Doctoral Seminar : PhD Biostat Sept6 2013

Pongsakorn Tantilipikorn

Outline

- Study plan and milestone
- Progression of Researches and Thesis

I) Study plan and milestone

- Course material from Takasila Classroom and KKU

- Course enrollment from UC Berkley : Inferential statistic

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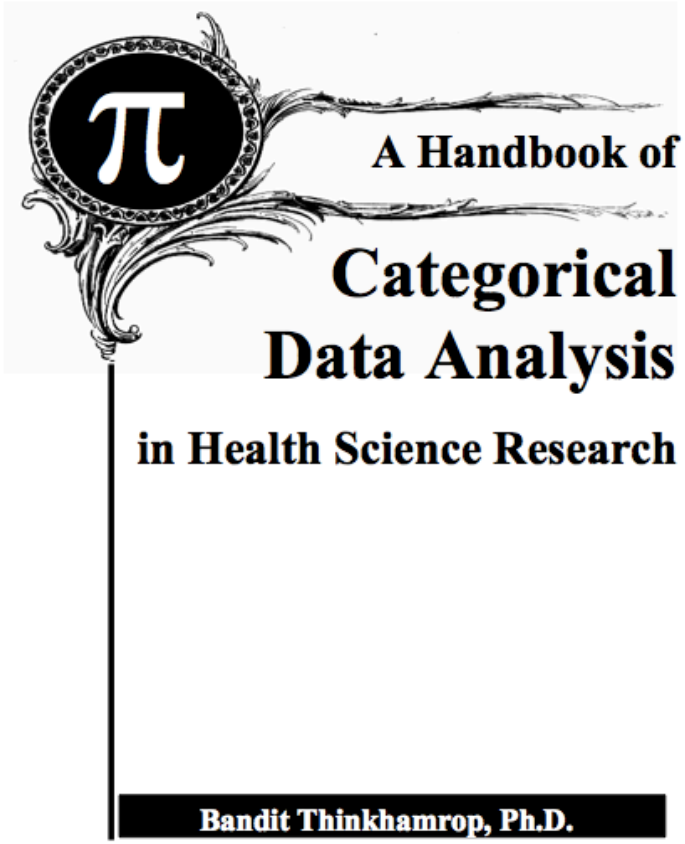
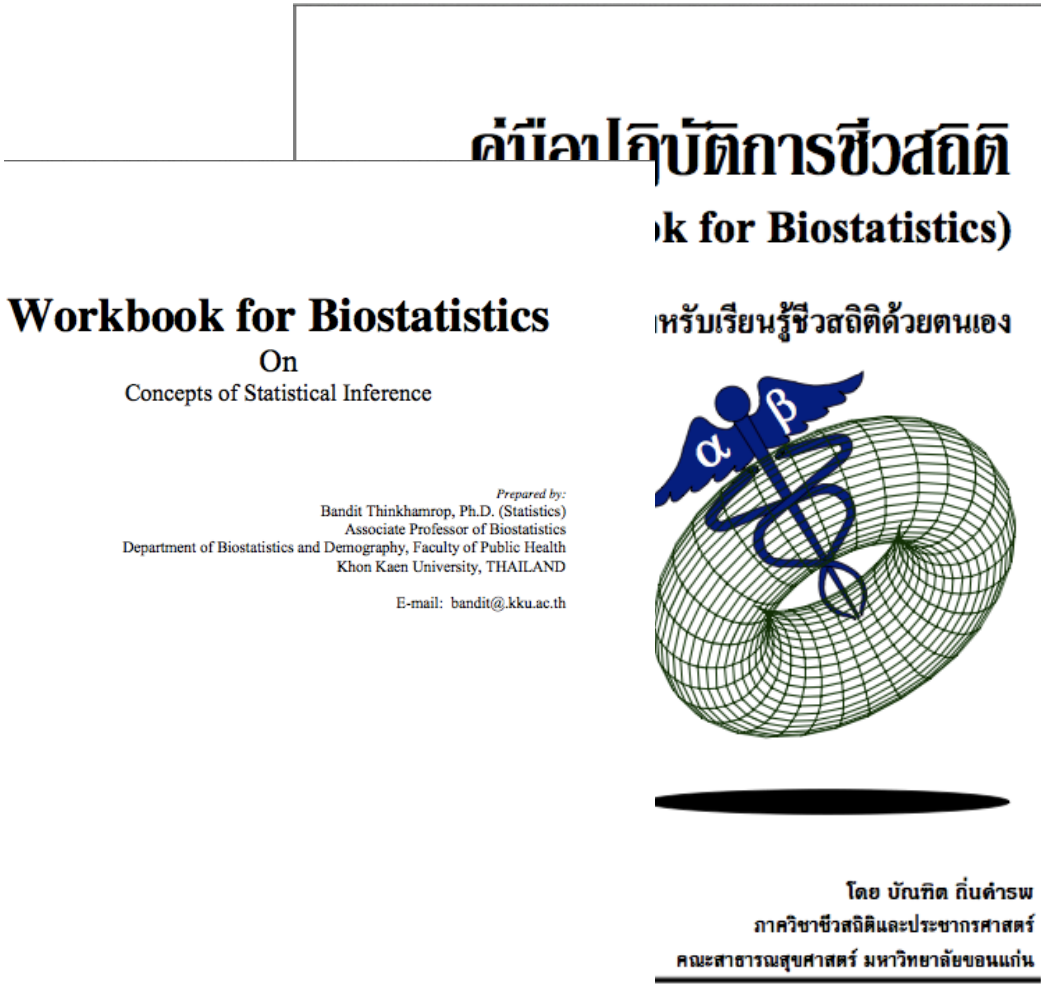
Self-study from KKU

