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OPERATIONALIZING REMAPCAP IN PAKISTAN

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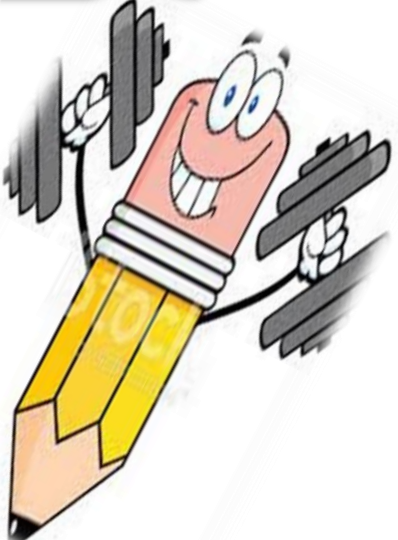
Pakistan: 220 Million population (2020)



SAARC Region: 8 countries in this region comprises 3% of the world's area, 21% of the world's population and 90% burden of diseases.



Barriers to Research in South Asia



Critical Care Bed Capacity in Asian Countries and Regions

www.ccmjournal.org

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Measurements and Main Results: Cumulatively, there were 3.6 critical care beds per 100,000 population. The median number of critical care beds per 100,000 population per country and region was significantly lower in low- and lower-middle-income economies (2.3; interquartile range, 1.4–2.7) than in upper-middle-income economies (4.6; interquartile range, 3.5–15.9) and high-income economies (12.3; interquartile range, 8.1–20.8) ($p = 0.001$), with a large variation even across countries and regions of the same World Bank income classification. This number was independently predicted by the World Bank income classification on multivariable analysis, and significantly correlated with the number of acute hospital beds per 100,000 population ($r^2 = 0.19$; $p = 0.047$), the universal health coverage service coverage index ($r^2 = 0.35$; $p = 0.003$), and the Human Development Index ($r^2 = 0.40$; $p = 0.001$) on univariable analysis.

Conclusions: Critical care bed capacity varies widely across Asia and is significantly lower in low- and lower-middle-income than in upper-middle-income and high-income countries and regions. (*Crit Care Med* 2020; 48:654–662)

A national survey of critical care services in hospitals accredited for training in a lower-middle income country: Pakistan

Madiha Hashmi^a, Arshad Taqi^b, Muhammad I. Memon^c, Syed Muneeb Ali^c, Saleh Khaskheli^d, Muhammad Sheharyar^e, Muhammad Hayat^f, Mohiuddin Shiekh^g, Chamira Kodippily^h, Dilanthi Gama,ⁱ Arjen M. Dondorpⁱ, Rshan Haniffa^{h,i,j}, Abi Beane^{h,i,k,*}



A B S T R A C T

Purpose: To describe the extent and variation of critical care services in Pakistan.

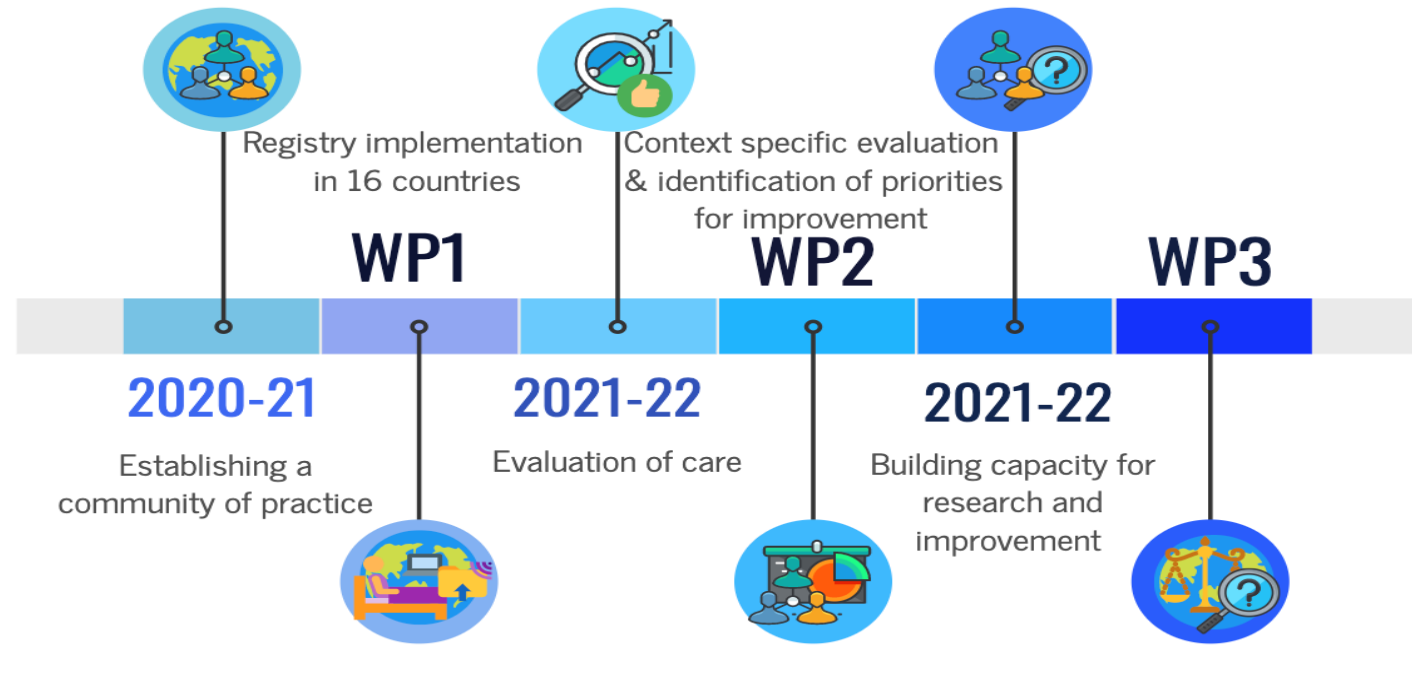
Materials and methods: A cross-sectional survey was conducted in all intensive care units (ICUs) recognised for postgraduate training to determine administration, infrastructure, equipment, staffing, and training.

