Management of the critically ill patient with confirmed or suspected COVID-19









Virus:SARS-CoV-2Disease:COVID-19







https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd402 99423467b48e9ecf6?utm_source=vancouver%20is%20awesome&utm_campaign=vanco uver%20is%20awesome&utm_medium=referral

Sat 14th March

🕡 Coronavirus COVID-19 Global Cases by the Center for Systems Science and Engineering (CSSE) at Jo...

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CLINICAL CHARACTERISTICS

BRIEF REPORT

A Novel Coronavirus from Patients with Pneumonia in China, 2019

Na Zhu, Ph.D., Dingyu Zhang, M.D., Wenling Wang, Ph.D., Xingwang Li, M.D., Bo Yang, M.S., Jingdong Song, Ph.D., Xiang Zhao, Ph.D., Baoying Huang, Ph.D., Weifeng Shi, Ph.D., Roujian Lu, M.D., Peihua Niu, Ph.D., Faxian Zhan, Ph.D., Xuejun Ma, Ph.D., Dayan Wang, Ph.D., Wenbo Xu, M.D., Guizhen Wu, M.D., George F. Gao, D.Phil., and Wenjie Tan, M.D., Ph.D., for the China Novel Coronavirus Investigating and Research Team

SUMMARY

In December 2019, a cluster of patients with pneumonia of unknown cause was From the NHC Key Laboratory of Biosafe linked to a seafood wholesale market in Wuhan, China. A previously unknown betacoronavirus was discovered through the use of unbiased sequencing in samples for Disease Control and Prevention, Chinese Center from patients with pneumonia. Human airway epithelial cells were used to isolate a (N.Z., W.W novel coronavirus, named 2019-nCoV, which formed a clade within the subgenus X.M., D.W., the Depart sarbecovirus, Orthocoronavirinae subfamily. Different from both MERS-CoV and the Departing Dita SARS-CoV, 2019-nCoV is the seventh member of the family of coronaviruses that University infect humans. Enhanced surveillance and further investigation are ongoing. han linvint: sion for Vir (Funded by the National Key Research and Development Program of China and the Provincial C National Major Project for Control and Prevention of Infectious Disease in China.) Preventio Biosafety N

MERGING AND REEMERGING PATHOGENS ARE GLOBAL CHALLENGES FOR sity and Sh

ty, National Institute for Viral Disease Control and Prevention, Chinese Center

March 3, 2020

Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore

Barnaby Edward Young, MB, BChir^{1,2,3}; Sean Wei Xiang Ong, MBBS^{1,2}; Shirin Kalimuddin, MPH^{4,5}; et.al

COVID-19 Resource Center

P Related

Key Points

Question. What was the initial experience in Singapore with the outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)?

January 23 and February 3, 2020, clinical presentation was a respiratory tract infection with prolonged viral shedding from the nasopharynx of 7 days or longer in 15 patients (83%). Supplemental oxygen was jes to enhance your e

ORIGINAL ARTICLE

Clinical Characteristics of Coronavirus Disease 2019 in China

B. Du, L. Li, G. Zeng, K.-Y. Yuen, R. Chen, C. Tang, T. Wang, P. Chen, J. Xiang, S. Li, Jin-lin Wang, Z. Liang, Y. Peng, L. Wei, Y. Liu, Ya-hua Hu, P. Peng, Jian-ming Wang, J. Liu, Z. Chen, G. Li, Z. Zheng, S. Qiu, J. Luo, C. Ye, S. Zhu, and N. Zhong, for the China Medical Treatment Expert Group for Covid-19*

ABSTRACT

BACKGROUND

Since December 2019, when coronavirus disease 2019 (Covid-19) emerged in Wuhan The authors' full names, academic decity and rapidly spread throughout China, data have been needed on the clinical grees, and affiliations are listed in the characteristics of the affected patients.

METHODS

We extracted data regarding 1099 patients with laboratory-confirmed Covid-19 from 552 hospitals in 30 provinces, autonomous regions, and municipalities in mainland China through January 29, 2020. The primary composite end point was admission to an intensive care unit (ICU), the use of mechanical ventilation, or death.

