How We Organise Clinical Investigations

Five Year Experience of Chinese Collaborative Study Groups for Neonatal/Pediatric Respiratory Failure

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Current Situation of Pediatric Intensive Care in China

- National University, Pediatric Centers

  Settings: PICU, NICU, P/NICU

  Function: National programmes of clinical investigation and CME, serve 10+ millions population

- Provincial Women and Children's Health Centers

  Settings: Childen's Hosp-PICU, NICU; Maternity-NICU

  Function: Regional CME and clin investig, 5-10 mln

- Prefectural/Sub-province Medical Centers

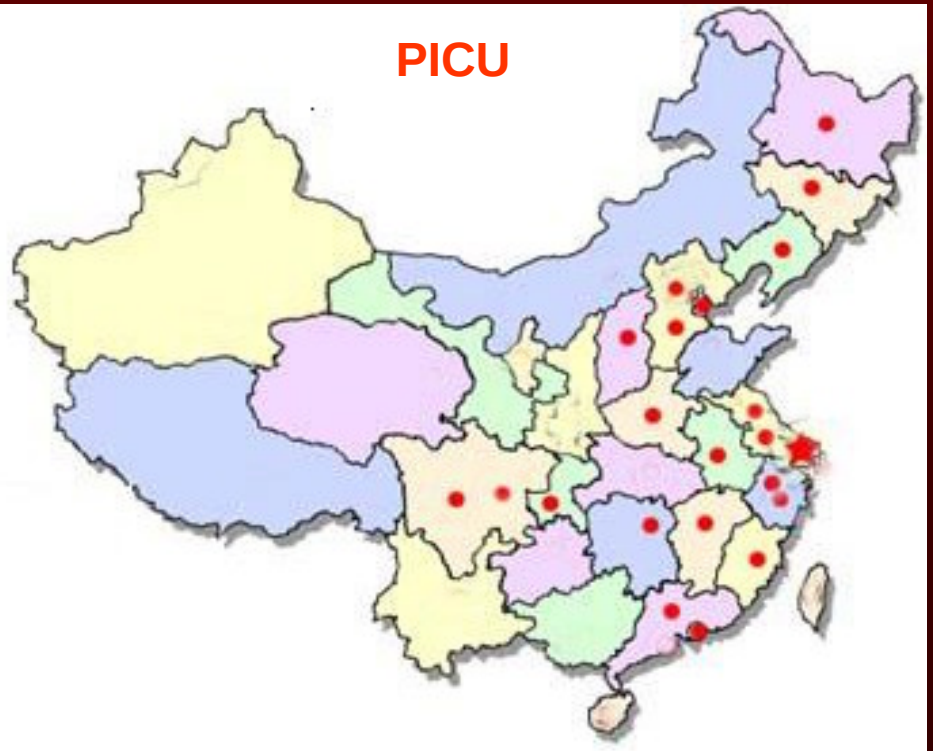
  Settings: NICU+P

  Function: Service and clin investig , 1-5 mln

NICU

Location of the member centers

PICU

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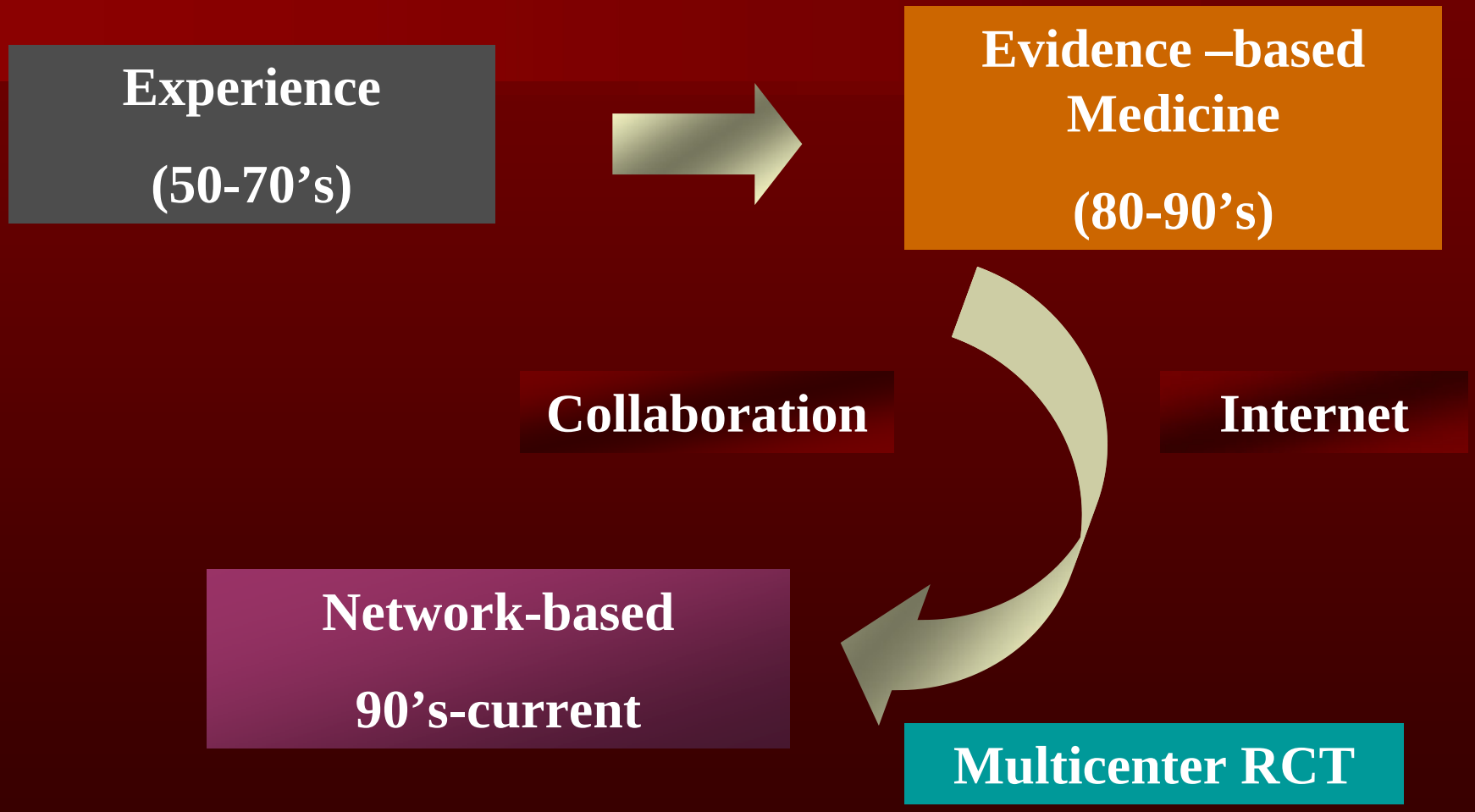
Background


Experience
(50-70’s)
Evidence –based Medicine
(80-90’s)
Collaboration
Internet
Network-based
90’s-current
Multicenter RCT

Current Situation of Pediatric Intensive Care in China

Advantage: sufficient cases

Experience ➡ evidence-based medicine

Few multicenter clinical study

challenge

network

- **Limited funds**
- **Change old mode**
- **Establish network**

Objectives

Descriptive clinical epidemiology

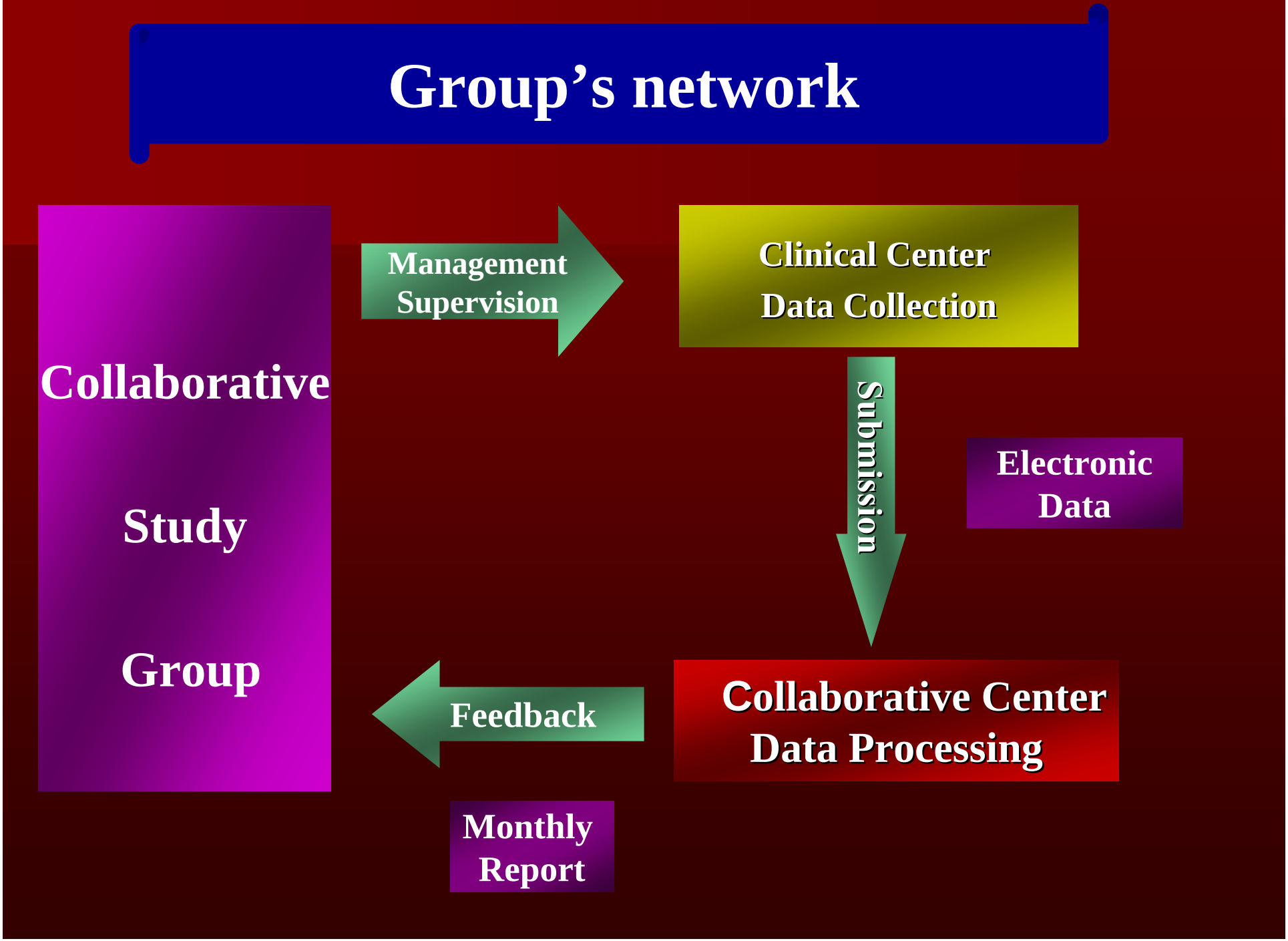
- Profile of respiratory failure
- Resource allocation
- Quality improvement

Interventional

RCT study

- Ethics and cultural/social
- Guidelines
- Nursing care

Group's network



Patient Information

Case report form :

- Demographic characteristics
- Medical history, health status, family, et al
- Disease components
- SNAPPE-II or PIM
- Intervention, et al
- Outcome and burden, et al

Monthly report form:

- New admission according to inclusion and exclusion criteria, et al

Man power input

Clinic directors:

- Commitment to the agreement
- Staffs and funds
- Responsible to all the cases and report forms
- Contact person
- Manuscript co-authorship

Key staffs:

- Daily collection of the case information
- Reporting to the collaborative center
- Responsible for data uploading and inquiry

Staff training

At the start period :

- Courses to study protocol and case reporting forms
- Practice communication

During the study period:

- Telephone communications
- Newsletters
- Attending workshops

At the conclusion:

- Assessment of unit performance

Part I

Prospective, Multicenter Clinical Survey of Neonatal Acute Respiratory Failure in 23 Neonatal Intensive Care Unit in China

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Chinese Collaborative Study Group for Neonatal Respiratory Diseases

2004-2005

Background

- Half of the mortality of children below 5 years old is in neonatal period
- NRF is a main cause of death with high mortality, morbidity and costs
- Epidemiological data are lacking but essential for promoting intensive care quality and health policy

Background

ARF surveys (mainly retrospective)

Author	country	time	object	Incidence(%)	Mortality(%)
Bonafe	Italy	1996	population	3.3	14.8
Rubaltelli	Italy	1998	population	2.2	14.6
Angus	USA	2001	population	1.8	11.1
Ali	Tobago	2003	population	1.4	33.0
Lee	Canada	2000	NICU	43	/

- Variable results were due to the differences in population, inclusion criteria and geography

Background

- Lack of epidemiological data of ARF in China
- A survey based on population is difficult — no reliable birth registration for vital statistics
- A survey based on clinical record is feasible — relatively easier with admission registries, etc…

STUDY DESIGN

Method → Prospective multicenter

Period → 2004.3-2005.2

Inclusion Criteria →
1. All NICU admission
2. NRF: defined as requiring MV or nasal CPAP

