VALIDATION OF CURB-65 SCORE IN HOSPITALIZED PATIENTS WITH COMMUNITY ACQUIRED PNEUMONIA IN MALAYSIA.

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Introduction

- Community-acquired pneumonia (CAP) is a common medical illness.
- 6th leading cause of death in the USA.[1]
- 4th most common cause of death in the UK.[2]
- Mortality ranges from 1- 9% (outpatient) to 50% in ICU setting.
- Malaysia's inpatient mortality = 12%.[3]

1. Barlet JG, Mundy LM, N Engl J Med, 1995.
2. Kamath A , Pasteur M , Slade M et al. Clin Med, 2003.
3. W S Lim, M M Van der Eerden, R Laing et al. Thorax, 2003..

CURB-65 score

- The CURB-65 score is a tool for assessing severity and risk, thus facilitating further management of patients.[4]
- CURB-65 is similar to the modified British Thoracic Society (BTS) scoring system and easier to use than the pneumonia severity index. (PSI).
- The CURB-65 score was derived and validated in 2003.[5]

4. BTS Guidelines for the Management of Community Acquired Pneumonia in Adults. *Thorax* 2001
5. W S Lim et al . Thorax 2003

CURB-65 SEVERITY SCORE

Initial	Description
C	Mental **C**onfusion. Disorientation in person, place or time.
U	Blood **U**rea>7mmol/L
R	**R**espiratory rate>=30/min
B	Low **B**lood pressure Diastolic blood pressure<=60mmHg Systolic blood pressure < 90mmHg
65	Age >=65

Score 1 for each feature present. Minimum score 0, maximum score 6

Clinical prediction rule to stratify patients with community acquired pneumonia (CAP)
Lim WS, Van der Eerden MM, Laing R, Boersma WG, Karalus N, Town GI, Lewis SA, Macfarlane JT. Defining community aquired pneumonia severity on presentation to hospital: an international derivation and validation study. Thorax 2003;58:377-82

