Study of Patterns of Drugs of Abuse in New Territories East Cluster Drug of Abuse Clinic Using Conventional and New Technologies

24 May 2010

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	Time-line and events
Month/Year	Events
Jan 2007	• Installation of UPLC-TOF/MS
Apr 2007	Approval of Beat Drug Fund
May – Aug 2007	 Ethics Approval of Research Protocol Preparation of subject recruitment Recruitment of Medical Laboratory Technician II (MLT II) Recruitment of study subjects starts in Jul 2007
Sep 2007	 Submitted 1st Progress report to Research Advisory Group MLT II reported duty
Nov 2007	 Submitted 2nd Progress report to Research Advisory Group Applied for extension of duration of study and revision of budget plan
Mar 2008	 Submitted 3rd Progress report to Research Advisory Group Submission of revised study proposal of original study (Project 1) and budget plan in collaboration of another study project (Project 2)

Month/Year	Events
May 2008	 Approval of revised study proposal and extension of Project 1 from Jun 2008 to Mar 2009
Jun 2008	 Submitted 4th Progress report to Research Advisory Group Recruitment of Project 2 started
Oct 2008	 Submitted 5th Progress report to Research Advisory Group Presentation on the progress of Project 1 to Research Advisory Group on 9 Oct 2008 Submission and approval of revised budget plan
Dec 2008	• Submitted 6 th Progress report to Research Advisory Group
Apr 2009	 Submitted 7th Progress report to Research Advisory Group Submission of proposal of extension of Project 1 with revised study protocol and budget plan
Jul 2009	 Approval of revised budget plan and proposal (Honorarium of \$100 for each recruited subjects)
Nov 2009	 Applications for ethics approval for revised study protocol (expansion of recruitment sources)

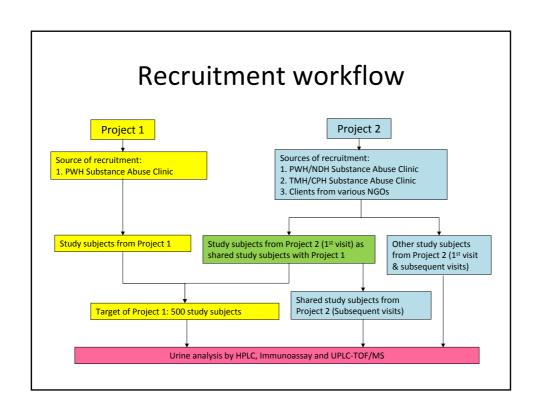
Submission of proposal of further extension of Project 1 to De 2010 Mar 2010 Ethics approval of revised study protocol by the Joint CUHKNTEC CREC Application of ethics approval in NTWC Apr 2010 Ethics approval of study protocol by NTWC CREC Submitted Semi-final report to Research Advisory Group Recruitment of study subjects in NTWC Substance Abuse Clinic started since late Apr 2010	Submission of proposal of further extension of Project 1 to De 2010 Mar 2010 Ethics approval of revised study protocol by the Joint CUHK-NTEC CREC Application of ethics approval in NTWC Apr 2010 Ethics approval of study protocol by NTWC CREC Submitted Semi-final report to Research Advisory Group Recruitment of study subjects in NTWC Substance Abuse Clinic started since late Apr 2010	Events
NTEC CREC • Application of ethics approval in NTWC Apr 2010 • Ethics approval of study protocol by NTWC CREC • Submitted Semi-final report to Research Advisory Group • Recruitment of study subjects in NTWC Substance Abuse Clinic started since late Apr 2010	NTEC CREC • Application of ethics approval in NTWC Apr 2010 • Ethics approval of study protocol by NTWC CREC • Submitted Semi-final report to Research Advisory Group • Recruitment of study subjects in NTWC Substance Abuse Clinistarted since late Apr 2010 May 2010 • Presentation on the progress of Project 1 to Research Advisor	• Submission of proposal of further extension of Project 1 to Dec
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May 2010 • Presentation on the progress of Project 1 to Research Advisory		 Submitted Semi-final report to Research Advisory Group Recruitment of study subjects in NTWC Substance Abuse Clinic
		 Presentation on the progress of Project 1 to Research Advisory Group on 24 May 2008
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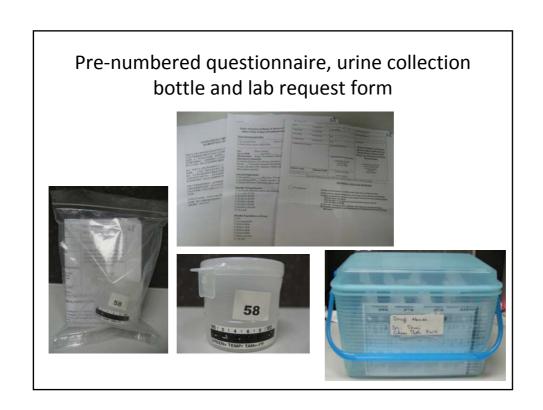
Subject recruitment

Month/Year	Cumulative no. of subjects	% of target recruitment
Sep 2007	23	4.6%
Nov 2007	37	7.4%
Mar 2008	51	10.2%
Jun 2008	56	11.2%

Expanding recruitment source

- Collaboration with a second project "Socioeconomic and Health Impacts of Substance Abuse in Hong Kong – A Longitudinal Study"
 - granted by the Beat Drugs Fund Association
 - leaded by Professor Kenneth Lee, School of Pharmacy, CUHK
- One of the objectives of this project is to study the acute toxicity in a group of drug abusers admitted or referred to a public hospital by performing a quality and reliable analysis on the urine specimens for toxicology screening
- Department of Chemical Pathology, CUHK, as one of the collaborating institutions, primarily provides the analytical services for this project
- Relevant data obtained from this second project including the urine analysis result and information from questionnaire can be used by our first project for data analysis





