

表 1. チェンライ県の結核登録(1995 年より 28,945 登録、1985 年より 36,650 登録)

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	Total
Total	1,555	1,627	1,840	2,031	2,133	2,075	2,105	2,000	2,157	2,322	2,544	2,227	2,231	2,098	28,945
Thai - lowland	1,231	1,306	1,445	1,631	1,727	1,605	1,615	1,497	1,644	1,789	1,854	1,577	1,612	1,512	22,045
HIV Negative	355	361	381	413	531	558	568	524	572	675	912	877	929	917	8,573
HIV Positive	469	594	752	838	809	764	741	650	714	767	740	596	584	479	9,497
HIV Unknown	407	351	312	380	387	283	306	323	358	347	202	104	99	116	3,975
Thai - hilltribe	266	261	267	300	295	320	344	348	327	333	357	339	310	325	4,392
HIV Negative	82	107	134	128	145	165	161	188	166	165	217	223	232	242	2,355
HIV Positive	24	36	37	59	54	63	70	70	63	62	98	76	52	66	830
HIV Unknown	160	118	96	113	96	92	113	90	98	106	42	40	26	17	1,207
Non-Thai	266	261	267	300	295	320	344	348	327	333	357	339	310	325	4,392
HIV Negative	6	16	70	30	55	62	64	77	83	108	173	219	202	174	1,339
HIV Positive	4	4	11	19	13	23	24	23	31	24	76	61	74	56	443
HIV Unknown	48	40	47	51	43	65	58	55	72	68	84	31	33	31	726
Thai - lowland with HIV negative															
No have CID	350	357	378	399	515	549	553	489	378	391	66	29	29	24	4,507
Have CID	5	4	3	14	16	9	15	35	194	284	846	848	900	893	4,066
Thai - lowland with HIV positive															
No have CID	464	590	749	833	799	747	719	598	422	294	27	14	9	10	6,275
Have CID	5	4	3	5	10	17	22	52	292	473	713	582	575	469	3,222
Thai - lowland with HIV unknown															
No have CID	405	350	310	377	384	281	302	312	248	213	26	4	5	1	3,218
Have CID	2	1	2	3	3	2	4	11	110	134	176	100	94	115	757
Thai - hilltribe with HIV negative															
No have CID	80	106	130	123	138	161	154	172	126	116	52	44	51	66	1,519
Have CID	2	1	4	5	7	4	7	16	40	49	165	179	181	176	836
Thai - hilltribe with HIV positive															
No have CID	22	36	37	58	54	61	69	63	53	27	11	19	8	10	528
Have CID	2	0	0	1	0	2	1	7	10	35	87	57	44	56	302
Thai - hilltribe with HIV unknown															
No have CID	157	118	96	111	95	90	110	85	77	81	14	8	11	6	1,059
Have CID	3	0	0	2	1	2	3	5	21	25	28	32	15	11	148
Non-Thai with HIV negative															
No have CID	6	16	70	30	55	62	64	77	83	107	167	212	195	172	1,316
Have CID	0	0	0	0	0	0	0	0	0	1	6	7	7	2	23
Non-Thai with HIV positive															
No have CID	4	4	11	19	13	23	24	23	31	24	61	54	67	51	409
Have CID	0	0	0	0	0	0	0	0	0	0	15	7	7	5	34
Non-Thai with HIV unknown															
No have CID	48	40	47	51	43	65	58	55	72	68	81	31	31	30	720
Have CID	0	0	0	0	0	0	0	0	0	0	3	0	2	1	6

表 2

HIV 陰性結核患者に対する Provider Initiated
Counseling & Testing (PICT) の評価-HIV 陰性
患者の HIV 陽転化に関連した因子分析

表2 HIV陰性結核患者に対するProvider Initiated Counseling & Testing (Pilot)の評価-HIV陰性患者のHIV陽転化に関連した因子分析