Objectives →
1. Incidence, mortality
2. Risk factors
3. Underlying diseases

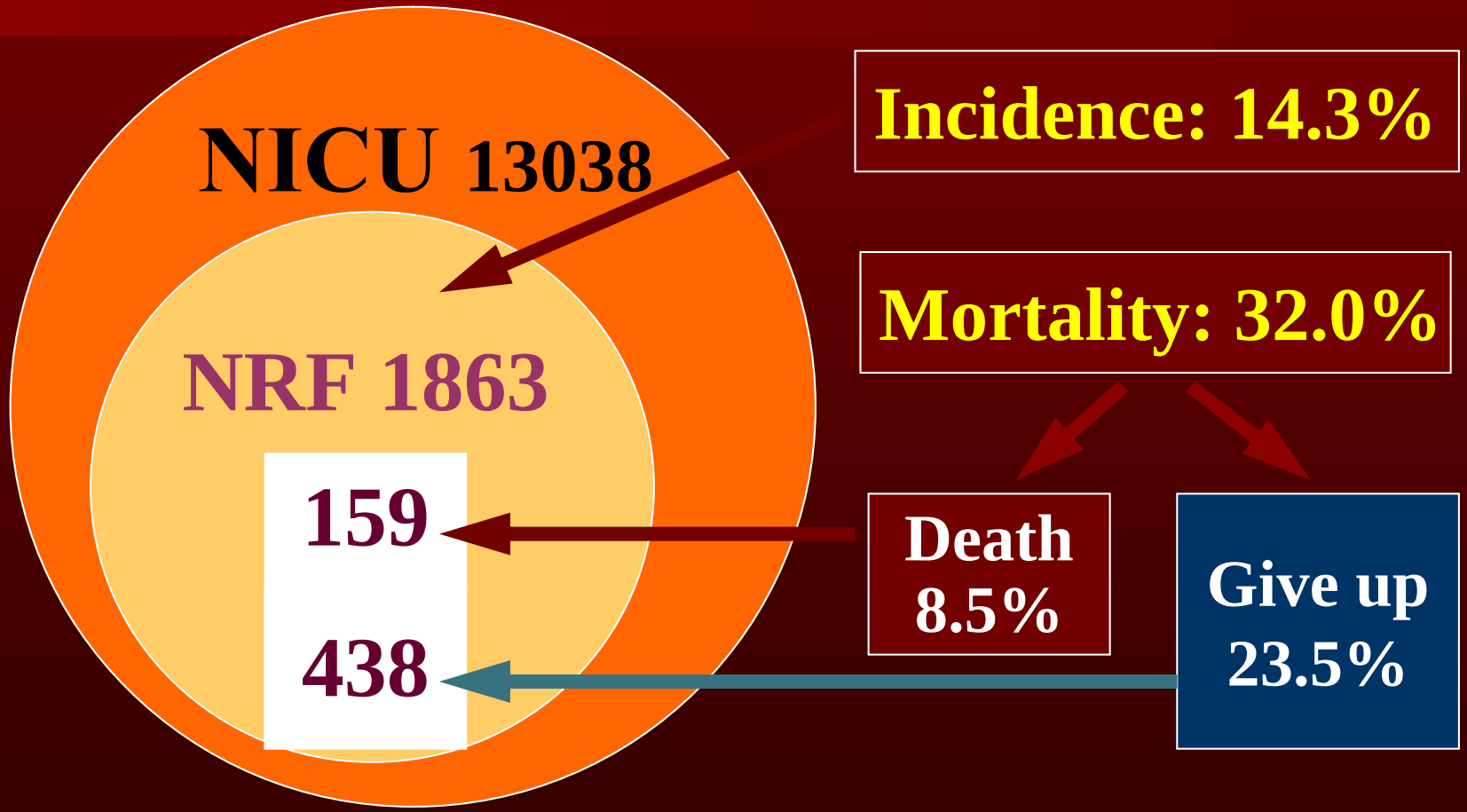
Data Submission & Communication

Network website

www.shlung.com/ neonet

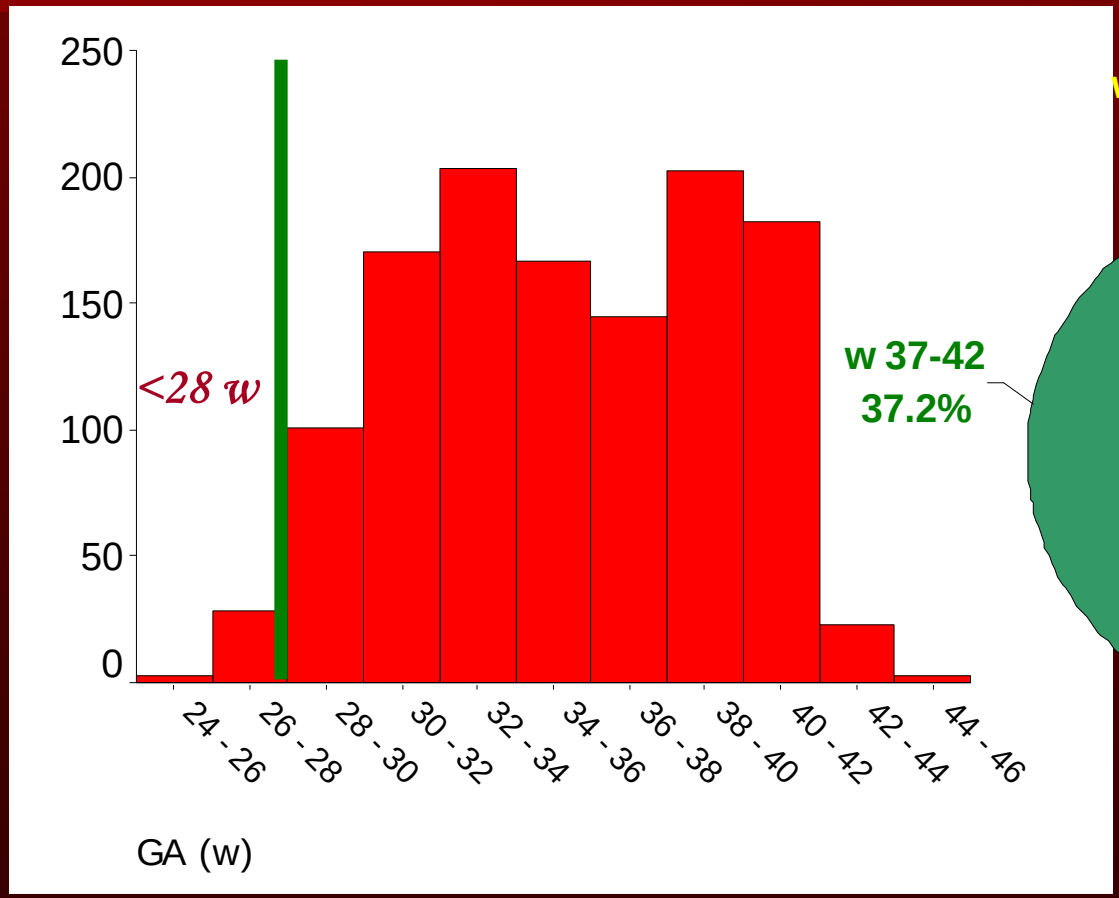
Results

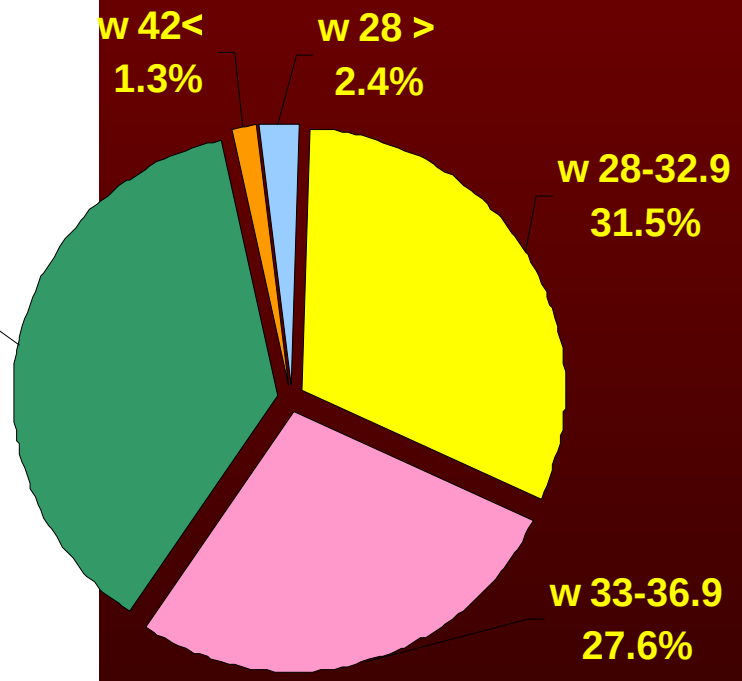
(2004.3.1 ~ 2005.2.28)



Gestational Age Distribution of NRF

34.9± 4.1 w

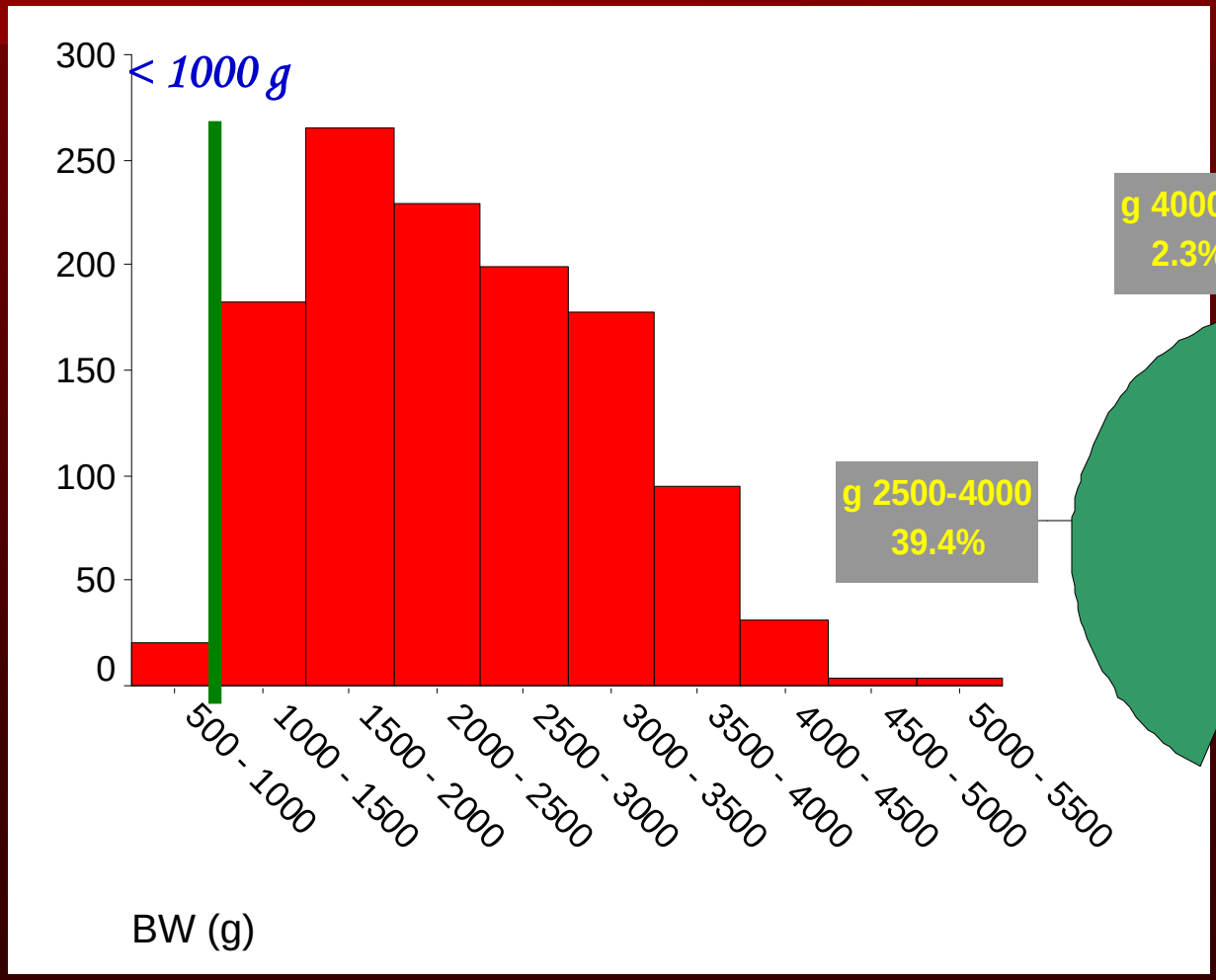


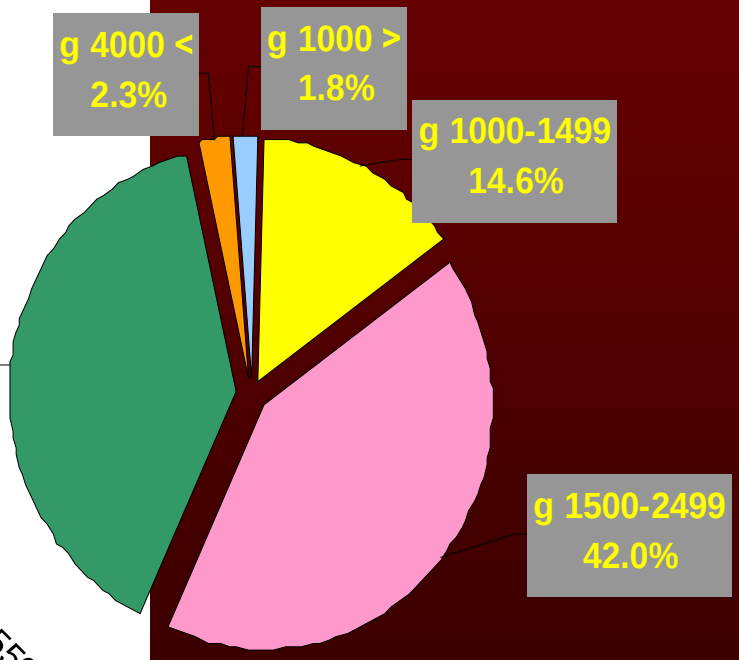


63.3% preterm

Birth Weight Distribution of NRF

2309± 832 g

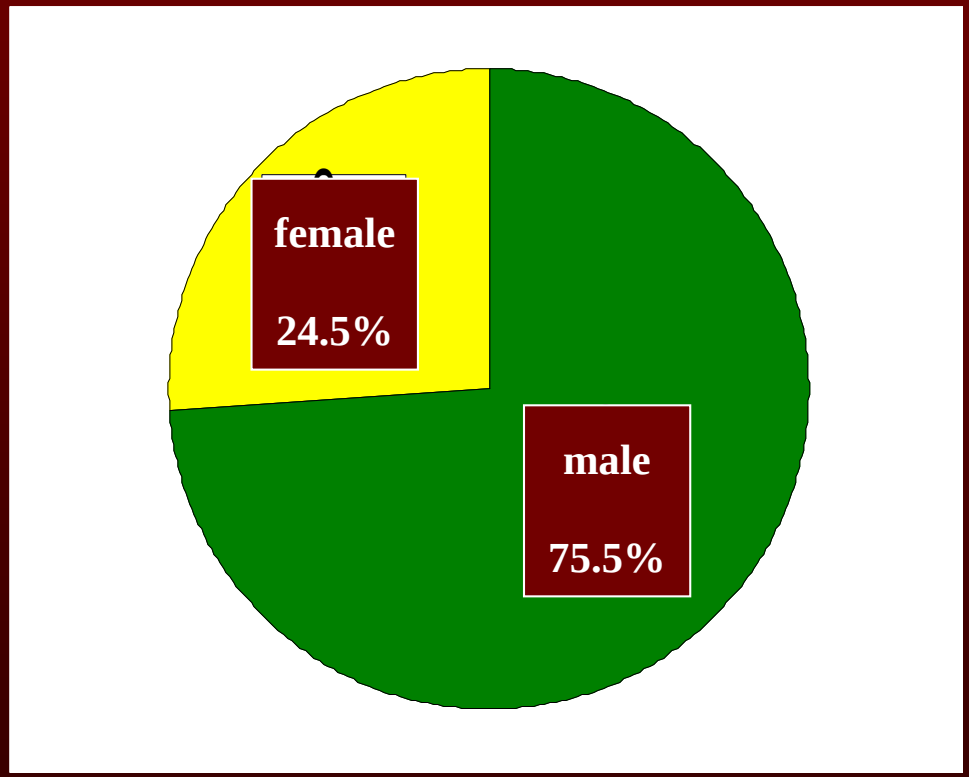




59.8% LBW

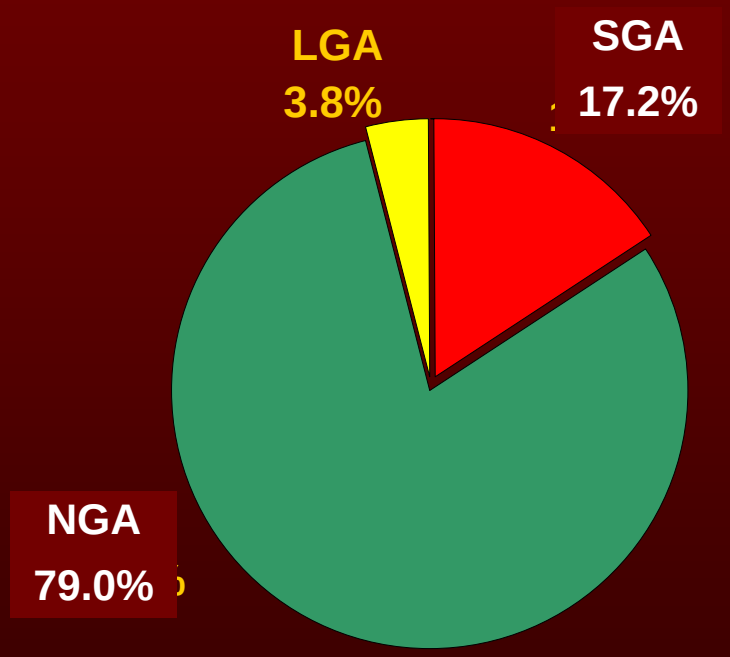
Clinical features

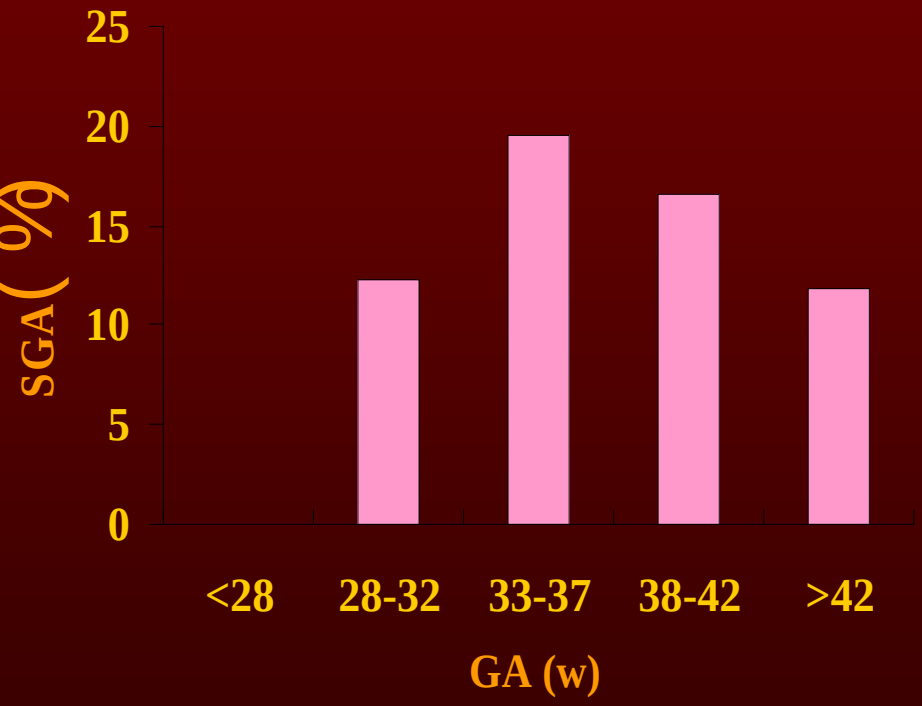
Sex M/F=3 : 1



Clinical features

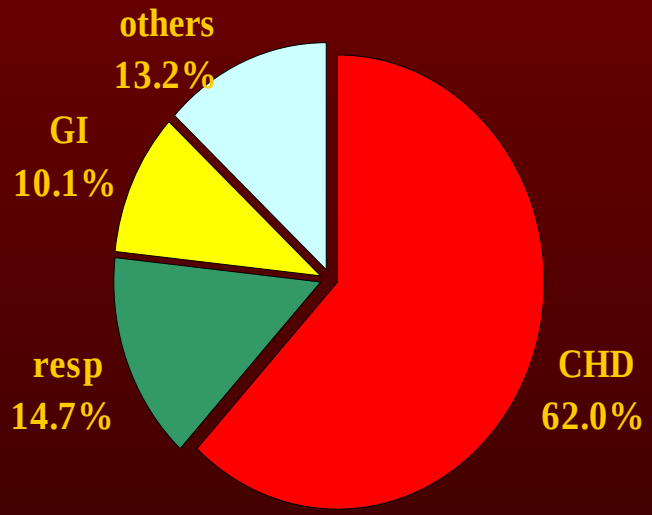
SGA

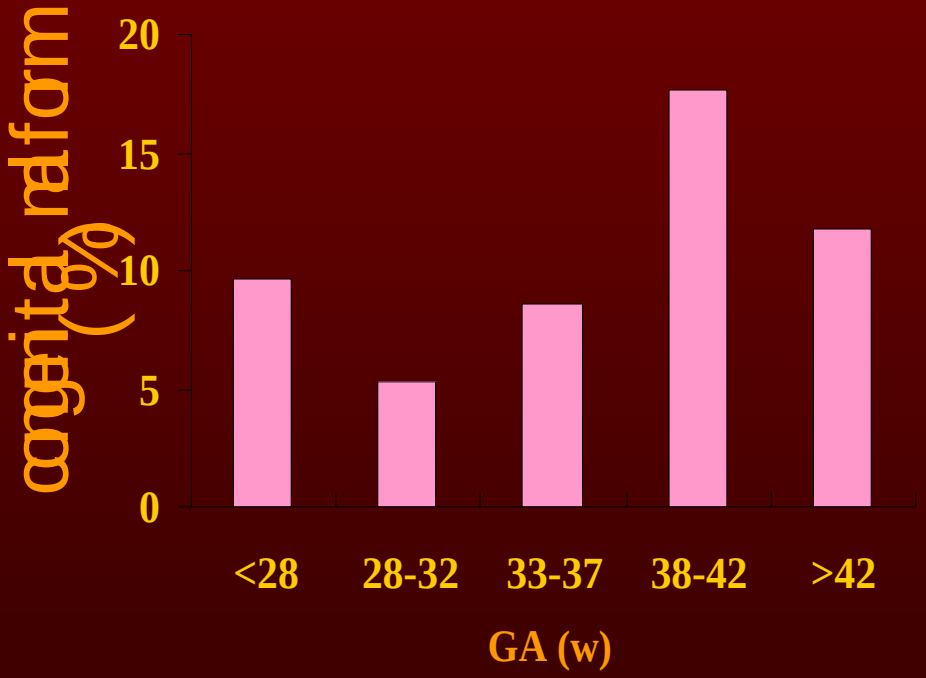




Clinical features

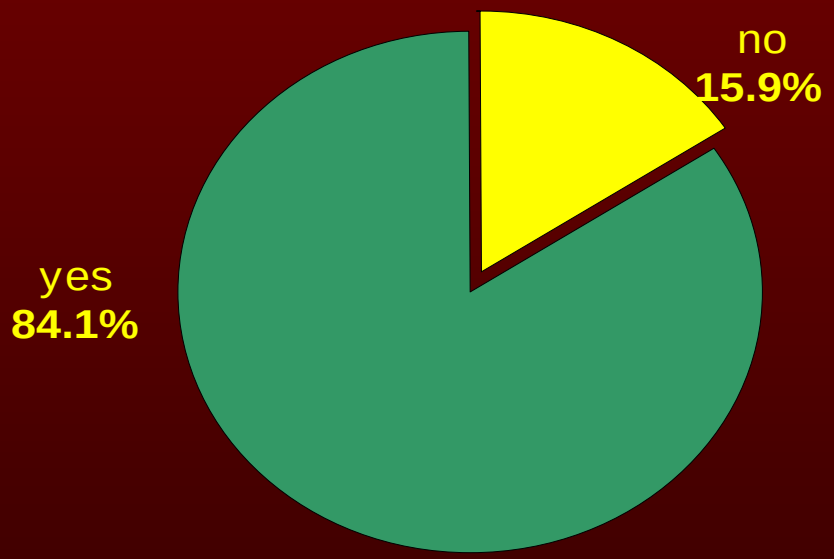
Congenital Malformation (8.5%)