RESULTS

The median age of the patients was 47 years; 41.9% of the patients were female. The primary composite end point occurred in 67 patients (6.1%), including 5.0% who were admitted to the ICU, 2.3% who underwent invasive mechanical ventila- Drs. Guan, Ni, Yu Hu, W, Liang, Ou, H

Annendix. Address reprint requests to Dr. Zhong at the State Key Laboratory of Respiratory Disease, National Clinical Research Center for Respiratory Disease, Guangzhou Institute of Respiratory Health First Affiliated Hospital of Guangzhou Medical University, 151 Yanjiang Rd., Guangzhou, Guangdong, China, or at nanshan@vip.163.com

*A list of investigators in the China Medi cal Treatment Expert Group for Covid-19 study is provided in the Supplementary Appendix, available at NEJM.org.

W. Guan, Z. Ni, Yu Hu, W. Liang, C. Ou, J. He, L. Liu, H. Shan, C. Lei, D.S.C. Hui,

Findings In this descriptive case series of the first 18 patients diagnosed with SARS-CoV-2 infection in Singapore betwee



> Author Affiliations | Article Information and the Shi

JAMA. Published online March 3, 2020. doi:10.1001/iama.2020.3204

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February 24, 2020

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More

Characteristics of and Important Lessons Fre Coronavirus Disease 2019 (COVID-19) Outbreas China

Summary of a Report of 72314 Cases From the Chinese Center for Disease Control and Prevention

Zunyou Wu, MD, PhD¹; Jennifer M. McGoogan, PhD¹

» Author Affiliations | Article Information

JAMA. Published online February 24, 2020. doi:10.1001/jama.2020.2648

中文 (chinese) COVID-19 Resource Center

P Related

he Chinese Center for Disease Control and Prevention recently published the largest case series to date of coronavirus disease 2019 (COVID-19) in mainland China (72 314 cases, updated through February 11, 2020). This Viewpoint summarizes key findings from this report and discusses emerging understanding of and lessons from the COVID-19 epidemic.

Epidemiologic Charac

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Background A recent cluster of pneumonia cases in Wuhan, China, was caused by a novel betacoronavirus, the Lancet 2020; 395: 497-506 2019 novel coronavirus (2019-nCoV). We report the epidemiological, clinical, laboratory, and radiological characteristics Published and treatment and clinical outcomes of these patients. Methods All patients with suspected 2019-nCoV were admitted to a designated hospital in Wuhan. We prospectively

Clinical features of patients infected with 2019 novel

Chaolin Huang", Yerning Wang", Xingwang Li", Lili Ren", Jianping Zhao", Yi Hu", Li Zhang, Guohui Fan, Jiuyang Xu, Xiaoying Gu, Zhenshun Cheng, Ting Yu, Jiaan Xia, Yuan Wei, Wenjuan Wu, Xuelei Xie, Wen Yin, Hui Li, Min Liu, Yan Xiao, Hong Gao, Li Guo, Jungang Xie,

Researchers also directly communicated with patients or their families to ascertain epidemiological and symptom

data. Outcomes were also compared between patients who had been admitted to the intensive care unit (ICU) and

infection. Most of the infected patients were men (30 [73%] of 41); less than half had underlying diseases (13 [32%]),

[44%]]: less common symptoms were sputum production (11 [28%] of 39), headache (three [8%] of 38), s (two [5%] of 39), and diarrhoea (one [3%] of 38). Dyspnoea developed in 22 (55%) of 40 patients (median

Iness onset to dyspnoea 8 · 0 days [IQR 5 · 0-13 · 0]). 26 (63%) of 41 patients had lymphopenia. All 41 patients onia with abnormal findings on chest CT. Complications included acute respiratory distress syndrome

tNAaemia (six [15%]), acute cardiac injury (five [12%]) and secondary infection (four [10%]). 13 (32%) patients red to an ICU and six (15%) died. Compared with non-ICU patients, ICU patients had higher plasma levels

on The 2019-nCoV infection caused clusters of severe respiratory illness similar to severe acute respiratory oronavirus and was associated with ICU admission and high mortality. Major gaps in our knowledge of

nidemiology, duration of human transmission, and clinical spectrum of disease need fulfilment by future

coronavirus in Wuhan, China

those who had not

Guangfa Wang, Rongmeng Jiang, Zhancheng Gao, Qi Jin, Jianwei Wang†, Bin Cao†

IL10. GSCF. IP10. MCP1. MIP1A, and TNFq.