Subject recruitment

Month/Year	Cumulative no. of subjects	% of target recruitment
Sep 2007	23	4.6%
Nov 2007	37	7.4%
Mar 2008	51	10.2%
Jun 2008	56	11.2%
Oct 2008	81	16.2%
Dec 2008	107	21.4%
Apr 2009	134	26.8%
Jan 2010	222	44.4%
Mar 2010	226	45.2%



Study of Patterns of Drugs of Abuse in New Territories East and West Clusters Drug of Abuse Clinic Using Conventional and New Technologies

Part II: Interim findings

NEW TERRITORIES EAST CLUSTER DRUG OF ABUSE CLINIC USING CONVENTIONAL AND NEW TECHNOLOGIES

Semi-Final Report Submitted To

The Research Advisory Group of The Beat Drugs Fund Association

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Data analysis

• Subjects recruited from July 2007 to March 2010

• Total: 226 subjects (excluding eight follow-up cases of our collaborated project)

• Male: Female = 143:83

• Age: 14 - 63 years

• NTEC: NTWC = 161:65

• New case : Old case = 55 : 161

Major findings

- Survey results
 - Demographics
 - History of previous drug use
 - History of last drug use
 - Other information
- Results of urine analysis
 - Comparison of conventional and new techniques
 - Overall results
- · Comparison of survey and urine analysis results
 - Patterns of substance abuse
 - Comparison of urine analysis results with history of last drug use

Demographics

- Young age (< 40 yrs, range from 14 to 63 yrs)
- Single
- Junior secondary education (up to F.2 / F.3)
- High unemployment rate
- No or low monthly personal income

Age and Sex

Age group (years)	Female	Male	Total	ı
10-19	24	17	41	(18%)
20-29	28	45	73	(32%)
30-39	23	60	83	(37%)
40-49	6	11	17	(8%)
50-59	1	9	10	(4%)
60-70	1	1	2	(1%)
Grand Total	83	143	226	(100%)

^{*}Age of the recruited subjects range from 14 to 63 years.

^{*87%} of 226 subjects are < 40 years.

Marital Status

Marital status	Female	Male	Total
Never married	49	87	136 (60.2%)
Co-habitant	3	2	5 (2.2%)
Married	15	33	48 (21.2%)
Divorced	8	7	15 (6.6%)
Separated	1	4	5 (2.2%)
Widowed	1		1 (0.4%)
Not specified	6	10	16 (7.1%)
Grand Total	83	143	226 (100%)

Education level by sex

Education level	Female	Male	Total	
Primary education	7	16	23	(10%)
Secondary education	75	110	185	(82%)
Tertiary education		5	5	(2%)
Not specified	1	12	13	(6%)
Grand Total	83	143	226	(100%)

Education level by age group

Education level	Age group (Years)						Total
	10-19	20-29	30-39	40-49	50-59	60-70	
Primary education	1	2	3	9	7	1	23
Secondary education	36	66	73	8	2		185
Tertiary education		3	1			1	5
Not specified	4	2	6		1		13
Grand Total	41	73	83	17	10	2	226

- 185 (82%) of the 226 recruited subjects attained secondary education level.
- These data is compatible with a general trend of increase in education level among the youngster population due to the provision of 9-year free education by the government since 1970s.

Education level

Secondary education up to	Female	Male	Total	
F.1	7	18	25	(13.5%)
F.2	15	29	44	(23.8%)
F.3	21	35	56	(30.3%)
F.4	8	7	15	(8.1%)
F.5	23	21	44	(23.8%)
Not specified	1		1	(0.5%)
Grand Total	75	110	185	(100%)

Employment status by sex

Employment status	Female	Male	Total	
Unemployed	51	77	128	(56.6%)
Full-time	12	32	44	(19.5%)
Part-time	4	17	21	(9.3%)
Student	8	11	19	(8.4%)
Housewife	7		7	(3.1%)
Retired		1	1	(0.4%)
Others	1	5	6	(2.7%)
Grand Total	83	143	226	(100%)

Employment status by age

Secondary education	Age group (Years)					Total	
up to	10-19	20-29	30-39	40-49	50-59	60-70	
Unemployed	19	37	49	15	6	2	128
Full-time	3	25	14	1	1		44
Part-time	3	3	15				21
Student	14	5					19
Housewife		2	3	1	1		7
Retired					1		1
Others	2	1	2		1		6
Grand Total	41	73	83	17	10	2	226

Monthly personal income by sex

Employment status	Female	Male	Total	
No income	63	82	145	(64%)
< \$1,000	3	1	4	(2%)
\$1,000 to \$2,999	3	5	8	(4%)
\$3,000 to \$4,999	4	9	13	(6%)
\$5,000 to 6,999	3	6	9	(4%)
\$7,000 to \$8,999	1	9	10	(4%)
\$9,000 to \$10,999	3	10	13	(6%)
>\$11,000	3	16	19	(8%)
Not specified	0	5	5	(2%)
Grand Total	83	143	226	(100%)

^{*} Most of the subjects have no income or low income.