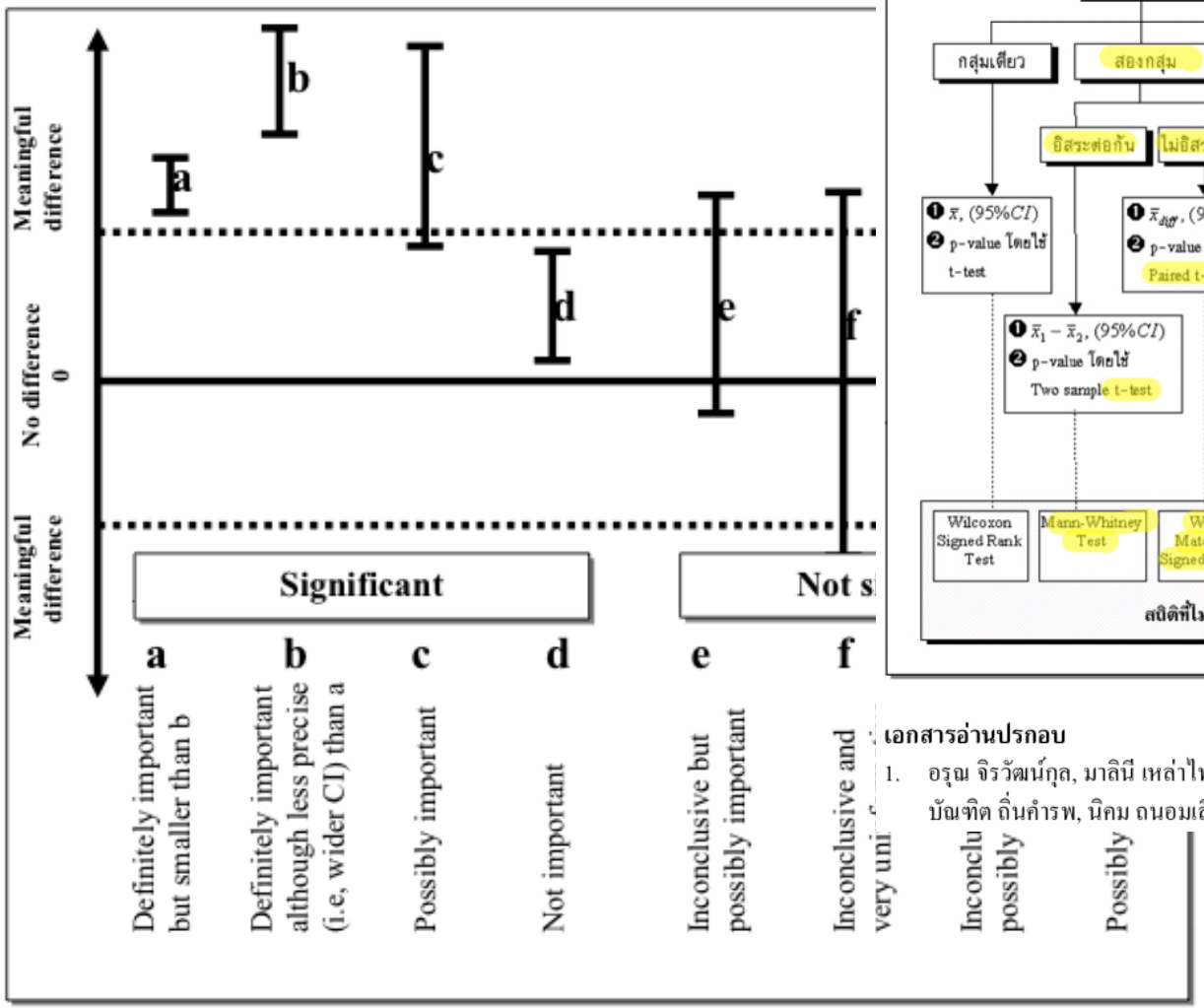




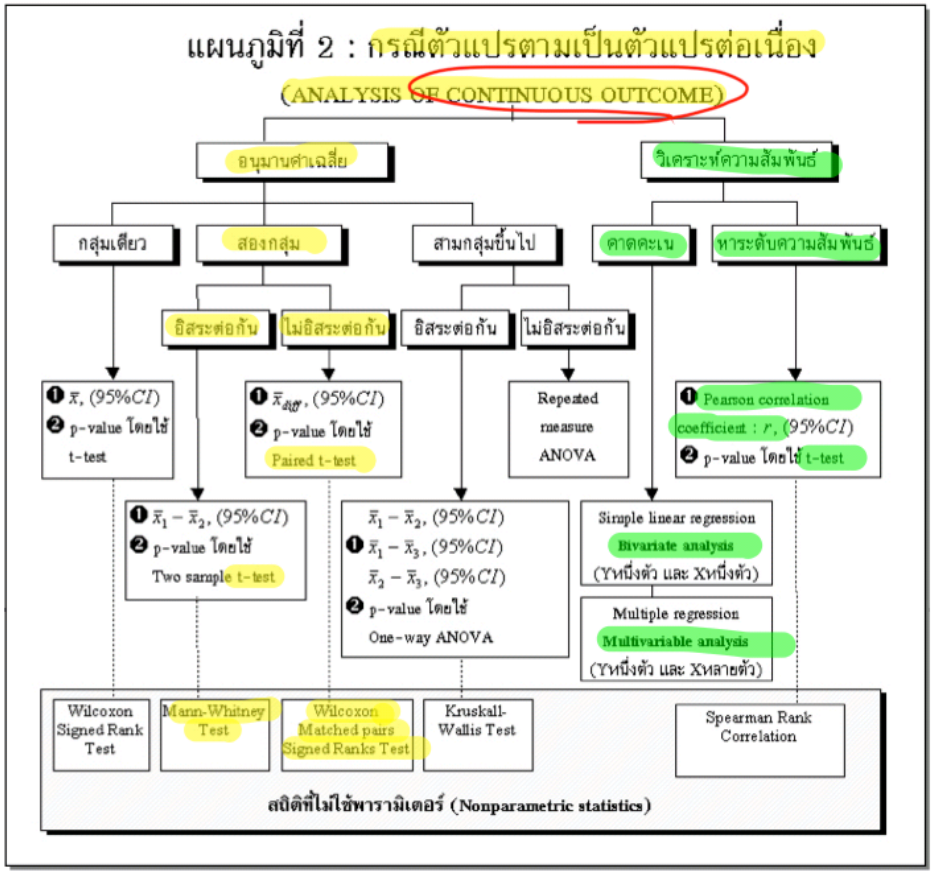
PART 3: CONFIDENCE INTERVAL VS.

Confidence intervals showing eight possible interpretatior
statistical significance and practical importanc

(Adapted from: Armitage, P. and Berry, G. Statistical methods in mec
edition. Blackwell Scientific Publications, Oxford. 1994.pa



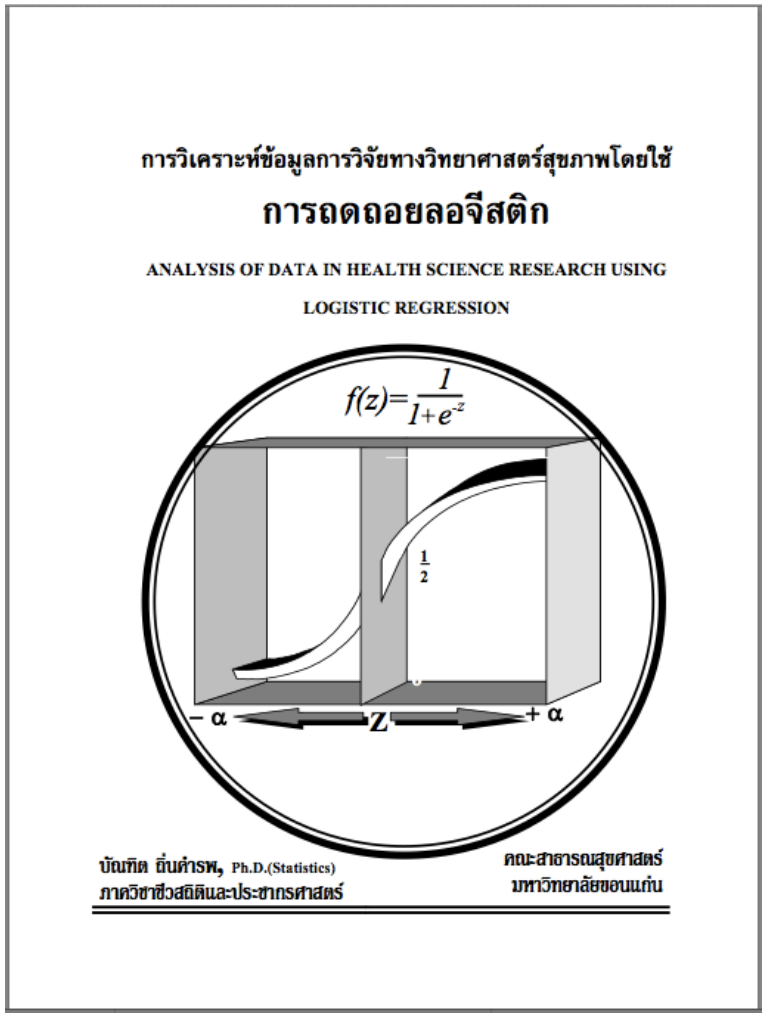
แผนภูมิที่ 2 : กรณีตัวแปรตามเป็นตัวแปรต่อเนื่อง

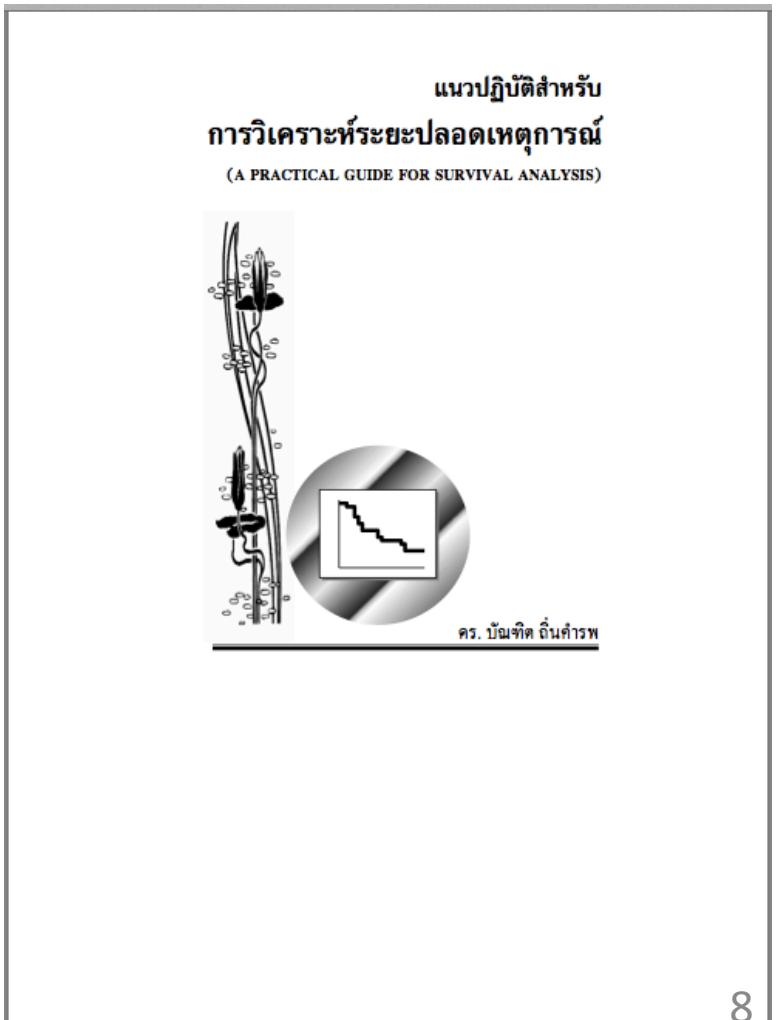


เอกสารอ่านปรกอบ

1. อรุณ จิรวัฒน์กุล, มาลินี เหล่าไพบูลย์, จิราพร เขียวอยู่, ยุพา ถาวรพิทักษ์, จารุวรรณ โชคคณาพิทักษ์, บัณฑิต ถิ่นคำรพ, นิคม ถนอมเสียง. (2542). *ชีวสถิติ*. ขอนแก่น. โรงพิมพ์คลังนานาวิทยา.