Characteristics	HIV status	% converter	%	Total	Odds ratios	95%CI	p. Sig. at alpha 0.05
Gender							
Female	4,705	98.9%	54	4,759	1.00		
Male	10,130	98.9%	108	10,238	0.93	(0.67-1.3)	0.660 NS.
Age (years)							
n	14,818		162	14,980	0.99	(0.98-1)	<0.001 Sig
minimum	0		1	0			
maximum	104		96	104			
median	47		39	47			
mean	47		42	47			
SD	19		17	18			
Age (years)							
<=15	442	99.5%	2	444	1.00		
16-25	1,584	98.8%	20	1,604	2.79	(0.65-11.99)	0.168 NS.
26-35	2,239	97.3%	48	2,287	4.74	(1.15-19.57)	0.032 Sig
36-45	2,624	98.7%	34	2,658	2.86	(0.69-11.97)	0.149 NS.
46-55	2,678	98.3%	24	2,702	1.98	(0.47-8.41)	0.354 NS.
56-65	2,407	98.3%	17	2,424	1.56	(0.36-6.78)	0.552 NS.
66+	2,844	99.4%	17	2,861	1.32	(0.31-5.74)	0.710 NS.
Race							
Thai	10,442	98.7%	134	10,576	1.00		
Hilltribe	2,800	98.2%	24	2,824	0.67	(0.44-1.04)	0.070 NS.
Non-Thai	1,593	99.7%	4	1,597	0.20	(0.08-0.53)	0.001 Sig
Race							
Thai	10,442	98.7%	134	10,576	1.00		
Hilltribe/ Non-Thai	4,393	99.4%	28	4,421	0.50	(0.34-0.75)	0.001 Sig
Marital status							
Single	1,179	99.4%	7	1,186	1.00		
Married	4,340	98.1%	40	4,380	1.55	(0.7-3.48)	0.285 NS.
Divorced	352	98.0%	4	356	1.91	(0.56-6.58)	0.303 NS.
Widow	804	99.1%	7	811	1.47	(0.52-4.2)	0.475 NS.
Missing	8,160	96.7%	104	8,264	-	(-)	<0.001 Sig
Education							
Uneducated	1,822	98.3%	12	1,834	1.00		
Primary school or lower	2,341	99.2%	20	2,361	1.30	(0.64-2.67)	0.478 NS.
High school	632	99.4%	4	636	0.96	(0.31-3)	0.945 NS.
Higher	201	99.0%	2	203	1.51	(0.34-6.8)	0.591 NS.
Missing	9,839	98.8%	124	9,963	-	(-)	<0.001 Sig
Occupation							
01 Agriculture	1,874	99.0%	19	1,893	1.00		
02 Government/ Enterprise	92	98.6%	1	93	1.07	(0.15-8.1)	0.946 NS.
03 Labor	2,029	98.3%	15	2,044	0.73	(0.37-1.44)	0.363 NS.
04 Merchant	174	99.4%	1	175	0.57	(0.08-4.26)	0.581 NS.
05 Home take care	770	98.6%	11	781	1.41	(0.67-2.98)	0.368 NS.
06 Student	182	99.5%	1	183	0.54	(0.08-4.08)	0.552 NS.
07 Soldier/ Policeman	8	100.0%	0	8	N/A	(-)	<0.001 Sig
08 Fisherman	1	100.0%	0	1	N/A	(-)	<0.001 Sig
09 Teacher	12	100.0%	0	12	N/A	(-)	<0.001 Sig
10 Prisoner	77	97.5%	2	79	2.56	(0.59-11.2)	0.211 NS.
11 Business	14	100.0%	0	14	N/A	(-)	<0.001 Sig
12 Employee	14	100.0%	0	14	N/A	(-)	<0.001 Sig
13 Unemployed	380	99.5%	2	382	0.52	(0.13-2.24)	0.379 NS.
14 Monk/ Nun	53	100.0%	0	53	N/A	(-)	<0.001 Sig
15 Others	92	98.3%	1	93	1.07	(0.15-8.1)	0.946 NS.
99 Missing	9,063	98.6%	109	9,172	-	(-)	<0.001 Sig
TB site and sputum AFB result							
Pulmonary TB with sputum AFB positive	8,408	99.1%	77	8,485	1.00		
Pulmonary TB with sputum AFB negative	3,962	98.3%	46	4,010	1.32	(0.93-1.91)	0.130 NS.
Pulmonary TB with sputum AFB unknown	362	98.4%	6	368	1.81	(0.79-4.19)	0.165 NS.
Extra-pulmonary TB	2,103	98.0%	31	2,134	1.61	(1.06-2.45)	0.026 Sig
TB site and sputum AFB result							
Pulmonary TB with sputum AFB positive	8,408	99.1%	77	8,485	1.00		
Other	6,427	98.7%	85	6,512	1.44	(1.06-1.97)	0.020 Sig
TB site							
Pulmonary TB only	12,347	99.1%	117	12,464	1.00		
Extra-pulmonary TB only	2,103	98.5%	31	2,134	1.56	(1.05-2.32)	0.030 Sig
Both	385	96.5%	14	399	3.84	(2.19-6.75)	<0.001 Sig
Chest X-ray							
Cavity	6,925	98.1%	63	6,988	1.00		
Non cavity	7,231	99.9%	62	7,313	1.25	(0.9-1.74)	0.151 NS.
Not done	679	97.6%	17	696	-	(-)	<0.001 Sig
Patient type							
1 New	11,595	99.0%	114	11,709	1.00		
2 Relapse	307	96.4%	5	312	1.66	(0.68-4.09)	0.273 NS.
3 Treatment after failure	227	94.7%	3	230	1.34	(0.43-4.27)	0.615 NS.
4 Chronic	135	98.5%	2	137	1.51	(0.37-6.17)	0.568 NS.
5 Treatment after default	539	98.5%	6	547	1.51	(0.74-3.11)	0.264 NS.
6 Other	436	99.3%	3	439	0.70	(0.23-2.22)	0.543 NS.
7 Transfer in	1,596	98.3%	27	1,623	1.72	(1.13-2.63)	0.012 Sig
Year of TB start treatment							
1990	268	99.3%	2	270	1.00		
1991	279	99.5%	1	280	0.48	(0.05-5.33)	0.550 NS.
1992	248	98.8%	1	250	0.34	(0.05-5.98)	0.514 NS.
1993	252	98.8%	3	255	1.60	(0.27-9.63)	0.611 NS.
1994	316	97.5%	8	324	3.39	(0.72-16.12)	0.124 NS.
1995	368	97.6%	9	377	3.28	(0.71-15.3)	0.131 NS.
1996	538	98.7%	7	545	1.74	(0.35-8.46)	0.491 NS.
1997	545	98.0%	11	557	2.70	(0.6-12.27)	0.198 NS.
1998	572	99.0%	6	578	1.41	(0.29-7.01)	0.678 NS.
1999	712	99.6%	3	715	0.66	(0.1-3.4)	0.632 NS.
2000	772	99.4%	5	777	0.87	(0.17-4.5)	0.866 NS.
2001	785	99.0%	6	793	1.37	(0.29-6.48)	0.695 NS.
2002	703	98.5%	11	714	2.10	(0.47-9.53)	0.338 NS.
2003	823	98.4%	13	836	2.12	(0.46-9.44)	0.326 NS.
2004	867	98.4%	36	1,003	4.99	(1.2-20.86)	0.028 Sig
2005	1,291	98.3%	22	1,313	2.28	(0.54-9.77)	0.266 NS.
2006	1,304	99.5%	7	1,311	0.72	(0.15-3.49)	0.682 NS.
2007	1,325	99.5%	2	1,327	0.20	(0.03-1.49)	0.111 NS.
2008	1,401	98.9%	3	1,404	0.29	(0.05-1.73)	0.173 NS.
2009	1,364	99.7%	4	1,368	0.39	(0.08-2.16)	0.282 NS.
Prisoner							
Yes	301	98.7%	4	305	1.00		
no	14,534	98.9%	158	14,692	0.82	(0.31-2.23)	0.694 NS.
Treatment outcome							
1 Cured	4,203	99.5%	31	4,234	1.00		
2 Completed	4,961	98.0%	49	5,010	1.34	(0.86-2.11)	0.205 NS.
3 Defaulted	1,906	98.6%	28	1,934	1.99	(1.2-3.33)	0.009 Sig
4 Failed	371	100.0%	0	371	N/A	(-)	<0.001 Sig
5 Died	1,711	97.7%	40	1,751	3.17	(1.98-5.09)	<0.001 Sig
6 Change diagnosis	360	99.4%	2	362	0.75	(0.18-3.16)	0.699 NS.
7 Transfer out	599	96.4%	10	609	2.26	(1.11-4.65)	0.026 Sig
DM							
No	5,185	99.7%	17	5,202	1.00		
Yes	349	99.1%	3	352	2.62	(0.77-8.99)	0.125 NS.
Missing	9,301	98.6%	142	9,443	-	(-)	<0.001 Sig
IDU							
No	5,379	99.6%	22	5,401	1.00		
Yes	163	98.1%	1	164	1.50	(0.21-11.2)	0.693 NS.
Missing	9,293	98.5%	139	9,432	-	(-)	<0.001 Sig
BCC scar							
No	3,026	99.5%	11	3,037	1.00		
Yes	1,697	98.4%	11	1,708	1.78	(0.78-4.13)	0.176 NS.
Missing	10,112	96.6%	140	10,252	-	(-)	<0.001 Sig