Monthly expenditure on drugs by sex

Expenditure	Female	Male	Total	
Nil	30	69	99	(44%)
<\$100	4	4	8	(4%)
\$100 to \$299	7	6	13	(6%)
\$300 to \$499	6	6	12	(5%)
\$500 to \$699	5	4	9	(4%)
\$700 to \$899	1	2	3	(1%)
\$900 to \$1,099	7	1	8	(4%)
>\$1,100	22	44	66	(29%)
Not specified	1	7	8	(4%)
Grand Total	83	143	226	(100%)

Monthly expenditure on drugs by income

Expenditure	No income	Monthly income						
		<\$5000	\$5000 to \$10,999	>\$11,000				
Nil	68 (47%)	13 (52%)	13 (41%)	5 (26%)				
<\$100	6 (4%)	1 (4%)		1 (5%)				
\$100 to \$299	10 (7%)	3 (12%)						
\$300 to \$499	8 (6%)	2 (8%)	2 (6%)					
\$500 to \$699	5 (3%)	2 (8%)	1 (3%)	1 (5%)				
\$700 to \$899	3 (2%)							
\$900 to \$1,099	6 (4%)	1 (4%)		1 (5%)				
>\$1,100	36 (25%)	3 (12%)	16 (50%)	11 (58%)				
Not specified	3 (2%)							
Grand Total	145 (100%)	25 (100%)	32 (100%)	19 (100%)				

^{*}Among 145 subjects who have no income, 74 of them still have expenditure on drugs (36 subjects reported to have monthly expenditure on drugs of > \$1,100).

History of previous drug use

- First try at young age
 - < 25 yrs, majority 15-19 yrs
- Try multiple drugs
 - Higher tendency of multiple drug use in younger age groups
- Pattern of drug use
 - <40 yrs: Ketamine and Amphetamines</p>
 - >= 40 yrs: Hypnotics and Heroin
- Reasons for drug use
 - Recreational and peer influence
- Subjective complications from drug
 - 50% Yes, 40% No

Age first started drug abuse by sex

Age group	Female	Male	Total
			N %
10-14	20	27	47 (20.8%)
15-19	39	63	102 (45.1%)
20-24	12	23	35 (15.5%)
25-29	6	9	15 (6.6%)
30-34	1	5	6 (2.7%)
35-39	2	3	5 (2.2%)
45-49	1	1	2 (0.9%)
50-54		3	3 (1.3%)
55-60	1		1 (0.4%)
Not specified	1	9	10 (4.4%)
Grand Total	83	143	226 (100%)

^{*}Age first started drug abuse was reported to be ranged from 10 to 55 years.

Number of groups of drug items ever tried by sex

Number of groups of drug items	Female		Male		Total	
	N	%	N	%	N	%
1	26	(31%)	42	(29%)	68	(30%)
2	14	(17%)	20	(14%)	34	(15%)
3	9	(11%)	22	(15%)	31	(14%)
4	13	(16%)	16	(11%)	29	(13%)
5	10	(12%)	16	(11%)	26	(12%)
6	5	(6%)	11	(8%)	16	(7%)
7	3	(4%)	4	(3%)	7	(3%)
8	3	(4%)	2	(1%)	5	(2%)
9			5	(3%)	5	(2%)
Not specified			5	(3%)	5	(2%)
Grand Total	83	(100%)	143	(100%)	226	(100%)

Number of groups of drug items ever tried by age

Number of groups		Total					
of drug items	10-19	20-29	30-39	40-49	50-59	60-70	
1	11	23	21	7	5	1	68
2	7	10	13	3	1		34
3	6	11	11	2	1		31
4	8	8	11	1	1		29
5	5	10	8	1	1	1	26
6	2	7	6	1			16
7	1	2	3	1			7
8		1	3	1			5
9			5				5
Not specified	1	1	2		1		5
Grand Total	41	73	83	17	10	2	226

^{*}Proportion of multiple drug users is greater than that of single drug users among the younger age groups.

Summary of group of drug item ever tried by sex

Group of drug item	Female (N=83)		Male (N=14		Total (N=22	
		%		%		%
Ketamine	52	63%	82	57%	134	59.3%
Amphetamines (Ice)	41	49%	61	43%	102	45.1%
Cannabis	26	31%	61	43%	87	38.5%
MDMA (Ecstasy)	28	34%	48	34%	76	33.6%
Benzodiazepines	24	29%	37	26%	61	27.0%
Hypnotics	25	30%	35	24%	60	26.5%
Cocaine	27	33%	30	21%	57	25.2%
Cough medicine	21	25%	36	25%	57	25.2%
Opiates	9	11%	48	34%	57	25.2%
Mandrax	6	7%	9	6%	15	6.6%
Thinner / Organic solvent			1	1%	1	0.4%
Others (e.g. Analgesics)			2	1%	2	0.9%
Grand Total	259		450		709	

Summary of group of drug item ever tried by age

Group of drug item	Age group (Years)							Total						
	10-1 (N=4		20-: (N=		30- (N=		40- (N=		50- (N=	59 :10)	60- (N=		(N=2	26)
Ketamine	34	83%	59	81%	35	42%	4	24%	2	20%			134	59.3%
Amphetamines (Ice)	22	54%	26	36%	45	54%	8	47%	1	10%			102	45.1%
Cannabis	13	32%	29	40%	39	47%	5	29%			1	50%	87	38.5%
MDMA (Ecstasy)	15	37%	31	42%	25	30%	4	24%	1	10%			76	33.6%
Benzodiazepines	8	20%	16	22%	26	31%	7	41%	3	30%	1	50%	61	27.0%
Hypnotics	3	7%	13	18%	28	34%	7	41%	7	70%	2	100%	60	26.5%
Cocaine	14	34%	22	30%	17	20%	3	18%			1	50%	57	25.2%
Cough medicine	4	10%	12	16%	37	45%	4	24%					57	25.2%
Opiates (Heroin)	2	5%	9	12%	33	40%	7	41%	5	50%	1	50%	57	25.2%
Mandrax	5	12%	5	7%	5	6%							15	6.6%
Thinner / Organic solvent Others (e.g. Analgesics)			1	1%	2	2%							1 2	0.9% 0.4%
Grand Total	120		223		292	2	49		19		6		709	