Study objectives

Primary Objectives

1. To determine the mortality rate of hospitalised CAP patients.

2. To correlate CURB-65 score to mortality (72hr and 30-days).

Study objectives

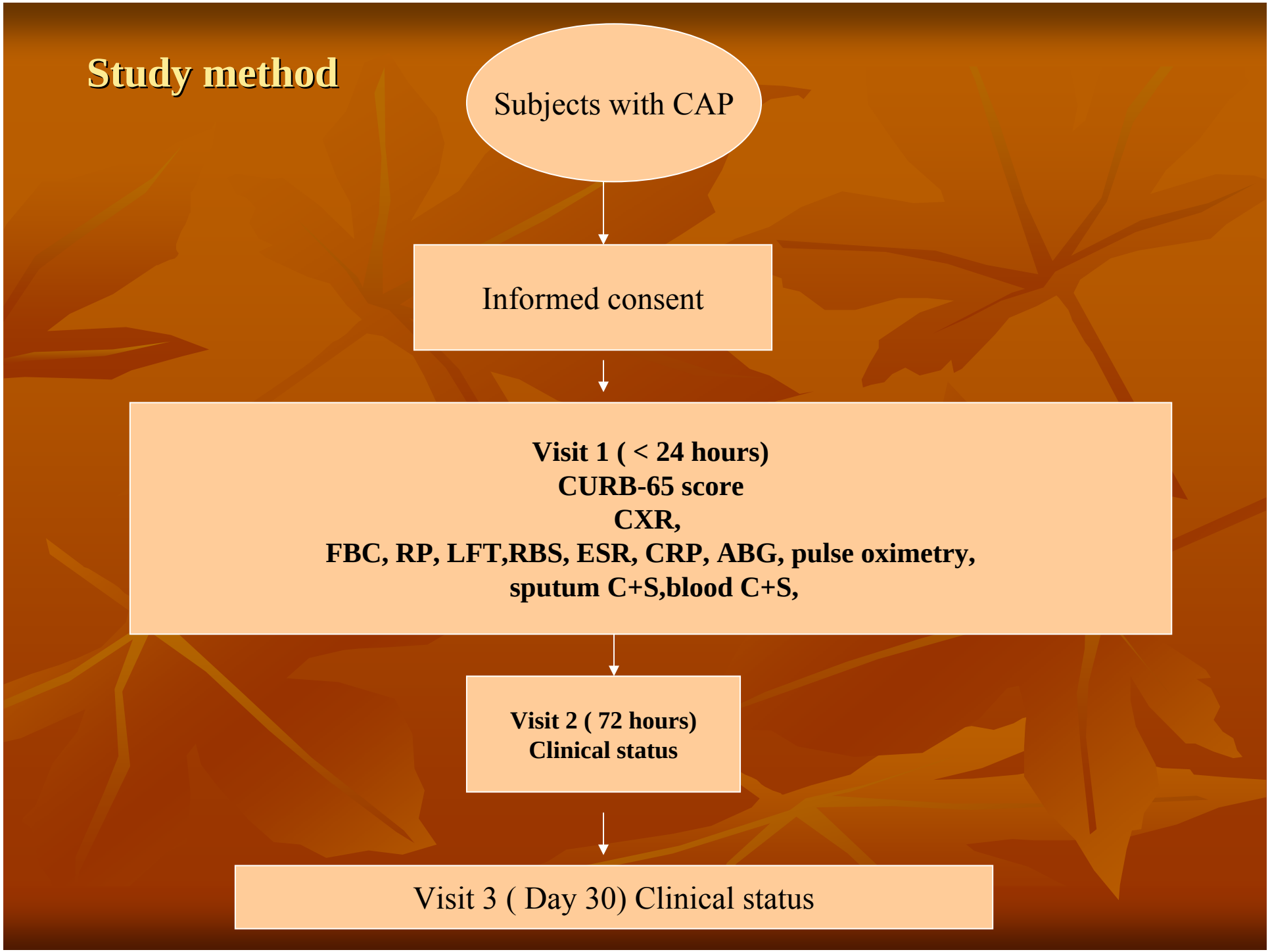
Secondary objectives

1. To compare mortality rates with the original validated CURB-65 model.

Study design

- Study design
  - Prospective observational cohort study in hospitalised patients with CAP in the medical wards in HUKM.
  - 8-month study (Dec 2005-August 2006).
- The study was conducted upon approval of the ethics committee of HUKM.

Study method



Study methods

- Subjects were started on antibiotics by the respective medical teams in keeping with HUKM antibiotic guidelines.

Inclusion Criteria

- Subjects ≥ 12 years old
- CAP diagnosed based on (3 out of 4)
  - Fever
  - Cough
  - Neutrophilia or raised TWBC
  - Presence of infiltrates on CXR consistent with consolidation

Exclusion criteria

- Consent not obtained
- Opportunistic pneumonia
- PTB
- Neutropaenic or immunosuppressed
- Hospital acquired pneumonia

Subject withdrawal

- Subjects were withdrawn if found to have
  - pulmonary tuberculosis
  - lung carcinoma
  - HIV
- Upon request

Definitions

- Current smokers: Subjects who are actively smoking at time of current admission
- Ex-smokers: Subjects who had given up the habit at least 1 year before recruitment into study
- Life-long non smoker: Subjects who have never smoked in their life
- Passive smoker: Subjects who inhale environmental smoke.

Sample size calculation

$$N = \frac{Z^2 1\text{-}/2\ P\ (1\text{-}P)}{d^2}$$

- Z=desired level of certainty
- Z:=1.96 (fixed value) for 95% confidence interval
- Confidence level of 95% (α=0.05)
- P = Prevalence of the disease,
- If P = 0.1
- d=absolutely error or precision. Taken as 0.05
- **N= 138**