Results: There were 151 hospitals recognised for training, providing 2166 ICU beds and 1473 ventilators. Regional distribution of ICU beds per 100,000 population ranged from 1.0 in Sindh to none in Gilgit Baltistan (median 0.7).

A senior clinician trained in critical care was available in 19 (12.1%) of units. One-to-one nurse-to-bed ratio during the day was available in 84 (53.5%) of units, dropping to 75 (47.8%) at night. Availability of 1:1 nursing also varied between provinces, ranging from 56.5% in Punjab compared to 0% in Azad Jamu Kashmir. Similarly, there was disparity in the availability of ventilators between provinces. All ICUs had basic infrastructure (electricity, running water, piped oxygen) and basic equipment (electronic monitoring and infusion pumps).

Conclusion: Pakistan, a lower middle-income country, has an established network of critical care facilities with access to basic equipment, but inequalities in its distribution. Investment in critical care training for doctors and nurses is needed.

Collaboration for Research, Implementation and Training in Critical care in Asia & Africa



CRIT CARE ASIA *Critical Care* (2020) 24:608
<https://doi.org/10.1186/s13054-020-03321-7>

Critical Care

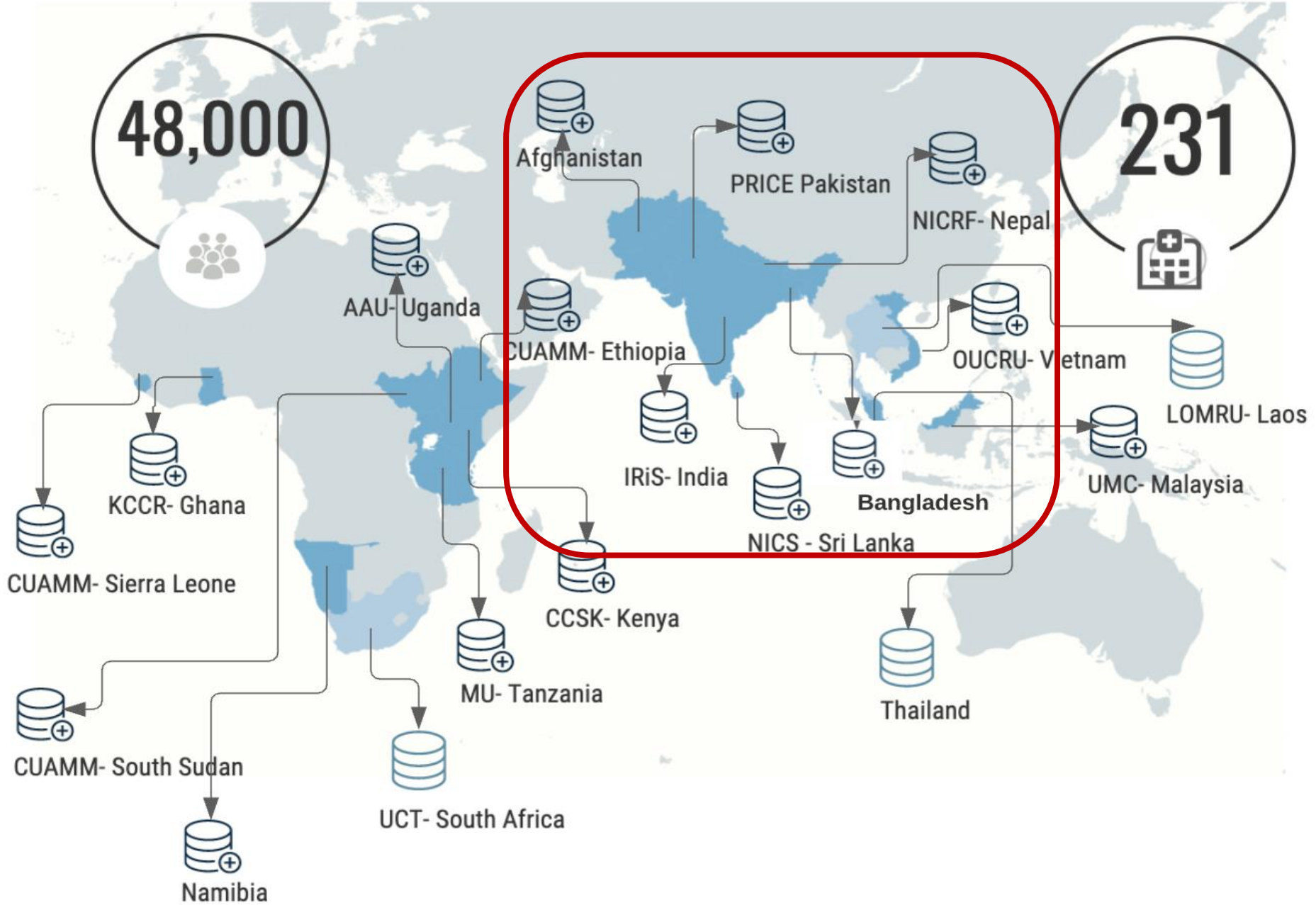
EDITORIAL

Open Access

Establishing a critical care network in Asia to improve care for critically ill patients in low- and middle-income countries



