Artificial Intelligence & MDR

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Carolina Garcia Vidal

Infectious Diseases Department, Hospital Clínic, Barcelona

CLÍNIC BARCELONA Hospital Universitari



Cancer patients



Difficult to treat infections



NEUTROPENIA FEBRIL



MULTIRESISTANCE

More antibiotics

- Broad spectrum
 - Higher resistance
- More toxicity

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• Higher cost

Martinez-Nadal G, et al. Inappropriate empiric antibiotic treatment in high-risk neutropenic patients

with bacteremia in the era of multi-drug resistance. Clin Infect Dis 2019; doi: 10.1093/cid/ciz319.

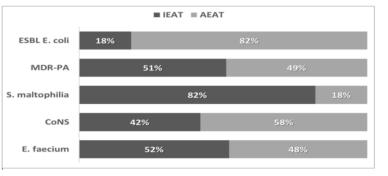
1615 episodes of BSI in neutropenic patients

MOST FREQ CAUSATIVE AGENTS

24%	IDSA
20%	recommendations
16%	were followed in 87% of cases
13%	
9%	
	20% 16% 13%



A total of



Cancer patients





NEUTROPENIA FEBRIL

MULTIRESISTANCE

Difficult to treat infections

More antibiotics

- Broad spectrum
- Higher resistance
- More toxicity

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• Higher cost

Personalized medicine

Can a computer make predictions that help in the

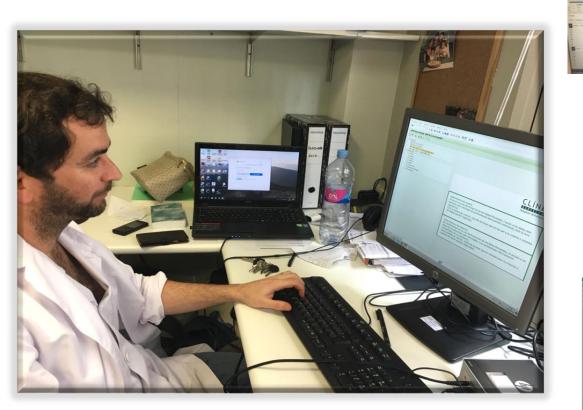
clinical decision-making process?

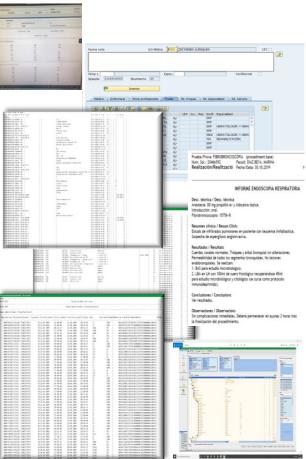






Searching for solutions





Tellez A, et al. Identifying the most important data for research in the field of infectious diseases: thinking on the basis of artificial intelligence. *Submitted*

Medical workflow variables	Structured data	Unstructured data in
Total variables = 4488	in our EHR	our EHR
	n (%)	n (%)
Epidemiology	203 (4.5)	185 (4.1)
Admission	84 (1.9)	0
Demographics	664 (14.8)	251 (5.6)
Comorbidities	547 (12.2)	9 (0.2)
Clinical manifestations	195 (4.3)	325 (7.2)
Laboratory	317 (7.1)	0
Microbiology	513 (11.4)	13 (0.3)
Other diagnosis	477 (10.6)	11 (0.2)
Treatment	487 (10.9)	2 (0)
Outcomes	180 (4)	21 (0.5)
Other	1 (0)	3 (0.1)

We need 100% optimal data quality!

This article has been retracted: N Engl J Med. DOI: 10.1056/NEJMc2021225.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19

Mandeep R. Mehra, M.D., Sapan S. Desai, M.D., Ph.D., SreyRam Kuy, M.D., M.H.S., Timothy D. Henry, M.D., and Amit N. Patel, M.D.