表 3

タイ北部チェンライ県全域の死亡統計
(県レベルでの直接入力個票データ)

Year	Age	Total	<1	1	2	3	4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	>85
2006	Total	5,938	0	18	5	8	8	12	37	82	92	114	190	285	321	403	450	419	421	587	779	705	488	466
	Male	3,403	0	8	5	3	5	5	20	67	72	71	118	194	224	272	296	262	235	309	401	373	230	205
	Female	2,535	0	10	0	5	3	7	17	15	20	43	72	91	97	131	154	157	186	278	378	332	258	261
2005	Total	7,962	0	11	4	9	3	38	42	135	125	221	331	424	487	492	570	514	550	771	963	882	695	612
	Male	4,602	0	6	1	5	2	17	26	103	92	135	209	286	338	327	368	321	341	419	523	462	343	237
	Female	3,360	0	5	3	4	1	21	16	32	33	86	122	138	149	165	202	193	209	352	440	420	352	375
2004	Total	7,465	0	11	7	10	4	48	50	96	136	260	410	417	447	509	485	470	519	699	843	779	631	575
	Male	4,364	0	7	2	5	2	25	35	81	101	138	240	294	299	365	308	284	309	378	474	411	318	255
	Female	3,101	0	4	5	5	2	23	15	15	35	122	170	123	148	144	177	186	210	321	369	368	313	320
2003	Total	8,729	15	18	9	15	11	88	65	133	177	386	638	621	520	542	556	488	597	787	930	848	623	632
	Male	5,028	7	12	7	9	5	43	40	106	122	195	384	426	357	354	329	312	347	436	505	447	300	271
	Female	3,701	8	6	2	6	6	45	25	27	55	191	254	195	163	188	227	176	250	351	425	401	323	361
2002	Total	9,626	17	24	17	11	22	111	59	127	243	595	818	718	661	630	527	530	671	853	935	786	612	632
	Male	5,709	12	15	11	7	13	67	32	100	157	293	527	488	448	424	341	342	410	479	509	433	305	277
	Female	3,917	5	9	6	4	9	44	27	27	86	302	291	230	213	206	186	188	261	374	426	353	307	355
2001	Total	10,384	58	18	22	12	19	125	42	123	309	817	1,053	883	684	607	552	503	689	876	877	816	614	641
	Male	6,034	39	10	9	5	9	67	19	91	167	430	678	597	491	404	347	299	387	463	480	416	307	292
	Female	4,350	19	8	13	7	10	58	23	32	142	387	375	286	193	203	205	204	302	413	397	400	307	349
2000	Total	9,816	45	28	15	19	20	111	37	118	329	989	1,020	832	686	554	445	491	638	818	814	682	522	583
	Male	5,649	31	12	10	15	12	73	16	81	162	508	683	574	447	351	269	281	342	442	429	395	263	242
	Female	4,167	14	16	5	4	8	38	21	37	167	481	337	258	239	203	176	210	296	376	385	287	259	341
1999	Total	11,589	70	37	25	20	35	128	49	140	429	1,222	1,382	994	771	597	504	578	726	915	899	783	565	710
	Male	6,966	37	15	15	11	16	70	27	111	225	707	979	711	529	391	326	354	424	497	497	415	277	324
	Female	4,623	33	22	10	9	19	58	22	29	204	515	403	283	242	206	178	224	302	418	402	368	288	386
1998	Total	11,990	81	35	31	25	29	110	38	154	583	1,415	1,475	999	758	559	526	567	814	874	870	778	590	660
	Male	7,356	43	14	12	14	18	68	19	107	285	857	1,127	772	554	355	338	350	480	481	492	417	281	257
	Female	4,634	38	21	19	11	11	42	19	47	298	558	348	227	204	204	188	217	334	393	378	361	309	403
1997	Total	7,983	82	30	25	19	20	57	35	98	428	1,019	914	689	489	354	328	420	523	566	535	533	385	423
	Male	4,987	43	12	14	9	11	37	20	74	210	710	701	543	351	243	213	252	302	319	286	280	175	176
	Female	2,996	39	18	11	10	9	20	15	24	218	309	213	146	138	111	115	168	221	247	249	253	210	247
1996	Total	9,335	90	36	22	25	23	54	47	142	616	1,158	1,052	748	590	427	354	491	628	703	624	567	424	500
	Male	5,966	52	20	17	15	14	36	31	110	337	867	838	585	430	281	245	311	355	391	328	297	189	208
	Female	3,369	38	16	5	10	9	18	16	32	279	291	214	163	160	146	109	180	273	312	296	270	235	292
1995	Total	10,328	73	55	23	20	9	73	37	182	644	1,163	1,104	779	614	481	455	566	791	766	755	626	492	526
	Male	6,770	41	29	15	11	4	43	21	129	408	918	924	630	465	326	305	366	459	433	416	319	230	226
	Female	3,558	32	26	8	9	5	30	16	53	236	245	180	149	149	155	150	200	332	333	339	307	262	300
1994	Total	7,929	50	51	21	21	12	45	39	147	460	771	663	538	399	329	398	483	628	637	615	518	451	520
	Male	5,098	32	27	9	11	4	28	23	90	315	629	564	440	304	231	262	290	366	353	335	276	210	220
	Female	2,831	18	24	12	10	8	17	16	57	145	142	99	98	95	98	136	193	262	284	280	242	241	300
1993	Total	5,869	55	28	19	14	14	39	32	132	283	378	366	325	265	232	306	447	566	552	497	427	396	409
	Male	3,612	24	13	10	7	7	26	14	98	215	311	300	264	193	146	171	270	317	329	268	218	188	167
	Female	2,257	31	15	9	7	7	13	18	34	68	67	66	61	72	86	135	177	249	223	229	209	208	242