Reason of drug abuse

Reason of drug abuse	Female N=83		Male N=143		Tota N=2	
		%		%		%
Recreational	44	53%	71	50%	115	51%
Peers Influence	22	27%	44	31%	66	29%
Experimental	5	6%	15	10%	20	9%
Dependence	11	13%	8	6%	19	8%
Others	14	17%	18	13%	32	14%
Grand Total	96		156		252	

Subjective complications of drug abuse

Presence of complications	Fer	Female		e	Tota	ı
	N	%	N	%	N	%
Yes	39	(47%)	73	(51%)	112	(50%)
No	38	(46%)	52	(36%)	90	(40%)
Not specified	6	(7%)	18	(13%)	24	(11%)
Grand Total	83	(100%)	143	(100%)	226	(100%)

History of last drug use

- Within 1 month
- Reported only single drug use
- Ketamine, amphetamines, hypnotics, cough medicine and heroin are the five most popular groups of drug items
- Got drugs from friends
- Taken drugs at home

Estimated time of last use

When was last drug use?	Female	Male	Total
Less than 1 day	11	16	27 (12%)
1 day to less than or equal to 1 week	31	52	83 (37%)
Above 1 week to less than or equal to 1 month	16	21	37 (16%)
Above 1 month to less than or equal to 1 year	16	36	52 (23%)
Above 1 year	7	9	16 (7%)
Not specified	2	9	11 (5%)
Grand Total	83	143	226

Number of drug item last used by sex

Number of drug item last used	Female	Male	Tota	ıl
1	66	118	184	(81%)
2	11	16	27	(12%)
3	2		2	(1%)
4	3	1	4	(2%)
Not specified	1	8	9	(4%)
Grand Total	83	143	226	(100%)

^{*}Note: Individual subject could report more than one drug item during his/her last use.

^{*}Most (81%) subjects reported only one drug item used.

Summary of group of drug item last used by sex

Group of drug item last used		Female (N=83)		Male (N=143)		l 26)
		%		%		%
Ketamine	31	30%	50	31%	81	31%
Amphetamines (Ice)	24	24%	18	11%	42	16%
Hypnotics	18	18%	18	11%	36	14%
Cough medicine	2	2%	30	19%	32	12%
Opiates (Heroin)	11	11%	15	9%	26	10%
Benzodiazepines	8	8%	7	4%	15	6%
Cocaine	4	4%	4	2%	8	3%
MDMA (Ecstasy)	2	2%	5	3%	7	3%
Cannabis	1	1%	3	2%	4	2%
LSD			1	1%	1	0%
Others (e.g. analgesics)			2	1%	2	1%
Not specified	1	1%	8	5%	9	3%
Grand Total	102		161		263	

Source of drugs

		18 Districts of	Hong Ko	ong	
New Territories (Subtotal: 118)		Kowloon (Subtatal: 80)		Hong Kong Island (Subtotal: 3)	
Sha Tin	41	Mong	61	Central & Western	1
Yuen Long	30	Kwun Tong	9	Eastern	1
Tuen Mun	26	Sham Shui Po	7	Wan Chai	1
Tai Po	9	Kowloon City	2	Southern	0
North	5	Wong Tai Sin	1		
Tsuen Wan	3				
Islands	2				
Sai Kung	2	Outside Hong	Kong		
Kwai Ching	0	Shenzhen			
(Grand Total: 22	21)	(Grand Total:	12)		

Channels to obtain drugs

Channels	Total	%
Friends	116	51.3%
Pharmacy	56	24.8%
Others	25	11.1%
Not specified	29	12.8%
Grand Total	226	100.0%

^{*}Pharmacy is reported as a common source of hypnotics and cough medicine.

Location of drug use

Location of drug use	Fema (N=8		Male (N=143)		Total (N=2	
		%		%		%
Home	52	63%	62	43%	114	50.4%
Friend's apartment	21	25%	19	13%	40	17.7%
Street	5	6%	23	16%	28	12.4%
Disco	4	5%	17	12%	21	9.3%
Pharmacy			13	9%	13	5.8%
Video Game Centre			3	2%	3	1.3%
Karaoke	1	1%	1	1%	2	0.9%
Bar	1	1%	1	1%	2	0.9%
Park			1	1%	1	0.4%
Not specified	2	2%	9	6%	11	4.9%
Grand Total	86		149		235	

Currently on therapeutic drugs by sex

On therapeutic drug therapy	Female	Male	Total
Yes	43	60	103
No	39	74	113
Not specified	1	9	10
Grand Total	83	143	226

^{*}Note: Therapeutic drug items used by the study subjects are mainly psychiatric medications prescribed from drug of abuse clinic.

Smoking & drinking history by sex

Smoking history	Female	Male	Total
Smoker	63	124	187
Ex-smoker	2	5	7
Non-smoker	13	6	19
Not specified	5	8	13
Grand Total	83	143	226

Drinking history	Female	Male	Total
Drinker	26	63	89
Ex-drinker	12	10	22
Non-drinker	41	59	100
Not specified	4	11	15
Grand Total	83	143	226

^{*}However, detail description of individual's therapeutic drug regime is unavailable.