anuary 24, 2020 This online publication has collected and analysed data on patients with laboratory-confirmed 2019-nCoV infection by real-time RT-PCR and next-generation sequencing. Data were obtained with standardised data collection forms shared by WHO and the former and the context of t International Severe Acute Respiratory and Emerging Infection Consortium from electronic medical records. on January 30, 2020

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Findings By Jan 2, 2020, 41 admitted hospital patients had been identified as having laboratory-confirmed 2019-nCoV Jin Yin tan Hospital, Wohat

Figure 2







The Lancet 2020 395, 497-506DOI: (10.1016/S0140-6736(20)30183-5) Copyright © 2020 Elsevier Ltd

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gane	Ster - 5	A A A A

	All patients (n=41)	ICU care (n=13)	No ICU care (n=28)	p value
Signs and symptoms				
Fever	40 (98%)	13 (100%)	27 (96%)	0-68
Highest temperature, "C		-	-	0-037
<37-3	1 (2%)	0	1(4%)	-
37-3-38-0	8 (20%)	3 (23%)	5 (18%)	-
38-1-39-0	18 (44%)	7 (54%)	11 (39%)	-
>39-0	14 (34%)	3 (23%)	11 (39%)	-
Cough	31 (76%)	11 (85%)	20 (71%)	0-35
Myalgia or fatigue	18 (44%)	7 (54%)	11 (39%)	0-38
Sputum production	11/39 (28%)	5 (38%)	6/26 (23%)	0-32
Headache	3/38 (8%)	0	3/25 (12%)	0-10
Haemoptysis	2/39 (5%)	1(8%)	1/26 (4%)	0-46
Diamhoea	1/38 (3%)	0	1/25 (4%)	0-66
Dyspnoea	22/40 (55%)	12 (92%)	10/27 (37%)	0-0010
Days from illness onset to dyspnoea	8-0 (5-0-13-0)	8-0 (6-0-17-0)	6-5 (2-0-10-0)	0-22
Days from first admission to transfer	5-0 (1-0-8-0)	8-0 (5-0-14-0)	1-0 (1-0-6-5)	0-0023
Systolic pressure, mm Hg	125-0 (119-0-135-0)	145-0 (123-0-167-0)	122-0 (118-5-129-5)	0-018
Respiratory rate >24 breaths per min	12 (29%)	8 (62%)	4 (14%)	0-0023

Data are median (IQR), n (%), or n/N (%), where N is the total number of patients with available data. p values comparing ICU care and no ICU care are from χ^2 test, Fisher's exact test, or Mann-Whitney U test. 2019-nCoV=2019 novel coronavirus. ICU-intensive care unit.

Table 1: Demographics and baseline characteristics of patients infected with 2019-nCoV

Case definition HPSC



https://www.hpsc.ie/az/respiratory/coronavirus/ novelcoronavirus/casedefinitions/

Case Definitions

 This interim case definition for COVID-19 for possible cases is based on the current information available on the outbreak and may be subject to revision as new data become available.



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Of 1099, 975 patients had CT scan on admission

- 86.2% were abnormal
- ground-glass opacity 56.4%.

No radiographic or CT abnormality

- 17.9% with non-severe disease
- 2.9% with severe disease.

Clinical Course



- Severe Acute Respiratory Infection (SARI)
- Type I respiratory failure (often hypocapnic)
- ARDS
- Near normal compliance lungs
- Severe shunt
- Secondary Complications
 - Septic Shock
 - Acute Renal Failure
 - Myocarditis
 - Glucose abnormalities and ketoacidosis
- 7-10 days IPPV required

Laboratory testing for COVID-19



- 3 Viral swabs available in a pre-prepared pack
 - 1 nasopharyngeal swab and
 - 2 throat swabs in viral transport medium
- Further samples may be indicated e.g. Nasopharyngeal aspirate (NPA) or Sputum or a lower respiratory tract sample (BAL) – please discuss with on-call clinical microbiologist if necessary
- Microbiologist-on –call should be contacted if COVID-19 testing to take place.
- A single negative test result, particularly if this is from an upper respiratory tract specimen, does not exclude COVID-19
- Repeat sampling and testing, lower respiratory specimen is strongly recommended in severe or progressive disease.
- A positive alternate pathogen does not necessarily rule out COVID-19 as little is yet known about the role of co-infections.