Self-study from KKU

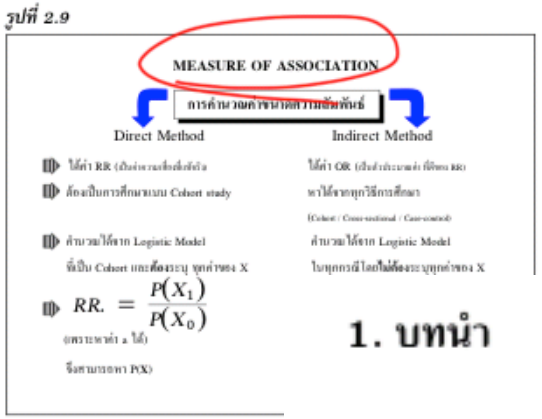




ตัวอย่างนี้ เป็น RR. ที่ควบคุมผลของอายุและ ECG แล้ว (Adjusted RR.)

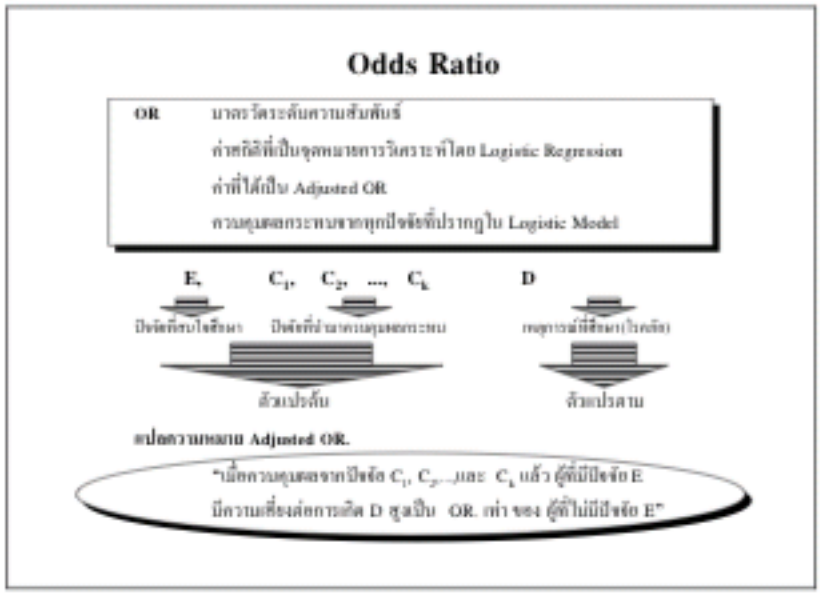
RR. เป็นมาตรวัดระดับความสัมพันธ์โดยตรง (Direct measure) แม้สามารถคำนวณได้ จาก Logistic Regression Model แต่ต้องมาจากการศึกษาแบบ Cohort study และต้องระบุทุกค่าของ X จึงทำให้มีข้อจำกัด ตรงข้ามถ้าได้จากการศึกษาแบบอื่น ต้องคำนวณค่า OR ค่านี้คำนวณได้จากทั้งการศึกษาแบบ Cohort

รูปที่ 2.9



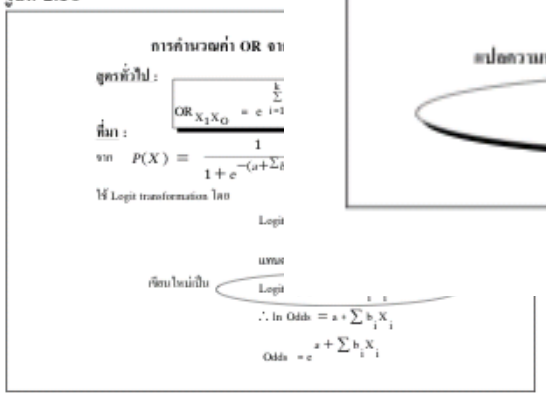
1. บทนำ

รูปที่ 3.1



เป้าหมายของการวิเคราะห์โดยใช้ Logistic Regression คือ ประมาณค่าระดับความสัมพันธ์ (Magnitude of association) ระหว่างปัจจัยที่ศึกษา (E) กับปัญหาที่ศึกษาซึ่งมักหมายถึงโรคภัยต่าง ๆ (D) โดยควบคุมผลกระทบจากตัวแปรอื่น ๆ ค่า OR ที่ได้จาก Logistic Regression เป็นค่าระดับความสัมพันธ์ที่ควบคุมผลจากทุกตัวแปรที่ปรากฏใน Model จึงเรียกว่าเป็น Adjusted OR

รูปที่ 2.10



เป็นผลรวมเชิงเส้น (Linear sum) ของค่าสัมประสิทธิ์ดังนี้ Logit $P(X) = a+\sum biXi$

ไม่เหมาะสมก่อน (ผิดเป็นครู) จากนั้นจึงเป็นแนวทางที่ถูกต้องเหมาะสม ตามลำดับดังนี้

3.1 การวิเคราะห์เปรียบเทียบระหว่างกลุ่มที่ไม่เหมาะสม

3.1.1 วิเคราะห์โดยใช้ระยะปลอดเหตุการณ์เป็นตัวแปรตาม

3.1.1.1 เปรียบเทียบค่าเฉลี่ยโดยใช้ t-test

```
. ttest  time, by(drug)

Two-sample t test with equal variances

------------------------------------------------------------------------------
   Group |     Obs        Mean    Std. Err.   Std. Dev.   [95% Conf. Interval]
---------+--------------------------------------------------------------------
       0 |       6    13.33333    2.092314    5.125102    7.954869     18.7118
       1 |       6    27.16667    5.775908    14.14803    12.31922    42.01411
---------+--------------------------------------------------------------------
combined |      12       20.25    3.595294    12.45446    12.33681    28.16319
---------+--------------------------------------------------------------------
    diff |           -13.83333    6.143199               -27.52123   -.1454339
------------------------------------------------------------------------------
Degrees of freedom: 10

                    Ho: mean(0) - mean(1) = diff = 0

     Ha: diff < 0                 Ha: diff ~= 0                 Ha: diff > 0
   t =  -2.2518                 t =  -2.2518                  t =  -2.2518
P < t =   0.0240         P > |t| =   0.0480          P > t =   0.9760
```

คำสั่ง ttest ข้างต้นเป็นคำสั่งสำหรับทดสอบว่าค่าเฉลี่ย TIME ระหว่างกลุ่ม DRUG แตกต่างกันอย่างมีนัยสำคัญหรือไม่ ในวงรีคือค่าที่ควรนำไปสรุปในผลการวิเคราะห์ (ศึกษารายละเอียดใน บัณฑิต ถิ่นคำรพ,

Censored observation ต้องมีวิธีการ
รุปที่ผิด อย่างไรก็ตามแม้ข้อมูลไม่มี
ete observation ทั้งหมด แต่ถ้ามีตัว
ยใช้ Survival analysis สามารถให้
รผนวกเอาข้อมูลระยะเวลาในแต่ละ
าพสูงกว่าวิธีการทั่วไปทางสถิติ

ว่างกลุ่มที่เหมาะสม

ce โดยใช้ Log-rank test

function ว่าเป็นสัดส่วนกันระหว่าง

Self-study from KKU

PH·KKU
Faculty of Public Health
Khon Kaen University
We are Expertise in Community Approach

DOCTOR OF PHILOSOPHY PROGRAM IN EPIDEMIOLOGY AND BIOSTATISTICS

(INTERNATIONAL PROGRAM)