ABSTRACT

BACKGROUND

Coronavirus disease 2019 (Covid-19) may disproportionately affect people with cardiovascular disease. Concern has been aroused regarding a potential harmful effect of angiotensin-converting-enzyme (ACE) inhibitors and angiotensin-receptor blockers (ARBs) in this clinical context.

METHODS

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Using an observational database from 169 hospitals in Asia, Europe, and North America, we evaluated the relationship of cardiovascular disease and drug therapy with in-hospital death among hospitalized patients with Covid-19 who were admitted between December 20, 2019, and March 15, 2020, and were recorded in the Surgical Outcomes Collaborative registry as having either died in the hospital or survived to discharge as of March 28, 2020.

From Brigham and Women's Hospital Heart and Vascular Center and Harvard Medical School, Boston (M.R.M.); Surgisphere, Chicago (S.S.D.); Baylor College of Medicine and Department of Veterans Affairs, Houston (S.K.); Christ Hospital, Cincinnati (T.D.H.); the Department of Biomedical Engineering, University of Utah, Salt Lake City (A.N.P.); and HCA Research Institute, Nashville (A.N.P.). Address reprint requests to Dr. Mehra at Brigham and Women's Hospital, 75 Francis St., Boston, MA 02115, or at mmehra@bwh .harvard.edu.

This article was published on May 1, 2020, and updated on May 8, 2020, at NEIM.org. Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis

Mandeep R Mehra, Sapan S Desai, Frank Ruschitzka, Amit N Patel

Summarv

Background Hydroxy chloroquine or chloroquine, often in combination with a second-generation matching and the second-generation matching and the second generation matching and the second gene widely used for treatment of COVID-19, despite no conclusive evidence of their benefit. Although derall used for approved indications such as autoimmune disease or malaria, the safety and ben £th regimens are poorly evaluated in COVID-19.

Methods We did a multinational registry analysis of the use of hydroxychloroguine. wittee wi macrolide for treatment of COVID-19. The registry comprised data from 671 hospings in s ntinents V patients hospitalised between Dec 20, 2019, and April 14, 2020, with a positive laboratory i or for SARS-CoV-2. Patients who received one of the treatments of interest within 48 h of diagna included in groups (chloroquine alone, chloroquine with a macrolide, hydroxychlor ine alone, or hydroxychloroquine with a macrolide), and patients who received none of these treatments formed control gree Patients for whom one of the treatments of interest was initiated more than 48 h after diagnosis of le they w on mechanical ventilation. as well as patients who received remdesivir, were excluded. The main outc a were in-hospital mortality and the occurrence of de-novo ventricular arrhythmias d ventricular tachycardia or vained o ventricular fibrillation).

Findings 96032 patients (mean age 53-8 years, 46-39 women were in the treatment groups (1868 received period and met the inclusion criteria. Of the patie macro chloroguine, 3783 received chloroguine with 3016 hydroxychloroquine with a macrolide) and 1 pat hospital. After controlling for multiple lerlying lung disease, smoking, immunosuppressed condition, cardiovascular disease and its risk fact diabete and baseline disease severity), w ortality in the control group (9-3%), hydroxychloroquine mpared w (18 · 0%; hazard ratio 1 · 335, 95% 102 457), hydro, vchloroquine with a macrolide (23 - 8%; 1 - 447, 1 - 368-1 - 531). chloroquine (16-4%; 1-365, 118-1-531). independently associated an increased a f in-hospital mortality. Compared with the control group (0.3%), 935-2-900, hydroxychloroguine with a macrolide (8-1%; 5-106, 4-106-5-983). hydroxychloroquine (6 4,2-36 chlorogutne (4-3%; 0-4-596), and chloroquine with a macrolide (6-5%; 4-011, 3-344-4-812) were independently associate an incr d risk of de-novo ventricular arrhythmia during hospitalisation.