PREVENTION OF SPREAD



Transmission

- Direct contact (hand to mucus membrane)
- Droplet (contact within 1m of infected patient)
- Aerosols: Smaller airborne particles which can travel around a room



FFP3 or surgical mask (over NP) Mask or Non-rebreather for Transfer





PROTECTING HCW

Transmission within hospitals

- In one study, 41% of patients were presumed to be related to transmission within the hospital,
 - 12% patients hospitalized for other reasons
 - 29% healthcare workers

Wang JAMA 2020

- Health care personnel infected
 - 3.8% (1716 of 44 672)
 - 14.8% cases classified as severe or critical (247 of 1668)
 - 5 deaths





Personal Protective Equipment

- FFP3 Filter Mask
- Visor or Goggles (glasses not sufficient)
- Long sleeved water resistant gown
- Gloves
- Hat





Technique for Donning and Doffing of PPE

Donning

- 1. Perform Hand hygiene
- 2. Put on Gown and hat

3. Put on FFP3 mask

• Fit Check Mask

- Place mask over nose, mouth and chin
- Fit flexible nose piece over nose bridge
- Secure on head with elastic
- Adjust to fit
- Inhale- mask should collapse
- Exhale- check for leakage around face
- 4. Put on Eye Protection goggles or face shield

Doffing

	In the patients' room						
1.	Remove Gloves						
2.	Perform Hand hygiene						
3.	Remove Goggles -avoid touching the front						
4.	Remove Gown -avoid touching the front of the apron/gown						
5.	Perform Hand hygiene						
1. Re	In ante room or directly outside patients' room- Ensure door is closed 1. Remove Mask Grasp and lift ties from behind your head and pull off respirator away from your face. Avoid touching the front of the respirator and use ties to discard. 2. Perform Hand hygiene						

https://www.youtube.com/watch?v=pNirkWLjMX0

Aerosol generating procedures



- Procedures that produce aerosols of respiratory secretions carry an increased risk of transmission:
 - NIV/CPAP/HFNC
 - bronchoscopy
 - induced sputum
 - positive-pressure ventilation via a face mask
 - intubation and extubation
 - airway suctioning
 - -CPR



Critical Care Equipment

- Protect respiratory equipment with a high efficiency filter (eg BS EN 13328-1).
- Use disposable respiratory equipment where possible
- Decontaminate re-usable equipment in accordance with the manufacturer's instructions
- Use closed suctioning systems
- Ventilator circuits should not be broken unless necessary
- Place ventilators on standby when carrying out bagging
- Wear PPE at all times
- Consider a HME filter rather than water humidification



Operating theatre



- Decisions regarding the need for surgery during the period of infectivity should be made by senior clinicians.
- Patient should be anaesthetised and recovered in the operating room
- Staff should wear appropriate PPE
- Disposable anaesthetic equipment should be used where possible
- The anaesthetic machine should be protected by a filter with viral efficiency of 99.99%
- Reusable anaesthetic equipment should be decontaminated as per manufacturer's instructions
- Operation room should be cleaned and disinfected after use
- Operating room should not be used for 15 minutes after patient leaves (based on a conventional ventilation system with 20 air changes per hour)

TREATMENT





Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury

	Outcomes of corticosteroid therapy*	Comment
MERS-CoV	Delayed clearance of viral RNA from respiratory tract ²	Adjusted hazard ratio 0·4 (95% Cl 0·2–0·7)
SARS-CoV	Delayed clearance of viral RNA from blood ⁵	Significant difference but effect size not quantified
SARS-CoV	Complication: psychosis ⁶	Associated with higher cumulative dose, 10 975 mg vs 6780 mg hydrocortisone equivalent
SARS-CoV	Complication: diabetes?	33 (35%) of 95 patients treated with corticosteroid developed corticosteroid-induced diabetes
SARS-CoV	Complication: avascular necrosis in survivors"	Among 40 patients who survived after corticosteroid treatment, 12 (30%) had avascular necrosis and 30 (75%) had osteoporosis
Influenza	Increased mortality ⁹	Risk ratio for mortality 1:75 (95% Cl 1:3-2:4) in a meta-analysis of 6548 patients from ten studies
RSV	No clinical benefit in children ^{10,11}	No effect in largest randomised controlled trial of 600 children, of whom 305 (51%) had been treated with corticosteroids