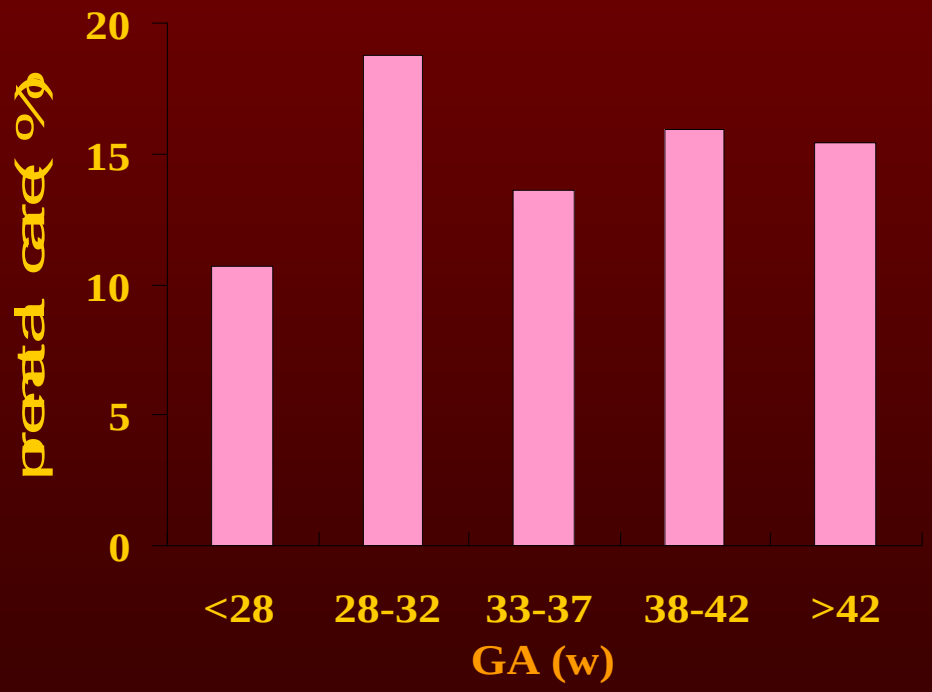




Risk factors

Prenatal Care

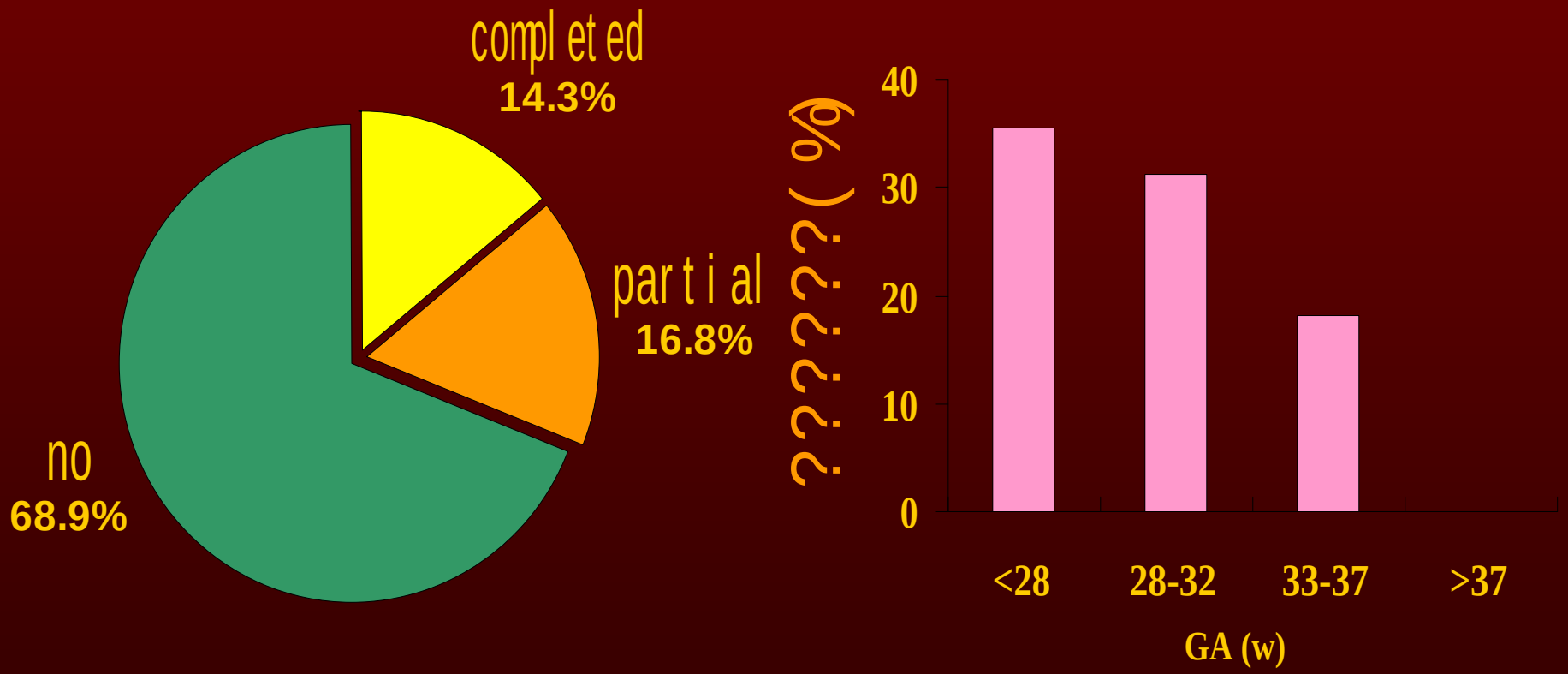




Risk factors

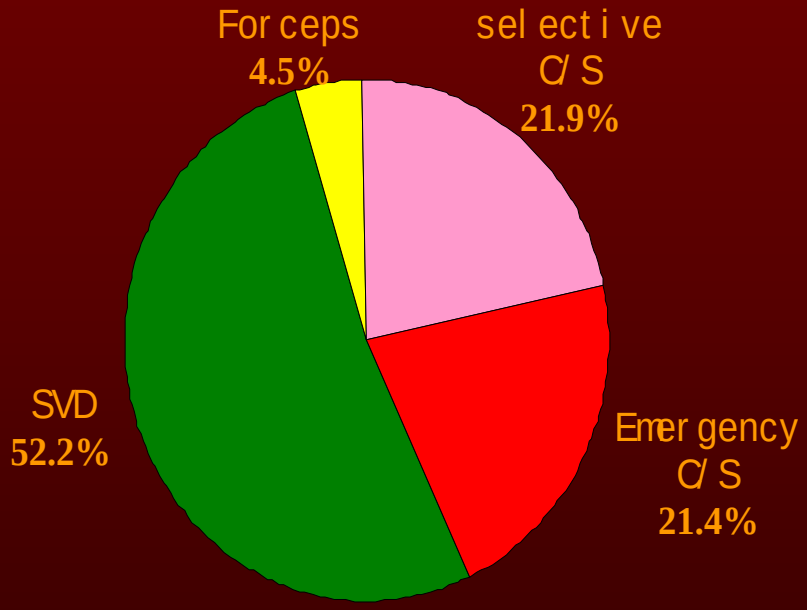
Antenatal Steroids

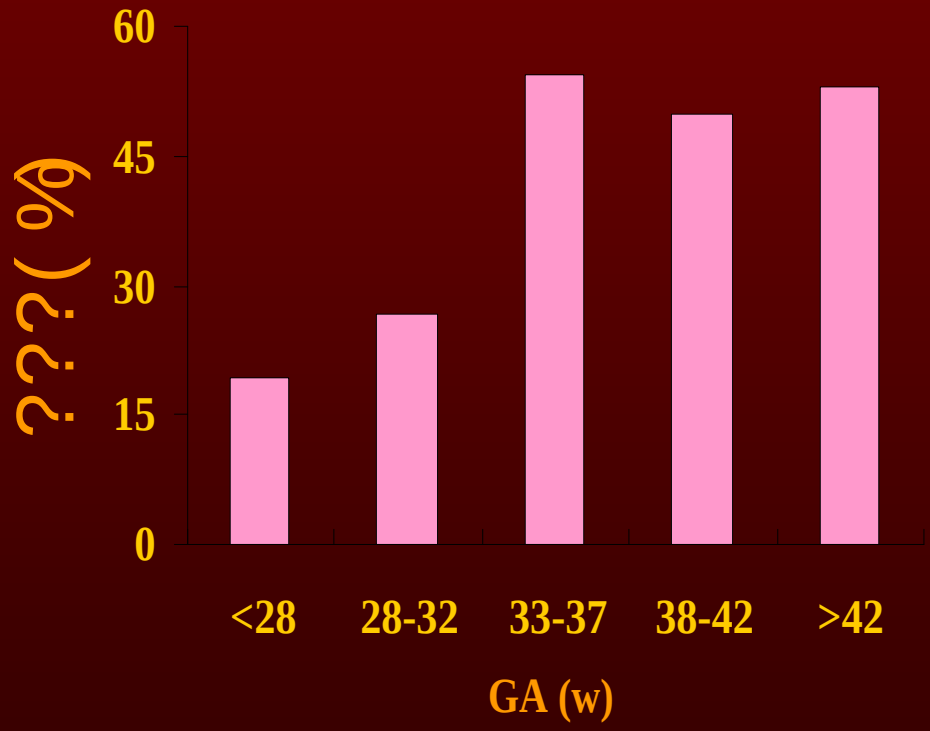
GA= 34 w



Risk factors

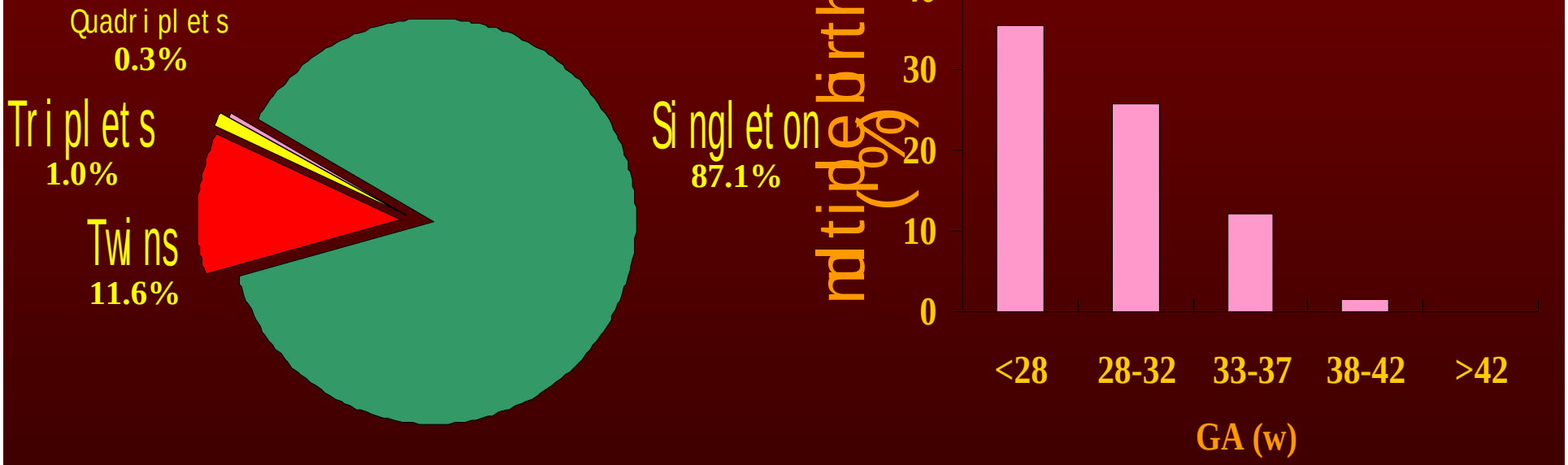
Delivery Mode





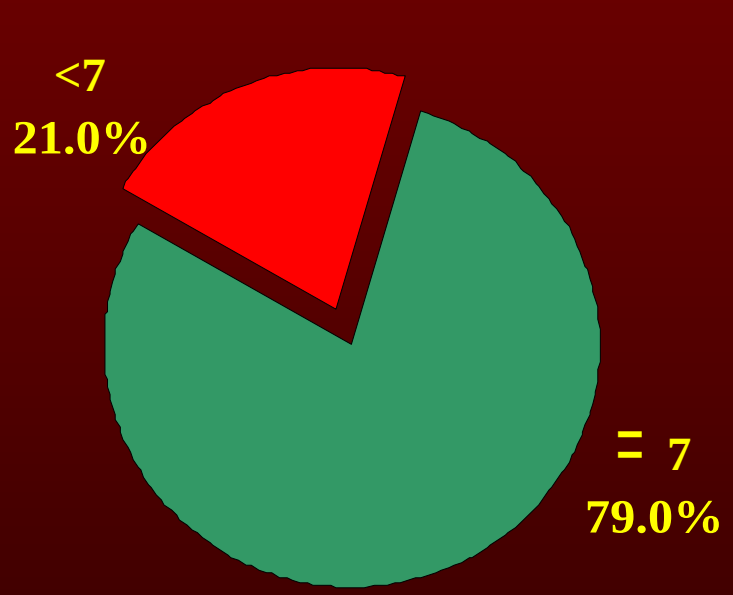
Risk factors

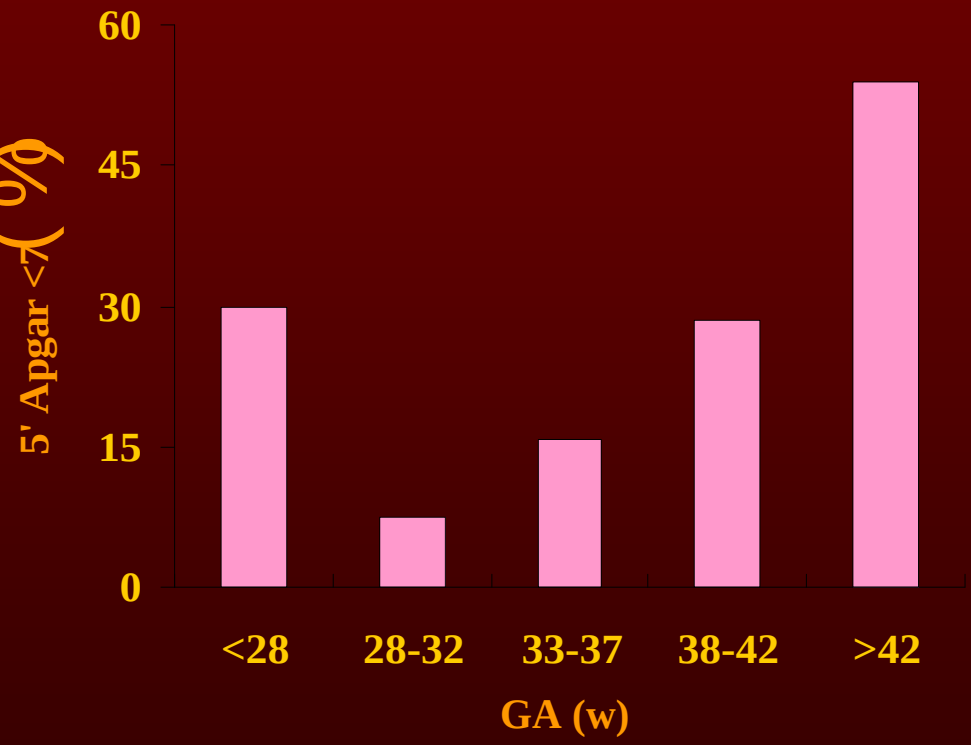