> firm a benefit of hydroxychloroquine or chloroquine, when used alone or with unab spital outcomes for COVID-19. Each of these drug regimens was associated with decreased eased frequency of ventricular arrhythmias when used for treatment of COVID-19.

ev Distinguished Chair in Advanced Cardiovascular Medicine at Brigham and Women's Hospital. Funding William

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Introduction

Interpreta

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drugs have been shown in laboratory conditions to have The absence of an effective treatment against severe antiviral properties as well as immunomodulatory acute respiratory syndrome coronavirus 2 (SARS-CoV-2) effects.¹⁴ However, the use of this class of drugs for infection has led clinicians to redirect drugs that are COVID-19 is based on a small number of anecdotal known to be effective for other medical conditions to the experiences that have shown variable responses in treatment of COVID-19. Key among these repurposed uncontrolled observational analyses, and small, opentherapeutic agents are the antimalarial drug chloroquine label, randomised trials that have largely been and its analogue hydroxychloroguine, which is used for inconclusive.³⁸ The combination of hydroxychloroguine the treatment of autoimmune diseases, such as systemic with a second-generation macrolide, such as azithrohupus ervthematosus and rheumatoid arthritis." These mycin (or clarithromycin), has also been advocated.

ps//doi.org/10.1016 50140-6736(20)31180-6 This online publication has been corrected. The corrected version first appeared at thelancet.co on May 29, 2020 See Online/Comment https://doi.org/10.1016 50140-6736(20)31174-0 Brigham and Women's Hospital Heart and Vascular Center and Harvard Madical School Boston MA, USA (ProfM RMehra MD); Surgisphere Corporation Chicago, IL, USA (SS Denai MD); University Heart Center University Hospital Zurich Zurich, Switzerland (Prof F Ruschitzka MD): Department of Riomedical e control group, 10698 (11-1%) patients died in Engineering University sex, race or ethnicity, body mass index, underlying of Utah Salt Lake Giy, UT, USA (A NPatel MD); and HCA Research Institute Nuclearily TN, USA (AN Patel)

TODAT

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e included

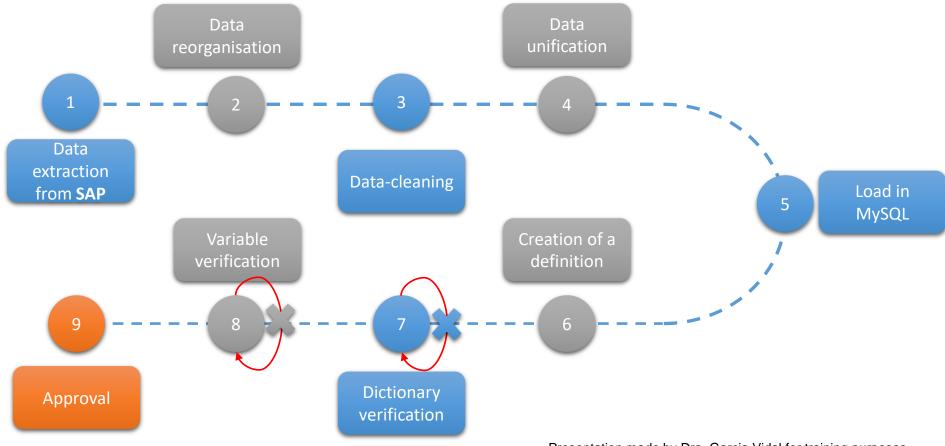
of four treatment

OVID-19 were hospitalised during the study

elved hydroxychloroguine, and 6221 received

Commencements chloroquine with a macrolide (22 · 2%; 1 · 368, 1 · 273-1 · 469) were each Prof Mandeep R Mehra Brisham and Woman's Housital Heart and Vancular Center and Haward Medical School, Boston, MA 02115 USA mmehra@bwh.haward.edu