- Final sample size 138 +14 = 152
- Total calculated sample size is 152

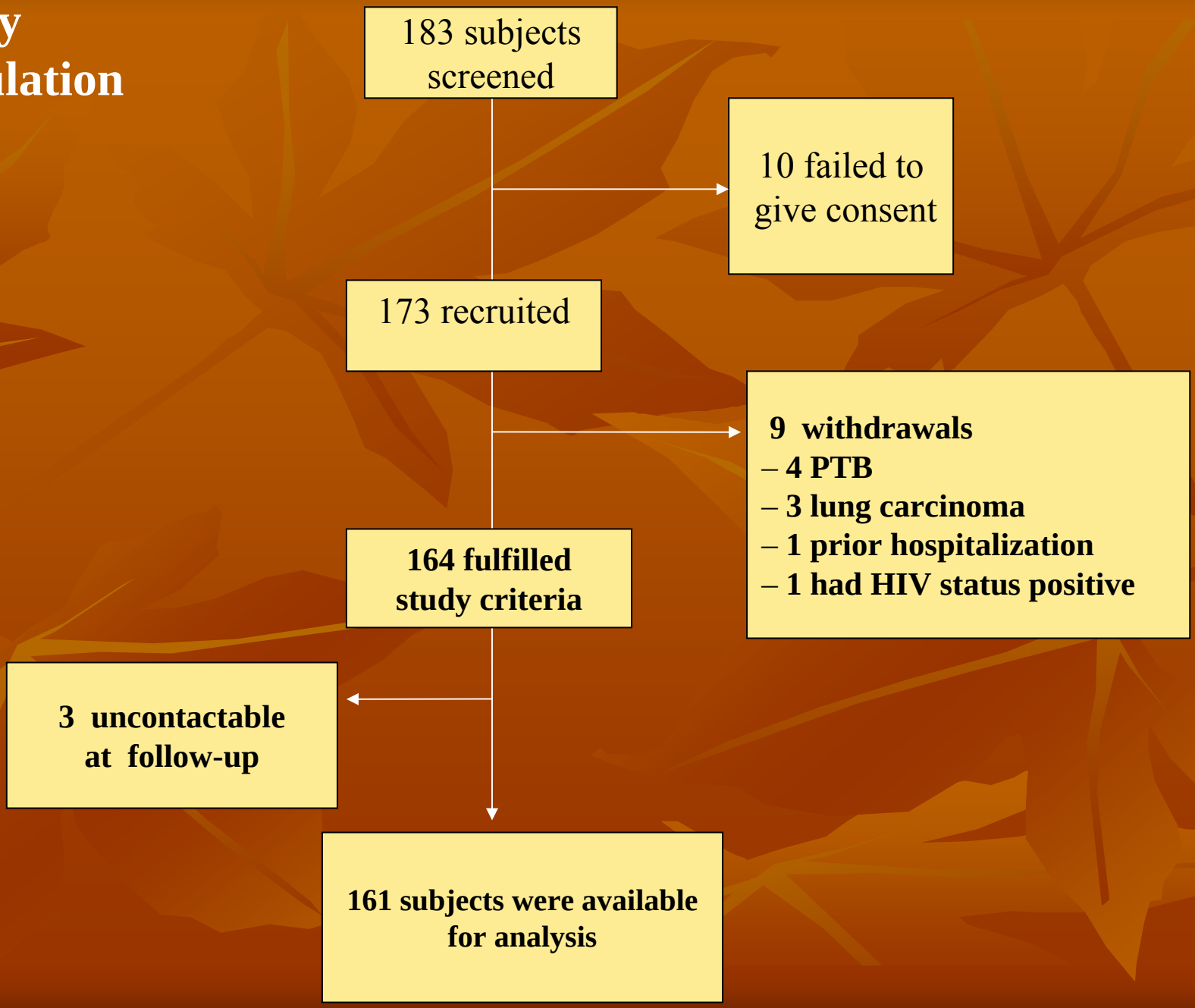
6. Lwanga SK, Lemeshow S. Sample size determination in Health Studies: A Practical Manual. Geneva: WHO 1991.

Statistical analysis

- Analyzed by SPSS version 11.5.
- All numerical data were non-parametric and were expressed as median with IQR.
- Mann-Whitney U test was used to determine differences between the two groups.
- Pearson Chi-Square test was used for categorical data.
- Significant differences were reported as $p<0.05$.
- Logistic regression was used to determine predictors of 30-day mortality.