Multiple Birth



Risk factors

5 min Apgar <7

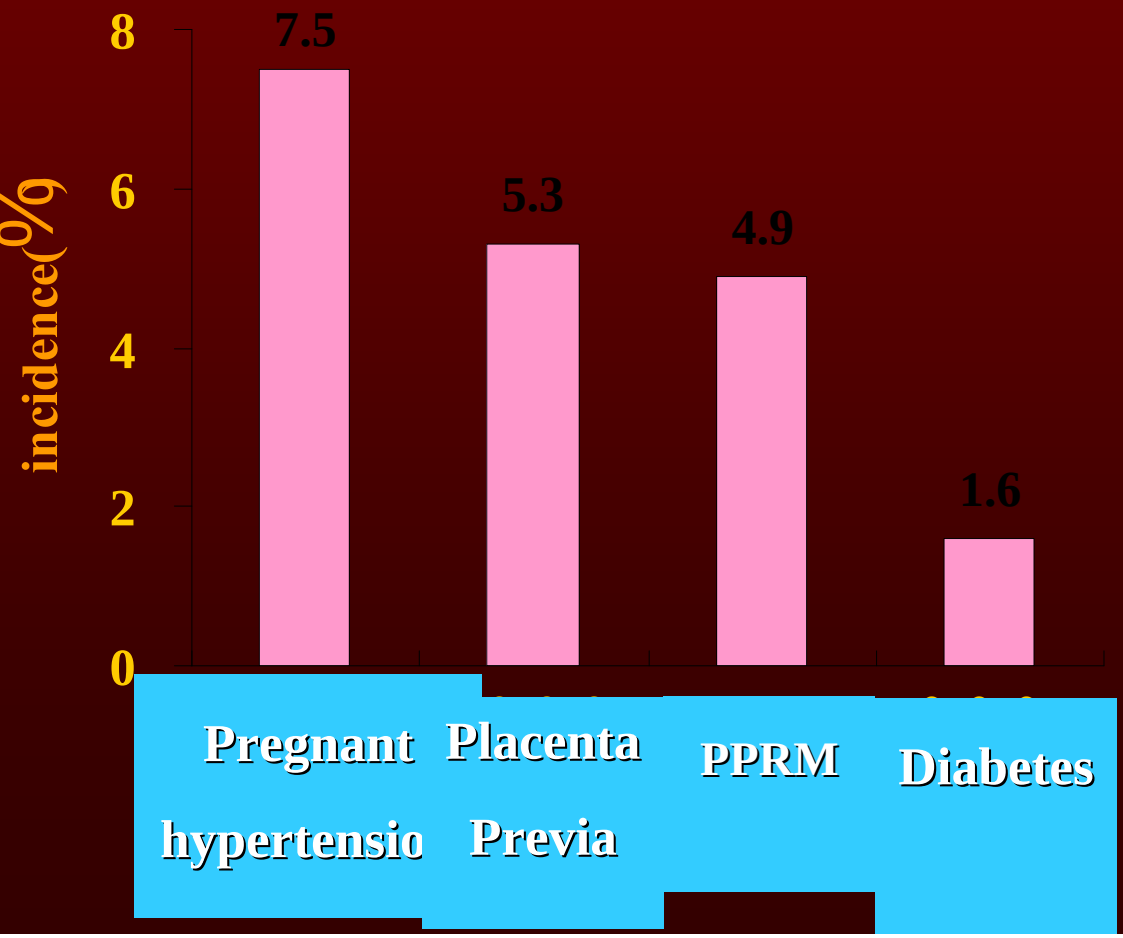




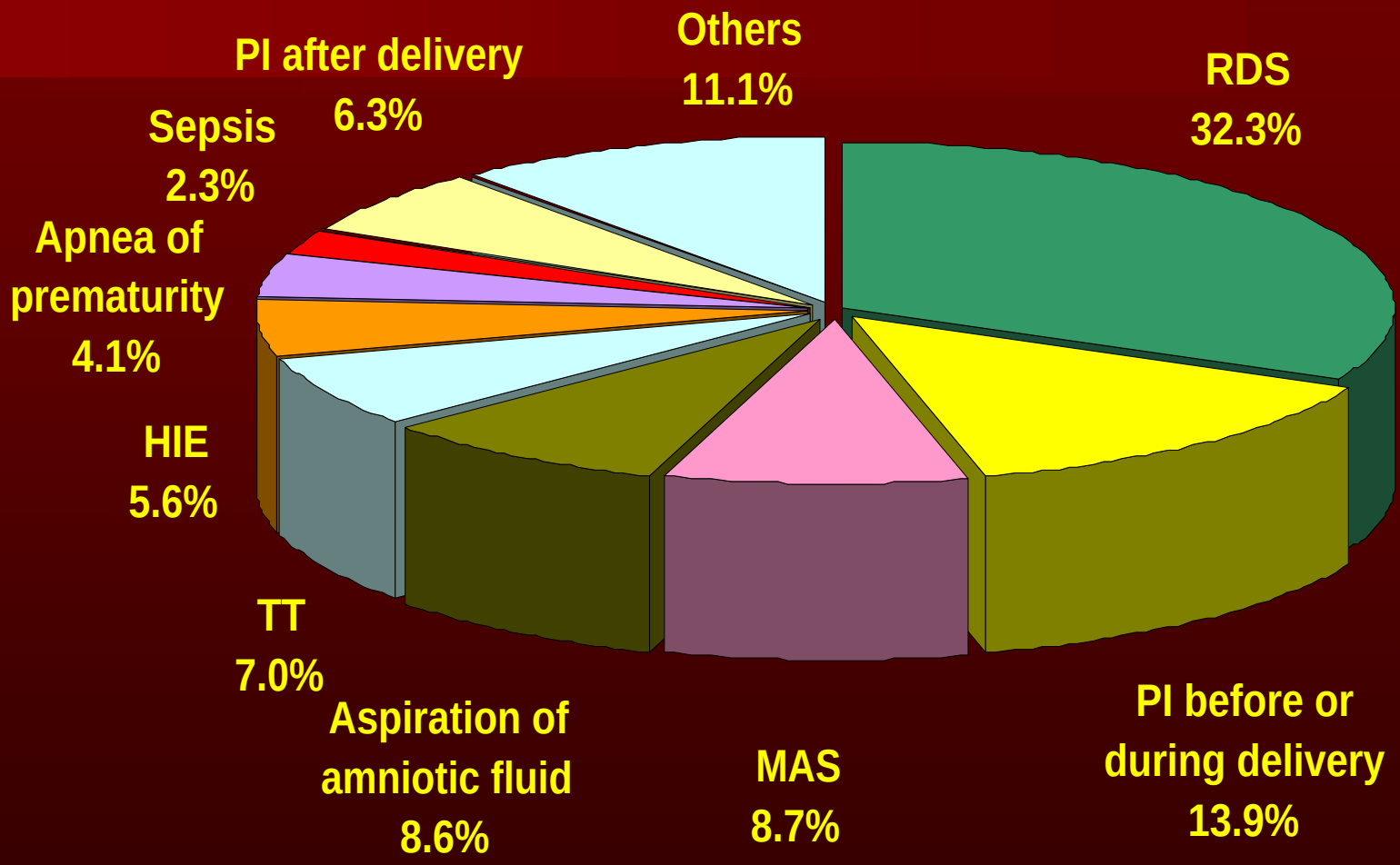
Risk factors

Maternal Diseases

Age: 27.8± 4.8 yrs, Median: 27.0(19-51) yrs

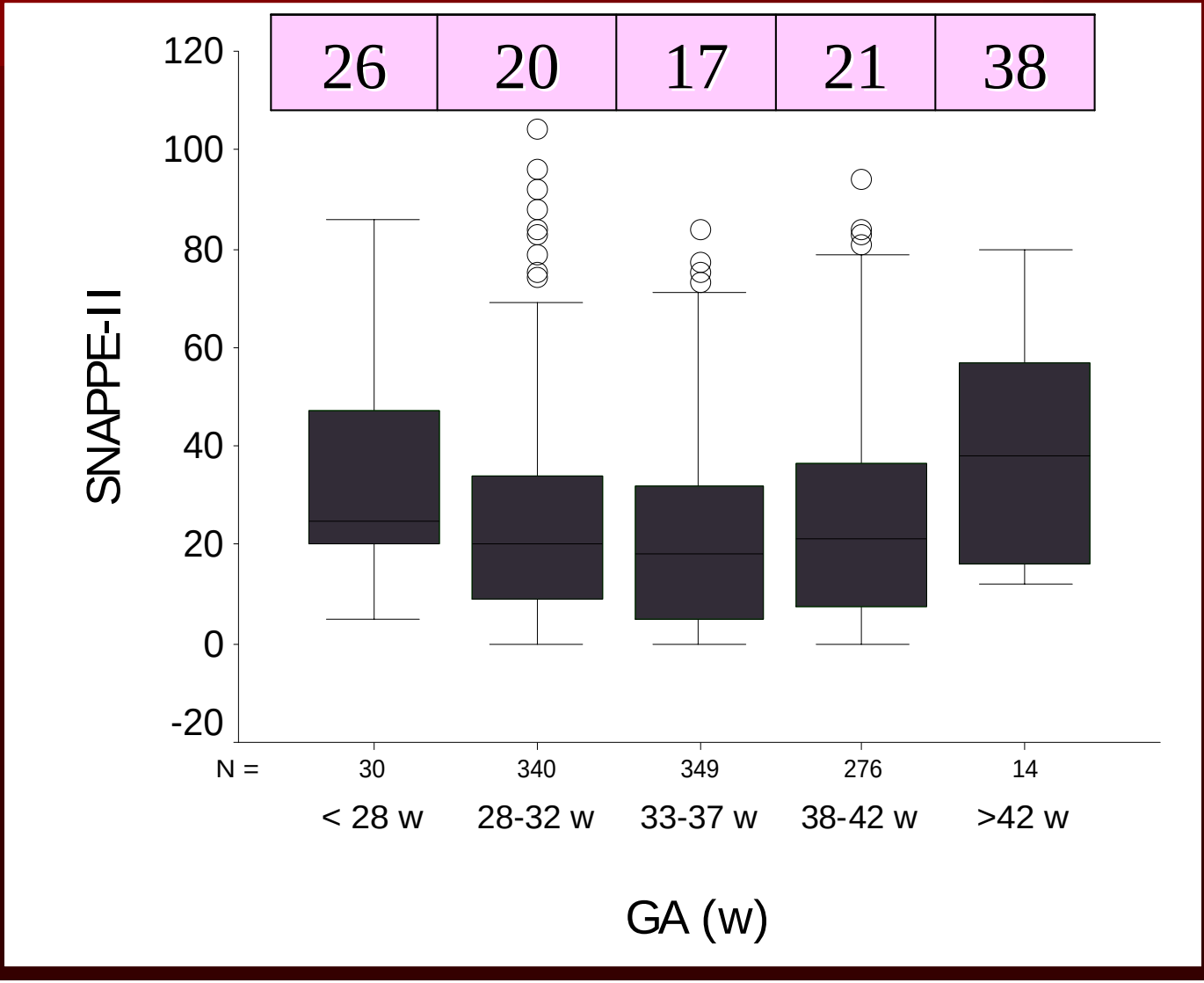


Primary Causes of Assisted Ventilation



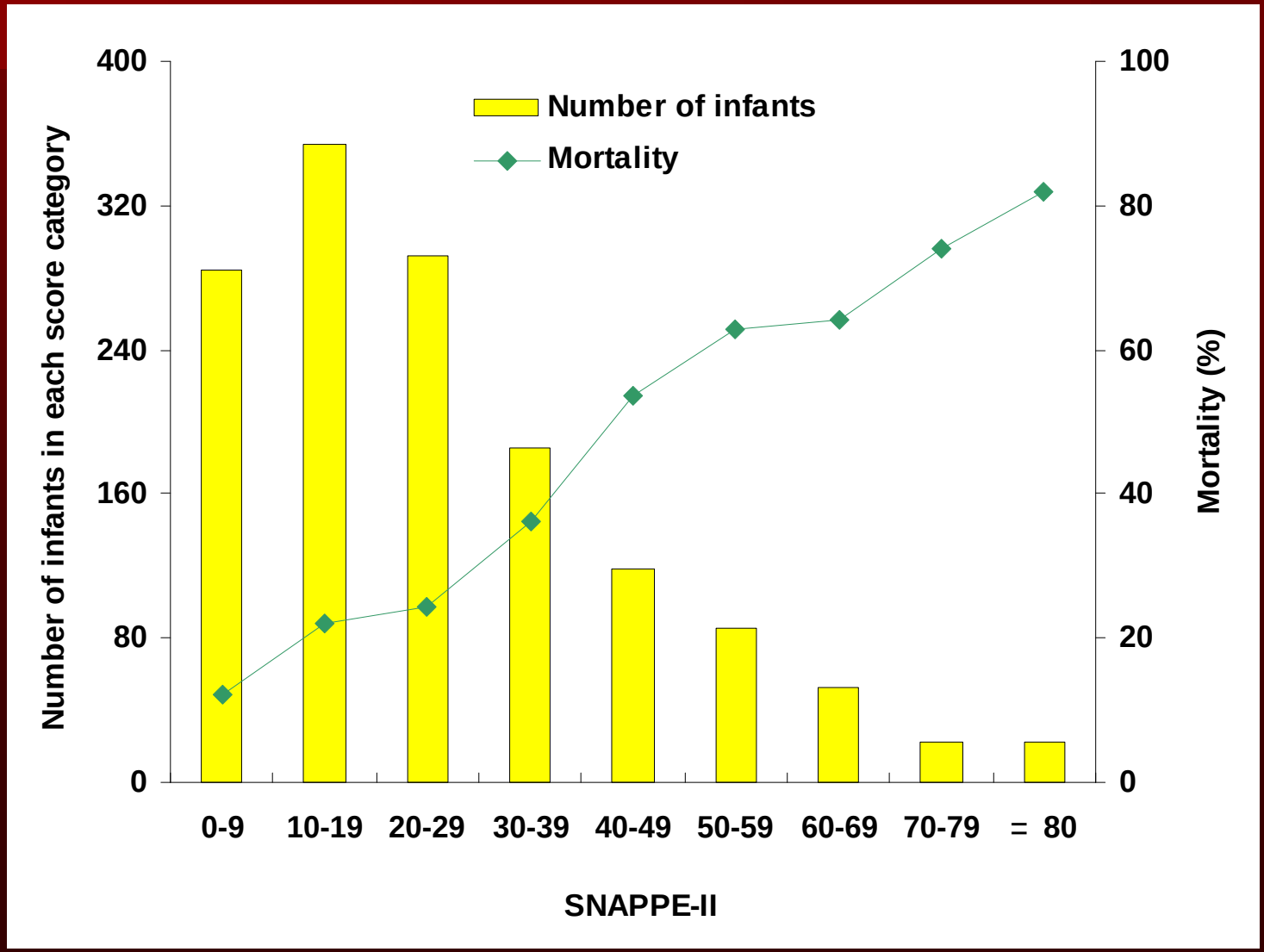
Critical scores

SNAPPE-II(Median 20)