Forensic history by sex

Forensic history	Female	Male	Total
Yes	30 (36%)	94 (66%)	124 (55%)
No	49 (59%)	39 (27%)	88 (39%)
Not specified	4 (5%)	10 (7%)	14 (6%)
Grand Total	83 (100%)	143 (100%)	226 (100%)

Summary of forensic history

Drug-related forensic history	Subtotal: 54
Drug trafficking	21
Drug possession	28
Drug abusing	5
Non-drug-related forensic history	Subtotal: 37
Theft	15
Assault	9
Robbery	9
Attacking police	2
Money laundering	1
Driving without license	1
Not specified	Subtotal: 52
	Grand Total: 143

Comparison of conventional (HPLC-UV/ immunoassays) and new (UPLC-TOF/MS) techniques

- Other than drugs caffeine, nicotine and cotinine, count the number of drugs identified in each urine sample by both conventional (C) and new (N) techniques.
- Number of drugs identified by conventional techniques (C) is defined as the number of drugs identified by HPLC-UV and number of additional drugs identified by immunoassay.
- Determine the ratio of C/N of each urine sample.
- Calculate the mean C/N ratio.
 - If the mean ratio is <1, the new technique identifies more drugs than conventional technique.
 - If the mean ratio is >1, the conventional technique identifies more drugs than the new technique.

Performance of the new for replacement of conventional technique

- Compare the identified drugs between the New and Conventional techniques.
- For drugs identified by the Conventional technique but not the New, add +1 point to Deficiency score (D) for each drug.
- For drugs identified by the New technique but not the Conventional, add +1 point to Improvement score (I) for each drug.
- Calculate the D/I ratio.
 - If the D/I ratio is <1, the New technique has better overall performance than the Conventional technique in terms of identification of drug item by detection of either parent drug or metabolites.
 - If the D/I ratio is >1, the Conventional technique has better performance and the New technique has missed drugs that are identified by the Conventional technique.

- 1	Α	DE	F	. 6	i I	J	K	L	М	N	0 P	R	S T
1	Master Subject no.	Sex	Urine temperature (F)	Urine creatinine (mmol/l)	TOF_Reute_Analyzed (Updated)	TOF_Roulta_Roviewed	TOF_No. of drug items identified (N Score)	score	Rinned_Results	Raned Besultz Roviewed	Remed_No. of drug items identified (R) AxSym Result	Added Score_No. of drug items found by AxSym but not Remedi (A)	C score (No. of drug kems Identified by Remedi and AxSym = R + A) (Updated) D score (Updated)
117	21	-	_	_	1.9 Chlorpheniramine	Chlorpheniramine	-	. (-	5	0	
118	21				1.9 Chlorpheniramine N-desmethol	,			Chlorpheniramine N-desmethyl	Chlorpheniramine			
119	21				1.9 Cocaine	Cocaine			Coraine	Coraine	Cocaine		
120	21				1.9 Cocaine hudroxu								
121	21	F :	35 3	94 1	1.9 Ecgonine Methyl Ester								
122	21	F :	35 3		1.9				Benzoylecquaine(-me-Cocaine)				
123	21				1.9 Codeine	Codeine		(Codeine	Codeine	Opiates		
124	21	F :	35 3	94 1	1.3 Codeine N-desmethyl								
125	21	F	35 3		1.3 Pseudoephedrine/ephedrine	Pseudoephedrine/ephedrine			Pseudoephedrine/ephedrine	Pseudoephedrine/ephedrine			
126	21				1.9 Phenopropanolamine/Pseudoephedrine No								
127	21		35 3		1.9 Promethagine	Promethazine		(
128	21	F :	35 3	94 1	1.9 Promethazine hydroxydesmethyl				Promethazine hydroxydesmethyl	Promethazine			
129	21	F :	35 3		9 Promothania sulforido				Promethaniae sulferride				
130	21	F :	35 3	94 1	1. Zolpidem metab#1	Zolpiden			l				
131	21	F :	35 3	94 1	1. Zolpidem metab#2								
132													
133	22	M :	37 5	94 14	1.5 Methamphetamine	Methamphetamine	3		Methamphetamine	Methamphetamine	2 Amplie	0	2
134	22	M :	37 3	94 14	1.5 Amphetamine								
135	22	M :	37 3	94 14	1.5 Zopiclone	Zopidose		- ((
136	22	M	37 3	94 14	1.5 Zopiclone desmethyl				Zopiclone desmethyl	Zopiclone			
37	22	M :	37 3	94 14	1.5 Fluoxetine	Fluoxetine			l				
38	22	M :	37 3	94 14	1.5 Fluoxetine N-desmethyl								
39								_					
40	23	M	21 3	92 16	i.I Ketamine	Ketamine		1	Nil	Nil	0 Mil	0	0
141	23	M	21 3	92 16	i.I Ketamine dehydro-N-desmethyl								
42	23	M	21 3	92 16	i.I Ketamine N-desmethyl								
43													
44					7.5 Codeine	Codeine	6	(Codeine	Codeine	4 Opiotes	0	4
45			33 3		7.5 Codeine, N-desmethyl				Codeine, N-desmethyl				
146			33 3		7.5 Morphine_CM								
47			33 3		7.5 Morphine 3-Bets-D-glucuronide								
48					7.5 Morphine N-desmethyl								
149	24		33 5		7.5 Hydrocodose	Hydrocodone			l e e e e e e e e e e e e e e e e e e e				
50			33 5		7.5 Hydrocodol								
51	24	м :	33 5		7.5 Hydrocodone N-desmethyl								
152	24	м :	33 5		7.5 Olanzapine	Olanzapine			l .				
153			33 3		7.5 Olanzapine N-desmethyl								
154			33 3		7.5 Promethazine	Promethazine		((
155					7.5 Promethazine hydroxydesmethyl				Promethazine hydroxydesmethyl	Promethazine			
156	24	M :	33 5	4 1	7.5 Promethazine sulforide				Promethazine sulforide				

