

## Data Analysis on SARS Clinical Management

Hospital Authority  
16 Aug 03

## HA SARS Collaborative Group

**Purpose**

- To steer, coordinate, enhance, report and disseminate latest information on SARS management

**Membership**

- Clinicians with contributions and expertise in SARS management
  - Physicians, paediatricians, geriatricians, intensivists, radiologists, microbiologists, pathologists, psychiatrists, rehabilitation and A&E specialists

## SARS Central Clinical Database

IN PROGRESS

## Contents

**Hong Kong Data**

- Risk and prognostic factors
- Study on Kaletra treatment
- Study on steroid usage

**International Comparison**

- Treatment
- Outcome and Case Fatality Rate

## Risk and Prognostic Factors

### Risk/Prognostic Factors + Drug Treatment vs Outcome

*Model on Aged 15-74 only (n = 889)*

Death vs Discharge	Discriminant Analysis	Logistic Model	
	Standardised Canonical Coefficients	Adjusted Odds Ratio	p-value
Age	0.51	1.98 (per 10 years ↑)	<0.0001*
LDH - 1 <sup>st</sup> reading	0.41	1.82 (per 10 IU/L ↑)	<0.0001*
Comorbidity	0.39	3.39 (vs without)	0.0002*
Lowest SaO2 before intubation	-0.29	0.92 (per 2% ↓)	<0.0001*
Neutrophil - 1 <sup>st</sup> reading	0.23	1.13 (per 10 <sup>9</sup> /L ↑)	0.02*
Sex	0.20	2.36 (vs F)	0.002*
Ever Steroid	0.07	1.42 (vs No Steroid)	0.38
Ever Ribavirin	0.06	1.28 (vs No Ribavirin)	0.38
	Overall model: $p < 0.0001$ Canonical correlation: 77.1 %	Overall model: $p < 0.0001$	

## Study on Kaletra Treatment

- ### Kaletra®
- Lopinavir/Ritonavir combination
  - Lopinavir - Aspartate Protease Inhibitor used in HIV infection
  - Protease found in Coronavirus
  - Lopinavir found to have weak in vitro effect on Coronavirus

### Analysis of Kaletra Use

	Matched Cohort
n	1039
Treatment	Ribavirin/ Steroid

\*Matched for age, sex, comorbidity & initial LDH level

- ### Discussion
- Early treatment with Kaletra and Ribavirin
    - Lower death rate
    - Lower intubation rate
    - Reduced use of pulsed corticosteroid
  - Need for a randomised controlled study of Kaletra and Ribavirin vs Placebo

## Study On Steroid Usage

- ### Analysis on Treatment with Steroid
- Group 0 : Had not received corticosteroid
  - Group I : Had received corticosteroid
  - Group II : Had received corticosteroid and additional pulsed methylprednisolone (MP) for 1 course (0.5 - 3g MP within 6 days)

## Discussion

- Limitations of a retrospective study
- Compared to Group 0, Group I patients given steroid had no differences in outcome except longer time to discharge and time to death → RCT on steroid vs no steroid
- The more severe respiratory failure in Group II when treated with pulsed steroid produced similar outcome as Group I → RCT on pulsed steroid?



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## International Comparison



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## Treatment

Country	n	Anti-bioider	Antiviral (Ribavirin)	Steroid	Pulsed MP	Ventilation
Hong Kong	120	Amoxicillin (8.5g/24h)	2.4g/once → 1.6g/d (4x)	MP (150mg/d)	14-16g	43.8% (24/55)
	138	β lactam or macrolide	1.2g/d (or 3.6g/d)	MP 50mg/d	1-1.2g	28.5% (39/138)
	31	or levofloxacin	1.2g/d (or 2.4g/d per 24h)	MP 150mg/d	2g	16.1% (5/31)
	75		1.2g/d (or 1.2g/d)	HC 30.0g/d (10 → 30mg/d)	1.2g	16.0% (12/75)
Canada	144	95%	88% 2g once → 1g/d (or 1.5g/d)	40% HC: 1-2.5g/d	NS	16.4% (24/146)
Singapore	192	11%	7% 1g/d	4% of non-ICU patients	16g	16.2%
USA (CDC)	193	100%	1.4-1.6g/d	0.25-1.0g/d	0.25-2.0g	16-23-40%

MP: Methylprednisolone; P: Prednisolone; HC: Hydrocortisone; N: Non-Invasive; M: Mechanical



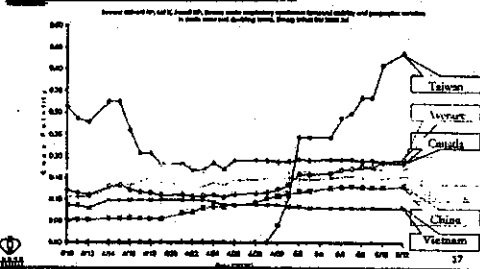
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## Case Fatality Rate



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## Cumulative Case Fatality Rates- 10 Apr to 12 May



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## International Comparison of CFRs in Relation to Case Mix