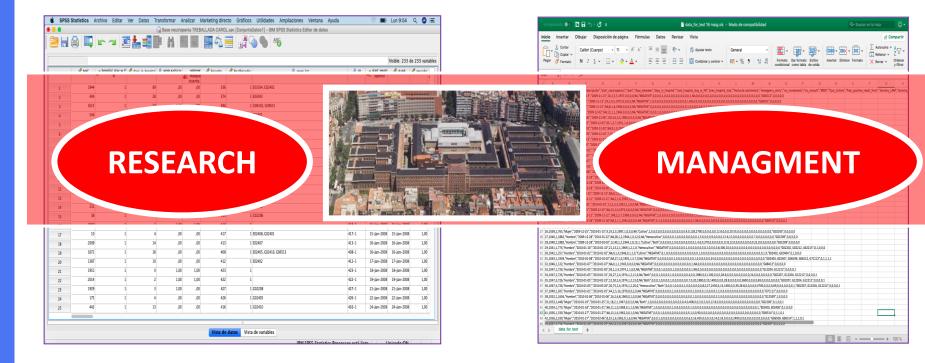
Data circuit



Presentation made by Dra. Garcia Vidal for training purposes

SILD-HOSPITAL CLINIC

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Commentary

Artificial intelligence to support clinical decision-making processes



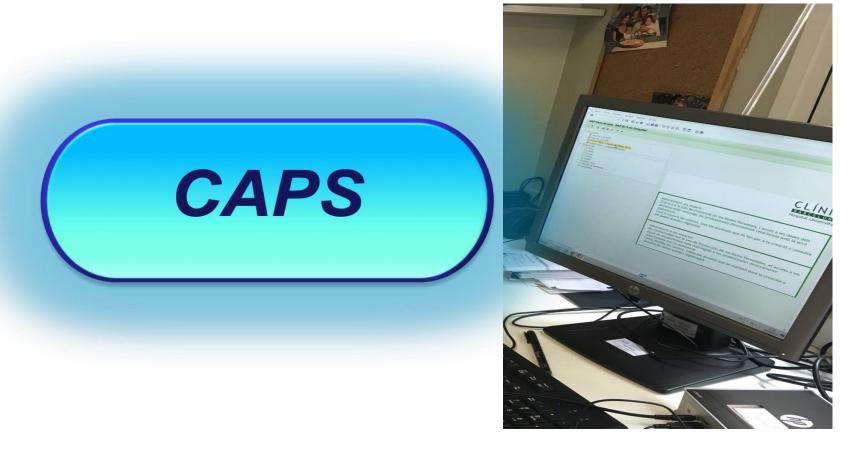
Carolina Garcia-Vidal^{a,*,1}, Gemma Sanjuan^{b,1}, Pedro Puerta-Alcalde^a, Estela Moreno-García^a, Alex Soriano^a

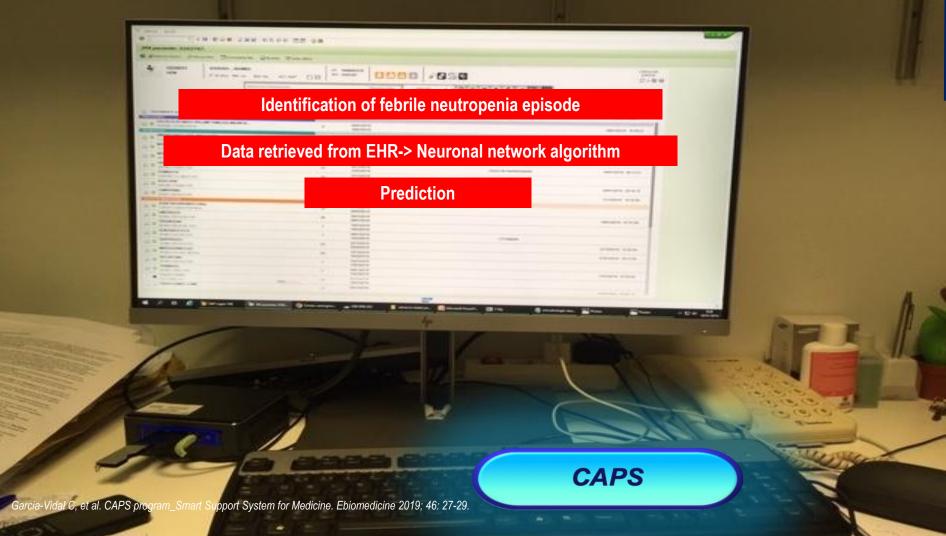
^a Infectious Diseases Department, Hospital Clínic-IDIBAPS, University of Barcelona, Barcelona, Spain.

