facility another time. We did not find any association between knowing the working hours of the nearest health facility and BCG coverage in either of the two counties.

Fifty-nine percent of mothers from Quxu County and 24% of the mothers from Damxung County have at least once taken their children for vaccination in a health facility. It seems that the utilization rate of the health facility was not high, at least not for the aspect of immunization. Especially in Damxung County it was very low. The children who have ever been vaccinated in a health facility had 2.5 times higher odds for being BCG vaccinated than those who had never been vaccinated in a health facility in Quxu County. The awareness of immunization among those mothers who had ever taken their children for vaccination in a health facility might be higher than those who did not. Or the mother who had ever brought their children to be vaccinated had more easy access to a health facility. But we did not find such association in Damxung County. It may also be because the immunization services in Damxung County mainly depended on the outreaching services.

Outreaching services

Tibet has low population density, often with long distance to a health facility in rural area. It is a big barrier if mothers have to travel for long distance and pay the transportation fee to bring children for vaccination to a health facility. Outreaching services is a good way to reduce the travelling distance for mothers from home to the site where the immunization services are given, and thus increase the accessibility of the immunization services. The immunization outreaching services rate was high in both counties, but more developed in Damxung County than in Quxu County. It was positively associated with BCG coverage in both two counties. The association was stronger in Quxu County than in Damxung County. It was communicated from the health workers that it is hard to travel a long distance to provide outreaching services. A health worker told us that it was difficult to ride the bicycle for the whole day to vaccinate the seven children, and he had some problems with his knee. Most health worker mentioned that the biggest problem for outreaching services are lack of vehicle.

Eighty-one percent of mothers in Damxung County and 91% in Quxu County received the outreaching services. In Damxung County the BCG coverage was higher when frequency of the outreaching services was monthly as compared with once every two to four months. When it was even more rare (twice or once per year) the BCG coverage decreased further. However, in Quxu County the BCG coverage decreased only when the frequency of outreaching services was rarely (twice or once per year).

Mother knowing the time of next outreaching services was positively associated with the immunization status in both two counties. Those mothers who knew the time of next outreaching services might be more aware about the immunization than those who did not know.

CONCLUSION

BCG coverage was significantly higher in semi-rural area Quxu County (77%) than in the rural-area of Damxung County (61%). Health service factors including short walking time from home to nearest health facility, low cost of transportation, location of birth (hospitals), type of delivery assistance (health workers), ever vaccinated in health facility, receiving outreaching services and high frequency of it, knowing the time of next outreaching services were associated with the high BCG immunization coverage of children in Quxu County. In Damxung County the health services factors which reached statistical significance were receiving outreaching services, high the frequency of it and knowing the time of next outreaching services.

We detected a number of subcutaneous nodules indicates that health workers lack training and have poor injection skills. Further research about the cause of such wrong practice and the clinical and immune impact of the BCG subcutaneous nodule is required.

In order to increase the immunization coverage in the rural and semi-rural area of Tibet, the frequency of the outreaching services should be increased, as well as more polite information about the time of such services should be given. To establish more health facilities to reduce the travel distance for the mothers or to set up transportation free of charge or to a low cost would be helpful. To encourage the mothers to give birth at hospitals would also increase immunization coverage. However, for many families in Tibet, this will be too expensive. At

the same time, birth at hospitals would help in decreasing the mother and child mortality in Tibet.

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APPENDIX

Questionnaire for mothers with children less than two years of old

Questionnaire (BCG coverage and obstacles which exist in process of getting BCG vaccine)

No.□□□□□□□□

Name of village:

Number of group:

Main questions of demographic characteristic

1. How old are your children? _____ months

2. The gender of your child? □

   1. Boy
   2. Girl

3. When this child was born _____.

4. How old are you?_____ years.

5. What ethnic group do you belong to? □

   1. Tibetan
   2. Chinese Han
   3. Moslem Han
   4. Moslem Tibetan
   5. Others_____.

6. What language do you speak in your family? □

   1. Tibetan
   2. Chinese
   3. Tibetan and Chinese
   4. Other_____.

Main questions of social economic status

1. What is main source of income in your family?

_____.

2. What is your occupation? _____.

3. Number of people in your family? □

1. Four and Less than four
2. Five- seven
3. More than seven

4. Which kind of house for dwelling? □

1. House made of concrete
2. House made of mud brick
3. House made of stone
4. Others_____.

5. How many rooms do you have in you in you household? _____.

6. Did you get any support from government to build the house?

1. Yes
2. No

If yes, how much money or other resource did government support you_____.

7. How many domestic animals do your family have? Cows _____. , Yaks _____. , Sheeps and goats_____. , Horses_____.

Main questions of available health services

1. Where did you give birth to your child who is less than two years of age? □

1. Hospital
2. Home
3. Others _____.

2. Who assisted you to deliver the children less than two years of old for you? □

1. Doctor
2. Nurse
3. Tradition birth attendant
4. Your own family members
5. Others _____.

3. Do you know the opening hours for the EPI facility? ☐

1. Yes
2. No

If yes when is it?_____.