Evaluation of Cancer and Chronic Disease Screening

June 2013

Professor Hsiu-Hsi Chen and

Taiwanese DHCG Group: Dr. Sam Li-Sheng Chen,

Dr. Amy Ming-Fang Yen, , Dr. Sherry Yueh-Hsia Chiu,

Dr. Jean Ching-Yuan Fann, Dr. Wendy Yi-Ying Wu

Schedule: 27th June ~ 2nd July

Program:

Module 1 (8:30am-12:00am, 27th Jun)

Basic Concept of Cancer and Chronic Disease Screening (2.5 hours)

Computer Practice of Data Analysis on Cancer and Chronic Disease Screening (1 hour)

Module 2 (13:00pm-17:00pm, 27th Jun)

Study Design for Evaluation of Disease Screening-Experimental Design (3 hours)

Computer Practice of Evaluation for Randomized Controlled Trial of Screening (1 hour)

Module 3 (8:30am-12:00am, 28th Jun)

Study Design for Evaluation of Disease Screening- Quasi-experimental Design (2.5 hours)

Computer Practice of Evaluation for Service Screening Program (1 hour)

Module 4 (13:00pm-17:00pm, 28th Jun), (8:30am-12:00am, 1st Jul)

Temporal Natural History Model in Cancer and Chronic Disease Screening (6.5 hours)

Computer Practice of Temporal Natural History Model (1 hour)

Module 5 (13:00pm-17:00pm, 1st Jul)

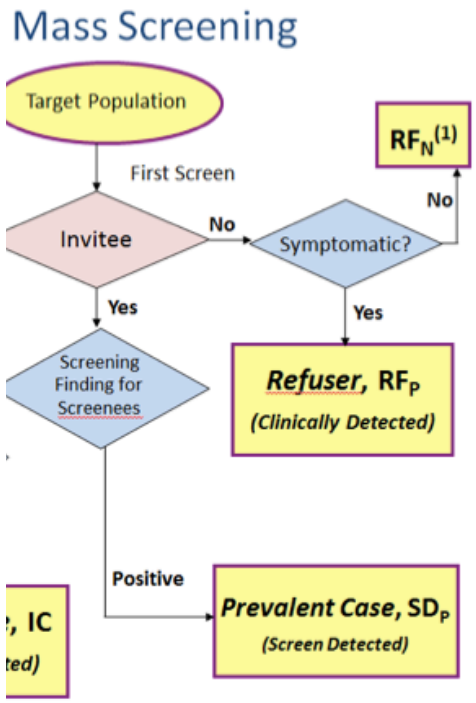
Bias Adjustment in Cancer and Chronic Disease Screening (3 hours)

Computer Practice of Data Analysis on Bias Adjustment in Screening (1 hour)

Module 6 (8:30pm-15:00pm, 2nd Jul)

Cost-effectiveness Analysis of Screening Program (5.5 hours)

Computer Practice of Cost-effectiveness Analysis of Screening Program (1 hour)



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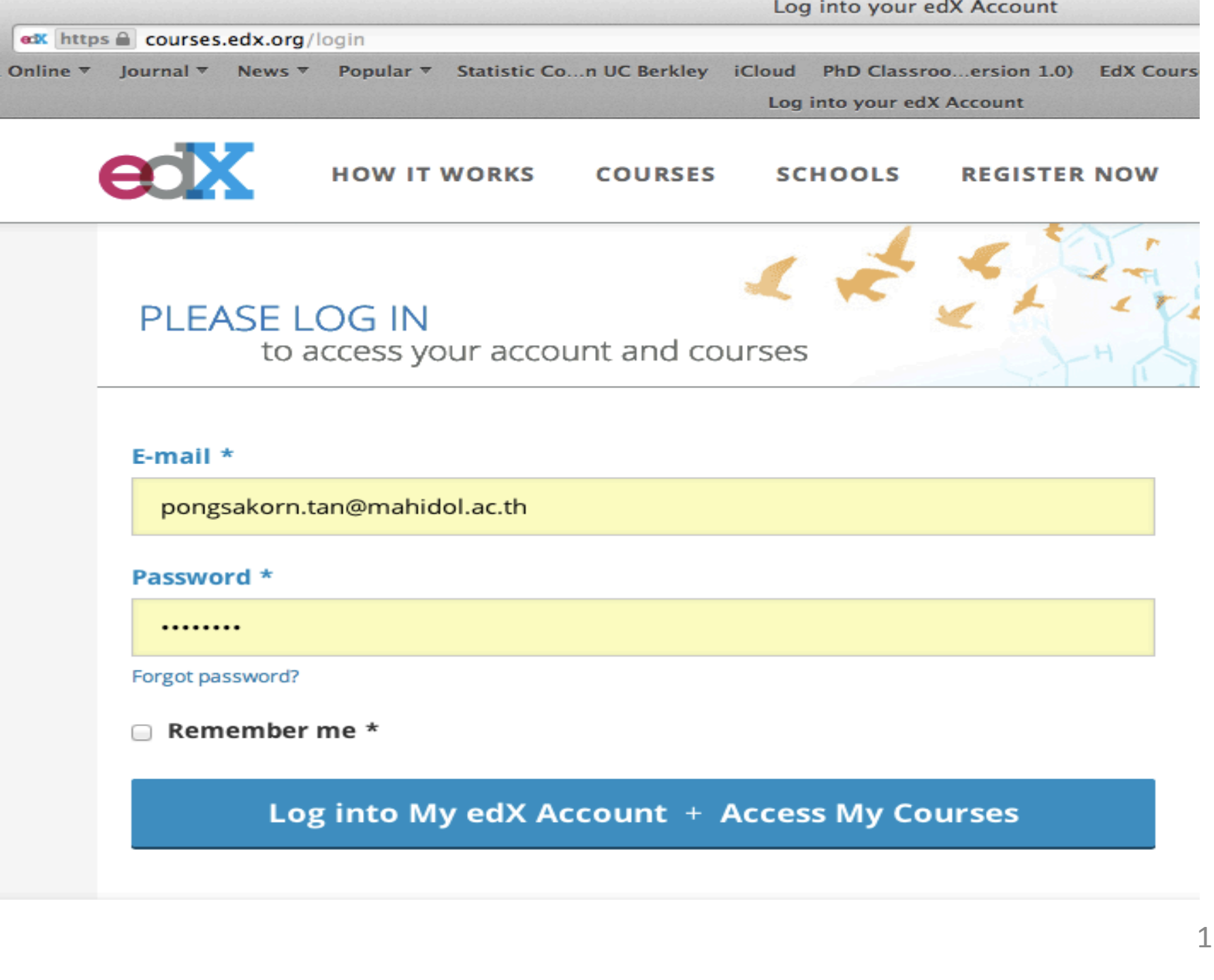
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Password *
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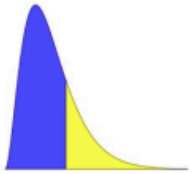
Remember me *
Log into My edX Account + Access My Courses

Course Updates & News

AUGUST 27, 2013

Congratulations, everyone! We've come a long way together, and I hope you've enjoyed 2X as much as I



BerkeleyX

Course Completed - Aug 27, 2013

Stat2.3x Introduction to Statistics: Inference

Final course details are being wrapped up at this time. Your final standing will be available shortly.

View Archived Course

Unregister

HarvardX

Course Starts - Oct 14, 2013

HSPH-HMS214x Fundamentals of Clinical Trials

Unregister

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27

Chapter 2

Hypothesis Testing: Does the Results

An important branch of Statistics, *Statistical Decisior* of making decisions—such as choosing between two world—on the basis of uncertain data. In CHAPTER 19 treated the "Let's Make a Deal" problem as a decisio hypothesis that switching one's guess of which door chance of winning, and the hypothesis that switching to the chance of winning. We saw that there were tw deciding that switching was better when in fact it was

This chapter discusses rules for deciding between co of data that have a random component (such as drav competing hypotheses are called the NULL HYPOTHESI The rules are called HYPOTHESIS TESTS or *hypothesis* null hypothesis is that something is not present, that there is no difference between two PARAMETERS. Typi that some effect is present, that a treatment has an e differ. The main requirement of the null hypothesis is compute the probability that the test rejects the null h hypothesis is true. That probability is called the SIGNI doubt, choose the simpler of the hypotheses to be th lead to easier computations.)