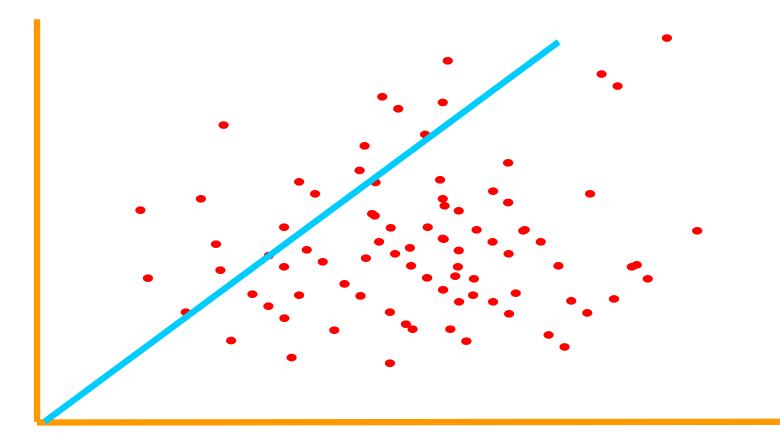
^b Smart Support System for Medicine, Spain

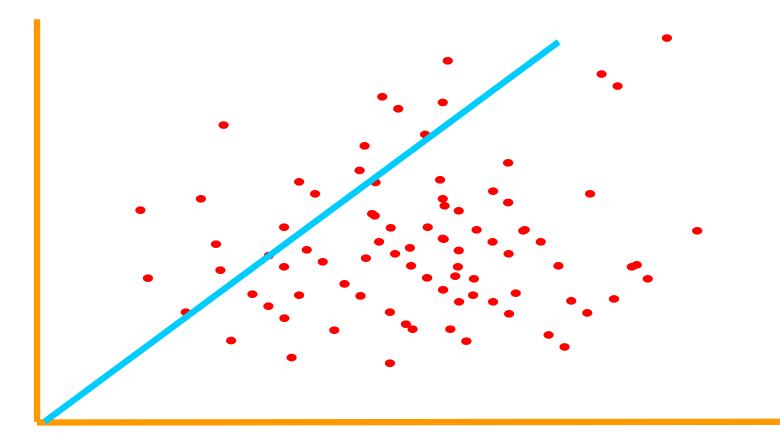
1. Introduction

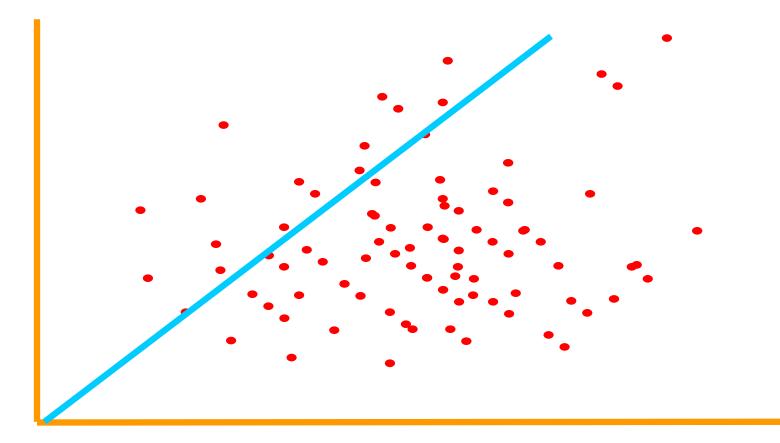
Artificial intelligence (AI) proffers the ability of computer systems to perform human brain tasks across various topics in all aspects of everyday life. Most clinical physicians are sceptical about the help that AI may provide in their current medical practice. In this commentary, we aim to provide readers with insight on our experience –including all the benefits and pitfalls– since the implementation of an AI programme in our Now, training a high number of data with machine learning (ML) or neural networks (NN), predictions on the results that will be obtained by cultures at febrile neutropenia onset are possible. This new and revolutionary reality is composed of two main tenets. First, a high number of data available from EHRs can be retrieved in real time. Second, advances made in computational performance allows extensive mathematical operations to dramatically optimise big data result training with ML and NN models. *Garcia-Vidal C, et al.* Artificial intelligence to support clinical decision-making process. EBioMedicine 2019; 46: 27-29.