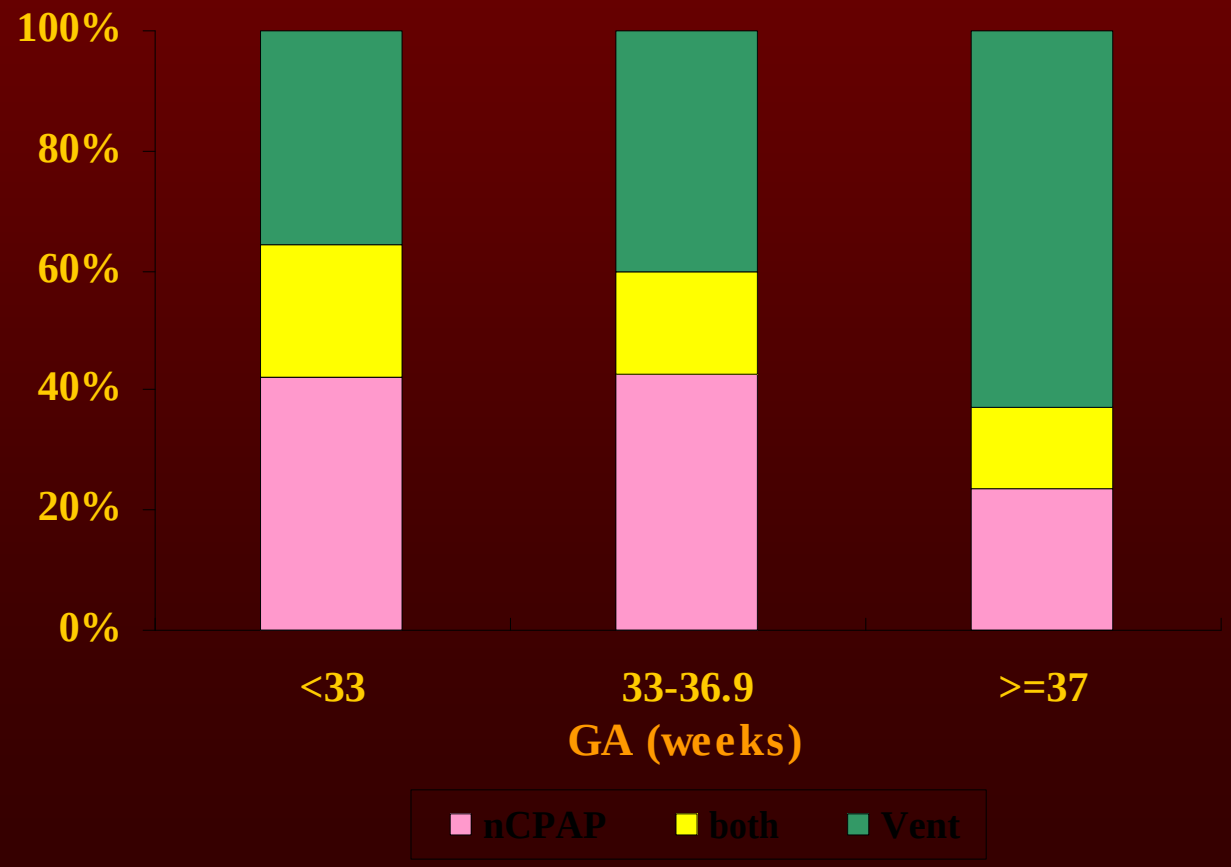
Critical scores

SNAPPE-II and Mortality

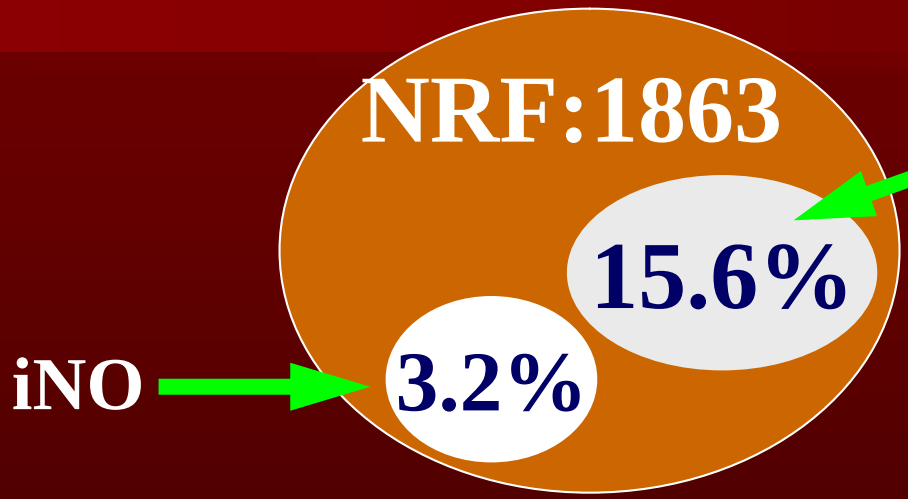


Respiratory Therapy

Duration of intervention: 91± 94 h, Median: 70 h



Surfactant and INO Therapy

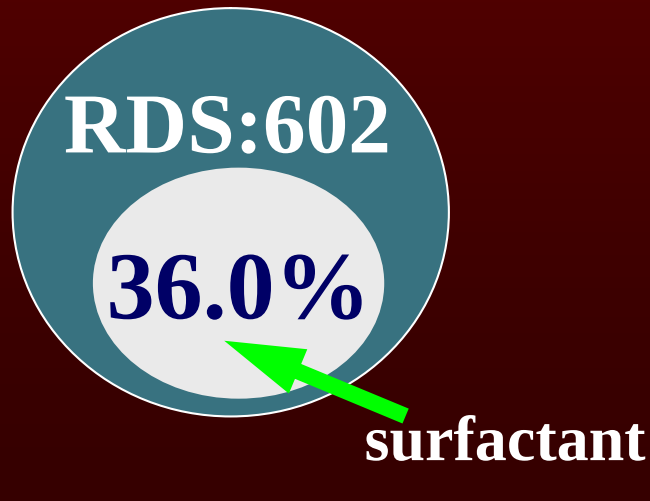


surfactant

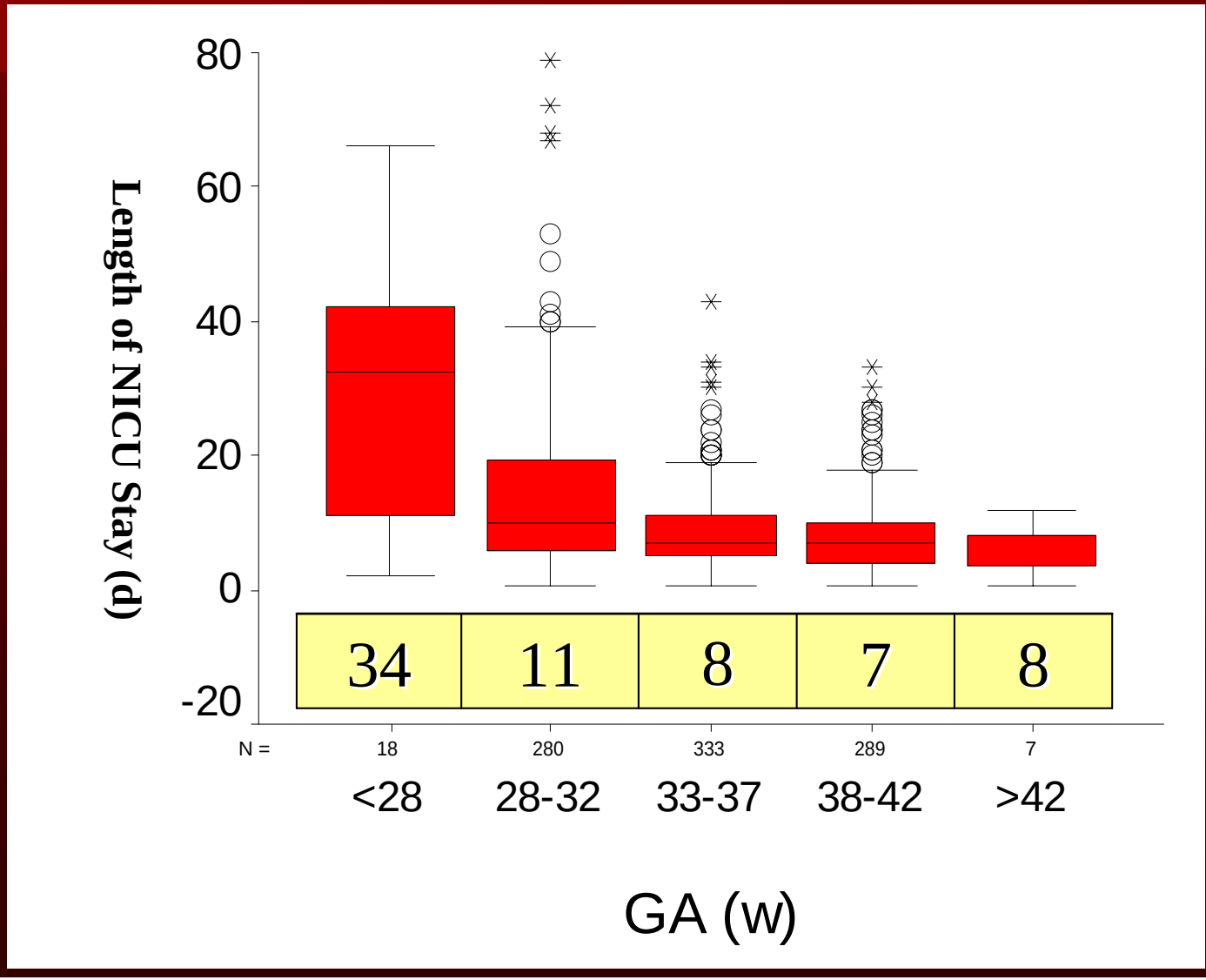
- GA: 31.8± 3.2 w
- BW: 1743± 637 g

Prophylactic surfactant：

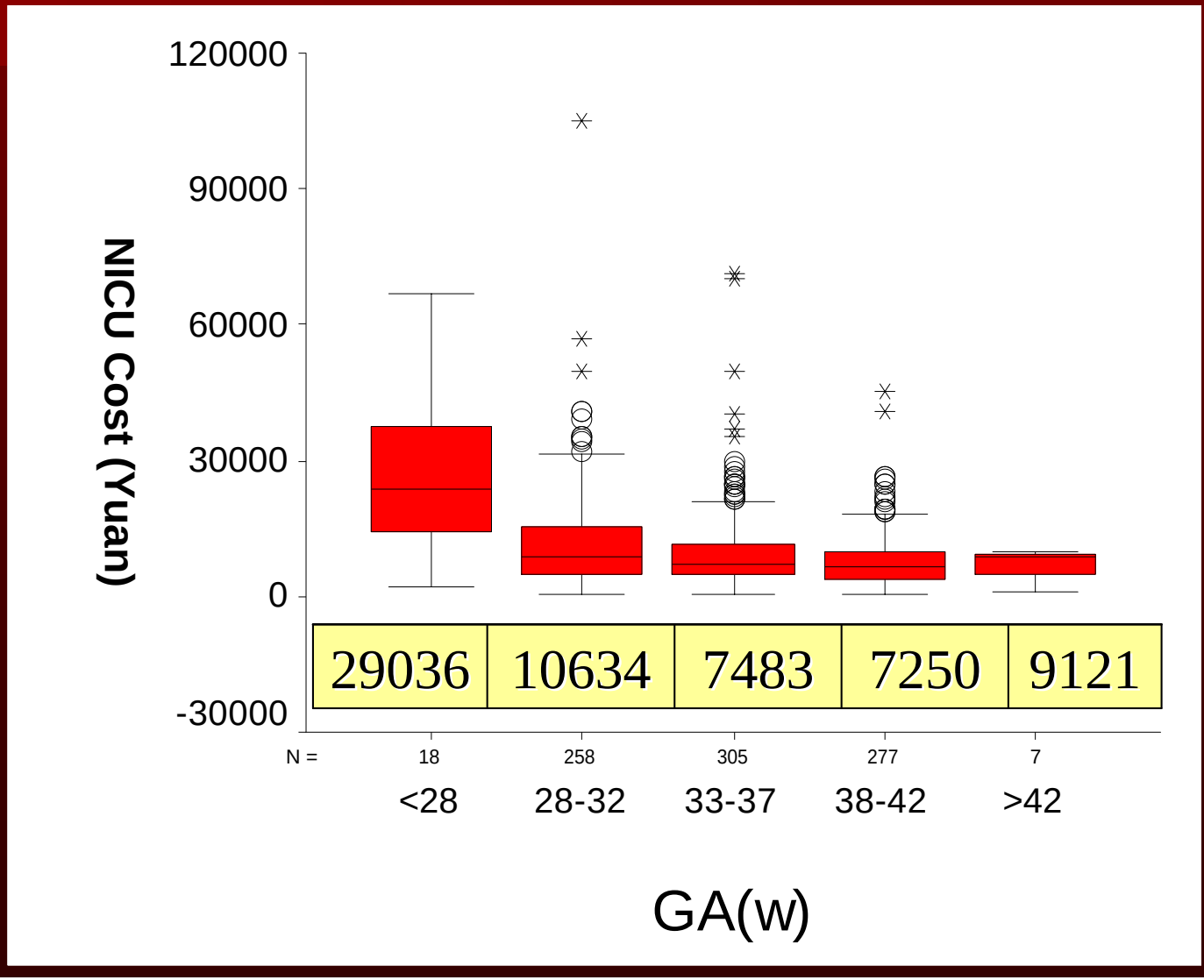
- BW<1200g: 14.4%
- GA<30 w: 9.5%



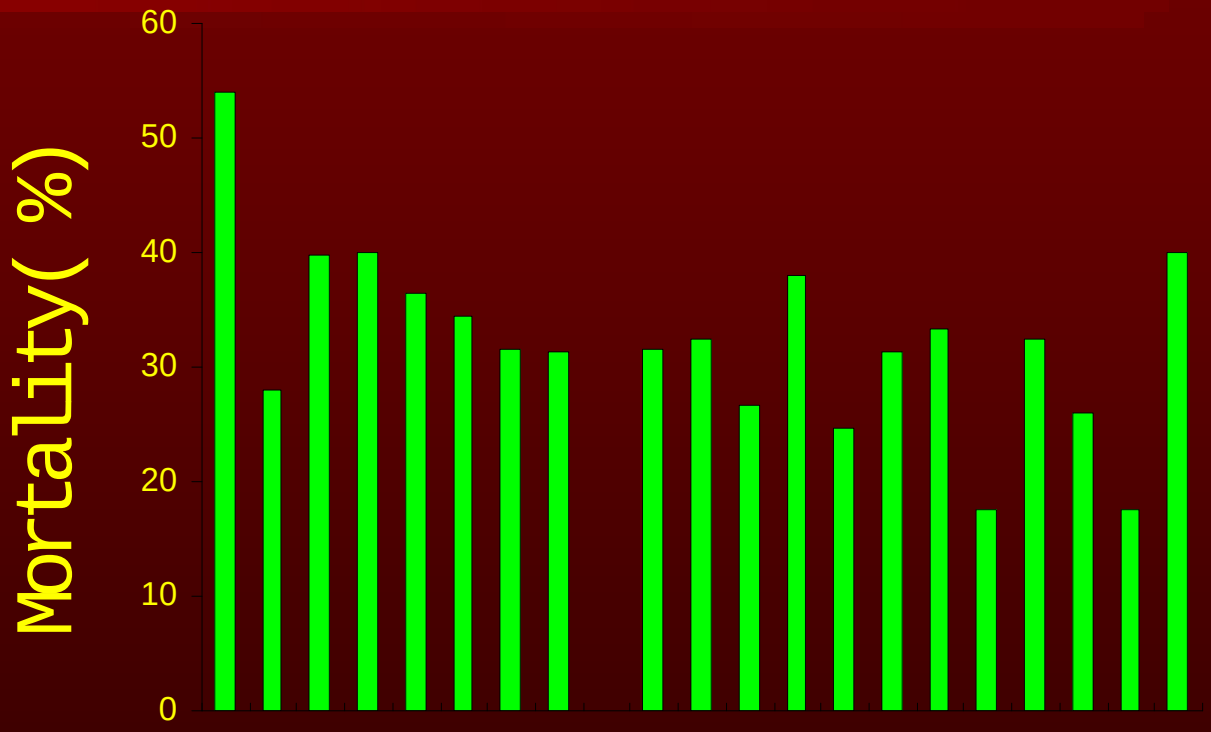
NICU Stay (Median 8 days)



NICU Cost (Median 8315 Chinese Yuan)

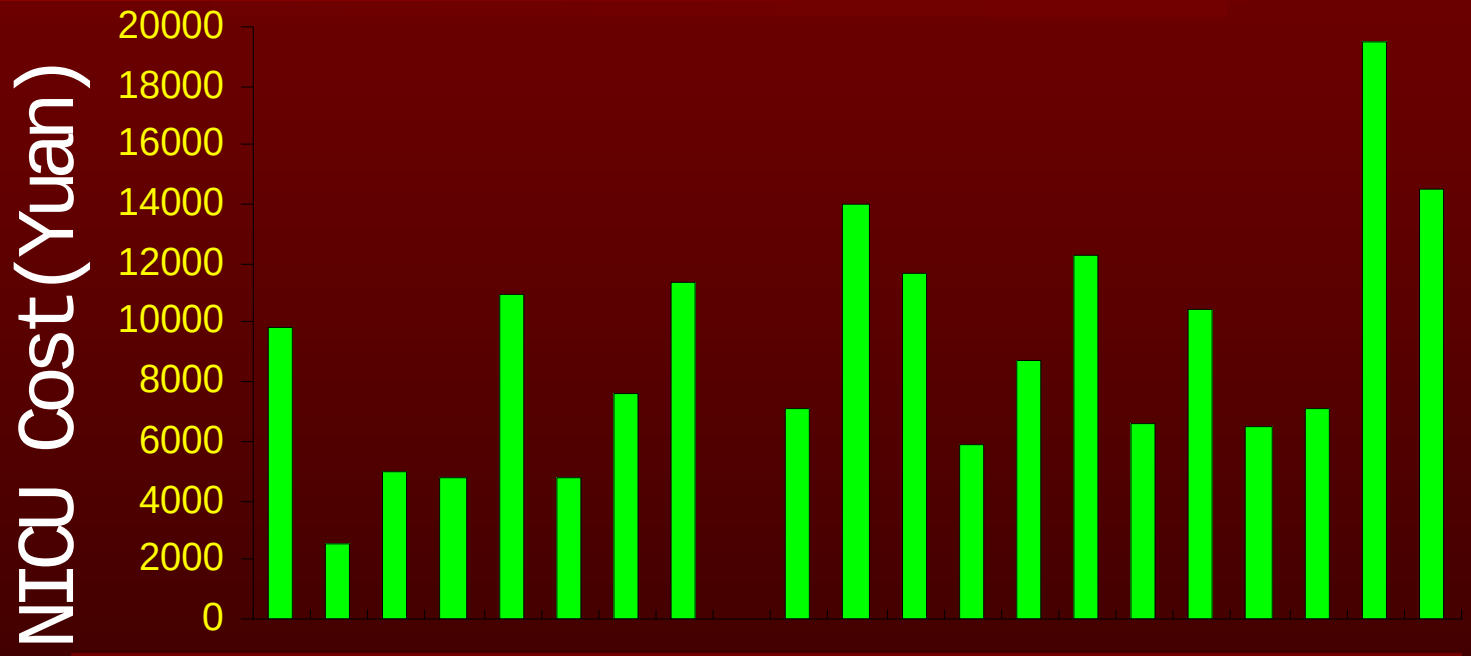


Mortality Among Hospitals



36.0 % vs. 29.2 % (p=0.002)

Cost Among Hospitals



6274 vs. 9128 (p=0.000)

CONCLUSIONS

- First multicenter prospective study of NRF in China
  - Overall reflects the incidence, disease components and critical care levels
  - Find out differences when compare with other countries for improvement national and regional intensive care
- First multicenter neonatal network based on advanced concepts of international standards, enabling cost-effectiveness and interventional investigation

Part II

Prospective, Multicenter Clinical Survey of Acute Respiratory Distress Syndrome in 25 Pediatric Intensive Care Unit in China

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Chinese Collaborative Study Group for Acute Respiratory Distress Syndrome

Participants (25 PICUs)