The two types of error are as follows:

- Rejecting a true null hypothesis. This is called a language, a Type I error is a false alarm.
- Failing to reject a false null hypothesis. This is

Controlling the chances of these two kinds of error is

Chapter 30

Approximate Hypothesis Tests: the *z* Test and the *t* Test

This chapter presents tw equals a particular value the *z* test and the *t* test. approximations to the PR HYPOTHESIS, so their SIGN sample size is reasonab has a *nearly normal dist* significance levels of the conditions are not met, t substantially from their r APPROXIMATION; the *t* test probability histograms b the deep connection bet how to compute approxi normal populations usin

In CHAPTER 29, TESTING E equality of two percenta POPULATIONS. The origina independent SAMPLE PER means are equal is true, addition, the SAMPLE SIZE pooled BOOTSTRAP estim

where ϕ is the pooled s $^{-c})$ under the null hypoth

Chapter 31

The Multinomial Distribution and the Chi-Squared Test for Goodness of Fit

CHAPTER 27, HYPOTHESIS TESTING: DOES CHANCE EXPLAIN THE RESULTS?, presented hypothesis tests in a general setting. CHAPTER 29, TESTING EQUALITY OF TWO PERCENTAGES, presented exact and approximate hypothesis testing procedures for population percentages. CHAPTER 30, APPROXIMATE HYPOTHESIS TESTS: THE *z* TEST AND THE *t* TEST, presented approximate tests of hypotheses about population means. All the examples of hypothesis testing so far have involved counts of outcomes that are dichotomous (categorical data with only two categories—good and bad—or quantitative data that have only two possible values—0 and 1), or have involved quantitative data. This chapter presents hypothesis tests and approximate hypothesis tests for probability models of CATEGORICAL DATA. Along the way, it introduces *joint probability distributions* and the *chi-square curve*, which approximates the probability histogram of a random variable introduced in the chapter, the *chi-square statistic*.

The Multinomial Distribution

The *multinomial probability distribution* is a probability model for random categorical data: If each of n independent trials can result in any of k possible types of outcome, and the probability that the outcome is of a given type is the same in every trial, the numbers of outcomes of each of the k types have a multinomial joint probability distribution. This section develops the multinomial distribution; later in the chapter we develop hypothesis tests that a given multinomial model is correct, using the observed counts of data in each of the categories.

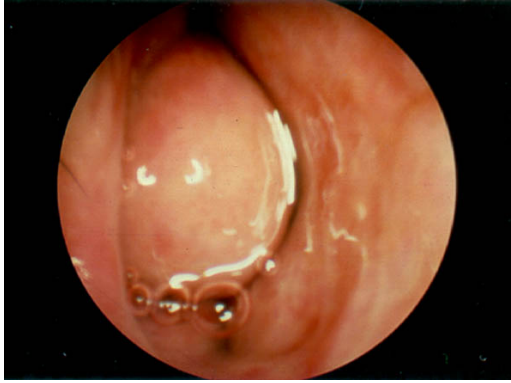
Suppose we have an experiment that will produce CATEGORICAL DATA: The outcome can fall in any of k categories, where $k > 1$ is known. Let p_i be the probability that the outcome is in category i, for $i = 1, 2, \ldots, k$. (We assume that the categories are DISJOINT—a given outcome cannot be in more than one category—and EXHAUSTIVE—each datum must fall in some category. That is, each datum must be in one and only one of the k categories. It follows that $p_1 + p_1 + \ldots + p_k = 100\%$.)

For example, consider rolling a fair die. The side that lands on top can be in any of six categories: 1, 2, … , 6, according to the number of spots it has. The corresponding category probabilities are

$$p_1 = p_2 = \ldots = p_6 = 1/6.$$

II) Progression of research :

Allergy



- Diagnosis by nasal challenge
- Diagnosis by skin test

→

- Peak nasal inspiratory flow rate
- Diagnostic Value of intradermal skin test in allergy

- Comorbidity of allergic rhinitis

→

- Pulmonary function test in Allergic Rhinitis

- Treatment : Curative options

→

- Randomized-controlled trial allergen injection immunotherapy

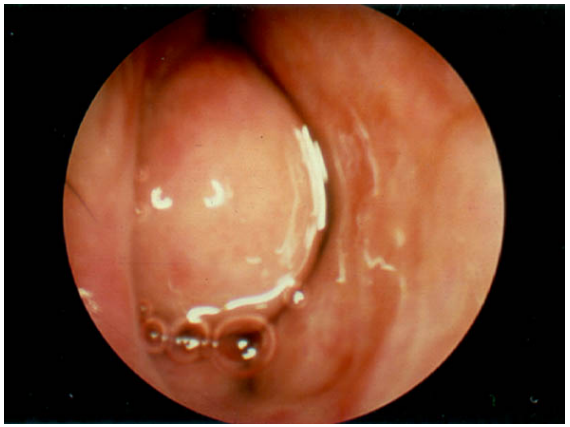
II) Progression of research projects

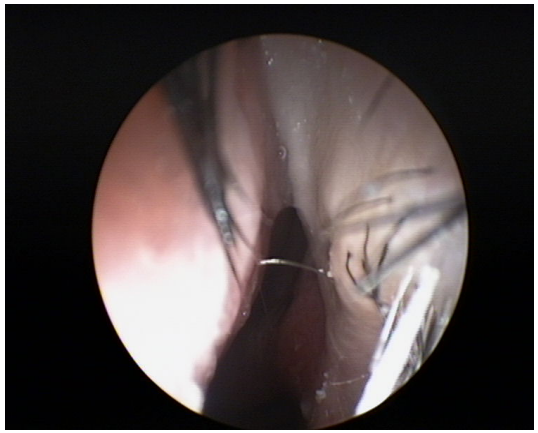
- Peak nasal inspiratory flow rate
- Pulmonary function test in Allergic Rhinitis
- Diagnostic Value of intradermal skin test in allergy (on-going and in process of recruitment)
- Randomized-controlled trial allergen injection immunotherapy (granted from NRCT วช. and will start in Jan2014

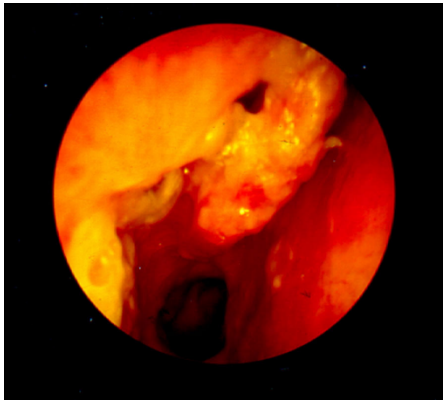
Peak nasal Inspiratory Flow: Normative value for Asian Ethnic

Introduction (I)

- Nasal obstruction : one of the most common complaints/symptoms
- Determination of airflow : Essential parameter of nasal provocation test (NPT)
- "Objective" measurement of nasal airflow is mandatory factor for NPT



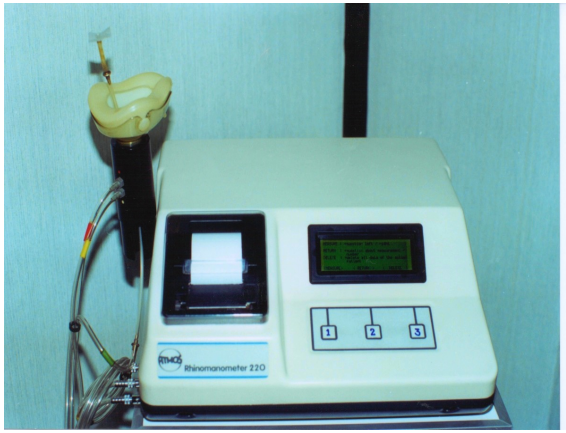




Introduction (II)

- Quantitative evaluation of nasal obstruction :

Rhinomanometer (RMM)



And Acoustic Rhinometer (ARM)

Nasal Airway Resistance in Asymptomatic Thai Population

Chaweewan Bunnag, M.D.*
Perapun Jareoncharsri, M.D.*

Siriraj Hosp Gaz
Vol. 47, No. 8, August 1995

NAR	Before decongestant	After decongestant
Rt. side	0.45 ± 0.21	0.33 ± 0.14 Pa/cc/sec
Lt. side	0.51 ± 0.31	0.34 ± 0.26 Pa/cc/sec
Total	**0.22 ± 0.10**	0.15 ± 0.06 Pa/cc/sec

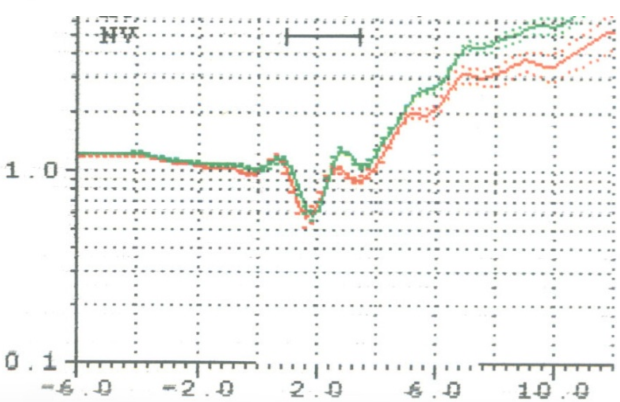
Acoustic rhinometry of Asian noses

Pongsakorn Tantilipikorn, M.D., Perapun Jareoncharsri, M.D., Siriporn Voraprayoon, M.Sc., Chaweewan Bunnag, M.D., Peter A. Clement, M.D. Ph.D.