Results of the comparison data

Summary of performance of new and conventional techniques	
Number of urine sample analyzed by both techniques	67
Total number of drug items identified by new technique (sum of N)	171
Total number of drug items identified by conventional technique (sum of C)	147
Mean C/N ratio	0.77
Deficiency score (D)	22
Improvement score (I)	46
D/I ratio	0.48

Improvement of drug detection by new technique

Ketamine

 9 of 67 urine samples detected ketamine by UPLC-TOF-MS, HPLC-UV missed 3 urine samples

Zopiclone and Zolpidem

- 11 of 67 urine samples detected zopiclone by UPLC-TOF-MS, HPLC-UV missed 2 urine samples
- 5 of 67 urine samples detected zolpidem by UPLC-TOF-MS, HPLC-UV missed all

Deficiency of drug detection by new technique

- UPLC-TOF-MS missed 10 urine samples that benzodiazepine was detected by Immunoassay
- Known deficiency of UPLC-TOF-MS

• Solutions:

- Supplementary use of immunoassay for benzodiazepine detection
- Modified UPLC-TOF-MS method with enzyme digestion to detect the conjugates of benzodiazepines

Overall urine analysis results

- 56 drug items (including both drugs of abuse or therapeutic agents) were identified from over 1,200 parent drugs and metabolites detected in 226 study subjects.
- Novel drug or impurities are not detected by UPLC-TOF-MS
- Cough mixture is the most common drug of abuse item detected

Drug category	Drug item detected	Drug category	Drug item detected
Amphetamines	Amphetamine	Therapeutic drugs	Amisulpride
	Methamphetamine		Amitriptyline
Analgesics	Tramadol		Atenolol
Barbiturates	Barbiturates		Atropine
Benzodiazepines	Diazepam		Benzhexol
	Flunitrazepam		Chlorpromazine
	Midazolam		Citalopram
	Nitrazepam		Desipramine
Cannabis	Cannabinoids		Dothiepin
Cocaine	Cocaine		Etoricoxib
Cough medicine	Brompheniramine		Famotidine
-	Cetirizine		Fluoxetine
	Chlorpheniramine		Metoclopramide
	Codeine		Nortriptyline
	Dextromethorphan		Ofloxacin
	Dihydrocodeine		Olanzapine
	Hydrocodone		Propranolol
	Hydromorphone		Quetiapine
	Methylephedrine		Ranitidine
	Promethazine		Risperidone
	Propoxyphene		Sertraline
	Pseudoephedrine/Ephedrine		Sulpiride
Hypnotics	Zolpidem		Trazodone
	Zopiclone		Trifluoperazine
Opiates	Heroin		Venlafaxine
	Morphine		
Ketamine	Ketamine		
MDMA	HMMA		
	MDA		
	MDMA		
Methadone	Methadone		

Number of groups of drug of abuse items detected in urine by sex

Number of groups of drug of abuse items	Fen	nale	Male		Total	
	N	%	N	100%	N	100%
0	26	31%	32	22%	58	25.7%
1	24	29%	62	43%	86	38.1%
2	24	29%	30	21%	54	23.9%
3	8	10%	14	10%	22	9.7%
4			5	3%	5	2.2%
5	1	1%			1	0.4%
Grand Total	83	100%	143	100%	226	100%

^{*}More than 1 drug (2 - 4 drugs) detected in 59 urine samples among the 184 subjects who reported single drug use during last use.

Number of groups of drug of abuse items detected in urine by age

Number of groups		Age group (Years)						
of drug of abuse items	10-19	20-29	30-39	40-49	50-59	60-70		
0	19	18	14	4	3		58	
1	15	34	28	6	2	1	86	
2	4	17	26	2	4	1	54	
3	2	4	10	5	1		22	
4			5				5	
5	1						1	
Grand Total	41	73	83	17	10	2	226	

Summary of group of drug of abuse item detected in urine by sex

Group of drug item	Female (N=83)			Male (N=143)		l 26)
		%		%		%
Cough medicine	36	43%	70	49%	106	46.9%
Ketamine	21	25%	32	22%	53	23.5%
Hypnotics	19	23%	18	13%	37	16.4%
Benzodiazepines	9	11%	24	17%	33	14.6%
Amphetamines	5	6%	20	14%	25	11.1%
Opiates	5	6%	15	10%	20	8.8%
Cocaine	4	5%	1	1%	5	2.2%
Analgesics	1	1%	1	1%	2	0.9%
MDMA	1	1%	1	1%	2	0.9%
Cannabis			1	1%	1	0.4%
Barbiturates			1	1%	1	0.4%
Grand Total	101		184		285	