表4

検体バンク (Specimen banking) のリスト
between 19 February 2002 and 03 May 2010

表4 検体バンク(Specimen banking)のリスト
between 19 February 2002 and 03 May 2010

Characteristic	Study										Total
	Clinical study	Daycare	DST	TB genetic		Household contact		TB recurrent			
				TB	non TB	TB	non TB	TB	non TB		
Total (specimens)	75	1,574	799	1,145	1,481	14	59	1,156	956	7,259	
Collection year											
2002	0	220	48	136	269	10	44	33	0	760	
2003	0	707	55	276	471	4	15	157	0	1,685	
2004	0	647	62	336	487	0	0	193	0	1,725	
2005	5	0	43	218	249	0	0	160	0	675	
2006	11	0	58	64	4	0	0	187	0	324	
2007	50	0	107	96	1	0	0	143	256	653	
2008	9	0	181	19	0	0	0	115	319	643	
2009	0	0	168	0	0	0	0	132	381	681	
2010	0	0	77	0	0	0	0	36	0	113	
Gender											
female	46	961	218	421	790	5	34	327	420	3,222	
male	29	612	578	721	689	9	25	829	536	4,028	
Pt. type for TB cases											
New			700	882		9		732		2,323	
Relapse			16	26		0		186		228	
Failure			14	3		0		147		164	
Chronic			9	1		0		59		69	
TAD			38	37		1		11		87	
Other			8	15		0		0		23	
Transfer in			7	18		0		0		25	
HIV status											
Negative	0	0	377	622	399	10	2	861	5	2,276	
Positive	38	6	160	388	32	0	0	91	2	717	
Unknown	37	1,568	262	135	1,050	4	57	204	949	4,266	
Age (years-old)											
n			404	1,101	1,422			175			
minimum			7	2	6			10			
maximum			104	99	99			78			
median			47	35	55			40			
mean			49.3	37.2	54.6			41.4			
SD			16.7	14.9	15.1			15.1			
Race											
Thai	0	6	308	432	445	5	14	28	4	1,242	
Aka	0	0	0	0	4	0	0	0	0	4	
Chinese	0	0	7	5	0	0	0	1	0	13	
Eko/Aka	0	0	57	31	0	0	0	5	0	93	
Hilltribe	0	0	17	21	35	1	7	5	0	86	
Kariang/Yang	0	0	1	0	0	0	0	0	0	1	
Laos	0	0	9	3	0	0	0	0	0	12	
Lau	0	0	0	0	3	0	0	0	0	3	
Leesor	0	0	3	0	0	0	0	0	0	3	
Lue	0	0	2	2	0	0	0	0	0	4	
Maw/Mong	0	0	1	0	0	0	0	0	0	1	
Muser/Lahu	0	0	35	18	0	0	0	2	0	55	
Musur	0	0	0	0	8	0	0	0	0	8	
ThaiYai	0	0	1	13	0	0	0	0	0	14	
ThaiYai/Lue	0	0	4	6	0	0	0	2	0	12	
Thailua	0	0	0	0	1	0	0	0	0	1	
Thaiyai	0	0	0	0	4	0	0	0	0	4	
Yao	0	0	3	1	0	0	0	0	0	4	
Myanmar	0	0	16	7	3	0	0	1	0	27	
Myanmar/Thailua	0	0	0	0	2	0	0	0	0	2	
Myanmar ThaiYai	0	0	3	3	0	0	0	0	0	6	
Other	0	0	1	0	1	0	0	0	0	2	
Missing	75	1,568	331	603	975	8	38	1,112	952	5,662	

添付資料 1

英文概念書

**Development of the field laboratory system to study
systemically the HIV and TB interventions**

Title:

Development of the field laboratory system to study systemically the HIV and TB interventions

Background

While HAART (Highly Active Anti-Retroviral Therapy) for HIV patients and World Health Organization (WHO) recommended DOTS strategies for TB control have contributed to reduce the burden of HIV and TB, these strategies are not adequate to eliminate these diseases. Development of tackling co-morbidity of HIV/AIDS and TB is one of the priorities in global health. We need further research and development to identify the breakthrough strategy. We had planned to set up the “Field laboratory (population-based monitoring system with specimen bank)” to combine the international collaborative research to maximize the utilization of the field site in Thailand and Japanese research and development capacity.

For example, Thai NIH has experienced the collaboration in HIV research of Thailand and Japan. Thai Researchers found the HLA-B*3505 allele associated with the nevirapine-induced skin adverse drug reactions in HIV-infected Thai patients [1]. Then, the team with the University Tokyo is now initiating the field trial for the field trial to use the genotype based drug prescription for better HIV treatment and control. Since we have difficulties to treating HIV-infected TB patients due to drug interactions (nevirapine-refampicin) and immune reconstruction syndrome [2], researches can identify personalized biomarkers for treating these cases, which can assist TB control in HIV-infected population.