Table 3 Acoustic rhinometry of 135 healthy Thai adults: Comparison between male and female subjects

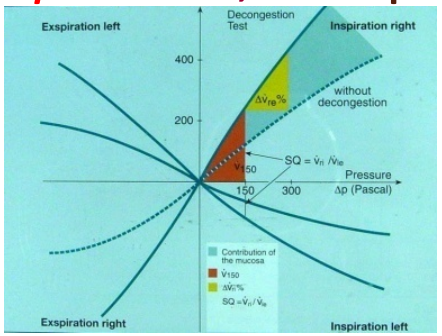
	Before Decongestion		After Decongestion	
	Male Subjects (n = 38)	Female Subjects (n = 97)	Male Subjects (n = 38)	Female Subjects (n = 97)
MCA (cm^2)	0.56 ± 0.15	0.55 ± 0.13	0.69 ± 0.17** (23.2% increase)	0.62 ± 0.12** (12.7% increase)
Distance (cm)	1.99 ± 0.67*	1.53 ± 0.51*	1.66 ± 0.88****	1.31 ± 0.65****
NV (cm^3)	3.78 ± 0.72	3.61 ± 0.65	4.50 ± 0.84*** (19.1% increase)	4.06 ± 0.68*** (12.5% increase)

*Distance, *p = 0.000; MCA; **p = 0.026; NV, ***p = 0.002; ****p = 0.012.*
MCA = minimal cross-sectional area; NV = nasal volume.



Introduction (III)

- Both RMM and ARM are *relatively expensive*, complex to use and *time-consuming.*
- Require *experience technician*



- In 1980, Youlten presented the **peak nasal inspiratory flow meter (PNIF**)

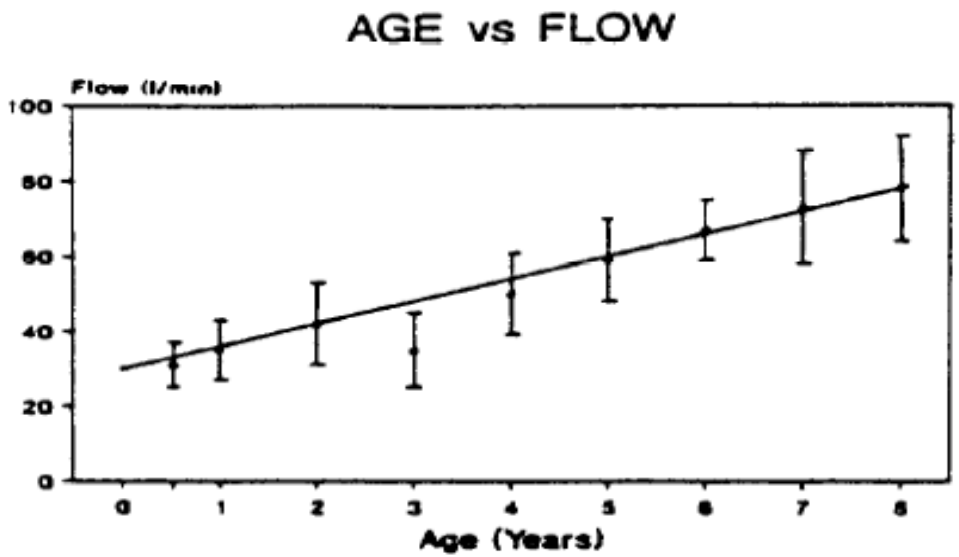
- The **patient sniff air through the nose** and the pe flow is recorded by a cursor

Introduction

Peak nasal inspiratory flow measurement: an investigation in children

C.A.J. Prescott*, K.E. Prescott

artment of Otolaryngology, The University of Cape Town, The Red Cross War Memorial Children's Hospital, Klipfontein Road, Rondebosch, 7700 Cape Town, South Africa



- *Prescott CAJ and Prescott KE* in 1995 studied the values for PNIF in normal **children of South Africa : MEAN PNIF = 80 L/min at 8 years-old**

Introduction

Peak nasal inspiratory flow; normal range in adult population*

Rhinology, 44, 32-35, 2006

Giancarlo Ottaviano[1,2], Glenis K. Scadding[2], Stuart Coles[3], Valerie J. Lund[2]

Table 1. Mean PNIF values at each attempt in males and females.

	Males (n=60)		Female (n=77)	
Variable	*Mean*	*SD*	*Mean*	*SD*
Age	43.3	22.1	40.2	18.6
Height	172.6	7.4	161.5	8.7
PNIF1	126.3	46.5	104.5	35.2
PNIF2	142	46.8	119.5	36.6
PNIF3	143	48.6	121.9	36

- *Giancarlo Ottaviano* ; London, UK, to establish baseline **normal values from 137 adult subjects.**

Objective

Primary objective :

to establish **normative PNIF** data for a healthy **Thai adults** population and imply those value as a reference for Asian Ethnic

Secondary objective :

- Determine association **PNIF** values with **age**, **height**, **weight** and **sex** in adults
- **Comparison** of PNIF by using Rhinomanometry (RMM) as the reference tests

Study design

- **Descriptive study**
- Study population : **Healthy** Thai volunteers

$$n = [z\alpha/2 \, SD / d]^2$$

α = chance of type I error = 0.05 (2-sided), z0.025 = 1.96

SD = standard deviation of maximum PNIF in normal pop. = 50

D = Error of the estimation of mean of PNIF = 10

$$n = [1.96(50)/10]2 = 96.04 = \mathbf{97}$$

Inclusion Criteria

- Age>15 years and Age <70 years
- No symptom of nasal congestion
- No history of asthma, rhinitis
- No structural abnormalities of nasal cavities

Exclusion Criteria

- Previous surgery to the nose and paranasal sinuses
- Take inhale nasal corticosteroid within 2 weeks or oral corticosteroid within 1 week
- Take nasal decongestant within 1 day
- Smoking

Material and methods

- One hundred and eighty subjects were tested for normative value of PNIF
- Three satisfactory maximal inspirations were obtained and the highest of the three results was taken as the PNIF
- For the first one hundred subjects, after PNIF was tested, RMM was tested to determined the correlation between two tests.

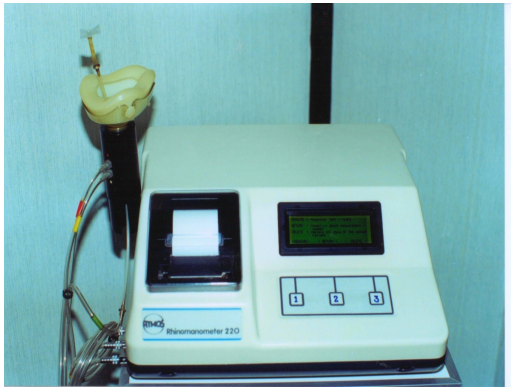
Research Study Design

PNIF x3

Subject#1-100

Subject #1-100

Proceed for RMM test



PNIF x3

Subject#100-180

Only PNIF was done

Results

Table 1 : Subjects demographic data. (N=180)

	Male (n=82)	Female (n=98)	Total (n=180)
Age (Yr)	39.18±14.04	38.74±13.53	38.94±13.73
Height (cm)	169.18±6.06	157.69±5.73	162.93±8.21
Weight (kg)	71.32±13.48	53.92±10.59	61.85±14.78
BMI	24.91±4.51	21.71±4.28	23.16±4.66

Table 2: Peak nasal inspiratory flow rate (PNIF , L/sec) of male & female subject (N=180)

	Male (n=82)	Female (n=98)	p-value
PNIF1	119.33±33.13	82.96±23.99	
PNIF2	129.45±36.12	85.38±27.81	
PNIF3	132.07±37.89	91.60±30.42	
PNIF max	139.02±37.62	97.11±27.13	<0.0001

Table 3: Peak nasal inspiratory flow rate (PNIF) & associated factors (N=180)

	PNIF	
	r	p
Age		0.37
Weight		0.85
Height		0.61
BMI		0.96
Sex	0.55	<0.001

Table 4: Peak nasal inspiratory flow rate (PNIF) and Rhinomanometry values. (N=100)