CoV=coronavirus. MERS=Middle East respiratory syndrome. RSV=respiratory syncytial virus. SARS=severe acute respiratory syndrome. *Hydrocortisone, methylprednisolone, dexamethasone, and prednisolone.

Table: Summary of clinical evidence to date







Co-infections

- One small study: Among COVID-19 patients in Qingdao, 24 (80.00%) of them had IgM antibodies against at least one respiratory pathogen, compared to 20% in Wuhan.
- 6% of patients with COVID-19 tested for other viruses had other infections (coronavirus, influenza A virus, rhinovirus, and influenza A H3N2).

https://www.medrxiv.org/content/10.1101/2020.02.29.20027698v2

https://www.medrxiv.org/content/10.1101/2020.02.12.20022327v2

• In MERS critically ill patients, 18% had bacterial co-infections and 5% viral co-infection

Arabi CCM 2017

 The recent 2019 ATS/IDSA clinical practice guidelines recommend standard antibacterial therapy to be initially prescribed for adults with community-acquired pneumonia who test positive for influenza.



Uyeki TM et al Clin Infect Dis 2019



Registered clinical trials

Antivirals

Remdesivir

Anti-retrovirals: Lopinavir-Ritonavir, Darunavir and Cobicistat,

ASC09/Ritonavir

Anti-influenza antivirals: Arbidol, Baloxavir, Favipiravir

Azvudine

R

Chloroquine phosphate

Hydroxycholoroquine

Recombinant human angiotensin-converting enzyme 2 (rhACE2) Ribavirin



Remdesivir

- High priority antiviral by WHO prioritizations list.
- In vitro activity against MERS-CoV, SARS-CoV and Ebola virus.
- Ongoing trials in China for severe and non-severe COVID-19 and in USA.

RESPIRATORY SUPPORT



Respiratory Support



- NIV/HFNC/Mask CPAP not contraindicated but results in aerosol production-must be delivered in a negative pressure isolation room
- Most patients will have type I resp failure but require higher levels of CPAP than can be delivered with HFNC
- Helmet CPAP may be the best NI option where available
- Full face mask NIV may be an option
- The rate of failure of NIV with COVID-19 is high
- In general early IPPV is encouraged





Use of NIV

- Selected patients in early stages and milder forms of acute hypoxemic respiratory failure.
- Avoid in shock, multiorgan failure, or large amount of secretions.
- Patients who do not show signs of early recovery, NIV may well delay but not avoid invasive ventilation.





Mechanical ventilation

- Standard protective ventilation
 - Tidal Volume 4-8 mls/kg IBW
 - Plateau pressure < 30 cm H2O</p>
 - Driving Pressure < 15 cm H2O
 - Early NDMR if indicated
 - Appropriate PEEP
 - Prone Ventilation if indicated
 - Daily CXR may not be neccessary

https://youtu.be/qx2z26IL6g8

Rescue Therapy



- NO
 - (but minimise circuit breaks)



ECMO

 as per advice of MMH ECMO team




Preventing Infection while on IPPV

Closed circuit suctioning

• High efficiency filter (eg BS EN 23328-1)



• Minimise circuit breaks

Clamp ETT if circuit breaks neccessary



Causes of death





Unknown



Treatment of shock

- As per surviving sepsis guidelines
- Early use of noradrenaline
- Avoid excessive volume administration
- Treat AKI as per standard ICU patient