	No of Cases <sup>1</sup>	CFR <sup>1</sup>	Median Age <sup>1</sup>	Co-morbidity <sup>2</sup> (%)	LDH ≥ 230 (%)	HCW (%) <sup>3</sup>
Canada	251	17	49 (1-98)	-	-	43
China	5327	7	-	13 <sup>4</sup>	46.5 <sup>5</sup> 18 <sup>6</sup> 26.3 <sup>7</sup>	19
Hong Kong	1755	17	40 (0-100)	17.8 <sup>1</sup>	67.8 <sup>2</sup>	22 (HA staff: 19)
Singapore	231	14	35 (1-90)	-	-	41
Taiwan	665	27	46 (2-79)	-	-	13
USA	33	0	36 (0-83)	-	-	3
Vietnam	63	2	43 (20-76)	-	-	57



1. WHO (based on 12 Aug 03)  
2. Zhu et al, 30 patients  
3. Zhu et al, 119 patients

4. Zhu et al, 68 patients  
5. Zhu et al, 68 patients  
6. Zhu et al, 68 patients  
7. Zhu et al, 68 patients

### Age-stratified Case Fatality Rate

Age Group	CFR	Cum. Age	CFR
<24	0%	0-24	0%
25-34	2%	0-34	1%
35-44	10%	0-44	4%
45-54	13%	0-54	6%
55-64	25%		
65-74	47%	0-74	12%
>75	66%	0-100	17%



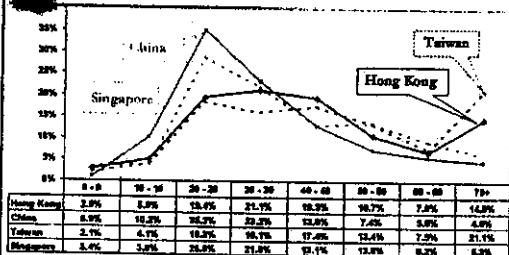
### Case Fatality Rate Comparison

Age Group	Hong Kong	WHO
0-24	0%	<1%
25-44	6%	6%
45-64	16%	15%
65+	58%	>50%

In HK: 60% deaths >65 yrs,  
40% deaths >75 yrs



### Age Distribution of SARS Cases



If age profile similar to China → CFR 9.3 %



### >65 & Comorbidity Among Fatalities

	≥65	<65
With Co-Morbidity	39%	11%
Without Co-Morbidity	19%	31%

\* If 13% with comorbidity (instead of 17.8%) → CFR 14.5 %



### Comorbidity Case Fatality Rate

- Chronic renal failure – 89%
  - Cerebral vascular accident – 71%
  - Ischaemic heart disease – 65%
  - Chronic liver disease – 60%
  - Diabetes mellitus – 50%
  - Cancer – 49%
  - Chronic obstructive airway disease / Asthma – 38%
- \* If 13% with comorbidity (instead of 17.8%) → CFR 14.5 %



### Health Care Workers

#### HA HCWs

- 19% of total SARS patients
  - CFR 2%
  - Young
  - Healthy
  - 74% female
- \* If HCW 50% → CFR 6.1 %



### International Comparison of Mortality Figures in ICU Subgroup

	Hong Kong	Toronto (JAMA, July 2003)	Singapore (JAMA, July 2003)
N (Total in cohort)	1755	196	199
Rate of ICU admission (%)	21.7	19	23
Rate of Intubation (%)	14.0 <sup>1</sup>	14.8	-
Mortality of ICU patients (%)			
- 28 days after symptom onset	23.3 <sup>1</sup>	-	31
- Overall	43.3 <sup>1</sup>	-	-
Mortality of whole cohort	17	-	-

1. n = 1592 2. n = 337 out of 1952 patients with complete records 25

### International Comparison of Mortality Figures in Relation to Intubation / NIV Status

	Hong Kong	China (GZ, Zhang et al)	China (GZ, Xiao et al)	China (GZ, Zhao et al)
N (Total in cohort)	1755	260	78	190
Rate of ICU admission (%)	21.7	-	34.6	-
Rate of Intubation (%)	14.0 <sup>1</sup>	4.2	19.2	6.8
Rate of NIV (%)	2.0 <sup>1</sup> (BIPAP)	13.8	30.1 (CPAP)	32.6 (CPAP)
Mortality				
- 28 days after symptom onset	10.7 <sup>1</sup>	-	-	-
- Overall	33	47.7	9	8.8

1. n = 1592 26

### Over-reporting of non-CoV

#### CoV positive

Hong Kong - 60%

USA - 12% (8 out of 68)

\* If PCR 12% POS in HK → CFR 9.6%

Source: WHO's Global Conference on SARS held in Malaysia on 17-18 June 03



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### Discussion- Confounding Factors in Interpreting CFRs

#### Case mix

- CFR affected by case mix: age, comorbidities, HCW, LDH ...
- If age profile similar to China → CFR 9.3 %
- If comorbidity 13% → CFR 14.5 %
- If HCW 50% → CFR 6.1 %



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### Discussion- Confounding Factors in Interpreting CFRs (cont'd)

#### Timing

- If 28-day fatality is used → CFR 10.7%

#### Inclusion Criteria

- If dilution of denominator by non-SARS or mild SARS to give CoV positivity of 12% → CFR 9.6 %



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### Summary

- Risk & prognostic factors influence interpretation of treatment outcome
- Useful initial findings:
  - Early treatment with Kaletra and Ribavirin
  - Pulsed methylprednisolone for severe cases
- Need to prepare RCT protocols for next epidemic
- The CFR of Hong Kong compared favourably with overseas countries



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