Therefore, we propose to set up the population-based field laboratory system in Chiang Rai province which has been initiated by Dr. Pathom Sawanpanyalert, director of Thai NIH [3-18].

Objectives:

- to develop the field laboratory system, which composed of (1) population-based field surveillance system of demographics and disease burden, especially HIV and Tuberculosis; and (2) specimen bank of HIV and TB cases and the comparison group to investigate the breakthrough interventions for HIV and TB control.

With this field laboratory system, we will evaluate the primary HIV prevention

(prevention of HIV infection) and secondary HIV prevention (prevention of HIV-infected person from developing morbidity and mortality).

– to evaluate the primary HIV prevention strategies such as provider-initiated HIV testing and counseling (PITC) for TB patients.

– to study the possibility of order-made care for HIV-infected tuberculosis patients to overcome the drug side effects and interactions between Nevirapine and Rifampicin, which has been studied clinically [2], but we need additional samples for immunology and genetics study. Clinical outcome such as pharmacokinetic can be investigated based on various genetic polymorphisms when we collect more number of samples.

Besides of above specific example, we will study the intervention identified by the systematic review and also will open the field laboratory for researchers to initiate the new innovative ideas.

Methodology:

(1) Population database system will be set up with the following the standard of INDEPTH (An International network of HDSS sites involved in demographic and health research in developing countries) network. Prof. Shibuya who has been working at WHO for disease burden monitoring is an expert for this field and will help us to formalize the system [19-23]. Thailand has 13 digit civil registrations system as below which can link the morbidity data, e.g., hospital information and mortality status. We had developed special computer program, named “looklike” to link these information while keeping the data anonymous and confidential.

HIV and TB cases will be ascertained in Chiang Rai province in Thailand. Chiang Rai is located in Northern Thailand and has a population of approximately 1.2 million. We have set the cohort of people living with HIV who registered for day-care center at the hospitals. As for TB, we maintained the TB register which has been active since May 1996. The outcome of the treatment data has also been documented in the register.

The study was reviewed and approved by the Ethical review committee, Ministry of Public Health, Thailand. All subjects have been and will be provided written, informed consent before being screened for study eligibility.

The meaning of 13 digit for Thai Citizen ID

1st digit person type as following

- 1 = people who got Thai nationality and born since December 17, 1983 and registered within 15 days
- 2 = people who got Thai nationality and born since December 17, 1983 and registered after 15 days
- 3 = people who got Thai nationality and already registered at the beginning of system
- 4 = people who got Thai nationality and did not have name in any household registration January- May 1984
- 5 = people who got Thai nationality and registered after disappeared from the registration
- 6 = Alien or small group
- 7 = the children from the parent who have 1st digit as “6”
- 8 = Alien who got Thai nationality
- 2nd – 5th digit code of register office that the children have name in the household registration (for the new born means birthplace).
- 6th – 10th digit the running number of birth certificate book.
- 11th – 12th digit the running numbers of birth certificate in each book follows the household registration system.
- 13th digit check digit that can calculate by computer to check the correction of 1st – 12th digit this digit can prove the real citizen ID.

(2) Specimen bank will be also trying to follow the standard of Biobank Japan <http://www.biobankjp.org> Initial target will be HIV-infected people, HIV-positive tuberculosis cases, and HIV-negative tuberculosis cases and normal Thai comparison group.

Patients and Controls

The Ethical review committee, Chiang Rai Hospital, Ministry of Public Health, Thailand, which has the international valid IRB (Institutional Review Board) status was informed and approved this field laboratory system on February 16, 2010.

Patients has been and will be recruited from Chiang Rai Province. All subjects will be provided written, informed consent before being screened for study eligibility.

There are four category of participants, (1) HIV infected people from the people living with HIV group; (2) HIV-positive TB cases; and control group, i.e., (3) HIV-negative TB cases; and (4) normal population.

Control population can be also recruited from the National Health Examination Survey of Thai population during year 2000 stored in Thai NIH.

Biological Specimen Collection and Processing

Preparation of genomic DNA

Venous blood (10 ml) will be taken from patients and controls Genomic DNAs will be prepared from white blood cells by standard methods.

Utilization of the field laboratory and specimen bank

Thai NIH and University of Tokyo have a memorandum of Understanding (MOU), which can be the basis for the organizational arrangement for the international collaborative researches. Series of researches has been conducted by this group [2-9] in addition to the study of Dr. Pathom Sawanpanyalert, when he was Ph.D. student [10-18]. Collaboration with the laboratory scientists, especially genetists [2], pharmacologists [3], bacteriologist [4], and virologists [5-6], has been done and will be further promoted systematically with emphasis for the HIV researchers in Japan and Thailand.

With the collaboration of Mahidol University, we will use the bacterial specimen bank to do DNA fingerprinting of *Mycobacterium tuberculosis* of Thai TB patients. We use standard IS6110-RFLP and also VNTR to compare the fingerprinting pattern [4]

In future, the network will be extended for the other Asian counties, such as Vietnam NIHE(National Institute of Hygiene and Epidemiology) with a similar function as Thai NIH, since they has been setting up the field laboratory system [24].