4. We will check the opening hours of EPI centre which is reported by EPI centre _____.

5. Have you ever taken your children to EPI facility to be vaccinated? ☐

1. Yes
2. No

If your child has ever been vaccinated, please answer questions 6 and 7

6. Did the health worker tell you about vaccination before they vaccinate your child? ☐

1. Yes
2. No
3. Don't remember

7. How about the cost of given one vaccination? ☐

1. Unaffordable
2. Affordable but expensive
3. Inexpensive
4. Free of charge

8. How long does it take from home to the nearest EPI facility by walking? ☐

1. Less than 30 minutes
2. 31-60minutes
3. More than 1 hr
4. Not possible by walking (more than three hours)

9. What kind of transportation have you ever taken when you went to the EPI facility? ☐

1. Tractor
2. Gharry
3. Motorcycle
4. Cars
5. Others_____.

10. How about the cost of transportation to go to the health facility? ☐

1. Unaffordable
2. Affordable but expensive
3. Inexpensive
4. Free

11. Is there any outreaching service of immunization available in your village? □

1. Yes
2. No

12. If it is available, how often it is □

1. Monthly
2. Two monthly
3. Tree monthly
4. Four monthly
5. Rarely (twice or once per year)

13. Next date for outreaching service of immunization _____.

14. We will check the date of next outreaching services of immunization which is reported by health worker_____.

The main question of BCG vaccine and Tuberculosis

1. Have you ever heard about BCG vaccine? □

1. Yes
2. No

If question one is yes, please answer question 2and 3

2. Do you know what illness is prevented by BCG vaccine?_____.

_____.

3. Where did you get information about BCG vaccine? □

1. Mass media
2. Health workers
3. At the health centre
4. From other mothers
5. Other resources_____.

4. Do you know any side effects of vaccination? ☐

1. Yes
2. No

5. If yes, please describe it

_____,

_____,

_____.

4. What do you know about Tuberculosis?_____.

_____.

5. Has child ever been given a BCG vaccination -that is, first vaccine which was injected in the left or right shoulder and a papule or a papule ulcerates appeared afterwards, it might be followed by a scar? ☐

1. Yes
2. No
3. Doesn't know

6. When your child received BCG vaccine? ☐

1. Just after birth
2. Later

7. Where did your children receive BCG vaccine? ☐

1. EPI facility
2. In your own village
3. Others_____.

8. Do you have a card where vaccinations are written down? ☐

1. Yes
2. Not available
3. Never had a card
4. Lost the card
5. Don't know

9. Record information exactly as it appears on vaccination card

Vaccination	Day	Month	Year
BCG			
OPV1			
OPV2			
OPV3			
DTP1			
DTP2			
DTP3			
MV 1			
MV2			
MV3			
HBV1			
HBV2			
HBV3			

10. Check scar in left or right shoulder just below the insertion of the deltoid of child (normally the scar is round and 4-7 millimetres wide, but it may be up to 10 mm. It is most often slightly depressed with slightly irregular edges and smooth surface texture) and record it:

wide _____.

Shape _____.

Surface and edge _____.

If it is keloid scar (the scar tissue balloons upward as a mushroom-like growth with overhanging margin) records it

Wide _____.

Shape _____.

Surface and edge _____.

Check the subcutaneous nodule at the site for BCG injection

Shape_____.

Wide_____.

Main questions of education and belief

1. What is your education level? □

   1. Primary school
   2. Middle school
   3. High school
   4. University or higher
   5. Never been to school

2. Do you believe vaccination can prevent some diseases? □

   1. Yes
   2. No
   3. Don't know

Question 4 to 6 will be conduct as a small interview

3. If you think it is not important to take your child to getting vaccine, can you explain?

_____,

_____,

_____.

4. If you think it is importation to take your child to getting vaccine, can you explain?

_____,

_____,

_____.

5. If you have ever taken your child to get vaccine, what kind of problems have you ever met when you take you child to get vaccine?

_____,

_____,

_____,

_____.

6. If you have never taken your child to get vaccine, why not?

_____,

_____,

_____,

_____.

The question below might be sensitive to informants, we should ask them carefully

1. What is the income per year in your family? □

   1. Less than 1500 Yuan
   2. 1500- 3000 Yuan
   3. 3000.4999 Yuan
   4. 5000-8000 Yuan
   5. More than 8000 Yuan

2. How many children do you have? □

   1. 1-3
   2. 4-5
   3. More than 5

3. Marital status: □

   1. Single
   2. Married
   3. Divorced
   4. Widowed
   5. Living separately with husband

Thank you very much for your collaboration

Interviewer's name:_____.

Date:_____. Time:_____.