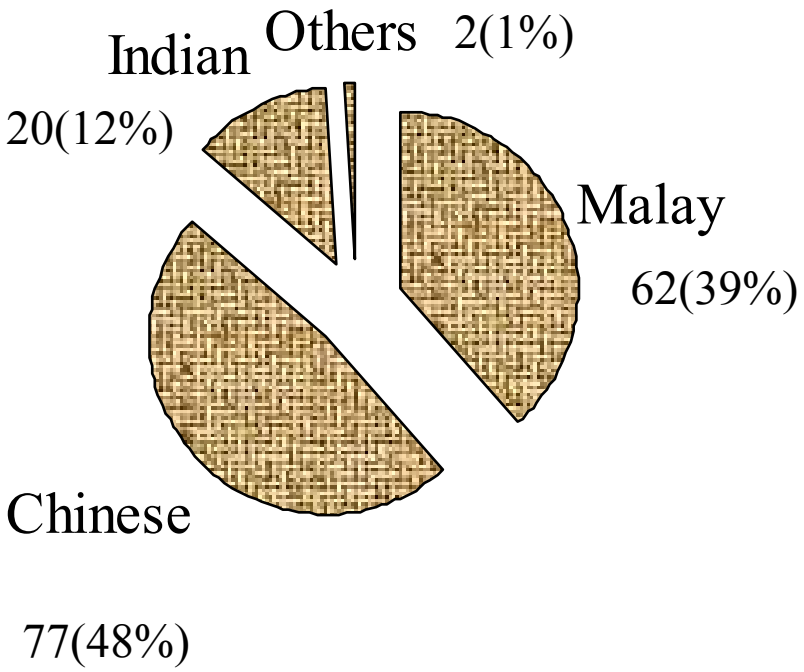
Results and discussion

Study population



Gender distribution of study population. n=161

Ethnic distribution of study population. n=161



	Total (n=161)	Survived (n=136)	Died n=(25)	p-value
Age in years **	**65(55-74)**	**64(52-71))**	**77(70-84))**	**p=0.00***
Sex n (%)				p=0.09
Male	78(100)	62(79.5)	16(20.5)	
Female	83(100)	74(89.2)	9(10.8)	
Race n (%)				
Malay	**62(100)**	**59(95.2)**	**3(4.8)**	
Chinese	**77(100)**	**59(76.6)**	**18(23.4)**	**p=0.01***
Indian	**20(100)**	**16(80)**	**4(20)**	
Others	**2(100)**	**2(100)**	**0(0)**	
Weight in kg**	58(48-66))	58(48-67)	57(46-65)	p=0.470
Height in meters**	**1.57(1.5-1.65)**	**1.57(1.50-1.64)**	**1.65(1.54-1.70)**	**p=0.007***
BMI (kg/m^2)**	**22.82(20.62-26.11)**	**23.16(20.62-26.66)**	**21.33(19.80-23.37)**	**p=0.017***
Smoking status				
Still smoking	22(100)	17(77.3)	5(22.7)	
Ex-smoker	63(100)	55(87.3)	8(12.7)	p=0.081
Life-long non smoker	49(100)	38(77.6)	11(22.4)	
Passive smoking	27(100)	26(96.3)	1(3.7)	
Type of work				
Professional	3(100)	3(100)	0(0.0)	
Non-professional	33(100)	31(93.9)	2(6.1)	p=0.083
Student	5(100)	5(100)	0(0.0)	
Not-working	120(100)	97(80.8)	23(19.2)	
Pets				p=0.097
Yes	46(100)	41(89.1)	5(10.9)	
No	114(100)	95(83.3)	19(16.7)	
Unknown	1(100)	0(0.0)	1(100)	
Alcohol				
Yes	25(100)	22(88)	22(16.2)	p=0.428

Parameters	Total(n=161)	Survived(n=136)	Died(n=25)	p-value
Cough (89.4%) Yes No	144(100) 17(100)	121(84.0) 15(88.2)	23(16.0) 2(11.8)	p=0.488
Dyspnoea (78.2%) Yes No	126(100) 35(100)	106(84.1) 30(85.7)	20(15.9) 5(14.3)	p=0.528
Sputum (73.3%) Yes No	118(100) 43(100)	101(85.6) 35(81.4)	17(14.4) 8(18.6)	p=0.335
Fever (71.4%) Yes No	115(100)	99(86.1)	16(13.9) 9(19.6)	p=0.252
Chest Pain (28.6%) Yes No			(15.2) 15.7)	p=0.577
Diarrhea (12.4%) Yes No			4(20.0) 21(14.9)	p=0.377
Loss of weight (12.4%) Yes No	20(100) 141(100)	15(75.0) 121(85.8)	5(25.0) 20(14.2)	p=0.176
Haemoptysis (6.2%) Yes No	10(100) 151(100)	7(70.0) 129(85.4)	3(30.0) 22(14.6)	p=0.188
Other symptoms (32.9%) Yes No	53(100) 108(100)	46(86.8) 90(83.3)	7(13.2) 18(16.7)	p=0.374