References:

1. Chantarangsu S, Mushiroda T, Mahasirimongkol S, Kiertiburanakul S, Sungkanuparph S, Manosuthi W, Tantisiriwat W, Charoenyingwattana A, Sura T, Chantratita W, Nakamura Y. HLA-B*3505 allele is a strong predictor for nevirapine-induced skin adverse drug reactions in HIV-infected Thai patients. *Pharmacogenet Genomics*. 2009 Feb;19(2):139-46.
2. Avihingsanon A, Manosuthi W, Kantipong P, Chuchotaworn C, Moolphate S, Sakornjun W, Meena Gorowara M, Yamada N, Yanai H, Mitarai S, Ishikawa N, Cooper D, Phanuphak P, Burger D, Ruxrungtham K. Pharmacokinetics and 12 Weeks Efficacy of Nevirapine: 400 mg versus 600 mg per day in HIV Infected Patients with Active Tuberculosis Receiving Rifampicin: A Multicenter Study *Antiviral Therapy* 2008; 13: 529-536
3. Mahasirimongkol S, Yanai H, Nishida N, Ridruechai C, Matsushita I, Ohashi J, Summanapan S, Yamada N, Moolphate S, Chuchotaworn C, Chaiprasert A, Manosuthi W, Kantipong P, Kanitwittaya S, Sura T, Khusmith S, Tokunaga K, Sawanpanyalert P, Keicho N. Genome-wide

- SNP-based linkage analysis of tuberculosis in Thais. *Genes Immun.* 2009 Jan;10(1):77-83. Epub 2008 Oct 9.
4. Billamas P, Smittipat N, Juthayothin T, Thong-On A, Yamada N, Yanai H, Palittapongarnpim P. Evolution of some variable-number tandem repeat loci among a group of Beijing strains of *Mycobacterium tuberculosis*. *Tuberculosis* 2007;87:498-501.
 5. Hamano T, Matsuo K, Hibi Y, Takahashi N, Sawanpanyalert P, Yanai H, Hara T, Yamazaki S, Yamamoto N, Okamoto T. A single nucleotide synonymous mutation in gag gene controlling human immunodeficiency virus type 1 virion production. *Journal of Virology*, 2007 Feb; 81(3):1528-33.
 6. Hamano T, Sawanpanyalert P, Yanai H, Piyaworawong S, Hara T, Sapsutthip S, Phromjai J, Yamazaki S, Yamamoto N, Warachit P, Honda M, Matsuo K. Determination of HIV-1 CRF01_AE gag p17 and env-V3 consensus sequences for HIV/AIDS vaccine design. *AIDS Research and Human Retroviruses* 2004;20(3):337-340.
 7. Sawanpanyalert P, Moolphate S, Saksoong P, Piyaworawong S, Yanai H. Sexual risk behaviors of male current and ex-opiate users in Chiang Rai, Thailand. *Journal of Epidemiology* 2002; 12:345-350.
 8. Yasui Y, Yanai H, Sawanpanyalert P, Tanaka H. A Statistical Method for the Estimation of Window-Period Risk of Transfusion-Transmitted HIV in Donor Screening under Non-Steady-State. *Biostatistics*, 2002; 3:133-143.
 9. Piyaworawong S, Yanai H, Nedsuwan S, Akarasewi P, Moolphate S, Sawanpanyalert P. Tuberculosis Preventive Therapy as Part of a Care Package for People Living with HIV in a District of Thailand. *AIDS* 2001; 15:1739-1741.
 10. Likitpongton K, Sawanpanyalert P, Moolphate S, Saksoong P, Piyaworawong S, Yanai H. Risk Factors for Hepatitis C Virus Infection Among Drug Users in Northern Thailand. *Bulletin of the Department of Medical Sciences, Thailand*. 2001; 43:8-20.
 11. Khaisuwan S, Sawanpanyalert P, Yanai H. The risk of HIV infection and safe donor recruitment and retention program in Chiang Rai. *Thai Journal of Hematology and Transfusion Medicine* 1999; 9:195-202.
 12. Sawanpanyalert P, Supawitkul S, Yanai H, Saksoong P, Piyaworawong S. Trend of HIV Incidence among drug users in an HIV Epicenter in Northern Thailand, 1989-1997. *Journal of Epidemiology*, 1999; 9:114-120.
 13. Yanai H, Uthaiworavit W, Mastro TD, Limpakarnjanarat K, Sawanpanyalert P, Morrow RH, Nieburg P. Utility of Tuberculin and Anergy Skin Testing in Predicting Tuberculosis Infection in HIV-infected Persons in Thailand. *the International Journal of Tuberculosis and Lung Disease*, 1997; 1:427-434.
 14. Ngamvithayapong J, Uthaiworavit W, Yanai H, Akarasewi P, Sawanpanyalert P. Adherence to tuberculosis preventive therapy among HIV-infected persons in Chiang Rai, Thailand. *AIDS* 1997; 11:107-112.

15. Sawanpanyalert P, Uthaiworavit W, Yanai H, Limpakarnjanarat K, Mastro TD, Nelson KE. HIV-Related Risk Factors of Blood Donors in Northern Thailand before and after Knowing HIV Test Results. *International Journal of Epidemiology* 1997; 26:408-413.
16. Yanai H, Uthaiworavit W, Panich V, Sawanpanyalert P, Chaimanee B, Akarasewi P, Limpakarnjanarat K, Nieburg P, Mastro TD. Rapid Increase in HIV-Related Tuberculosis, Chiang Rai, Thailand, 1990-1994. *AIDS* 1996; 10:527-531.
17. Sawanpanyalert P, Yanai H, Kitsuwannakul S, Nelson KE. An Estimate of the Number of Human Immunodeficiency Virus (HIV)-Positive Blood Donations by HIV-Seronegative Donors in a Northern Thailand. *The Journal of Infectious Disease* 1996; 174:870-3.
18. Sawanpanyalert P, Uthaiworavit W, Yanai H, Limpakarnjanarat K, Mastro TD, Nelson KE. Donation Deferral Criteria for Human Immunodeficiency Virus Positivity among Blood Donors in Northern Thailand. *TRANSFUSION* 1996; 36:242-249.
19. Murray CJ, Lopez AD, Black R, Mathers CD, Shibuya K, Ezzati M, Salomon JA, Michaud CM, Walker N, Vos T. Global Burden of Disease 2005. *Lancet* 2007;370:109-10.
20. Murray CJ, Laakso T, Shibuya K, Hill K, Lopez AD. Can we achieve Millennium Development Goal 4? New analysis of country trends and forecasts of under-5 mortality to 2015. *Lancet* 2007;370:1040-54.
21. Mahapatra P, Shibuya K, Lopez AD, Coullare F, Notzon FC, Rao C, Szreter S; on behalf of the Monitoring Vital Events (MoVE) writing group. Civil registration systems and vital statistics: successes and missed opportunities. *Lancet* 2007;370:1653-63.
22. Hill K, Lopez AD, Shibuya K, Jha P; on behalf of the Monitoring Vital Events (MoVE) writing group. Interim measures for meeting needs for health sector data: births, deaths, and causes of death. *Lancet* 2007;370:1726-35.
23. Lopez AD, AbouZahr C, Shibuya K, Gollogly L. Keeping count: births, deaths, and causes of death. *Lancet* 2007;370:1744-6.
24. Yanai H, Thiem VD, Matsubayashi T, Huong VTT, Suzuki M, Mai LP, Anh NH, Tho LH, Minh TT, Yoshida LM, Kilgore P, Anh DD, Ariyoshi K. The Khanh Hoa Health Project: Characterization of Study Population and Field Site Development for Clinical Epidemiological Research on Emerging and Re-Emerging Infectious Diseases *Tropical Medicine and Health* 2007;35(2):61-63.