CRIT CARE ASIA



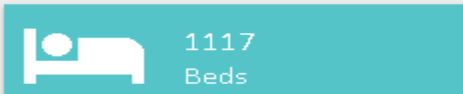
Pakistan Registry of Intensive Care (PRICE): Expanding a lower middle-income, clinician-designed critical care registry in South Asia

M Hashmi^{1,2,*}, A Beane^{3,4,5,6,*}, A Taqi⁷, MI Memon⁸, P Athapattu⁹, Z Khan¹⁰, AM Dondorp⁶ and R Haniffa^{4,5,6}

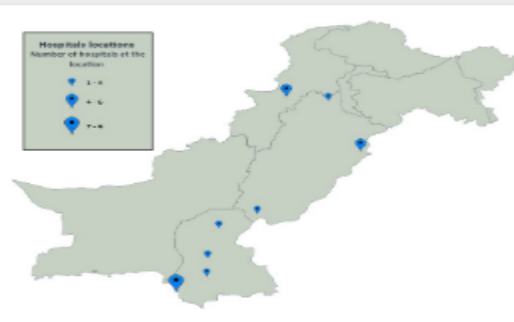
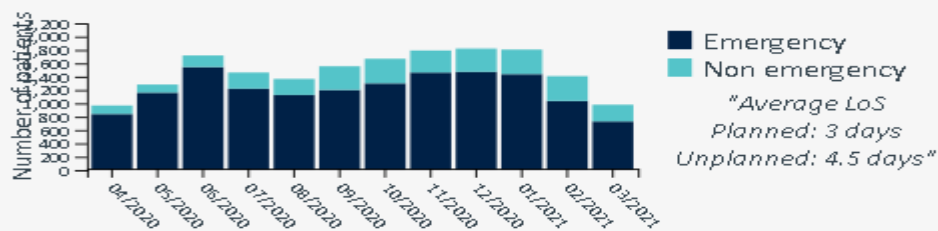
PRICE

Date: 01/04/2020 - 31/03/2021

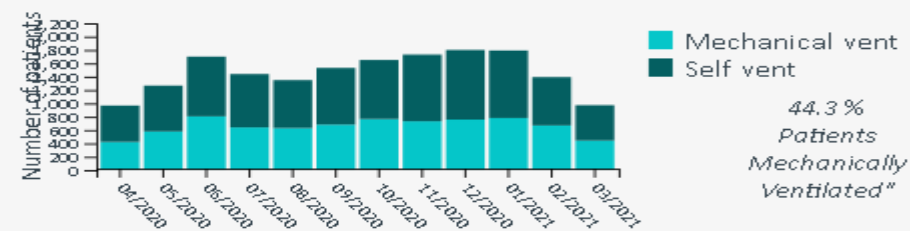
Filter



ICU admissions



Mechanically ventilated within 24 hours of admission



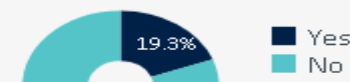
Antibiotics within 24 hours of admission



Reason for admission



Cardiovascular support within 24 hours of admission



Critical illness

IN THIS SECTION

[Overview](#)

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[Significant achievements](#)

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[Siem Pang](#)



In ICU COVID-19 reporting

18-Mar-2020 to 18-Mar-2021



48,756
All ICU admissions



230
Intensive care units



9,121 (18.7%)
Suspected or confirmed COVID-19



2,689 (29.5%)
Suspected COVID-19

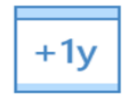


6,432 (70.5%)
Confirmed COVID-19

Clinical characteristics



6,061 (66.5%)
Male



59 years
Age



1,672 (18.3%)
Invasive vent



1,762 (19.3%)
NIV



466 (5.1%)
RRT

CCA participating sites



Clinical outcomes



8,663
ICU outcome census



2,638 (30.5%)
ICU Mortality



932 (58.0%)
ICU mortality [MV population]