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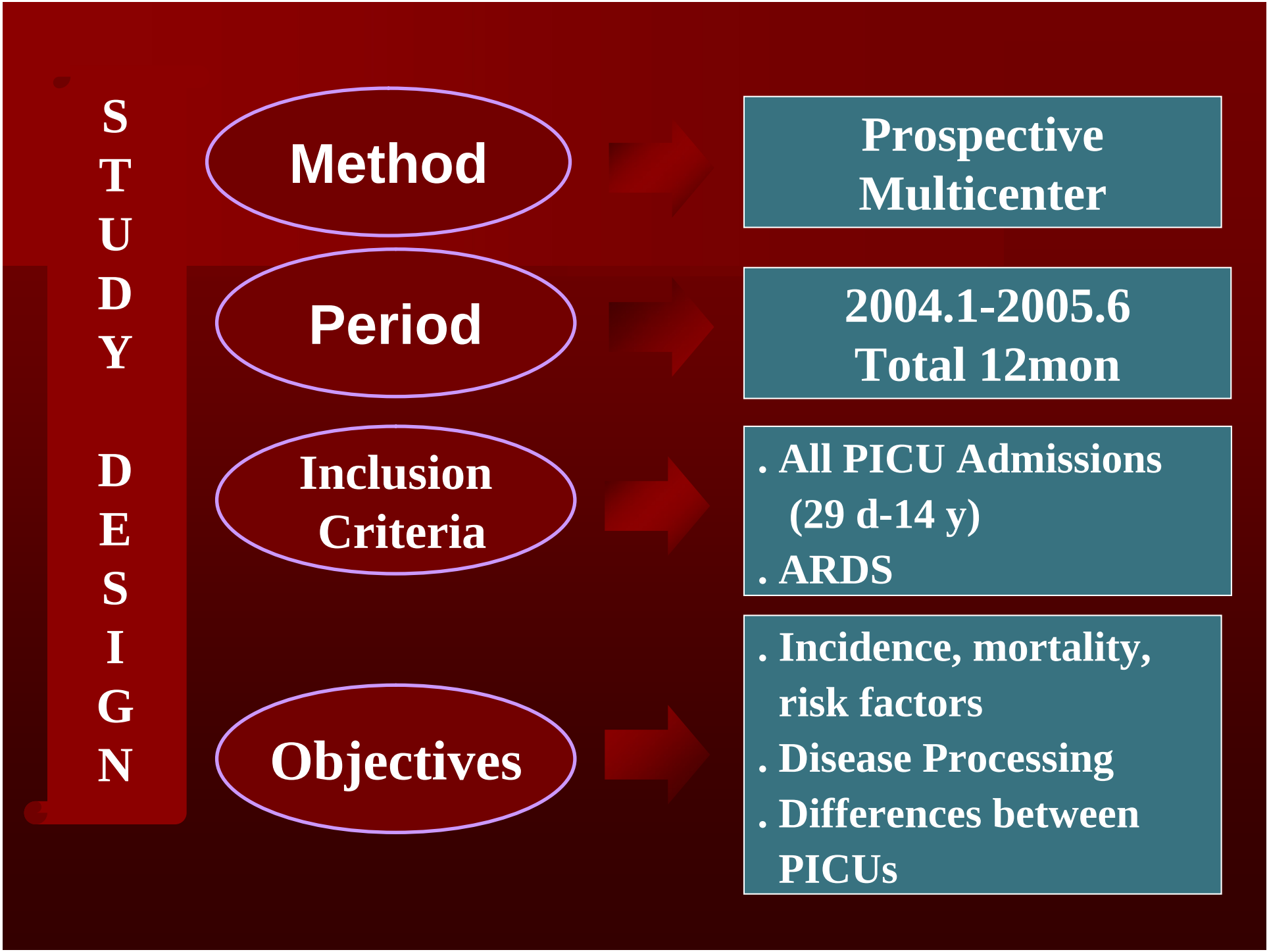
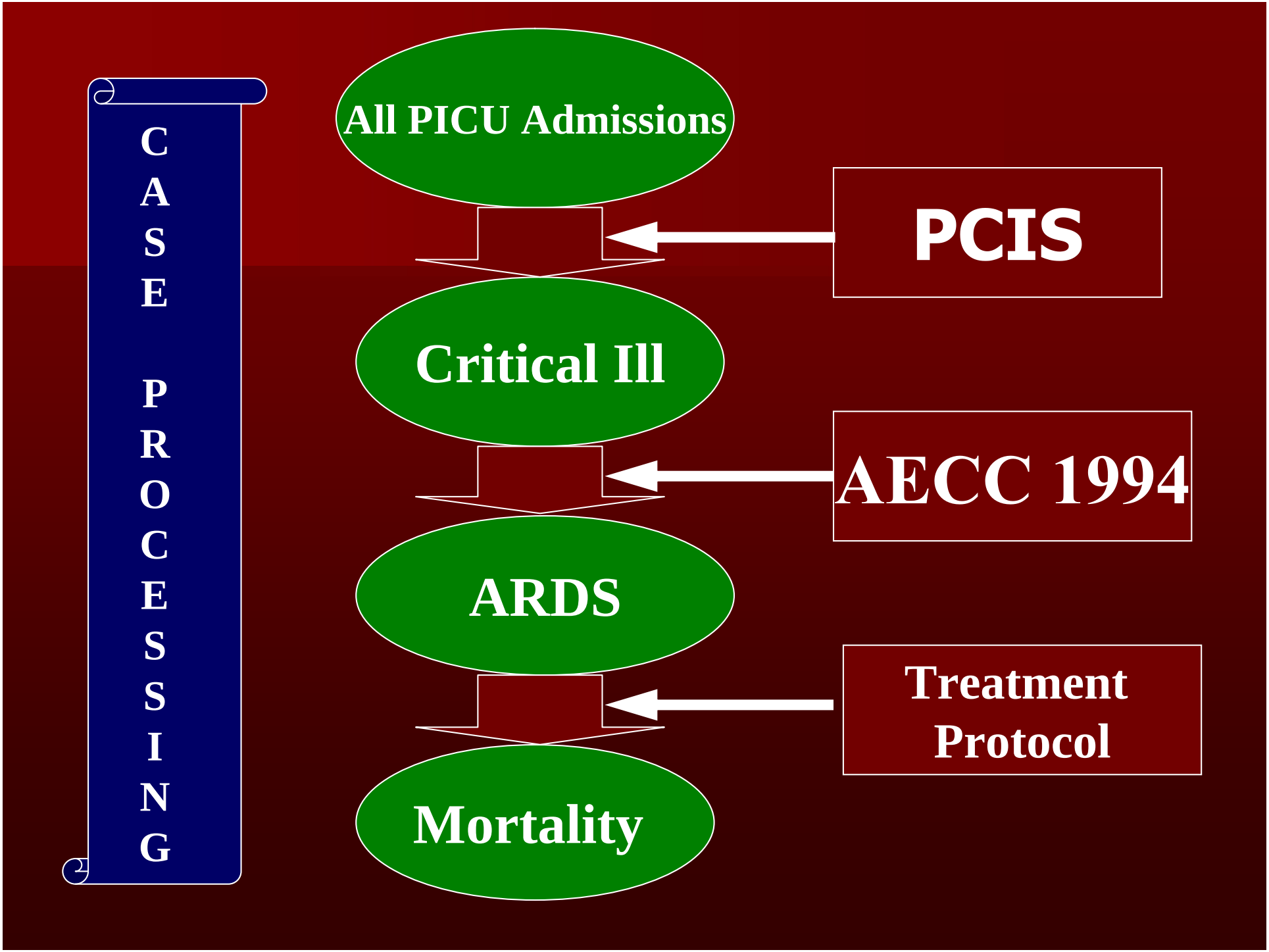
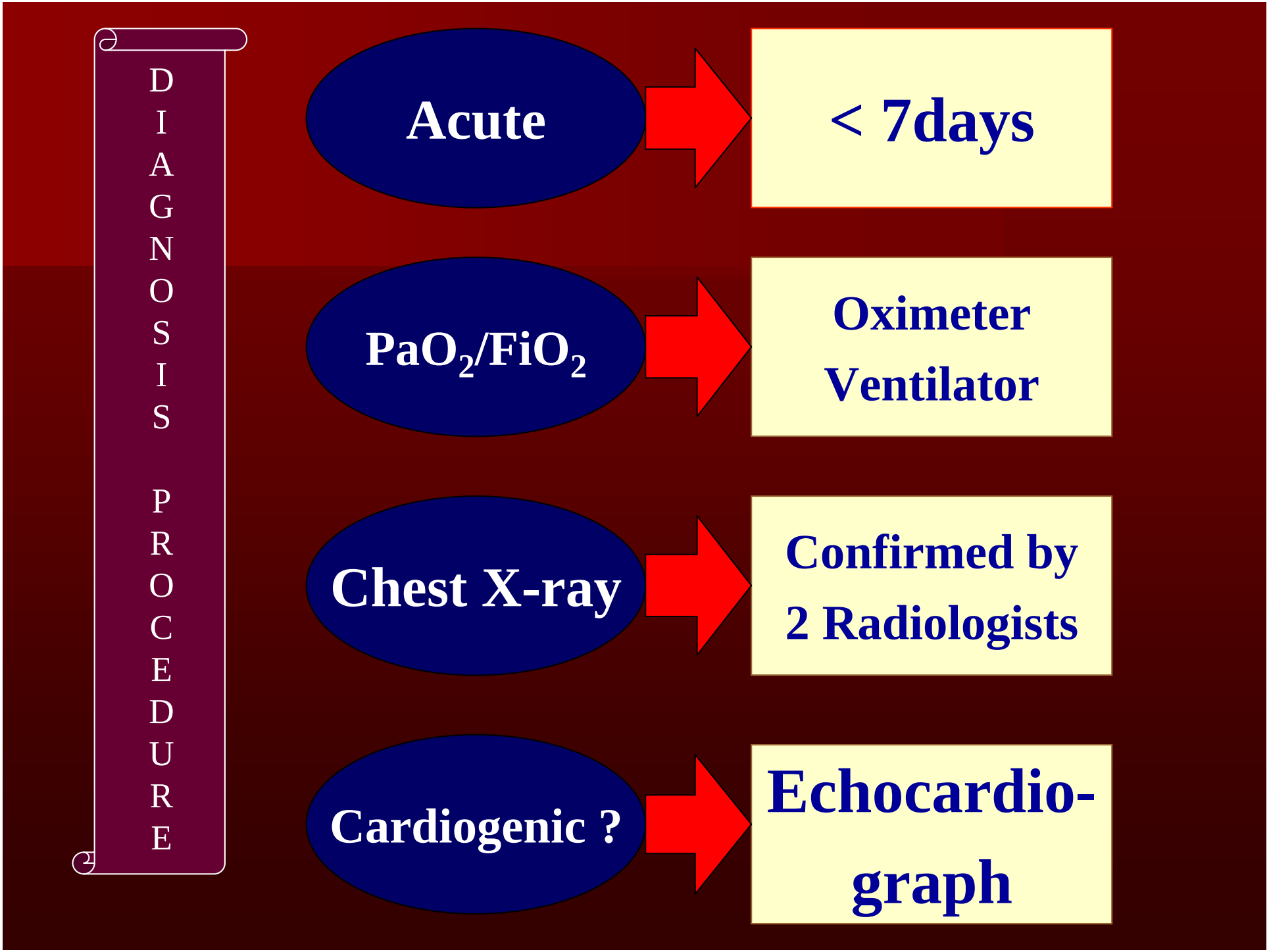

STUDY DESIGN
Method
Prospective
Multicenter
Period
2004.1-2005.6
Total 12mon
Inclusion
Criteria
. All PICU Admissions
(29 d-14 y)
. ARDS
Objectives
. Incidence, mortality,
risk factors
. Disease Processing
. Differences between
PICUs


CASE PROCESSING
All PICU Admissions
PCIS
Critical Ill
AECC 1994
ARDS
Treatment Protocol
Mortality


DIAGNOSIS PROCEDURE
Acute
< 7days
PaO2/FiO2
Oximeter
Ventilator
Chest X-ray
Confirmed by
2 Radiologists
Cardiogenic ?
Echocardio-
graph

ARDS Workshops

Shanghai

Wuhan

Changsha

Kunmin

ARDS Final Workshop
(2005.06.16)

2004.1 ~ 2005.6(25 PICUs)

PICU 12018

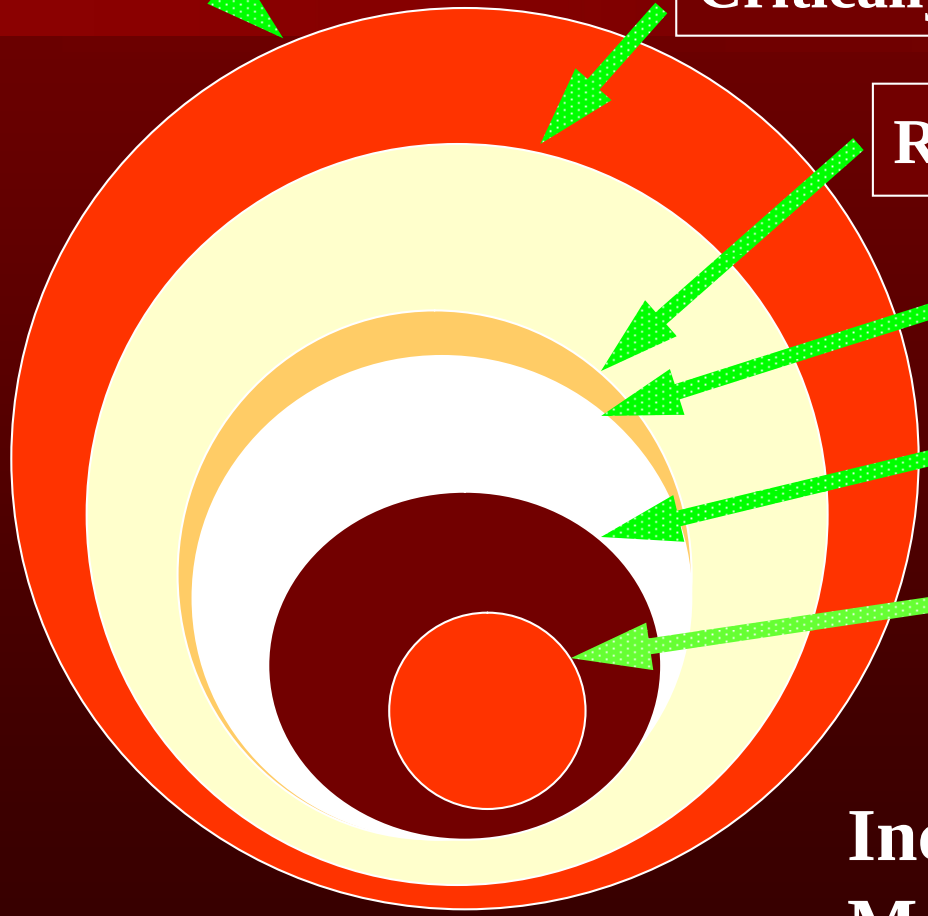
Critically ill 7269

Respir failure 2009

Mechan vent 1957

ARDS 105

ARDS Death 64



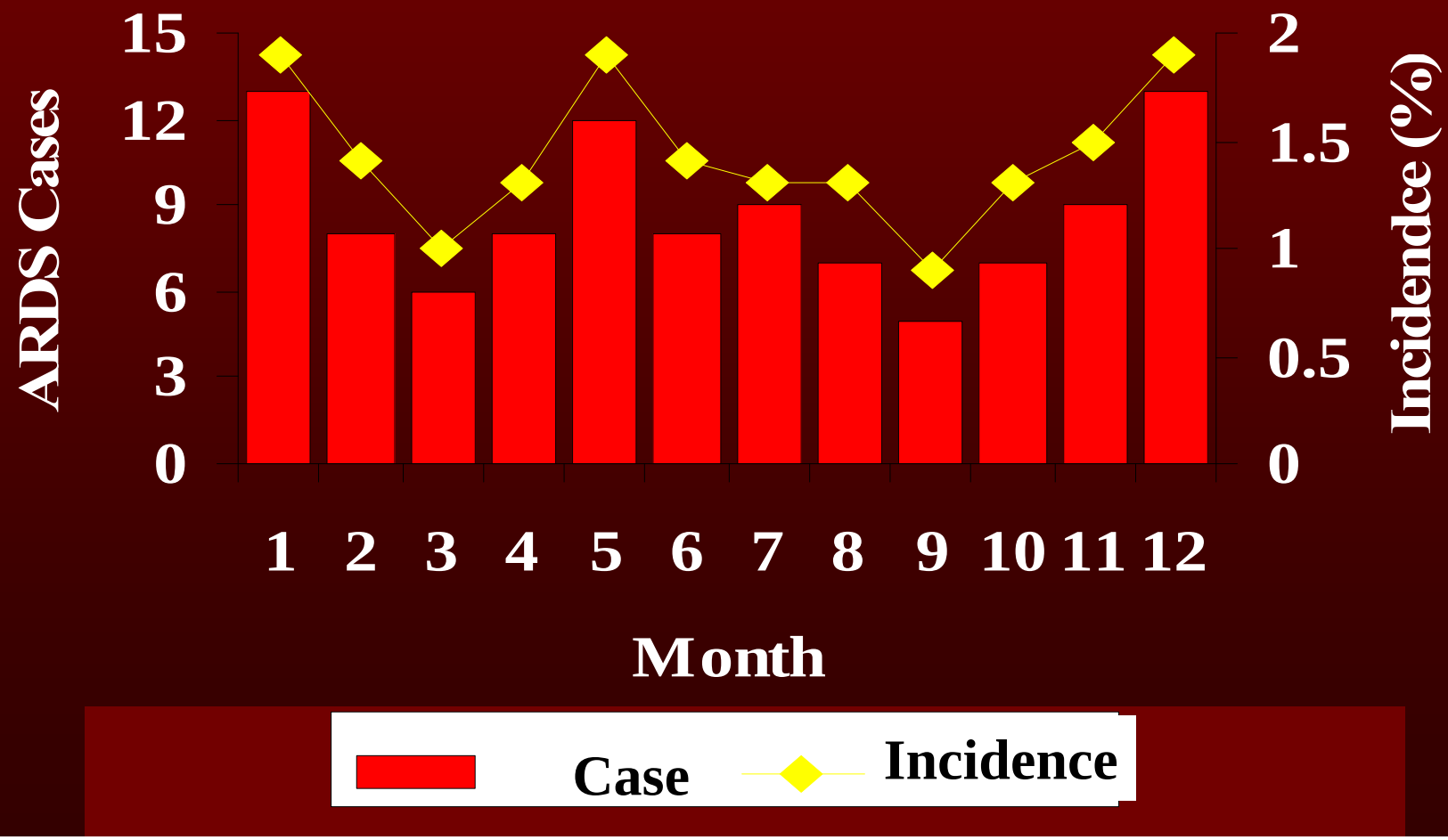
ARDS

Incidence: 1.44% (105/7269)

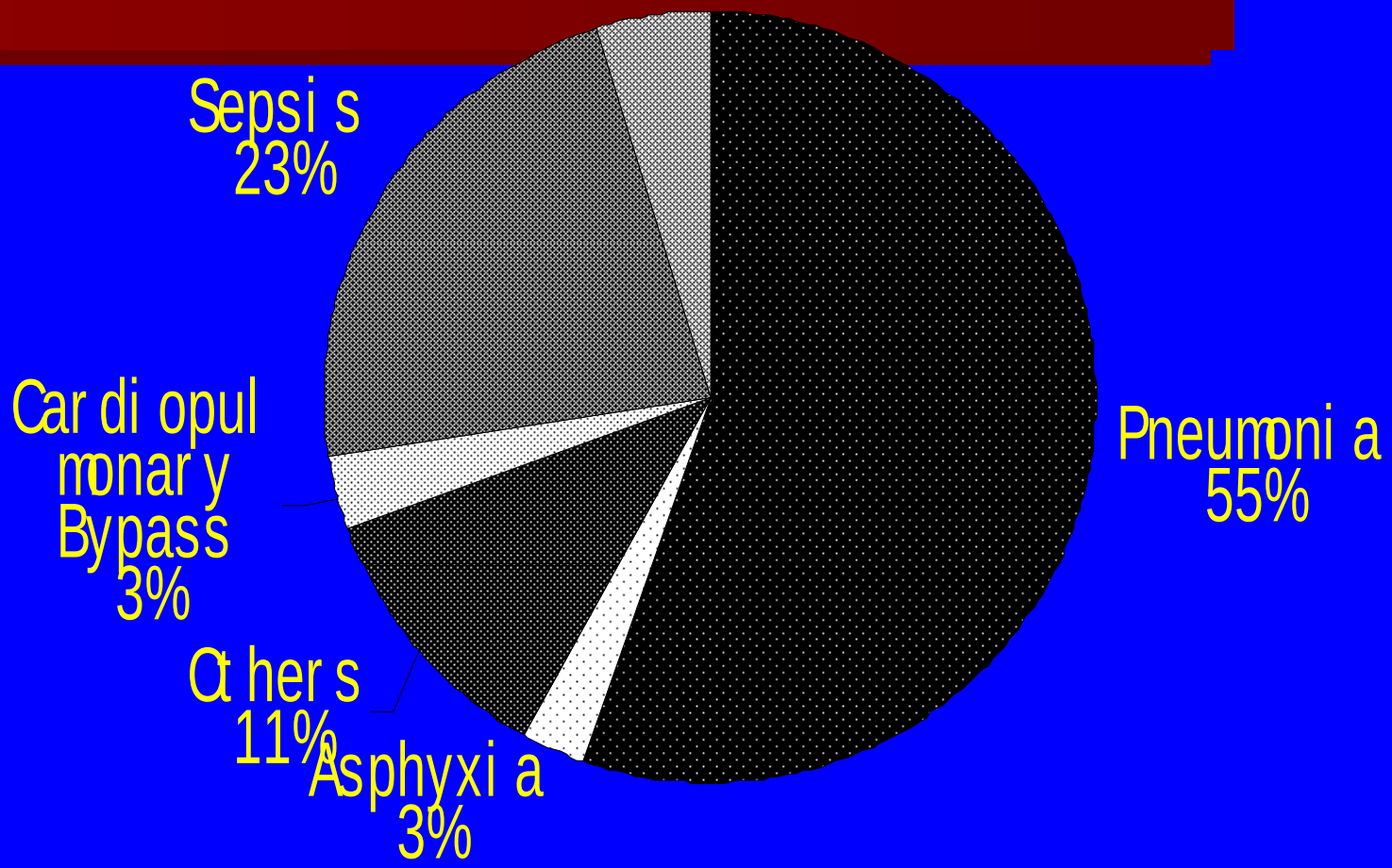
Mortality: 61.0% (64/105)