添付資料 2

Provider-initiated testing and counseling
(PITC) の評価に関する文献的研究と研究計画書

Title:

Assessment of Provider-initiated testing and counseling (PITC) for HIV/AIDS prevention at Tuberculosis Service, Chiang Rai, Thailand.

Investigators:

Dr. Supalert Nedsuwan, Chief, Department of Preventive and Social Medicine, Chiang Rai Hospital, Thailand

Ms. Oranuch Nampaisan, Stasisian, TB/HIV Research Project, Chiang Rai, Thailand

Ms. Saiyud Moolphate, project manager, TB/HIV Research Project, Chiang Rai, Thailand

Dr. Hideki Yanai, Chief, Division of Medical Diagnostics, Fukuji Hospital, Japan
Anti-tuberculosis Association (JATA), Japan

Dr. Lisa Kawatsu, Research Associate, Research Institute of Tuberculosis (RIT), JATA, Japan

Dr. Norio Yamada, Head, Department of International Cooperation, RIT, Japan

Assoc Prof. Rintaro Mori (to be confirmed after the review),

Prof. Kenji Shibuya (to be confirmed after the review)

Consultants:

Dr. Chamnan Harnsuthivatchakul, Provincial Chief Medical Officer

Dr. Jintana Ngamvithayapong, Department of International Cooperation, RIT, Japan

Introduction:

UNAIDS and World Health Organization (WHO) recommend tuberculosis (TB) and HIV collaborative activities as one of the core strategies for tuberculosis control, HIV prevention and scaling up of universal access to anti-retrovirus treatment (ART). HIV-testing for tuberculosis patients is listed as one of such collaborative activities, and in HIV high prevalence settings, WHO recommends HIV testing for every tuberculosis patient, primarily as part of clinical management of TB patients.

HIV testing is already well recognized as an essential component of HIV prevention strategy; a number of studies have shown that HIV positive people who have come to know their status have modified their risky behaviour thus preventing further HIV transmission to others. However, studies reporting benefits of HIV testing as intervention for HIV prevention among TB patients are very limited. Since HIV-negative TB patients may easily develop clinical TB again if they become HIV-positive, primary prevention of HIV among HIV-negative TB patients should be considered not only as a rational but a key strategic activity. Needless to

say, as for HIV-positive TB patients, HIV testing can become an effective entry point for secondary prevention of HIV.

It should be noted here that until recently, the so-called Voluntary Counselling and Testing (VCT) was considered as the most ideal method of implementing HIV-testing. As its name indicates, VCT was intended to enable individuals to make informed choice about being testing and cope with his or her result but also provides opportunity for education. However, to date, various factors have been pointed out which potentially hindered the acceptance and access to VCT, such as lack of HIV care and treatment including ARV, access to condoms and treatment of opportunistic infections, stigma and fear of negative reactions to disclosure, gender inequalities, transport difficulties in accessing testing site and fear of being seen at testing site and individual attitudes and perceptions of risk. Indeed, various studies on the effectiveness of VCT have been conducted, but the results are so far inconclusive. In the light of the above circumstances, in 2007, WHO, together with UNAIDS, produced new guidelines for HIV testing. In the report, WHO and UNAIDS state that though they "...strongly support the continued scale-up of client-initiated HIV testing and counselling, (they) recognise the need for additional, innovative and varied approaches", one of which is the so-called provider-initiated testing and counselling (PITC).

Studies on PITC are still quite limited, however, our study¹, conducted in Chiang Rai between June 2000 and January 2002, Thailand, has demonstrated that not only TB patients but spouses of HIV positive TB patients can also benefit from HIV testing. In this study, HIV testing was offered from the provider-side, and thus the study may be considered one of the first attempts of PITC. The results showed that almost half of the spouses of the HIV positive TB patients were HIV negative. We concluded that HIV testing should be regarded as a key opportunity to offer HIV prevention and care for those who need them.

If we could provide evidence of effectiveness of PITC for TB patients, we may then move onto consider implementing PITC to other high-risk populations, such as blood donors and pregnant women².

Research questions:

¹ Suggaravetsiri P, Yanai H. et al. Integrating counselling and screening for tuberculosis and HIV among household contacts of tuberculosis patients in an endemic area of HIV infection: Chiang Rai, Thailand. *Int J Tuberc Lung Dis* 2003;7; S424-431

² Sawanpanyalet P, et al. *Biostatistics*, 2002; 3:133-143; *Int J of Epi* 1997; 26:408-413; *The J of Infect Dis* 1996; 174:870-3; *TRANSFUSION* 1996; 36:242-249; Siriarayapon P, et. al. *J Acquir Immune Defic Syndr*. 2002; 31(1):80-89

- This project aims to clarify the following;

1. Coverage of HIV testing for TB patients and for the spouse of patients with TB and HIV co-infection.
2. The situation (frequency and reasons) of HIV sero-conversion as resulting from failure of primary prevention for HIV-negative TB patients.
3. The situation (rate and reasons) of progression to AIDS and deaths as resulting from failure of secondary prevention for HIV-positive TB patients

Objectives:

The objectives of this study are to;

1. describe HIV testing practice of TB patients and their spouses in Thailand.
2. estimate the frequency of HIV sero-conversion among HIV-negative TB patients.
3. examine the risk factors and reasons of HIV sero-conversion among HIV-negative TB patients.