No significant association

Association between comorbidities and mortality

	Total (n=161)	Survived (n=136)	Died (n=25)	p-value
Hypertension(49.7%)				
Yes	80(100)	66(82.5)	14(17.5)	p=0.320
No	81(100)	70(86.4)	11(13.6)	
Diabetic status (35.4%)				
Yes	57(100)	48(84.2)	9(15.8)	p=0.557
No	104(100)	88(84.6)	16(15.4)	
COPD (19.25%)				
Yes	**37(100)**	**36(97.3)**	**1(2.7)**	**p=0.008***
No	**124(100)**	**100(80.6)**	**24(19.4)**	
IHD (18.0%)				
Yes	31(100)	28(90.3)	3(9.7)	p=0.241
No	130(100)	108(83.1)	22(16.9)	
Previous PTB (12.42%)				
Yes	20(100)	8(90)	2(10)	p=0.365
No	14(100)	118(83.7)	23(16.3)	
Stroke (10.56%)				
Yes	17(100)	14(82.4)	3(17.6)	p=0.512
No	144(100)	122(84.7)	22(15.3)	
Asthma (10.56%)				
Yes	**29(100)**	**28(96.6)**	**1(3.4)**	**p=0.034***
No	**132(100)**	**108(81.8)**	**24(18.2)**	
Others (56.52%)				
Yes	91(100)	73(80.2)	18(19.8)	p=0.068
No	70(100)	63(90.0)	7(10)	

Association between baseline vital signs, blood investigations and mortality

	Total	Survived	Died	p-value
Pulse rate in b.p.m	102.47(21.18)	103.05(19.56)	99.36(28.74)	p>0.05
Respiratory rate in breaths/min	27(20-32)	26(20-32)	30(22-40)	p=0.243
Systolic blood pressure in mmHg	**135.5(115-156.75))**	**138(118-158.75)**	**122(99-140.5)**	**p=0.010***
Diastolic blood pressure in mmHg	75(54-86)	76(66-86)	68.5(52.25-84.50)	p=0.075
TWBC ($X10^9$/L)	13.5(10.8-18.38)	13.35(10.63-18.28)	14.65(11.15-14.65)	p=0.364
ESR (mm/hr)	62(32.25-98)	57(30-98)	77(54-108)	p=0.098
CRP (mg/L)	**6.49(.1.26-16.67)**	**5.25(0.90-14.84)**	**10.17(3.60-23.84)**	**p=0.018***
Urea (mmol/L)	**6.3(3.7-10)**	**5.5(3.6-8.38)**	**11.4(7-15)**	**p=0.00***
Albumin(g/dl)	**36(32-39.5)**	**37(33-40)**	**30(27.50-34.05)**	**p=0.00***
Random blood sugar(mmol/L)	8.2(6.25-11.85)	8.2(6.45-12.40)	8.15(5.65-9.65)	p=0.289
Blood cultures (%) **Positive** **Negative**	 **16(11)** **130(89.0)**	 **10(8.3)** **111(91.7)**	 **6(24)** **19(76)**	**p=0.011***

Multivariate analysis

	B	Sig	Lower CI	Upper CI
BMI	-.139	.041	.762	.994
Albumin	.091	.043	.836	.913
CURB High Risk		0.00		
CURB Mod vs High risk group	-2.087	.002	.033	.461
CURB low vs High risk group	-4.303	0.00	.001	.134

Sun Ha Jee et al. New England Journal of Medicine, 2006.

Logistic regression

	B	S.E.	Wald	df	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
							Lower	Upper
BMI	-.139	.068	4.193	1	.041	.870	.762	.994
ALBUMIN	-.091	.045	4.104	1	.043	.913	.836	.997
CURBLOG			19.795	2	.000			
CURBLOG(1)	-2.087	.670	9.709	1	.002	.124	.033	.461
CURBLOG(2)	-4.303	1.169	13.558	1	.000	.014	.001	.134
Constant	6.077	1.980	9.422	1	.002	435.651		

The prediction equation is as follows:

Z= 6.077 - 0.139*BMI-0.091*ALBUMIN - 2.087*CURBLOG (1) -.303*CURBLOG (2)

Probability (mortality at 30 days) = 1/1+e-z (where e denotes the exponential function)

Discussion

- Age, race, height , BMI, COPD, asthma, systolic BP, CRP, albumin, blood urea and blood cultures were significantly associated with 30-day mortality.
- BMI, albumin and CURB-65 categories were significant predictors of 30-day mortality after multivariate analysis.
- BMI had an inverse relationship with mortality.
- This was supported by a recent study.[7]

7. Sun Ha Jee Jae Woong Sull Junhyonh Park Sang-Yi Lee Heechoul Ohrr Eliseo Guallar PH Jonathan M Samet, *Body-Mass Index and Mortality In Korean Men and Women.* New England Journal of Medicine, 2006. 355: p. 779- 87.