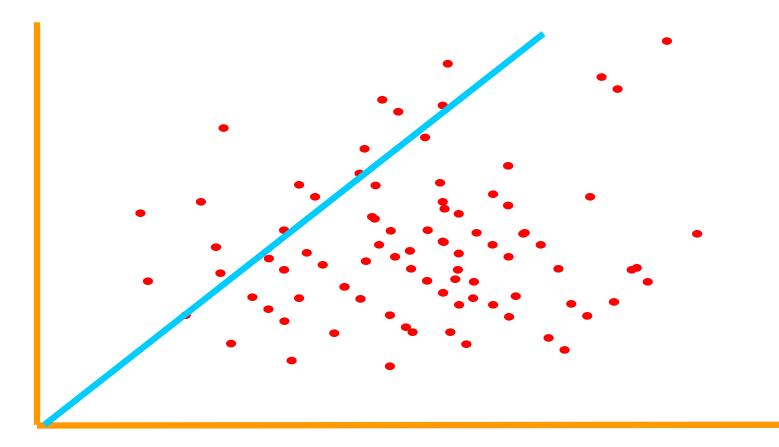


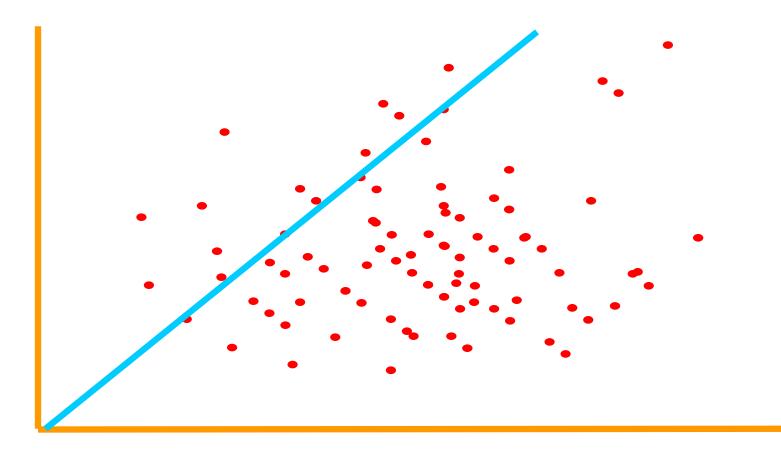


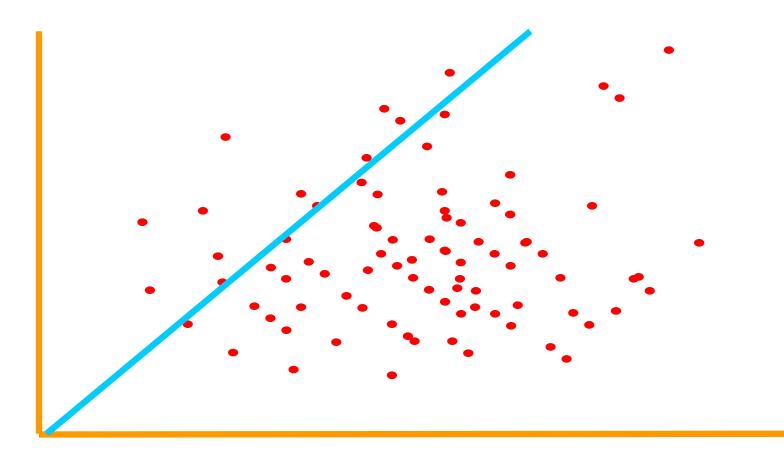


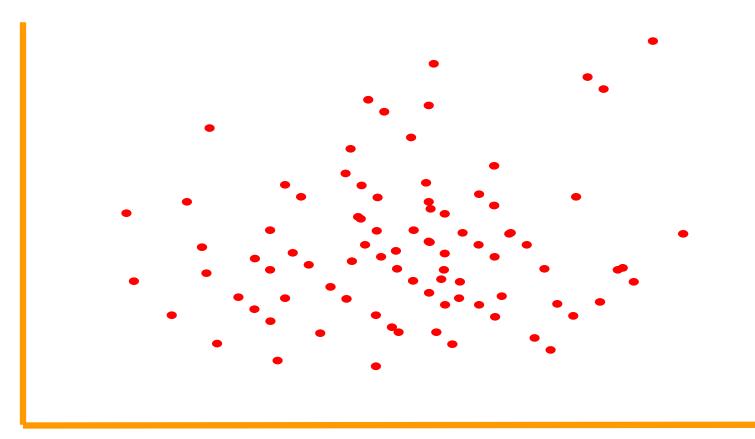


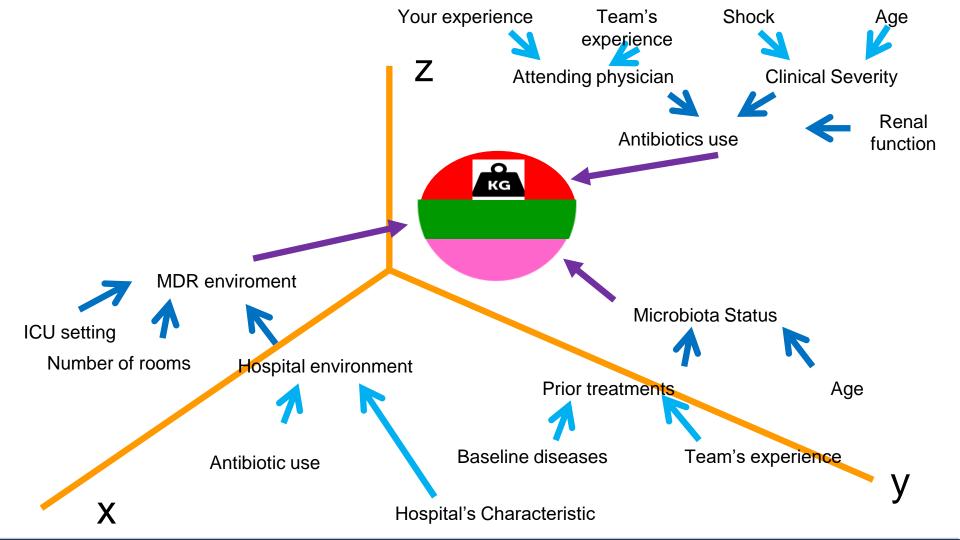