Subsidiary Objectives*

4. examine the AIDS progression and survival among HIV-positive TB patients and their risk factors.

Method

Setting:

Chiang Rai is the northernmost province of Thailand, where HIV epidemic occurred very early in the 1990s. Immediately after HIV epidemic broke out, HIV-positive TB cases rapidly increased³ and surveillance system for TB/HIV was set up, which later became the official TB/registry database system under the responsibility of Chiang Rai Provincial Health Office and the TB/HIV Research Project⁴.

Study Population

Population-based retrospective cohort of TB patients from the TB registry of Chiang Rai Province will be constructed. Between the period of 1995 and 2008, there is a total of 28,945 registry of TB case episodes. Excluding the 2,508 Non –Thai nationals, there are 10,928

³ Yanai H, Uthairavit W, Panich V, Sawanpanyalert P, Chaimanee B, Akarasewi P, Limpakarnjanarat K, Nieburg P, Mastro TD. Rapid Increase in HIV-Related Tuberculosis, Chiang Rai, Thailand, 1990-1994. *AIDS* 1996; 10:527-531

⁴ TB/HIV Research Project: a collaborative research project between the Ministry of Public Health, Thailand and the Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association, which began in 1995.

HIV-negative TB cases and 10,327 HIV-positive TB cases, and 5,182 HIV-unknown cases. Of them, 4,902 HIV-negative TB cases and 3,524 HIV-positive TB cases have CID (citizen ID card). These populations will be the primary target of our study. It should be noted that CID coverage of TB registry is recently increasing; for example, current estimates indicate that more than 97% of Thai lowlanders hold CID. However, HIV-unknown cases will be examined to assess potential biases, although the proportion of HIV unknown reduces the proportion recently only 7.2% in 2008. There are additional 7,705 TB cases registered between 1985-1994. Quality of data and HIV status information will be checked

Outcome Measures and ascertainment strategies:

We will have a separate file to obtain primary prevention information (follow-up HIV status for HIV-negative TB patients) by linkage with other databases, including Hospital Database, HIV/AIDS surveillance database, and Mortality Database. Since this process will give us the opportunity to examine data on secondary prevention (AIDS occurrence and mortality status), we will also attempt to investigate secondary prevention, as indicated above as subsidiary objective. Contacts through health systems and mail will be considered in the subset of cohort members, especially for those with very rich independent variable information.

Independent variables

Independent variables available for TB registry databases are listed in the appendix. In addition, data from questionnaire asking about health seeking behaviours are available for sputum smear-positive TB patients from 1996. Information on drug resistance is also available from 1996. Very detailed social and clinical information on those who have joined the previous household contact study already exist. It may thus be necessary to follow-up these individuals more actively. Collaboration with the Thai NIH will be considered if we are to examine the possibility of survival outcome of human genetic polymorphisms, since the Thai NIH has already extensively examined Single Nucleotide polymorphism (SNP) patterns of nearly 1,000 TB patients from Chiang Rai. (Number of HIV converter, which may have SNPs information may be too small, but association with mortality outcome can be investigated).

Supplemental Clinical and Qualitative information

It is not possible to perfectly ascertain the occurrence, but the process will be examined to assess the level of underestimation. For example, of which database detected how many cases of outcomes (HIV status or AIDS occurrence or Mortality) will be recorded. Possible reasons behind “failures of preventions” will be investigated by quantitative analysis and also

qualitative case studies. Clinical factors will be investigated through clinical case investigations of particular cases, e.g., those who became HIV-positive TB cases but were HIV-negative TB cases before. If the patients have survived, interviews will be conducted to investigate further reasons.

In addition, we will review the national guidelines on TB/HIV and interview national policy makers of TB and AIDS programs. We will also identify HIV preventions interventions through literature review and stakeholder analysis

Ethical Considerations

We will obtain approval from the ethic committee of Chiang Rai Regional Hospital, which is registered to the Institutional Review Board, Chiang Rai Regional Hospital, Ministry of Public Health, Thailand, which has the formal registration no. of international IRB body. Data management including the data security will be assured (NOTE before submission: any standard now in Thailand?) CID, Name, and other identifier will be changed to the other confidential coding system without losing the uniqueness when doing analysis to avoid the violation of confidentiality. .

Literature Review how the concept of PITC come out and current status:

Voluntary Counselling and Testing (VCT) supposedly enables individuals to make informed choice about being testing and cope with his or her result but also provides opportunity for education. It is thought that irrespective of the test result, VCT offers chance for the individual to access various information about HIV/AIDS which could potentially stimulate behaviour change. Effect of VCT, however, often varies by research design and population: Higgins et al (1991), in their analysis of VCT data published between 1986-1990, concluded that while the effect of VCT in changing risky behaviour was evident among discordant heterosexual couples, it was not so conclusive among men who have sex with men and injecting drug users. Another review of VCT studies from 1990-1996 showed that the evidence for most consistent behaviour change was found among discordant couples (Wolitski et al 1997). Weinhardt et al (1999), in their meta-analysis of VCT efficacy data, also concluded that VCT was an effective intervention in moderating risky behaviour of persons infected with HIV. It should here be noted that the aforementioned reviews mainly examined studies conducted in developed countries in North America and Europe. The picture can be substantially different in resource-constrained settings, where establishing VCT, a highly labour-intensive service, may strain the already weak health care infrastructure. However, Denison et al (2008), in their recent meta-analysis of VCT studies in developing countries