5.6 days
Length of ICU stay



Year **2019** Registries **11** All



PT **EN**



LOGIC

LINKING OF GLOBAL INTENSIVE CARE

International Benchmarking



787.8k

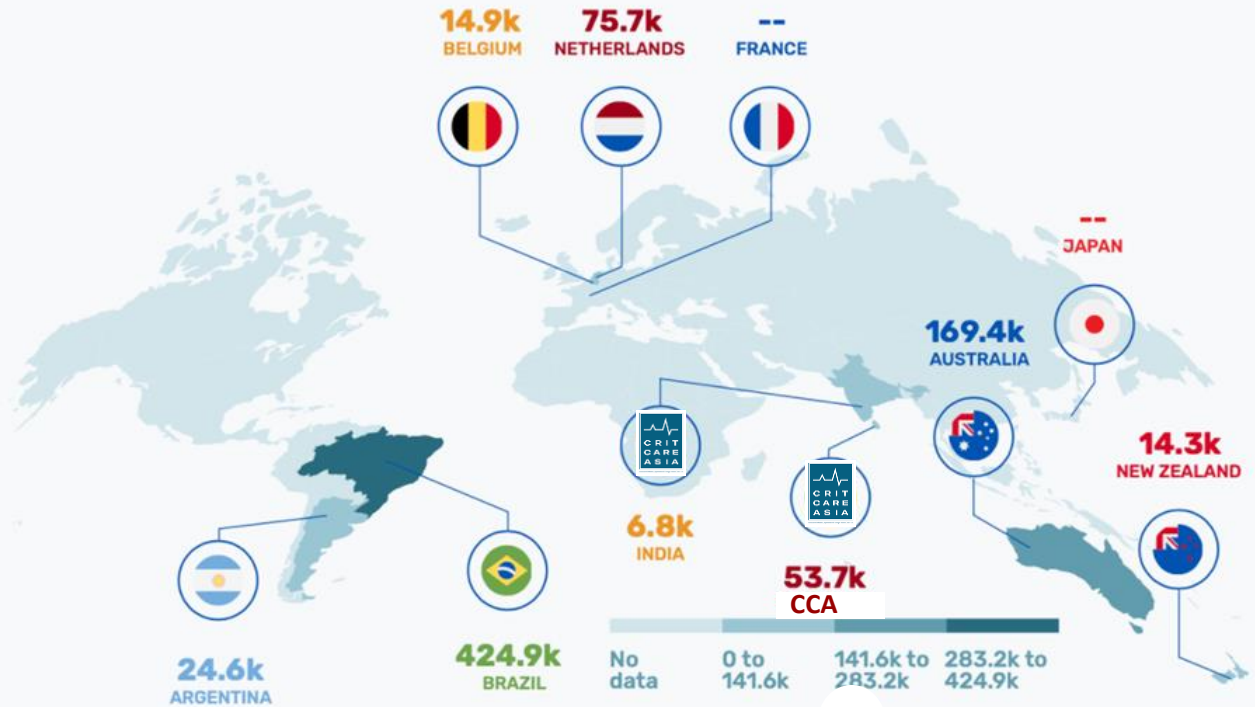
Admissions

(All countries)

H 778 HOSPITALS

U 1.1k UNITS

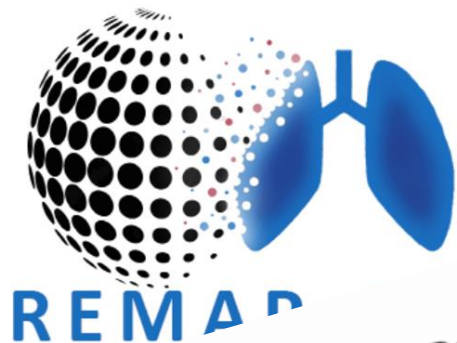
[More information](#)



- 3.4k
- 6.8k
- 14.3k
- 14.9k
- 24.6k
- 53.7k
- 75.7k
- 169.4k
- 424.9k
-
-



REMAP in CRIT CARE ASIA



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Wellcome Open Research 2021, 6:14 Last updated: 14 OCT 2021



Wellcome Open Research

OPEN LETTER

Operationalisation of the Randomized Embedded Multifactorial Adaptive Platform for COVID-19 trials in a low and lower-middle income critical care learning health system. [version 1; peer review: 3 approved]

Diptesh Aryal^{1*}, Abi Beane^{2,3*}, Arjen M. Dondorp^{2,3*}, Cameron Green^{4*}, Rashan Haniffa^{2,3*}, Madiha Hashmi^{5*}, Devachandran Jayakumar^{6,7*}, John C. Marshall^{8*}, Colin J. McArthur^{9,10*}, Srinivas Murthy^{11*}, Steven A. Webb^{4,12,13*}, Subhash P. Acharya¹⁴, Pramodya G. P. Ishani¹⁵, Issrah Jawad¹⁵, Sushil Khanal¹⁶, Kanchan Koirala¹, Subekshya Luitel¹⁷, Upulee Pabasara¹⁵, Hem Raj Paneru¹⁸, Ashok Kumar¹⁹, Shoaib Siddiq Patel²⁰, Nagarajan Ramakrishnan⁷, Nawal Salahuddin²¹, Mohiuddin Shaikh²⁰, Timo Tolppa¹⁵, Ishara Udayanga¹⁵, Zulfiqar Umrani²²

Writing Committee: M. J. D. H. M. J. M. B. A. D. F. H.

FREE

Time on Mortality and in Patients With Severe

The REMAP-CAP COVID-19 Corticosteroid Domain Randomized Clinical Trial

The Writing Committee for the REMAP-CAP Investigators

Article Information

JAMA. 2020;324(13):1317-1329. doi:10.1001/jama.2020.17022



SITE-LEVEL IMPLEMENTATION *ETHICAL APPROVAL*



National Bioethics Committee (NBC) Pakistan



Ref: No.4-87/COVID-43/NBC/20/301

Date: September 10, 2020

Patron

Minister of State, Ministry of National
Health Services Regulations and
Coordination

Chairperson

Secretary, Ministry of NHSR&C,
Government of Pakistan

Vice Chairperson,

Director General, Ministry of NHSR&C,
Government of Pakistan

Secretariat

Dr Madiha Hashmi

South East Asian Research & Education in Critical care Health (SEARCH),
199-E, Street No 6, Cavalry Grounds

Lahore Cantt

Subject: **Randomized, Embedded, Multifactorial Adaptive Platform trial for
Community-Acquired Pneumonia including COVID 19 (REMAP
CAP+Pandemic).**

SITE-LEVEL IMPLEMENTATION *RESEARCH COLLABORATION AGREEMENTS*

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ZIAUDDIN UNIVERSITY

AND

NATIONAL IN

ABBASI SHAHEED HOSPITAL

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RESEARC

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**RESEARCH COLLABORATION AGREEMENT
FOR REMAP-CAP**

=====


REMAP-CAP: R

DATI



SITE-LEVEL IMPLEMENTATION






DATA COLLECTION

Ziauddin Medical University Clifton Campus
MICU

PRICE 

Administration | REMAP Adverse Event | REMAP Protocol Deviation | REMAP ICU Discharge | REMAP Hospital Discharge | Discharge