	PNIF	
	r	p
Airway resistance	-0.27	0.0075
Nasal Flow Rate	0.26	0.0094

Table 5: Nasal airway resistance value by rhinomanometry (RMM), (N=100)

NAR (Pa/cc/sec)	Before Decongestion	After Decongestion
Right Side	0.44±0.26	0.29±0.16
Left Side	0.45±0.24	0.30±0.19
Total	0.20±0.10	0.14±0.06

Disscussion

Mean PNIF (L/min)	Male	Female
Gaincarlo et al	143±48.6	121.9±36
This study	139.02±37.62	97.11±27.13

- Gaincarlo et al, were produced relating PNIF to age, sex, and height, In this study was showed correlating PNIF to sex.
- PNIF is a cheap, simple, easy to performed method to assess nasal patency with hygienic advantages over expiratory flow device

Plan for the second trimester

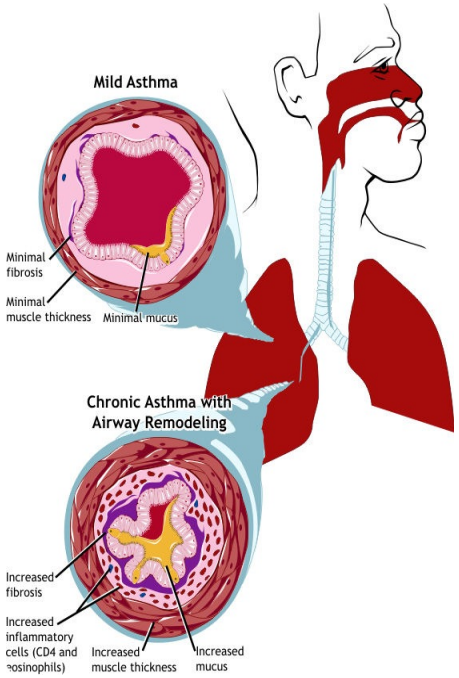
- Submit the first article of PNIF
- Analyze the data of Pulmonary function test in AR
- Complete recruitment of the subject in the project intradermal test
- Start the multicenter trial of immunotherapy

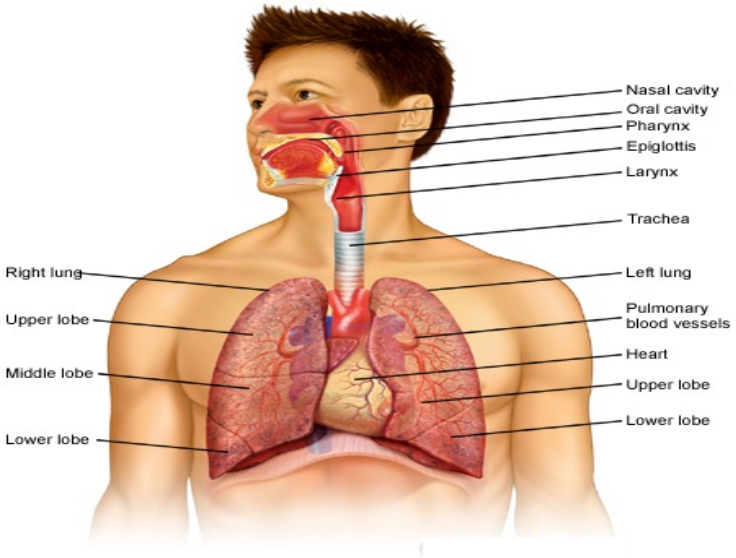
Thank you

Sriraj Hospital

Prevalence study of Pulmonary function test in Allergic Rhinitis

Introduction



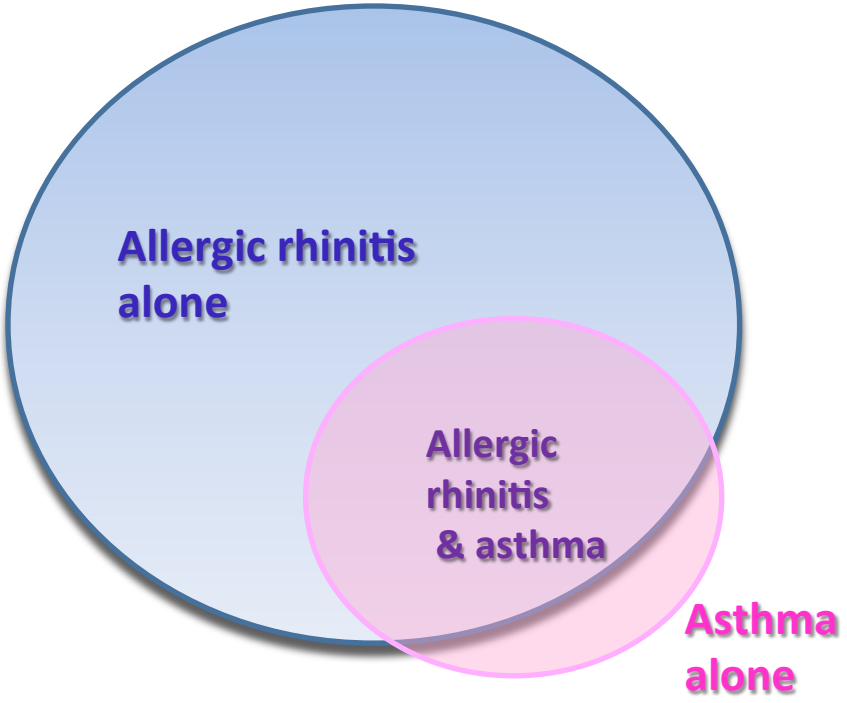


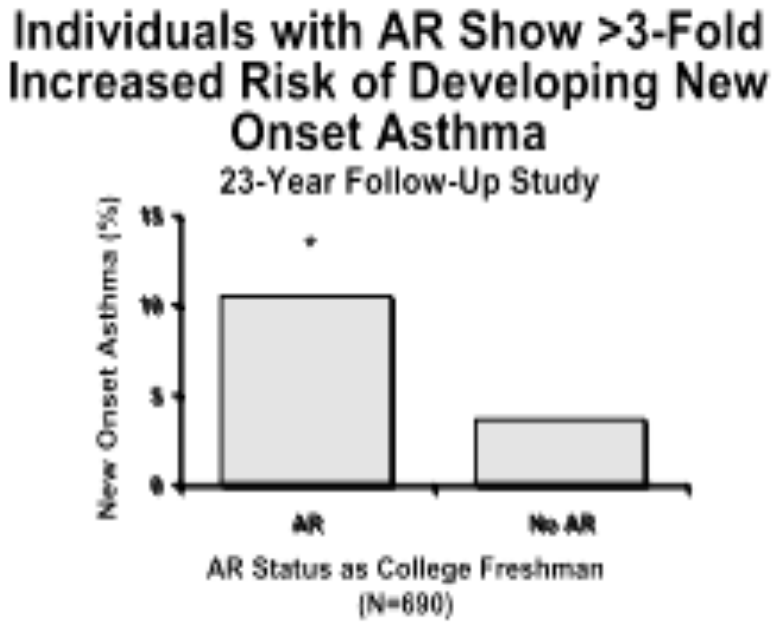
Linkage of upper airway and lower airway

- Anatomic
- Pathophysiologic
- Natural course of disease: “Allergic March” (Allergic Rhinitis to Allergic Asthma

A study of pulmonary function (FEV_1) in allergic rhinitis patients

Introduction





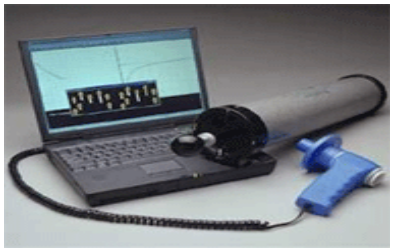
- 80% of asthma patients → allergic rhinitis
- 35-40% of allergic rhinitis patients → asthma

Guerra S. Rhinitis as an independent risk factor for adult-onset asthma. Journal of Allergy and Clinical Immunology - Volume 109, Issue 3 (March 2002)

Introduction : Spirometry

- Test of pulmonary function
- Force expiratory volume in one second
- Evaluation of reversible airflow obstruction

- Values depend on : Race, Sex, Age, Height
- FEV_1 predicts asthmatic condition



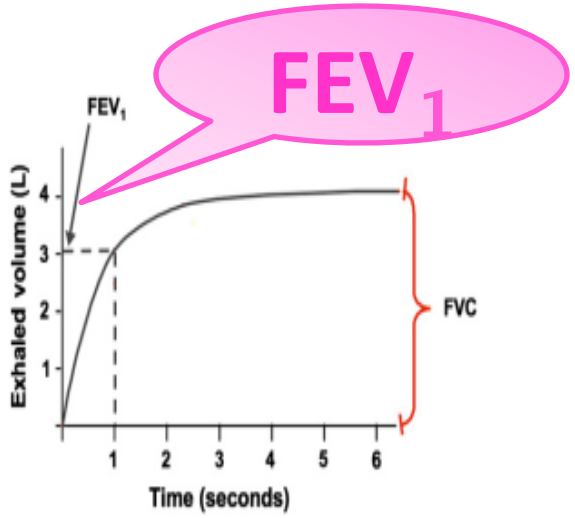


Fig. 2. The forced expiratory volume (FEV_1) is the volume of air that can be expired in the first second of a forced maximal expiration. FVC, forced vital capacity.