Empirical antibiotic therapy

	Total n=161	Survived n=136	Died n=25	p-value
Choice of antibiotics n (%)				
Augmentin + azithro	106(66)	92(86.8)	14(13.2)	
Cephalosporin + azithro	34(21)	30(88.2)	4(11.8)	p=0.106
Carbapenems + azithro	6(4)	3(50)	3(50.0)	
Others + azithro	3(2)	2(66.7)	1(33.3)	
Single antibiotic	11(7)	9(81.8)	2(18.2)	
Augmentin and others	1(0.6)	0(0.0)	1(100)	

There is no significant association between choice of antibiotic and mortality

Time of antibiotic administration

	Total n= 154	Survived n=131	Died n=23	p-value
Time of antibiotic administration				
≤ 4 hours	84(55)	70(83.3)	14(16.7)	
4.1-8 hours	44(29)	40(90.0)	4(9.1)	p=0.389
>8 hours	26(17)	21(80.8)	5(19.2)	

There is no significant association between time of antibiotic administration and mortality

Aetiological agents

	Total	Alive	Dead	p-value
Urine for *strep pneumoniae* (n=55)				
Positive (5%)	3(100)	3(100)	0(0.00)	p=0.893
Negative (95%)	52(100)	50(96.2)	2(3.8)	

Blood cultures isolates n=17	**Number of subjects**
Positive but no organism cultured	1
Gram negative rods	2
Gram positive cocci	2
Coagulase negative staph	4
E.coli	2
Bukholderia pseudomallei	1
Klebsiella	1
Citrobacter	1
Candida	1
Strep pneumoniae	1
Pseudomonas	1

Sputum culture

Sputum culture n= 110	
Pseudomonas	1
Strep pneumoniae	1
Klebsiella species	2
Branhamella species	1
Enterobacter	1
Pseudomonas/klebsiella	1
Candida	2

Aetiological agents

- Liam et al[8]
  - Klebsiella 10.2%
  - Strep pneumoniae 5.5%
  - Haemophilus Infleunza 5.5%
  - Mycoplasma pneumoniae 3.9%
  - Pseudomonas aeruginosa 3.9%
- Hooi et al.[9]
  - Mycobacterium tuberculosis 15.3%
  - Klebsiella pneumoniae 7.2%
  - Pseudomonas aeruginosa 6.1%
  - Staphylococcus aureus 5.1%

8. Chong-Kin Liam et al. Respirology, 2001.

9. Hooi LN Looi I NG AJ. Med J Malaysia, 2001.

Atypical serology

Atypical serology n=93	**Total**
***Mycoplasma* n (22.6%)**	21
***Legionella* n (25.8% %)**	24
***Chlamydia* n (17.2%)**	16
Two infections n (%) ***Myco+legionella*(6.5%)** ***Myco+Chlamydia*(1.1%)** ***Legion+Chlamydia*(3.2%)**	6 1 3
Three infections n (1.1%)	1
No infections (48.3%)	45

* Results obtained using paired serology

Atypical serology

- Ngeow et al[10]
  - Mycoplasma 12.2%
  - Chlamydia 4.7%
  - Legionella 6.6%

10. Ngeow YF et al, Int J Infect Dis, 2005.

Chest radiographs and mortality

Chest radiographs (n=109)	Total	Alive	Dead	p-value
One lobe (48%)	52(100)	48(92.3)	4(7.7)	p=0.105
Two lobes or more (51%)	56(100)	46(82.1)	10(17.9	p=0.092
Bilateral (45%)	49(100)	41(83.7)	8(16.3))	p=0.243
Effusion (41%)	45(100)	38(84.4)	7(15.6)	p=0.334

There is no significant association between CXR severity and mortality.