Monthly distribution of the cases

? ^{2}= 5.867, P = 0.862



Preliminary Diseases



Preliminary Diseases

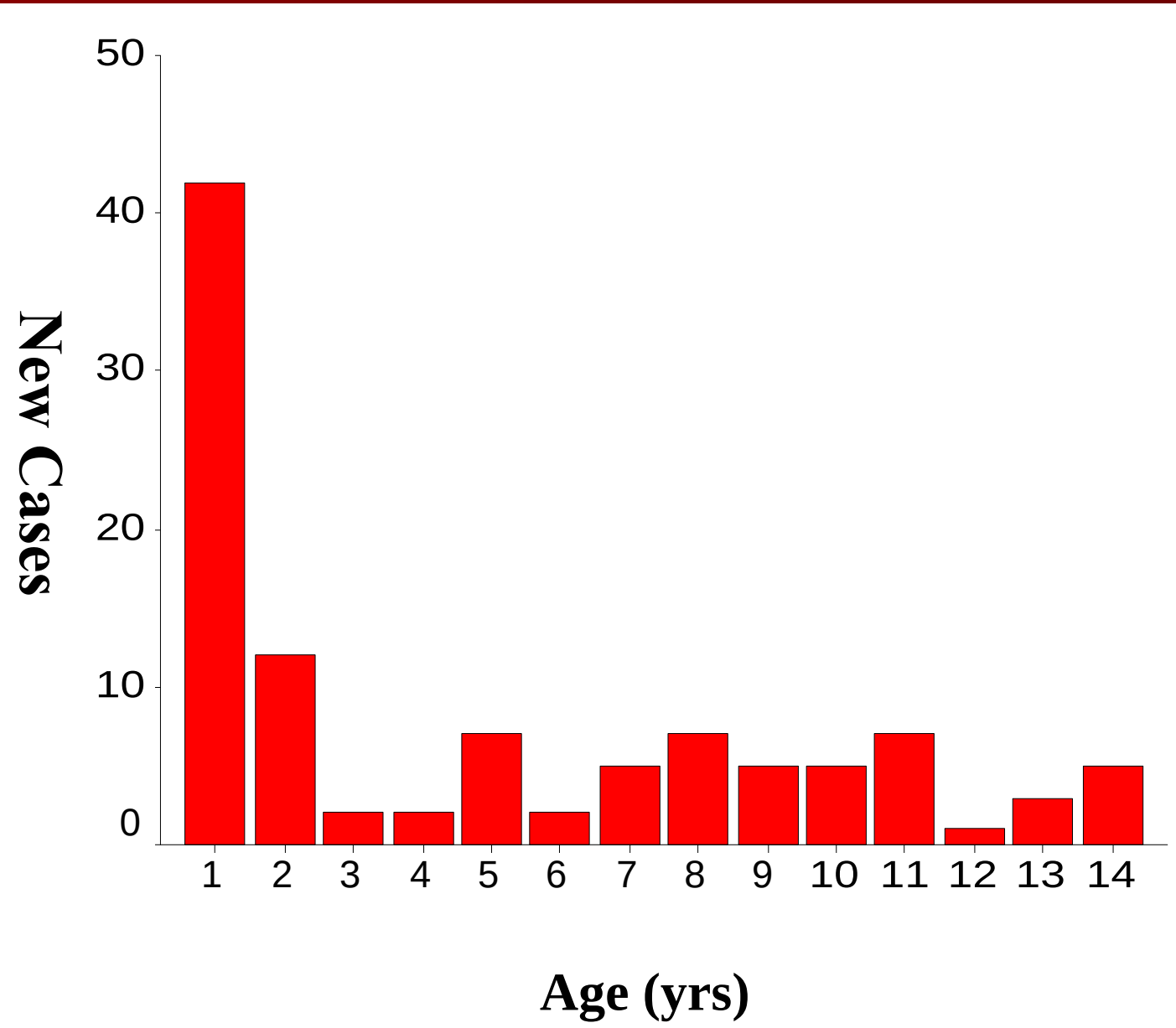
Diseases	Cases/Death (No.)
Intrapulmonary	**62/36**
Pneumonia	58/35
TB	1/0
Contusion	2/1
Near-drown	1/0
Extrapulmonary	**43/28**
Sepsis	24/19
Toxication	5/2
Asphyxia	3/2
Cardiopulmonary bypass	3/0
Hemorrhagic shock	2/1
Conjunctive tissue diseases	2/2
Fluid overload	2/0
Trauma	1/1
Ketoacidosis	1/1

Incidence and Mortality in Pneumonia and Sepsis Induced ARDS

	Pneumonia	Sepsis
PICU		
Total No.	3013	688
Death	159	122
Mortality (%)	5.3 (4.5, 6.1)*	17.7 (14.9, 20.8)
ARDS		
Total No.	58	24
Incidence(%)	1.9 (1.5, 2.5)	3.5 (2.2, 5.1)
Death	35	19
Mortality (%)	60.3 (46.6, 73.0)	79.2 (57.8, 92.9)

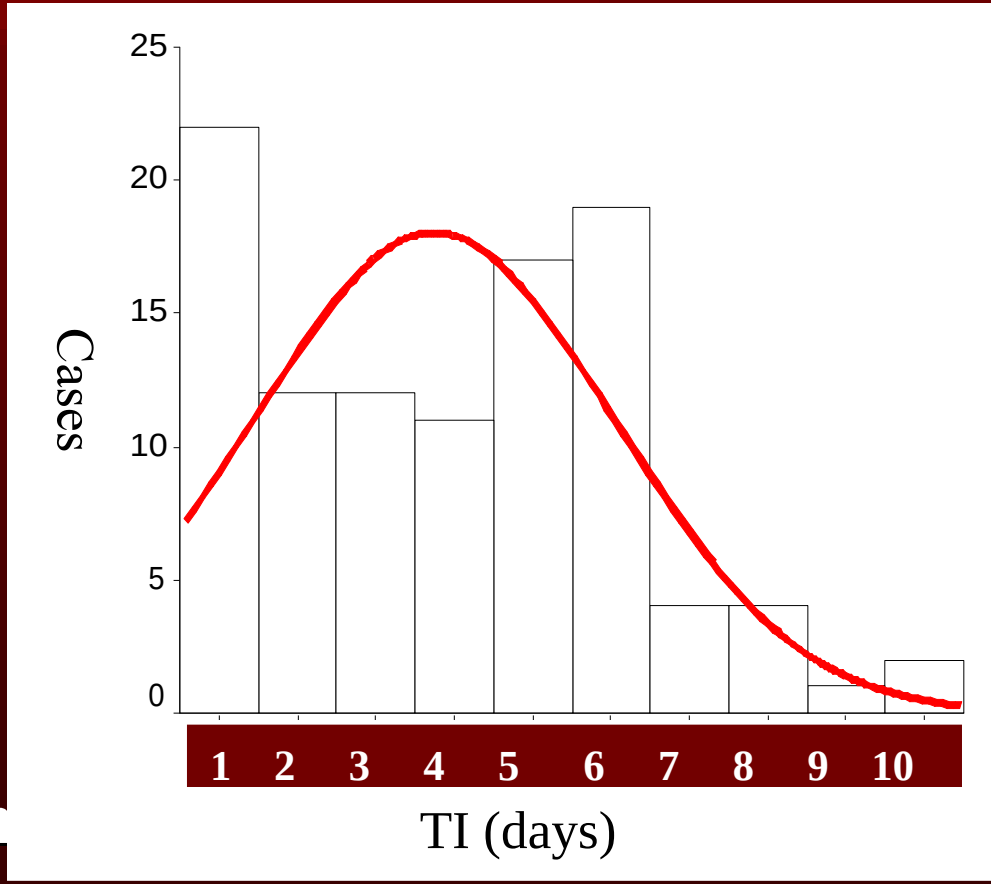
*95% CI

Age Distribution



Onset of ARDS

- Time interval from preliminary disease to onset of ARDS: 75.6± 53.0 h
- 25th, 50th, 75th, 90th, 95th percentile: 24, 72, 120, 144, 168 h
- ARDS death within 24hrs/ total ARDS death =37.7% (23/61)

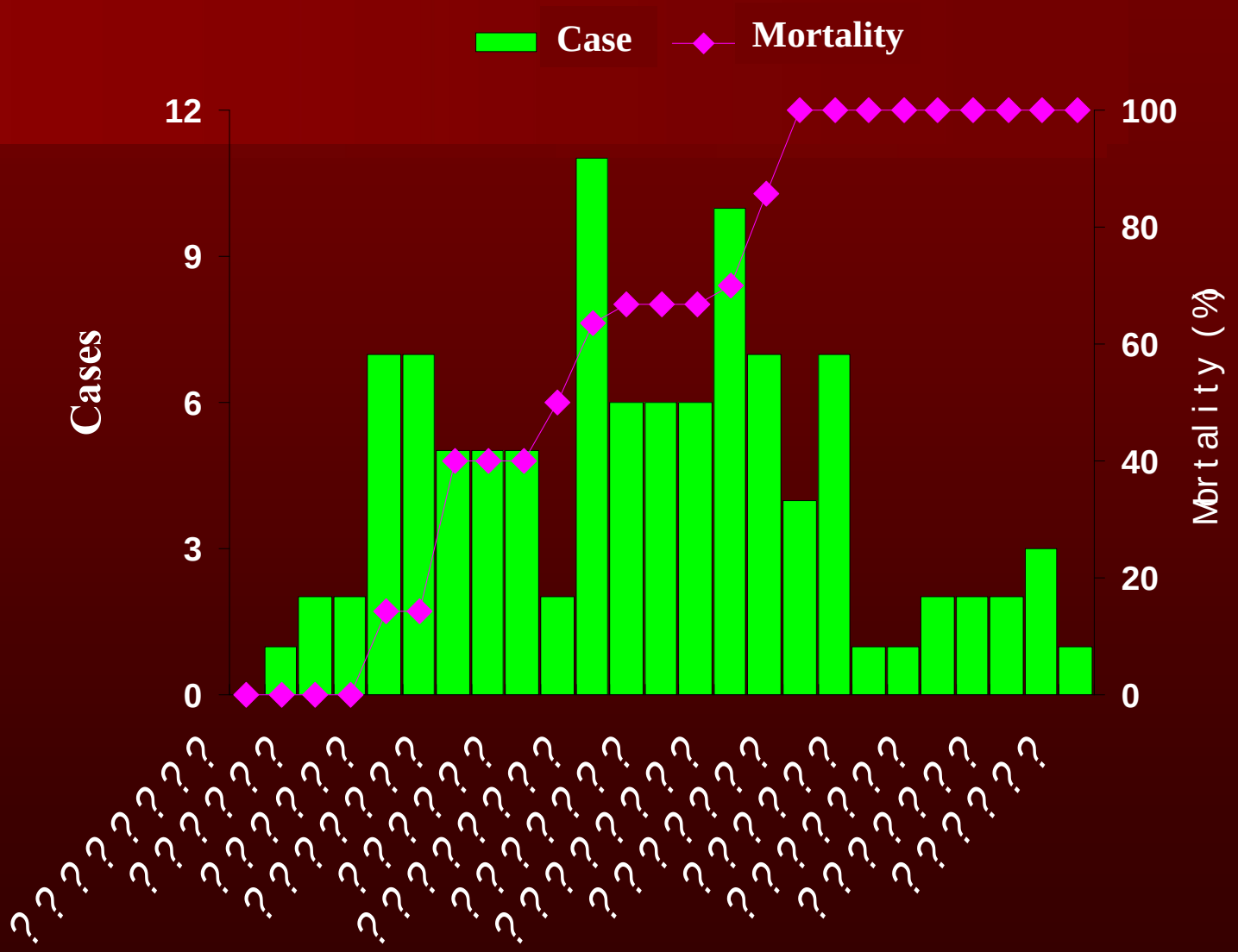


Burden of ARDS

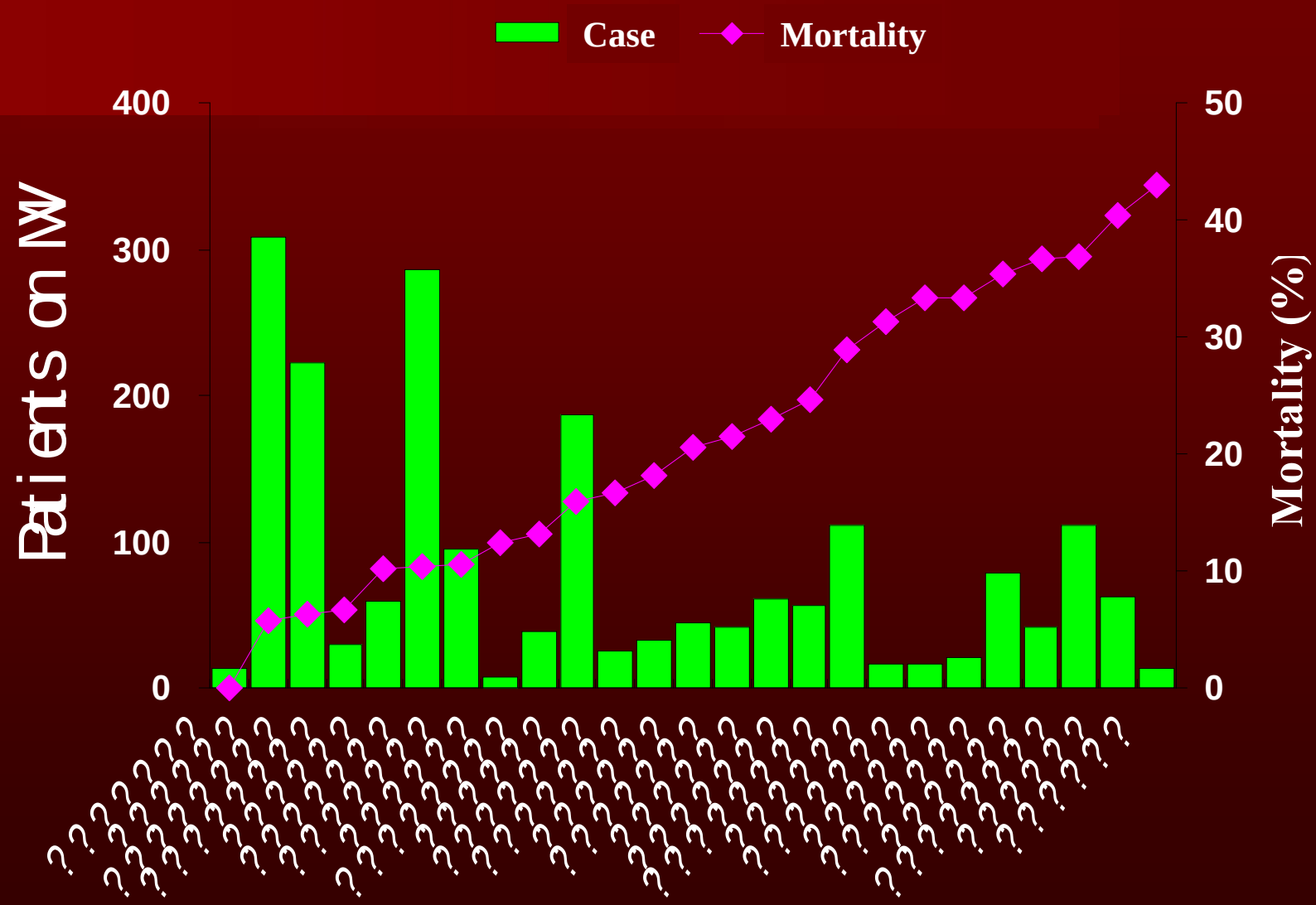
	ARDS	Critical ill	Fold
Mortality (%)	61.0	6.8	9.1
Hospital days	18.8	6.9	2.9
Cost(Yuan)	40914	9157	4.5

- The mortality of ARDS in China is significantly higher than those in developed country (30-40%)
- The burden of ARDS is heavy