Trial ID Enter field 0600800048	Date of randomisation in local time Enter field 29/04/2021 	Time of randomisation in local time 17 : 54  <input type="button" value="now"/>	Randomisation domain Vitamin C 
Randomisation intervention <input type="radio"/> Therapeutic intervention <input checked="" type="radio"/> Routine care	Randomisation domain Vitamin C 	Randomisation intervention <input type="radio"/> Therapeutic intervention <input checked="" type="radio"/> Routine care	Randomisation domain 
Randomisation intervention <input type="radio"/> Therapeutic intervention	Therapeutic intervention for antiplatelet domain	Has the patient/representative been approached	Reason not approached Enter field 14

SITE-LEVEL IMPLEMENTATION INFORMED CONSENT



**RANDOMISED, EMBEDDED, MULTIFACTORIAL, ADAPTIVE, PLATFORM TRIAL
FOR COMMUNITY-ACQUIRED PNEUMONIA (REMAP-CAP)**

مریضوں اور لواحقین کے لئے معلومات

تعارف

جب مریض موبیلا سہ ماہی ہوتے ہیں تو، ان کا مائیکروبائیوٹامک نظام ہلا ہوتا ہے جس کی وجہ سے شدید بیماریوں کی ابتدا ہوتی ہے۔ لی، ایف، اے، ایچ، ایچ کے بعد اور ہی گھبراہٹ تک محدود ہے۔ تحقیق سے پتا چلا ہے کہ وہ ای سی، آئی، اے سے دلچسپ دوائی، مائیکروبائیوٹامک کو تقویت بخشنے کے علاوہ دوسرے دوائی کی حاجت ہے۔

دعوت نامہ اور تحقیق کا مقصد

موبیلا کے مریضوں میں دوائی کی کارآمدی پر ایک تحقیق کر رہے ہیں۔ اس تحقیق کا نام ہے
Randomised, Embedded, Multifactorial, Adaptive, Platform Trial for Community-Acquired Pneumonia (REMAP-CAP) - Vitamin C
یہ ایک نیا اور تازہ تحقیق کا حصہ ہے۔ آپ کے رشتہ دار کو اس تحقیق میں حصہ لینے کے لئے مدعو کیا گیا ہے اور اس تحقیق میں ہم یہ دیکھنا چاہتے ہیں کہ آیا مریضوں کو عام علاج کے علاوہ دوائی کی دینے سے موبیلا کو بہتر بنانے میں مدد ملتی ہے۔

کیا میرے رشتہ دار کو اس تحقیق میں حصہ لینا ہے؟

آپ کے رشتہ دار کو اس تحقیق میں حصہ لینے کی اہلیت دینے کا فیصلہ مکمل طور پر دیکھنا ہے۔ وہی کی معلومات کے ساتھ، یہ دیکھ کر فیصلہ لیں کہ آپ کے رشتہ دار کو اس تحقیق میں حصہ لینے سے فائدہ ہونے سے بات کرنے کے بعد فیصلہ کریں۔ اگر آپ قبول کرنے کے بعد اپنا فیصلہ بدل چاہتے ہیں تو، آپ ہرگز کسی وجہ سے کسی بھی وقت اپنی رضاعتی دلائل سے سبک نہیں دیتے۔ آپ کے رشتہ دار کی حرکت یا اس تحقیق کو مسودہ کرنے سے مریض کے علاج پر کوئی اثر نہیں پڑے گا، اور آپ کو کچھ دیا گیا ہے کہ اس میں حصہ لینے سے کیا فائدہ ہو گا۔

اس تحقیق میں میرے رشتہ دار کو کیا پڑے گا؟

آپ کے رشتہ دار کو تحقیق کے لئے کچھ کرنے کی ضرورت نہیں ہے۔ آپ کی اہلیت سے، ان کی حالت کو غیر متاثر دیکھنے میں اس کی معلومات ICU دہریں مہربانی چاہیں گی۔ مریض کے علاج کے دوران مریضوں کو ایک نیا دوا دینے کے لئے سب سے زیادہ ممکنہ طور پر دیکھنا ہے۔
- مریضوں کے مطابق دیکھنا
- مریضوں کے مطابق دیکھنا + دوائی کی
دواؤں کی فہرست اور دوائیوں کو استعمال کرنے کی دوا سے محفوظ رہنا ہے۔ دوائی کی فہرست کے ذریعے کیا جائے گا (<https://remapcap.spinakersoftware.com/>)
مریضوں کو اپنی ہی سے سب سے زیادہ فائدہ ہونے کے لئے مریضوں کو دیکھنا ہے۔ مریضوں کی طبیعت پر مبنی دوا اور اس تحقیق کا حصہ لینے سے ان کے علاج پر کوئی اثر نہیں پڑے گا۔ اس تحقیق میں حصہ لینے کے لئے کسی ابتدائی یا ضمنی تحقیق کی ضرورت نہیں ہے۔ ہسپتال میں ان کے ہمراہ آئی سی یو کی مدت سے تحقیق لیا جاتا ہے تاکہ وہ رشتہ دار کو دیکھنا چاہتے ہیں اور اس وقت تک کہ ان کے حالات کے ساتھ دیکھنا چاہتے ہیں۔

اس تحقیق میں حصہ لینے کے فوائد کیا ہیں؟

دیکھنا میں دوائی کی دوسرے مریضوں کی اہلیت میں کمی ہے۔ مریضوں کو کم دوا دیکھنا ہے کہ ان کی بیماری کا علاج دیکھنا ہے۔ نتیجتاً حالت میں جاکر مریضوں کو COVID کہا جاتا ہے، اور دوائی کی حاجت کے بعد جان بچا سکتا ہے، اور جب دوا دیکھنا چاہتی ہے تو وہ عمل دیکھتا ہے۔ یہ دھت آئی سی یو میں مریضوں کی گھبراہٹ کی جاتی ہے، اور اگر آپ کا مریض آریستھرو دوائی سے سبک نہیں دیتے تو ان کوئی علامت ظاہر کرتے ہیں تو، دوائی کی کوئی فوری طور پر دیکھنا چاہتے ہیں۔