Summary of group of drug of abuse item detected in urine by age

Groups of drug items	10- (N=		20-2 (N=		30-39 (N=8		40- (N=	49 :17))-59 =10)		-70 =2)	Grand 1 (N=226	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Cough medicine	12	29%	24	33%	54	65%	9	53%	6	60%	1	50%	106	46.9%
Ketamine	11	27%	34	47%	8	10%							53	23.5%
Hypnotics	2	5%	7	10%	22	27%	3	18%	2	20%	1	50%	37	16.4%
Benzodiazepines	1	2%	6	8%	20	24%	5	29%			1	50%	33	14.6%
Amphetamines	4	10%	5	7%	14	17%	2	12%					25	11.19
Opiates			1	1%	9	11%	6	35%	4	40%			20	8.8%
Cocaine	2	5%	2	3%	1	1%							5	2.2%
Analgesics			1	1%	1	1%							2	0.9%
MDMA	2	5%											2	0.9%
Cannabis					1	1%							1	0.4%
Barbiturates									1	10%			1	0.4%
Grand Total	34		80		130		25		13	}	3		285	

Common ingredients of cough medicine detected

Ingredients of cough medicine detected in urine	Female (N=36)		Male (N=70)		Grand Total (N=106)	
		%		%		%
Promethazine	14	39%	38	54%	52	49.1%
Codeine	8	22%	43	61%	51	48.1%
Pseudoephedrine/Ephedrine	6	17%	39	56%	45	42.5%
Chlorpheniramine	14	39%	26	37%	40	37.7%
Hydrocodone	3	8%	21	30%	24	22.6%
Brompheniramine	6	17%	10	14%	16	15.1%
Propoxyphene	11	31%	4	6%	15	14.2%
Dextromethorphan	1	3%	10	14%	11	10.4%
Dihydrocodeine	1	3%	3	4%	4	3.8%
Cetirizine	3	8%			3	2.8%
Methylephedrine	1	3%	1	1%	2	1.9%
Hydromorphone			1	1%	1	0.9%
Grand Total	68		196		264	

Novel drugs or impurities

- No unidentified peak of unknown substances was detected in the 226 urine samples so far.
- However, unexpectedly high prevalence of cough medicine was detected in urine of our study subjects. Ingredients of cough medicine were detected in 106 urine samples (47% of 226 subjects).
- 194 (86%) of 226 subjects did not report cough medicine in their last use, of which, 77 subjects (40% of 194 subjects) turned out to have positive findings of ingredients of cough medicine in their urine.
 - Of these 77 subjects, the five most frequently reported drug items in their last use were ketamine (22 subject, 29%), heroin (19 subjects, 25%), hypnotics (19 subjects, 25%), amphetamines (13 subjects, 17%) and benzodiazepines (10 subjects, 13%).

Five most common drug of abuse items reported or detected in our study population (N = 226)

Results of survey			Results of urine analys	is	
	N	%		N	%
Ketamine	81	31%	Cough medicine	106	46.9%
Amphetamines (Ice)	42	16%	Ketamine	53	23.5%
Hypnotics	36	14%	Hypnotics	37	16.4%
Cough medicine	32	12%	Benzodiazepines	33	14.6%
Opiates (Heroin)	26	10%	Amphetamines (Ice)	25	11.1%

Five most common drug of abuse items in female (N = 83)

Results of survey			Results of urine analys	is	
	N	%		N	%
Ketamine	31	30%	Cough medicine	36	43%
Amphetamines (Ice)	24	24%	Ketamine	21	25%
Hypnotics	18	18%	Hypnotics	19	23%
Opiates (Heroin)	11	11%	Benzodiazepines	9	11%
Benzodiazepines	8	8%	Amphetamines (Ice)	5	6%
			Opiates	5	6%

Five most common drug of abuse items in male (N = 143)

Results of survey			Results of urine analys	is	
	N	%		N	%
Ketamine	50	31%	Cough medicine	70	49%
Amphetamines (Ice)	18	11%	Ketamine	32	22%
Hypnotics	18	11%	Hypnotics	18	13%
Cough medicine	30	19%	Benzodiazepines	24	17%
Opiates (Heroin)	15	9%	Amphetamines (Ice)	20	14%

Age of 10 - 19 years (N = 41)

Drug items detected in urine		%
Cough medicine	12	29%
Ketamine	11	27%
Amphetamines	4	10%
MDMA	2	5%
Non-benzodiazepine hypnotics	2	5%
Cocaine	2	5%
Benzodiazepines	1	2%
Grand Total	34	

Age of 20 - 29 years (N = 73)

Drug items detected in urine		%
Ketamine	34	47%
Cough medicine	24	33%
Non-benzodiazepine hypnotics	7	10%
Benzodiazepines	6	8%
Amphetamines	5	7%
Cocaine	2	3%
Opiates	1	1%
Analgesics	1	1%
Grand Total	80	

Age of 30 - 39 years (N = 83)

Drug items detected in urine		%
Cough medicine	54	65%
Non-benzodiazepine hypnotics	22	27%
Benzodiazepines	20	24%
Amphetamines	14	17%
Opiates	9	11%
Ketamine	8	10%
Analgesics	1	1%
Cannabis	1	1%
Cocaine	1	1%
Grand Total	130	

Age of 40 - 49 years (N = 17)

Drug items detected in urine		%
Cough medicine	9	36%
Opiates	6	24%
Benzodiazepines	5	20%
Non-benzodiazepine hypnotics	3	12%
Amphetamines	2	8%
Grand Total	25	

Age of 50 - 59 years (N = 10)

Drug items detected in urine		%
Cough medicine	6	60%
Opiates	4	40%
Non-benzodiazepine hypnotics	2	20%
Barbiturates	1	10%
Grand Total	13	

Age of 60 - 70 years (N = 2)

Drug items detected in urine		%
Benzodiazepines	1	50%
Non-benzodiazepine hypnotics	1	50%
Cough medicine	1	50%
Grand Total	3	