CURB-65 and Mortality

CURB-65 score	0-1 MILD	2 MODERATE	3-6 SEVERE	Total	p-value
Numbers (%)	71(44%)	44(27%)	46(29%)	161(100)	
Early mortality Dead Alive	 0(0.0) 71(100)	 2(4.5) 42(95.5)	 8(17.4) 38(82.6)	 10(6.2) 151(93.8)	p<0.01
30-day mortality Dead Alive	 1(1.4) 70(98.6)	 4(9.1) 40(90.9)	 20(43.5) 26(56.5)	 25(15.5) 136(84.5)	p<0.01

There is a significant association between CURB-65 score and both early as well as 30-day mortality

Odds ratio by multiple comparisons between the CURB-65 severity groups

CURB 65 score	Odds ratio value	95% Confidence Interval	p-value
0-1	0.08	0.02-0.37	p<0.01
2	0.46	0.15- 1.42	p=0.125
3-6	16.9	5.8-49.3	p<0.01

***p<0.01 is taken as significant to adjust for type I error for multiple comparisons**

Discussion

- This is one of the few studies in Malaysia looking at CURB-65 score and mortality.
- Loh et al[11] showed that BTS criteria fared poorly in predicting mortality compared to clinical assessment.

11. Li-Cher Loh et al. Respirology, 2004.

Our study

CURB-65 score	Description
0-1	0.6%
2	2.5%
> Or =3	12.4%

Lim et al

CURB-65 score	Description
0 or 1	Mortality low (1.5%)
2	Mortality intermediate (9.2%)
> Or = 3	Mortality high (22%)

Clinical prediction rule to stratify patients with community acquired pneumonia (CAP)
Lim WS, Van der Eerden MM, Laing R, Boersma WG, Karalus N, Town GI, Lewis SA, Macfarlane JT. Defining community aquired pneumonia severity on presentation to hospital: an international derivation and validation study. Thorax 2003;58:377-82

Other studies

- Aujesky et al.[12]
  - PSI has higher discriminatory power for short-term mortality. Defines a greater proportion of patients at low risk compared to CURB-65.
- Buising et al.[13]
  - PSI and CURB-65 are equally powerful as prediction tools for mortality, ventilatory support and inotropic support.

12. Aujesky D et al. Am J Med, 2005.

13. Buising KL et al. Thorax, 2006.

Conclusions

- Our study suggests that high **CURB-65 scores, elderly, thin and malnourished** subjects with CAP are at increased risk of death at 30-days.
- The early mortality rate in our medical inpatients from CAP is 6.2% and at 30 days is 15.5%.
- Death rates each category
  - 0.6% (CURB 0-1)
  - 2.5% (CURB 2)
  - 12.4% (CURB 3-6)
- Odds ratio increased with the CURB-65 categories
  - 0.08 (CURB 0-1)
  - 0.46 (CURB 2)
  - 16.9 (CURB 3-6)
- CURB-65 is a useful tool to identify patients at high risk of dying within 30-days.

Conclusion

- The aetiology of CAP in this study:
  - Legionella 25.8%,
  - Mycoplasma 22.6%,
  - Chlamydia 17.2%,
  - *Strep pneumoniae* 2.7%

Recommendations

- CURB-65
  - Incooperated into the assessment of CAP patients in the medical wards during admission.
- Those with high CURB-65 scores
  - monitored closely
  - transferred to the high dependency ward.
- Those with low CURB-65 could be treated as outpatient.

Limitations

- We did not include patients with pulmonary tuberculosis although it is a common CAP in Malaysia.

Thank you

Acknowledgements

- Prof Madya Dr Roslina Abdul Manap.
- Prof Madya Roslan Harun, Dr Fauzi and Dr Adina.
- The Respiratory Unit HUKM.
- The staff of Klinik Perubatan Satu, HUKM.
- Prof Madya Datin Dr Elina.
- Dr Niazlin.
- Cik Zuriza.
- Dr Marilyn Umar.
- Dr Azmi Tamil.
- Prof Madya Syed Zulkifli.

ABSTRACT

Background Obesity is associated with diverse health risks, but the role of body weight as a risk factor for death remains controversial.

Methods We examined the association between body weight and the risk of death in a 12-year prospective cohort study of 1,213,829 Koreans between the ages of 30 and 95 years. We examined 82,372 deaths from any cause and 48,731 deaths from specific diseases (including 29,123 from cancer, 16,426 from atherosclerotic cardiovascular disease, and 3362 from respiratory disease) in relation to the body-mass index (BMI) (the weight in kilograms divided by the square of the height in meters).