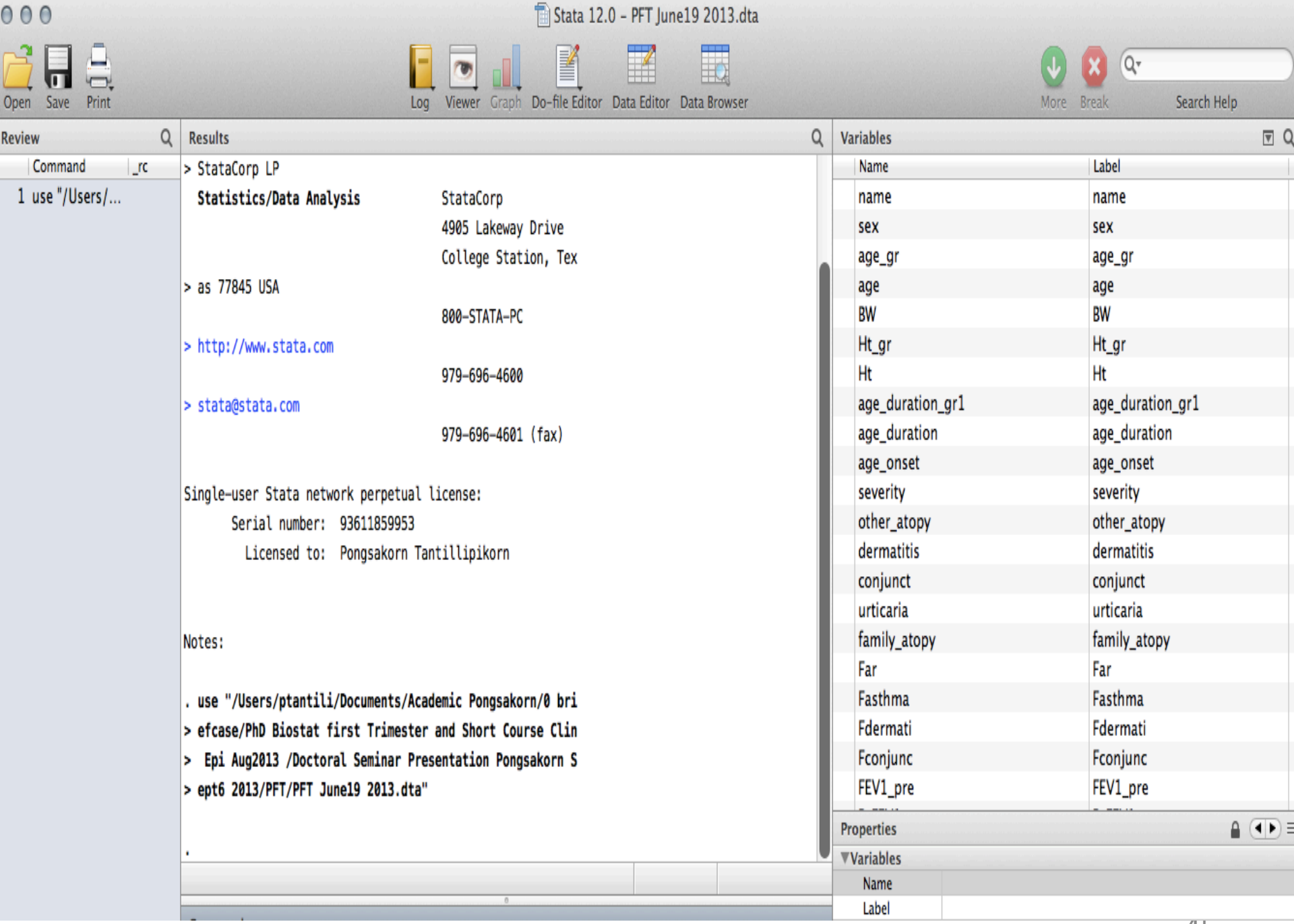
Gold W, et al. Pulmonary function testing.
Murray & Nadel's textbook of respiratory medicine, vol. 1. 4th edition.
Philadelphia: Elsevier Saunders; 2005. p. 671–733.

Objective

- Study of pulmonary function (esp FEV1 value) in Allergic Rhinitis (AR) Patients; and compares with the normative value of Thai Chest society

Study design and Research questions

- Descriptive
- Correlation study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Variables
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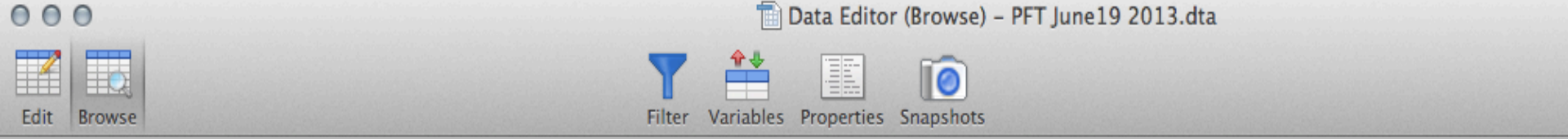

name[1] amornrat

	name	sex	age_gr	age	BW	Ht_gr	Ht	age_durati~1	age_duration	age_onset	severity
132	pakinee	2	2	32	55	2	161	1	3	30	4
133	payao	2	2	33	67	2	158	4	16	17	4
134	pimporn	2	4	53	84	2	163	6	30	20	4
135	pornsumon	2	3	46	72	2	163	5	22	25	4
136	rukkana	2	2	35	50	4	185	1	1	29	4
137	rungnapa	2	2	30	51	2	162	3	14	16	4
138	siriwat	1	2	39	51	1	150	1	1	39	1
139	somchai	1	3	48	90	1	153	1	3	47	1
140	suchana	2	2	32	43	2	156	2	10	20	4
141	tammanat	1	3	41	53	3	172	1	4	37	1
142	tanaporn	2	3	42	62	2	160	2	8	31	4
143	wannapa	2	4	50	62	3	167	4	20	24	2
144	watid	1	2	37	64	3	170	7	31	6	4
145	weeraporn	1	2	39	100	4	180	1	3	35	2
146	wichuporn	2	2	39	65	1	150	2	6	32	1
147	wirapa	2	2	39	59	2	162	4	20	25	3
148	suttipun	1	3	40	66	2	160	6	30	10	1
149	patcharee	2	2	36	54	1	150	6	26	10	1
150	kanoknard	2	4	52	68	2	156	1	3	50	4
151	sirikorn	2	4	51	79	2	163	1	5	46	2
152	penprapai	2	4	56	67	2	157	1	5	50	1
153	kunee	2	4	56	78	2	162	2	8	48	3

Crosstab

			four_fev1_pchgandFEF2575_pchgFEF2575		
			.00	1.00	Total
severity	mild intermittent	Count	16	22	38
		% within severity	42.1%	57.9%	100.0%
		% within four_fev1_pchgand FEF2575_pchgFEF2575	28.1%	22.9%	24.8%
	moderate to severe intermittent	Count	15	22	37
		% within severity	40.5%	59.5%	100.0%
		% within four_fev1_pchgand FEF2575_pchgFEF2575	26.3%	22.9%	24.2%
	mild persistent	Count	7	12	19
		% within severity	36.8%	63.2%	100.0%
		% within four_fev1_pchgand FEF2575_pchgFEF2575	12.3%	12.5%	12.4%
	moderate to severe persistent	Count	19	40	59
		% within severity	32.2%	67.8%	100.0%
		% within four_fev1_pchgand FEF2575_pchgFEF2575	33.3%	41.7%	38.6%
Total		Count	57	96	153
		% within severity	37.3%	62.7%	100.0%
		% within four_fev1_pchgand FEF2575_pchgFEF2575	100.0%	100.0%	100.0%