Subjects recruited from NTEC

Drug items detected in urine	Fem (N=5		Mal (N=8	_	Grar (N=1	nd Total .42)
		%		%		%
Cough medicine	27	47%	45	53%	72	50.7%
Benzodiazepines	9	16%	20	24%	29	20.4%
Non-benzodiazepine hypnotics	10	18%	16	19%	26	18.3%
Ketamine	12	21%	14	16%	26	18.3%
Opiates	5	9%	11	13%	16	11.3%
Amphetamines	4	7%	12	14%	16	11.3%
Cocaine	4	7%	1	1%	5	3.5%
MDMA	1	2%			1	0.7%
Analgesics	1	2%			1	0.7%
Grand Total	73		119		192	

Subjects recruited from NTWC

Drug items detected in urine	Female (N=26)			Male (N=53)		nd Total 79)
		%		%		%
Cough medicine	9	35%	23	43%	32	40.5%
Ketamine	9	35%	16	30%	25	31.6%
Non-benzodiazepine hypnotics	9	35%	2	4%	11	13.9%
Amphetamines	1	4%	7	13%	8	10.1%
Opiates			3	6%	3	3.8%
Benzodiazepines			3	6%	3	3.8%
MDMA			1	2%	1	1.3%
Analgesics			1	2%	1	1.3%
Barbiturates			1	2%	1	1.3%
Cannabis			1	2%	1	1.3%
Grand Total	28		58		86	

Number of drug use reported and number of drug detected in urine with reference to the timing of last drug use

Time of last drug use		of dro	ug ite	em last	used		_	roup d in		_		Grand Total
	NS	1	2	3	4	0	1	2	3	4	5	
< 1 Day		23	3		1		9	12	4	1	1	27
1 day to <= 1 week	1	69	11		2	7	38	23	12	3		83
> 1 week to <= 1 month	1	33	3			11	18	5	2	1		37
> 1 month to <= 1 year		42	8	1	1	27	14	8	3			52
> 1 year		14	1	1		10	2	3	1			16
Not specified	7	3	1			3	5	3				11
Grand Total	9	184	27	2	4	58	86	54	22	5	1	226

*Note: NS = Not specified from the history

Concordance of individual's history of last use and corresponding urine result

History of last use	Urine detection by UPLC-TOF- MS				
mistory or last use	Positive	Negative	Grand Total		
Positive	А	В	A + B		
Negative	С	D	C + D		
Grand Total	A + C	B + D	226		

- = Number of subjects who reported to have positive drug use and had positive urine result
- B = Number of subjects who reported to have positive drug use but had negative urine result
- C = Number of subjects who reported no drug use but had positive urine result
- D = Number of subjects who reported no drug use and had negative urine result A + B = Number of subjects who had positive drug use history
- A + C = Number of subjects who had positive urine drug detection
 *A and D signify that the history and urine result are concordant.
- *B and C signify that the history and urine result are discordant.

Ketamine

History of last use	Urine detection by UPLC-TOF-MS					
History of last use	Positive	Negative	Grand Total			
Positive	47	34	81			
Negative	6	139	165			
Grand Total	53	173	226			

Amphetamines

History of last was	Urine detection by UPLC-TOF-MS					
History of last use	Positive	Negative	Grand Total			
Positive	15	27	42			
Negative	10	174	184			
Grand Total	25	201	226			

Cough medicine

History of lost was	Urine detection by UPLC-TOF-MS				
History of last use	Positive	Negative	Grand Total		
Positive	29	3	32		
Negative	77	117	194		
Grand Total	106	120	226		



Subject recruitment

Month/Year	Cumulative no. of subjects	% of target recruitment
Sep 2007	23	4.6%
Nov 2007	37	7.4%
Mar 2008	51	10.2%
Jun 2008	56	11.2%
Oct 2008	81	16.2%
Dec 2008	107	21.4%
Apr 2009	134	26.8%
Jan 2010	222	44.4%
Mar 2010	226	45.2%
May 2010	291	58.2%

Current update

- Revised study protocol (to expand recruitment source in NTWC) was approved by the Joint-CUHK-NTEC Clinical & Research Ethics Committee (CREC) on 16 March 2010
- Research protocol was approved by NTWC CREC on 14 April 2010
- Subject recruitment in CPH started since 22 April 2010
- Current recruitment from CPH: 62 subjects up to 18 May 2010
- Recruitment from both projects in NTEC and NTWC

Project 1: 153 subjects (30.6%)Project 2: 138 subjects (27.6%)Total: 291 subjects (58.2%)

Factors affecting subject recruitment

- Improving factors:
 - More clinic sessions per week in CPH
 - Larger pool of potential subjects
 - Adoption of paying honorarium
- Hindering factors:
 - Limited active cases in clinic
 - High default rate (30 50% per clinic session)
 - Unsuitable subjects (e.g. too psychotic, criminal cases, etc.)
 - Variable response rate (0 25%)

Achieving the target

- Target recruitment: 500 subjects
- From July 2007 to March 2010 (33 months):
 - 226 subjects recruited (45.2% of target)
- From April 2010 to May 2010 (1 month):
 - 62 subjects recruited (12.4% of target)
 - Up to May 2010, 291 subjects recruited (58.2% of target)
- No. of subjects to be recruited: ~200
- Estimated recruitment: ~10 subjects per week
- Estimated time to achieve our target: 5-6 months (by Dec 2010)

Other usage of UPLC-TOF-MS in detection of substance abuse

- Potential use of salivary specimen for analysis
 - Assessing the sensitivity and specificity of a commercial kit for ketamine using spot salivary sample

Part IV: Discussions Thank you!

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