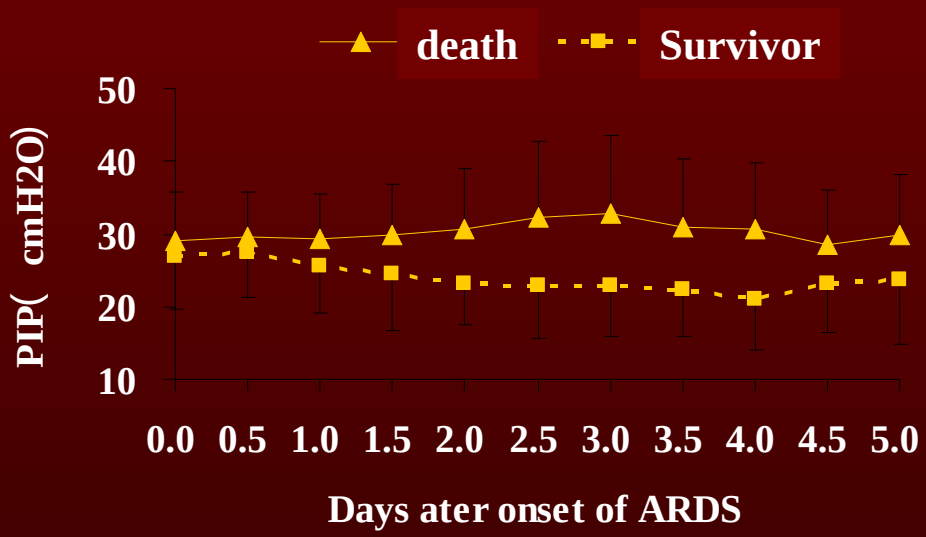
Mortality of ARDS in different PICUs

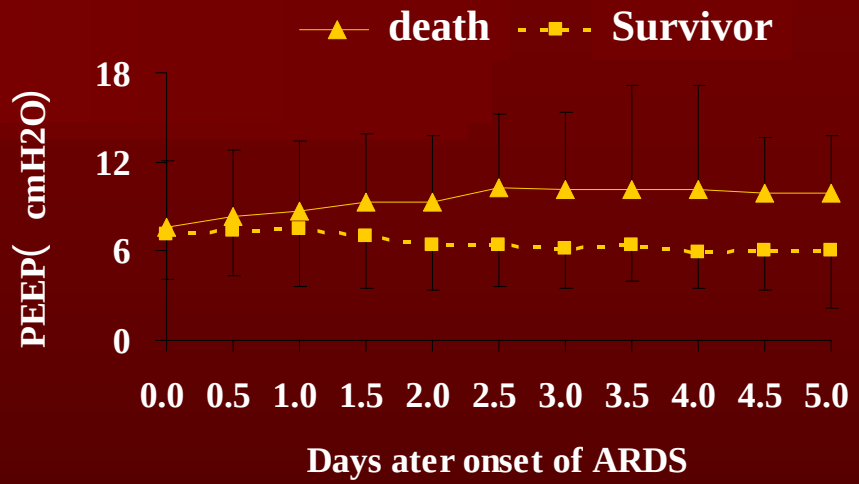


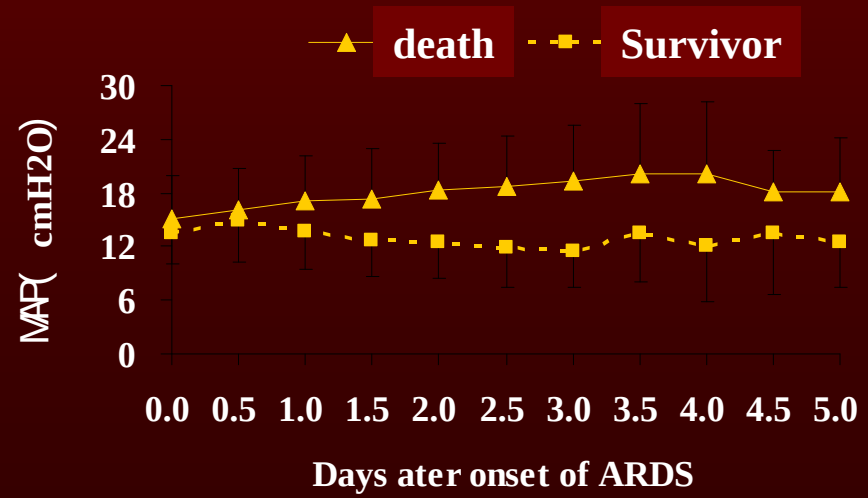
Mortality of ARDS on MV in different PICUs



Lung Mechanism Pressure



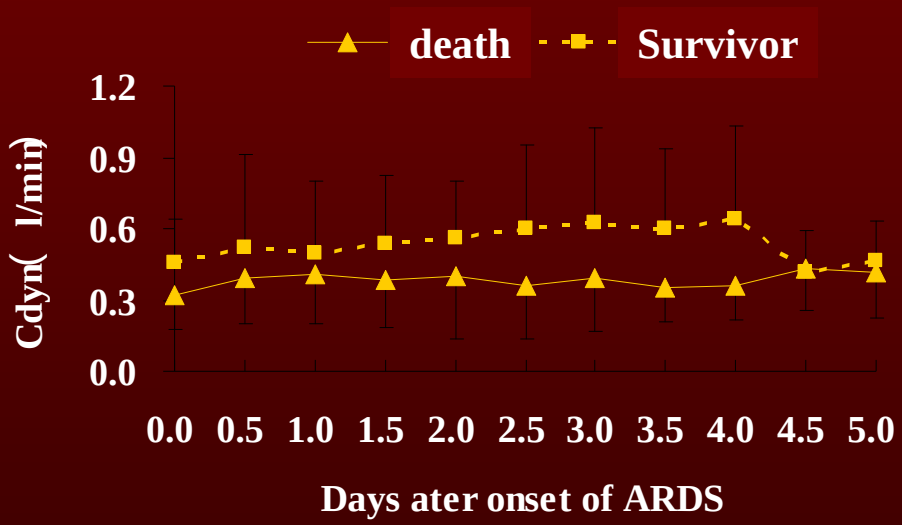


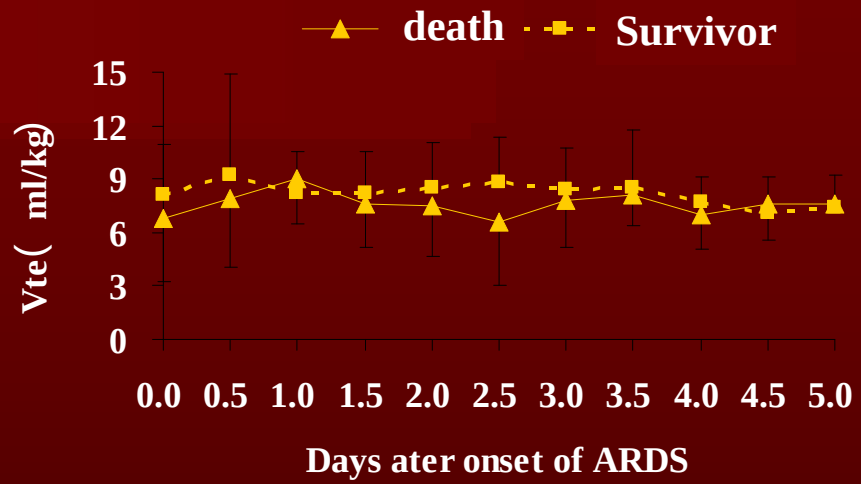


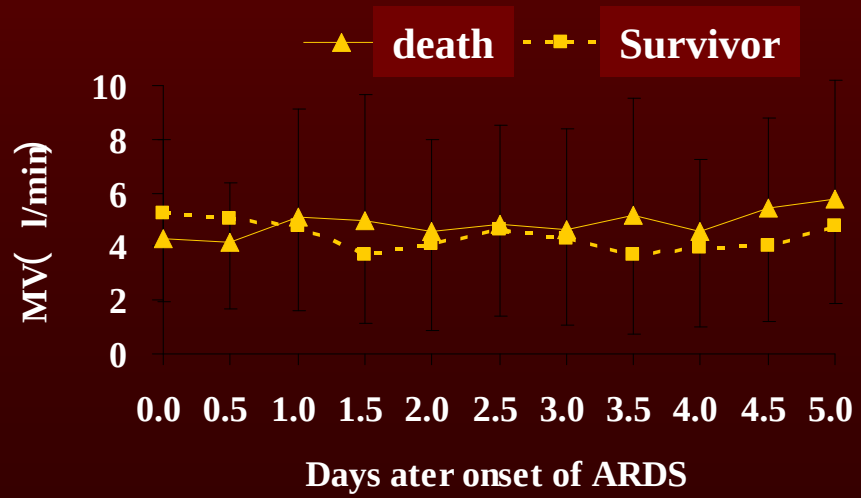
? /¦ , P<0.05

? /¦ , P<0.01

Lung Mechanism Volume







? /¦ , P<0.05

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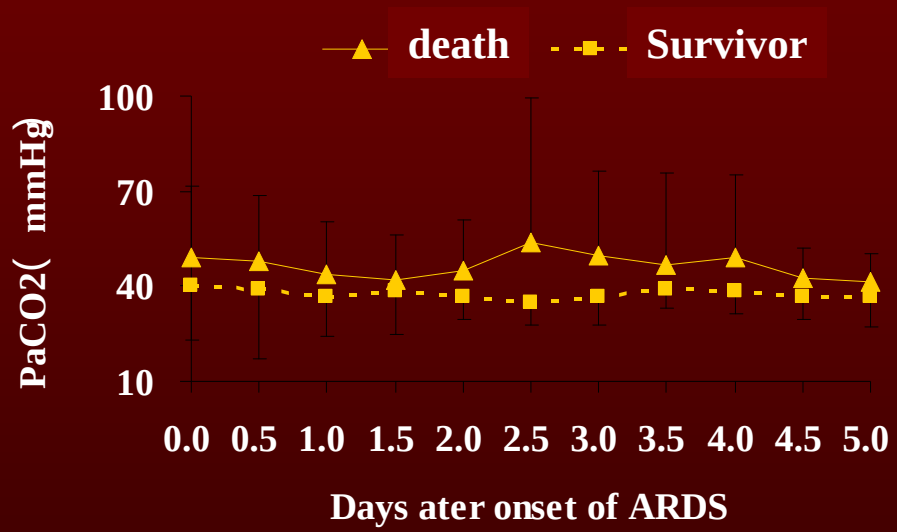
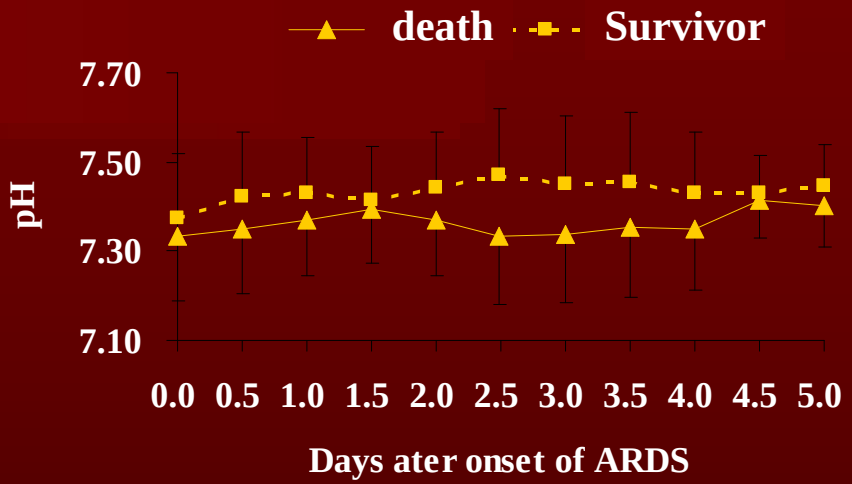
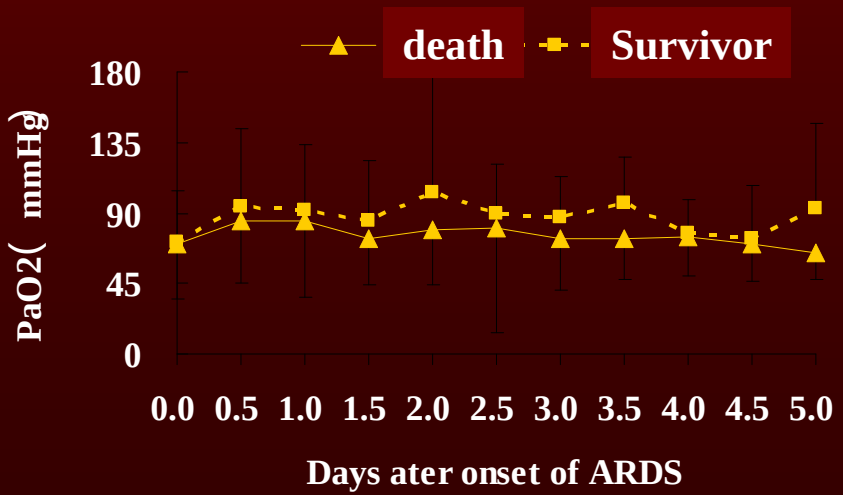
Gas Exchange
Blood Gas







? /¦ , P<0.05

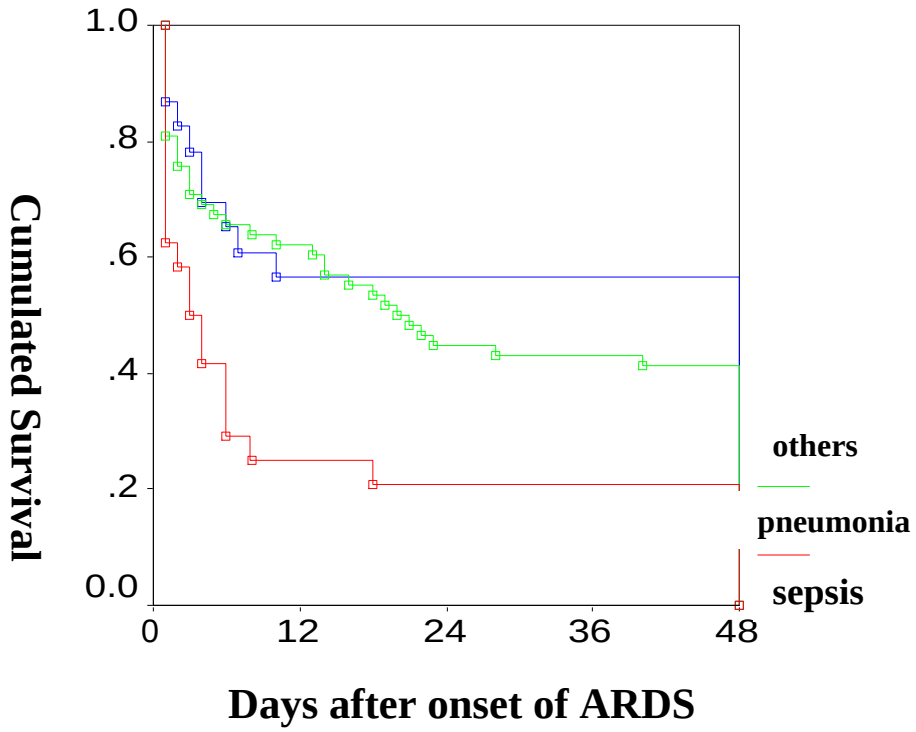
? /¦ , P<0.01

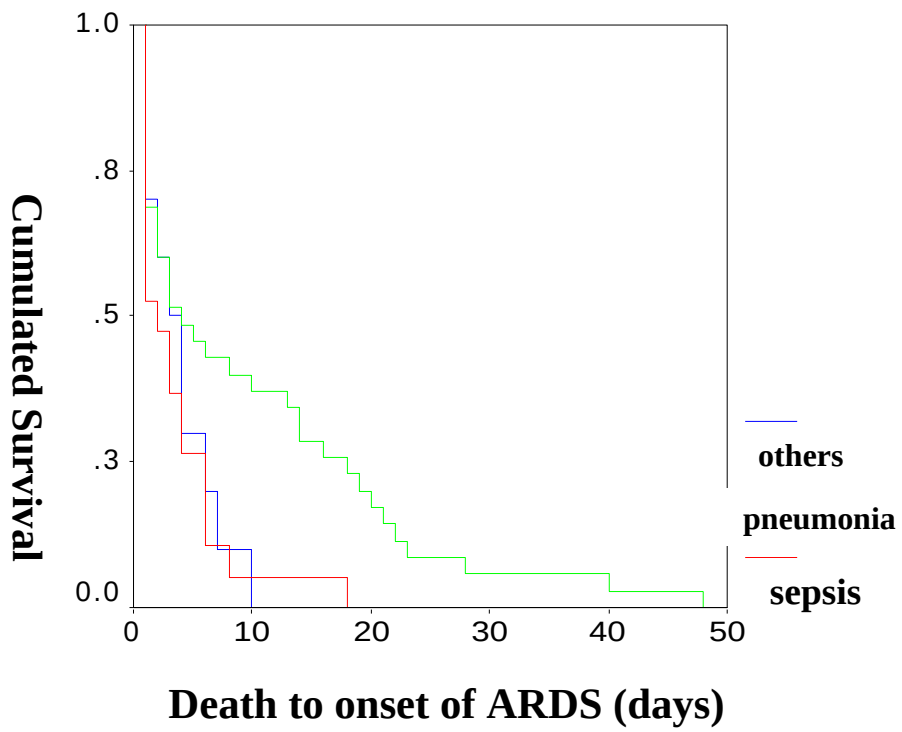
Multi-organ Failure

Number	Cases/Death	Mortality(%)
= 2 organs	55/37	67.3
= 2 EPO*	35/26	74.3
2 EPO	14/12	84.7
3 EPO	6/3	50
4 EPO	10/6	60
5 EPO	5/5	100

*EPO: extra pulmonary organs

Survival Analysis





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Univariate Logistic Regression Analysis of Risk Factors (34)

Variables	OR	p value
Sepsis	3.040	0.037
MOF	3.771	0.011
Infiltrations		
2 quadrants	0.264	0.002
3 quadrants	1.494	0.487
4 quadrants	2.533	0.023
PCIS (domestic)	0.891	0.001
pH	0.017	0.020
$PaCO_2$ (mmHg)	1.026	0.049
OI	1.040	0.116

Multivariate Logistic Regression Analysis of Risk Factors

	OR	p value
Infiltrations		0.004
2 quadrants	0.175	0.001
4 quadrants	0.642	0.530
PCIS (domestic)	0.881	0.001
$PaCO_2$	1.031	0.030

Conclusions

- The incidence and mortality of ARDS is 1.44% and 61.0% respectively in PICUs. The mortality of ARDS is 9 folds as those of critically ill patients and is twice that in the developed countries.
- Hospital stay days in ARDS took up 3% of total PICU occupancy and 5.2% of total ICU cost.
- Relatively low critical care level and inhomogeneity in using lung protective strategies are main issues associated with the high mortality.

Future

- How to set up a standardized network
- How to make well use of Chinese clinical resources
- How to improve the critical care in China

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Thank you