Results In both sexes, the average baseline BMI was 23.2, and the rate of death from any cause had a J-shaped association with the BMI, regardless of cigarette-smoking history. The risk of death from any cause was lowest among patients with a BMI of 23.0 to 24.9. In all groups, the risk of death from respiratory causes was higher among subjects with a lower BMI, and the risk of death from atherosclerotic cardiovascular disease or cancer was higher among subjects with a higher BMI. The relative risk of death associated with BMI declined with increasing age.

Conclusions Underweight, overweight, and obese men and women had higher rates of death than men and women of normal weight. The association of BMI with death varied according to the cause of death and was modified by age, sex, and smoking history.

A prospective comparison of severity scores for identifying patients with severe community acquired pneumonia: reconsidering what is meant by severe pneumonia

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Background: Several severity scores have been proposed to predict patient outcome and to guide initial management of patients with community acquired pneumonia (CAP). Most have been derived as predictors of mortality. A study was undertaken to compare the predictive value of these tools using different clinically meaningful outcomes as constructs for "severe pneumonia".

Methods: A prospective cohort study was performed of all patients presenting to the emergency department with an admission diagnosis of CAP from March 2003 to March 2004. Clinical and laboratory features at presentation were used to calculate severity scores using the pneumonia severity index (PSI), the revised American Thoracic Society score (rATS), and the British Thoracic Society (BTS) severity scores CURB, modified BTS severity score, and CURB-65. The sensitivity, specificity, positive and negative predictive values were compared for four different outcomes (death, need for ICU admission, and combined outcomes of death and/or need for ventilatory or inotropic support)
.

Results: 392 patients were included in the analysis; 37 (9.4%) died and 26 (6.6%) required ventilatory and/or inotropic support. The modified BTS severity score performed best for all four outcomes. The PSI (classes IV+V) and CURB had a very similar performance as predictive tools for each outcome. The rATS identified the need for ICU admission well but not mortality. The CURB-65 score predicted mortality well but performed less well when requirement for ICU was included in the outcome of interest. When the combined outcome was evaluated (excluding patients aged >90 years and those from nursing homes), the best predictors were the modified BTS severity score (sensitivity 94.3%) and the PSI and CURB score (sensitivity 83.3% for both).

Conclusions: Different severity scores have different strengths and weaknesses as prediction tools. Validation should be done in the most relevant clinical setting, using more appropriate constructs of "severe pneumonia" to ensure that these potentially useful tools truly deliver what clinicians expect of them.

i. Virion/Serion IgM/IgG Legionella Pneumophilia Germany

a. Samples were tested for IgG and IgM antibodies against Legionella pneumophila serogroups 1 to 7. According to the manufacturer, an acute legionella infection is defined as seroconversion of a titre increase in Ig G and Ig M.

ii. Binax Now Strep Pneumoniae test Kit (USA)

a. This test is an in-vitro immunochromatiographic (ICT) assay for the detection of streptococcus pneumoniae (S.pneumoniae) antigen in the urine of patients with pneumonia. A positive urine test is taken as a positive result. A negative urine test is a taken as a presumptive negative for pneumococcal pneumonia suggesting no current or recent pneumococcal infection. In fection due to S.pneumoniae cannot be ruled out since the antigen present in the sample may be belkow the delection limit of the tests.It has a sensitivity of 86% and a specificity of 94% and an accuracy of 93%

iii. Mycoplasma/Chlamydia Biolink IgM.-ELISA Badalona(Spain)

a. The BLK Mycoplasma pneumoniae Ig M ELISA is intended for qualitative determination of Ig M class antibodies against M.Pneumoniae in human serum. The specificity is>95% and the sensitivity is 94.4%

b. The chlamydia pneumoniae IgG-ELISA test is intended for the qualitative determination of IgG class antibodies against Chlamydia in human serum. The principle of the assay is the ELISA method. However this test does not give results of titres for Ig G.An acute or recent infection is based solely on the presence of the Ig M..

Iv Serodia-myco II kit. (Manufacturer Fujirebi Inc) This is a particle agglutination test kit for the detection of anti-mycoplasma pneumoniae antibodies. (Ig G) Positive titre>1:80, indeterminate 1:90.Negative <1:80.