شرکت لادتی ہے؟

نہیں، یہ دیکھنا چاہتا ہے۔ اس تحقیق میں حصہ لینے کے علاوہ دوائی ہے۔ اگر آپ کو کوئی قیمت یا سہولت ہے تو، یہ دیکھنا چاہتے ہیں۔



**RANDOMISED, EMBEDDED, MULTIFACTORIAL, ADAPTIVE, PLATFORM TRIAL
FOR COMMUNITY-ACQUIRED PNEUMONIA (REMAP-CAP)**

PATIENT INFORMATION LEAFLET - VITAMIN C

INTRODUCTION:

When patients develop pneumonia, their immune system is affected which leads to severe complications. Currently, treatment options are limited to antimicrobials and supportive care. Research suggests that vitamin C, a readily available medication, is potentially lifesaving by strengthening the immune response.

INVITATION AND PURPOSE OF STUDY:

We are conducting a study to assess the effect of Vitamin C in patients with pneumonia. The name of this study is "Randomised, Embedded, Multifactorial, Adaptive, Platform Trial for Community-Acquired Pneumonia (REMAP-CAP) - Vitamin C domain. This is part of an international study. Your relative is invited to participate in this international study to find out if giving patients Vitamin C in addition to their normal treatment helps improve outcomes in pneumonia.

DOES MY RELATIVE HAVE TO TAKE PART IN THIS STUDY?

Your decision to allow your relative to participate in this study is purely voluntary. With the information given, please weigh the benefits and risks and make a decision after discussing with the rest of your family. If you change your mind after accepting, you can withdraw your consent at any time without giving a reason. Your decision to let your relative participate or not will not affect the standard of treatment they receive.

WHAT WILL MY RELATIVE HAVE TO DO IN THIS STUDY? WHAT IS BEING STUDIED?

They don't need to do anything for the study. With your permission, their de-identified information will be collected for the intensive care database and for study purposes. Your relative will be allocated to receive one of these two treatment groups:

- Standard usual care
- Standard usual care + Vitamin C

Response Adapted Randomisation will be done through a password-protected, secure randomisation website called Spinnaker (<https://remapcap.spinakersoftware.com/Login/>). Patients will undergo routine blood tests while in the ICU and hospital. Participation in this study generally does not require any additional or special investigations. The rest of the treatment depends on their clinical condition and will not be affected by them being part of this study.

The length of their stay in the ICU/hospital and survival data will be collected. Depending upon the outcome, they might receive a phone call after 6 months as a follow-up. They might have to answer a few simple questions at that time.

WHAT ARE THE RISKS OF TAKING PART IN THIS STUDY?

Other studies that have used Vitamin C have not reported any side effects. There is a theoretical risk that patients may develop low blood sugar recordings and a small risk of renal stone formation. Some patients with a rare genetic disorder called G6PD can develop bleeding after taking Vitamin C. This issue gets resolved when the medication is stopped. Patients in the ICU are monitored closely at all times and if your relative shows any signs of these complications the Vitamin C will be stopped immediately.

IS PARTICIPATION COMPULSORY?

No. Taking part in this study is purely voluntary. If you have any doubts or questions please do not hesitate to ask.

HOW WILL THE INFORMATION COLLECTED IN THE STUDY BE USED?

The de-identified information collected will be kept confidential. Patient's identity will never be revealed. The information collected will be stored in a coded form which will not include name, address or other identifiable information. It will be shared with the international database for analysis. The results of this study without individual patient identifiable information may be published in medical journals or presented in academic meetings.

If you require more information before giving your consent, you may contact the study investigators on 03009292799, South East Asian Research & Education in Criticalcare Health.

A 4-day course of Vit C will be provided free of cost to the patient if they fall in the intervention group.