OUTCOME







COVID-19 Fatality Rate by AGE









COVID-19 IN NUMBERS

PEOPLE EACH INFECTED CASE PASSES ON TO	2–3 peopl	e 🔴 🔴 🌔		
ASCERTAINMENT RATE	10–25%		DOOC	0000
ATTACK RATE	30–60%		000	0000
HOSPITALISATION*	12%	00	0000	0000
SYMPTOMS*				
Mild	80%			0000
Severe	15%	000	0000	0000
Critical	2–10%	00	0000	0000
MORTALITY*	3.5%	000	0000	0000
INCUBATION	Up to 14 d	lays		•••••
INFECTIVE	14–24 day	s		
* IN THOSE IDENTIFIED			Relaction on a	k and Øalboobdadh

ALL DATA ARE ESTIMATES

@doctimcook and @elboghdadly Data as of 07/03/2020

Inter Hospital transfer and COVID-19

- May be occasionally required
- Standard inter-hospital protocols apply with additional infections prevention and control precautions (full PPE worn by all crew and appropriate ventilator tubing filters)



Conclusions

- COVID-19 is a novel coronavirus that causes severe hypoxic respiratory failure in about 5% of cases
- Mortality is high in patients who require ICU admission
- The scale of infection will put ICU capacity under severe pressure
- There is no directed treatment or vaccine

Main priorities for critical care teams

- Be prepared
- Triage appropriately
- Prevent HCW and nosocomial infection
- Intubate early
- Conservative fluid strategy for shock
- Supportive care is the mainstay of treatment
- Typically require long periods of IPPV (7-10 days)

Suggested ARDS Mechanical Ventilation Protocol

For Confirmed or Suspected COVID-19 March 2020



Acute Hypoxic Respiratory Failure due to COVID19 PaO₂/FiO₂<200

Intubate – VAC Ventilation TV 350ml Female (adjust) TV 425ml Male (adjust) Sedate to RASS -4 Limited use of RM* PEEP = 10cmH₂O

After 2 hours reassess

PaO₂/FiO₂ <125 Bilateral Infiltrates CXR Moderate-Severe ARDS

Continue sedation RASS-4 Administer Cis-Atracurium



Sedate to RASS -2 Continue Vent Strategy

Moderate to Severe ARDS PaO₂/FiO₂<125





Ventilator Liberation Protocol

ARDSnet PEEP Protocol

OXYGENATION GOAL: PaO₂ 55-80 mmHg or SpO₂ 88-95% Use a minimum PEEP of 5 cm H₂O. Consider use of incremental FiO₂/PEEP

combinations such as shown below (not required) to achieve goal.

	-	5-20						
FiO ₂	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
PEEP	5	5	8	8	10	10	10	12

FiO ₂	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	14	14	14	16	18	18-24

MAXIMAL ALLOWABLE TIDAL VOLUMES BASED ON PREDICTED BODY WEIGHT (PBW)

350ml	

FEMALE					
HEIGHT feet	HEIGHT cm	TV 6ml/kg			
5' 0	152.4	275			
5' 1	155	290			
5' 2	158	300			
5' 3	160	315			
5' 4	163	330			
5' 5	165	340			
5' 6	168	360			
5' 7	170	370			
5' 8	173	385			
5' 9	175	400			
5' 10	178	410			
5' 11	181	425			
6' 0	183	440			
6' 1	186	450			
6' 2	188	465			
6' 3	191	480			
6' 4	193	495			



MAXIMAL ALLOWABLE TIDAL VOLUMES BASED ON PREDICTED BODY WEIGHT (PBW)

MALE					
HEIGHT feet	HEIGHT cm	TV 6ml/kg			
5'0	152.4	300			
5' 1	155	315			
5' 2	158	330			
5' 3	160	340			
5' 4	163	355			
5' 5	165	370			
5' 6	168	385			
5' 7	170	400			
5' 8	173	410			
5' 9	175	425			
5' 10	178	440			
5' 11	181	450			
6'0	183	465			
6' 1	186	480			
6' 2	188	495			
6' 3	191	505			
6' 4	193	520			





Useful Resources:

https://www.intensivecare.ie/wp-content/uploads/2020/02/ICS-Guidelines-COVID-19-V2-1.pdf

https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratoryinfection-when-novel-coronavirus-(ncov)-infection-is-suspected

https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/algorithms/

https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/

https://www.nejm.org/coronavirus?cid=DM88295&bid=163494080