OUR RESEARCH PARTNERS



MONASH University



MORU
Multi-Organ Research Unit



SEARCH+
SOUTH EAST ASIAN RESEARCH IN CRITICAL CARE HEALTH



PRICE
Pneumonia Research in Criticalcare Health



ZIAUDDIN UNIVERSITY



NICHD
National Institute of Child Health & Human Development

SITE-LEVEL IMPLEMENTATION SUPPLY CHAIN



PRODUCTION FACILITIES

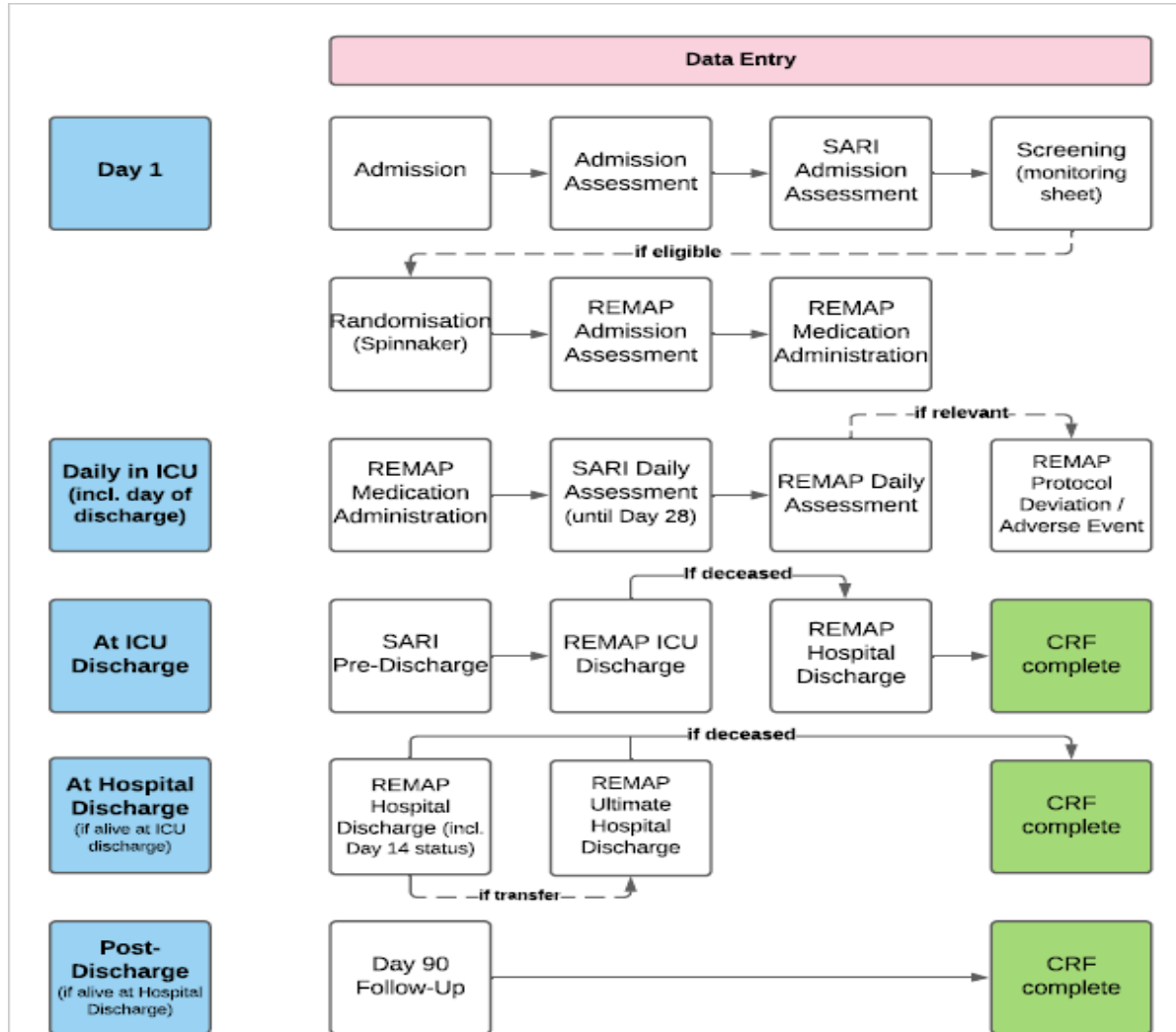
Wilshire Labs has a state-of-the-art production facility designed to facilitate the production of the highest quality products. This production facility is located at Quaid-e-Azam Industrial Estate, Kot Lakhpat, Lahore. Wilshire Labs adheres strictly to the principles of cGMP with its modernized production facilities including efficient production control, quality assurance, industrial safety, occupational health and environmental control systems.

10

SITE-LEVEL IMPLEMENTATION *ENGAGEMENT*



SITE-LEVEL IMPLEMENTATION TRAINING



This patient is participating in REMAP-CAP

PRICE

Vitamin C Domain	<input type="checkbox"/> No intervention <input checked="" type="checkbox"/> Vitamin C (50mg/kg IV every 6 hours for 16 DOSES or until ICU discharge)	Stop Vitamin C and report if: - Hypoglycaemia (glucose < 69 mmol/L) - Haemolysis
Statin Domain	<input type="checkbox"/> No intervention <input type="checkbox"/> Simvastatin (80 mg once a day PO <u>TILL ICU DISCHARGE</u> or max. day 28) <i>Note: if patient receives more than 1 DOSE of AMODIARONE reduce simvastatin dose to 20mg</i>	Stop Statin and report if: - Elevated Creatine Kinase more than 10 times the upper limit of normal - ALT or AST or both more than 8 times the upper limit of normal
Antiplatelet Domain	<input type="checkbox"/> No intervention <input type="checkbox"/> Aspirin (75 mg once a day PO for 14 DAYS or until hospital discharge) <input type="checkbox"/> Clopidogrel (75 mg once a day PO for 14 DAYS or until hospital discharge)	Stop Antiplatelet and report if: - Any major bleeding - Fatal bleeding, or intracranial, intraspinal, retroperitoneal, intra-arterial or pericardial, or intramuscular bleeding with compartment syndrome
Anticoagulation Domain*	<input type="checkbox"/> Low-dose thromboprophylaxis (14 DAYS or until hospital discharge) <input type="checkbox"/> Intermediate dose thromboprophylaxis (14 DAYS or until hospital discharge)	Stop Anticoagulant and report if: - Clinically significant bleeding - Heparin-induced thrombocytopenia

*See overleaf for the dosing guide

If you have any queries or would like a copy of the Participant Information Sheet, contact:

Research Coordinator: Dr. Shouab Siddique (shouab@hustk.com)
 Principal Investigator (UK): Dr. Maryam Ali (maryamali_84@hotmail.com)
 Principal Investigator (National): Prof. Muddisa Hashmi (muddisa.hashmi@u.edu.pk)

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 0215582917-4367
 0215582937-4355

REMAP-CAP PAKISTAN

PRICE

ANTICOAGULATION domain

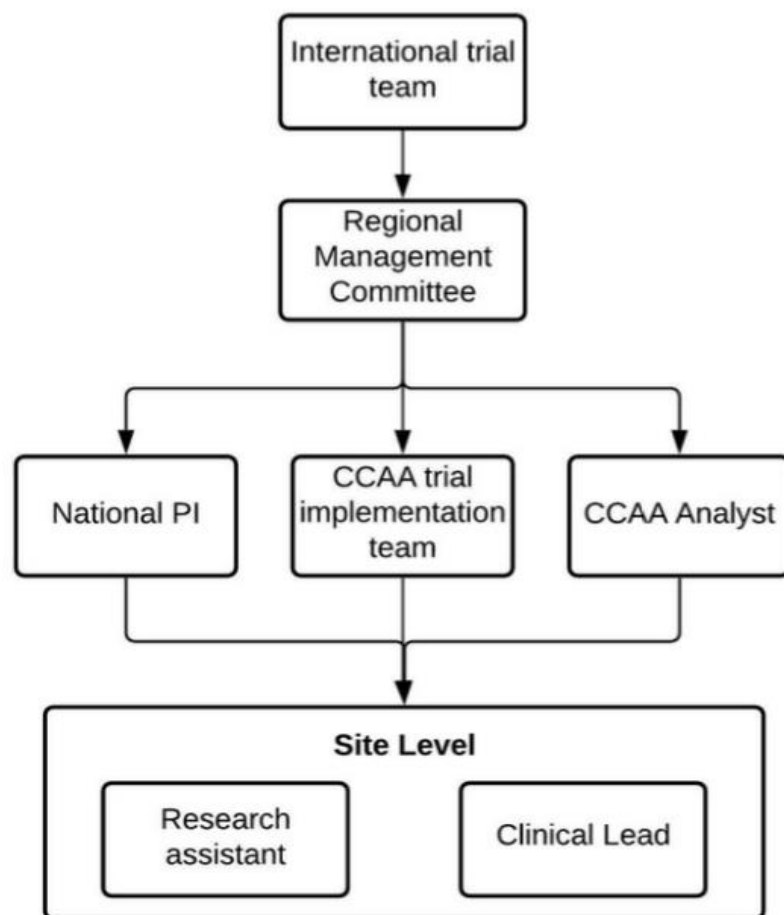
Enoxaparin dosing guide

Tick the correct dose for the patient based on weight, renal function and study allocation group

Weight	Renal function	Low-dose thromboprophylaxis		Intermediate dose thromboprophylaxis	
		Low-dose	Intermediate	Low-dose	Intermediate
< 50kg	CrCl <30ml/min	0.25mg/kg once daily		0.5mg/kg once daily	
	CrCl ≥30ml/min	20mg once daily		40mg once daily	
50-100kg	CrCl <30ml/min	20mg once daily		0.5mg/kg once daily	
	CrCl ≥30ml/min	40mg once daily		40mg twice daily	
101-150kg	CrCl <30ml/min	40mg once daily		0.5mg/kg once daily	
	CrCl ≥30ml/min	40mg twice daily		60mg twice daily	
> 150kg	CrCl <30ml/min	60mg once daily		0.5mg/kg once daily	
	CrCl ≥30ml/min	60mg twice daily		80mg twice daily	

SITE-LEVEL IMPLEMENTATION MONITORING

Figure 1. REMAP CCAA Organogram



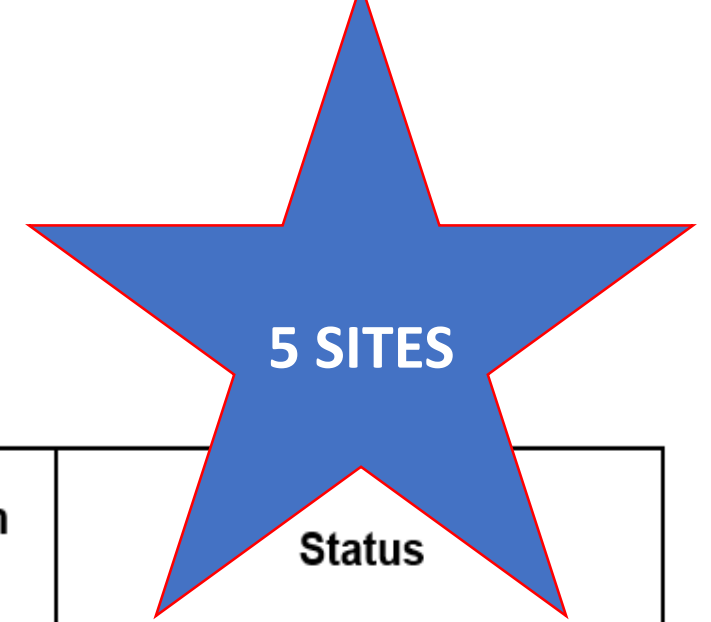
Clinical Monitoring Plan

Version 2.0. DRAFT 28/09/2021

Study Title: Randomized, Embedded, Multifactorial Adaptive Platform trial for Community-Acquired Pneumonia including COVID 19 (REMAP CAP+Pandemic)

Study Acronym: REMAP-CAP

SITE-LEVEL IMPLEMENTATION



Recruitment/Number of participants in the study



Intervention Domain	Total recruited to date	Total withdrawn to date	Status
Vitamin C	323	03	Recruitment ongoing.
Statin	13	0	Recruitment ongoing.
Ivermectin	114	01	Recruitment ongoing.
Anticoagulation	0	0	Recruitment has not started
Totals	450	04	*co-enrollment included

8TH October 2021

SITE-LEVEL IMPLEMENTATION *EXPERIENCE GAINED*

- Investing in Research infrastructure where the burden of disease is-**CCAA & WELLCOME TRUST**
- Research Collaborations- **ISARIC & REMAPCAP**
- Local Engagement
- Ministries of Health, National Health Systems, WHO