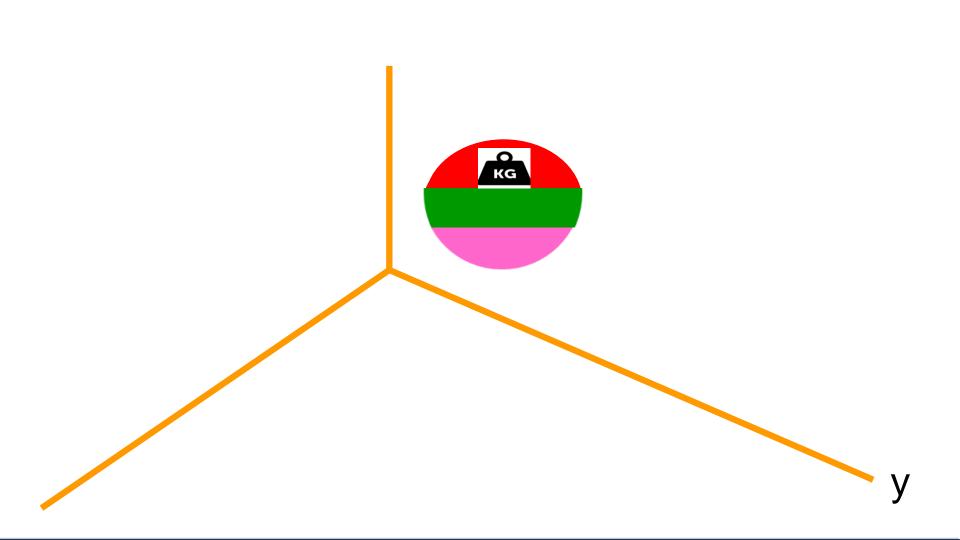




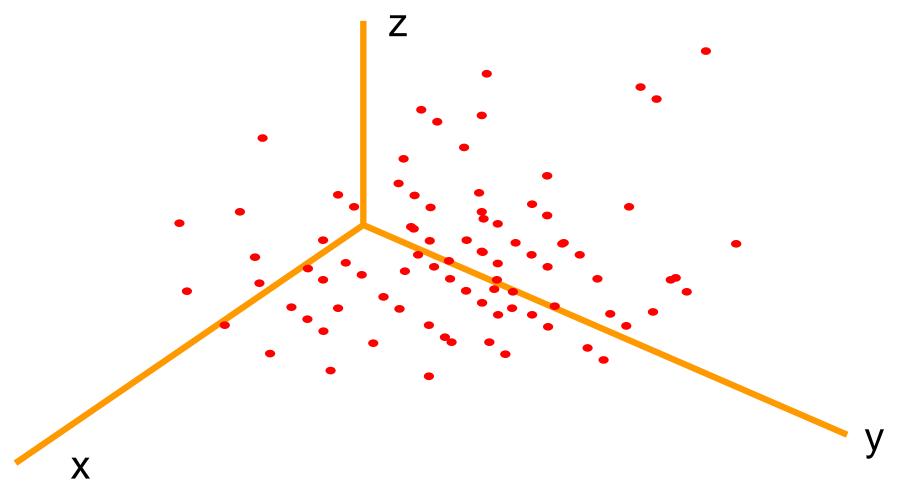


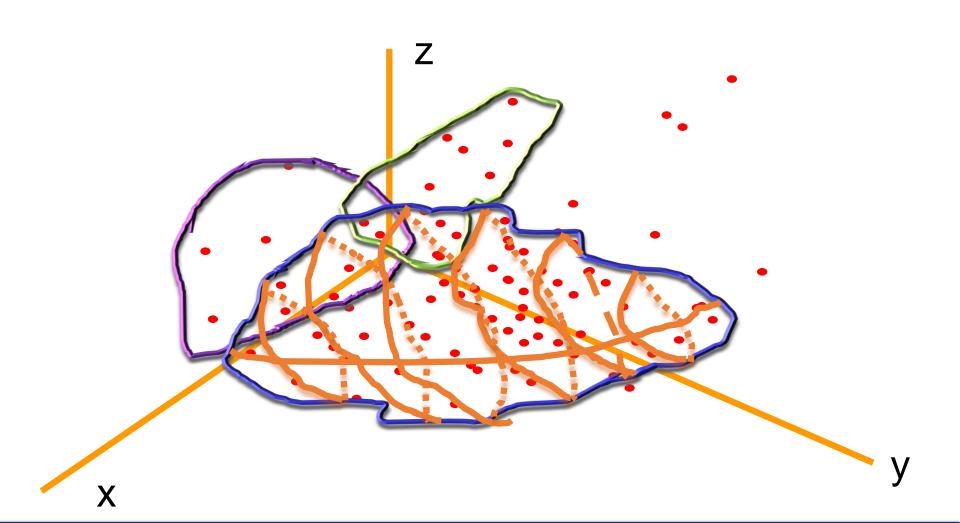






Análisis en tres dimensiones





Garcia-Vidal C, et al. Machine learning to assess the risk of multidrug-resistant Gramnegative bacilli infections in febrile neutropenic haematological patients. *Infectious Diseases and Therapy*, 2021.

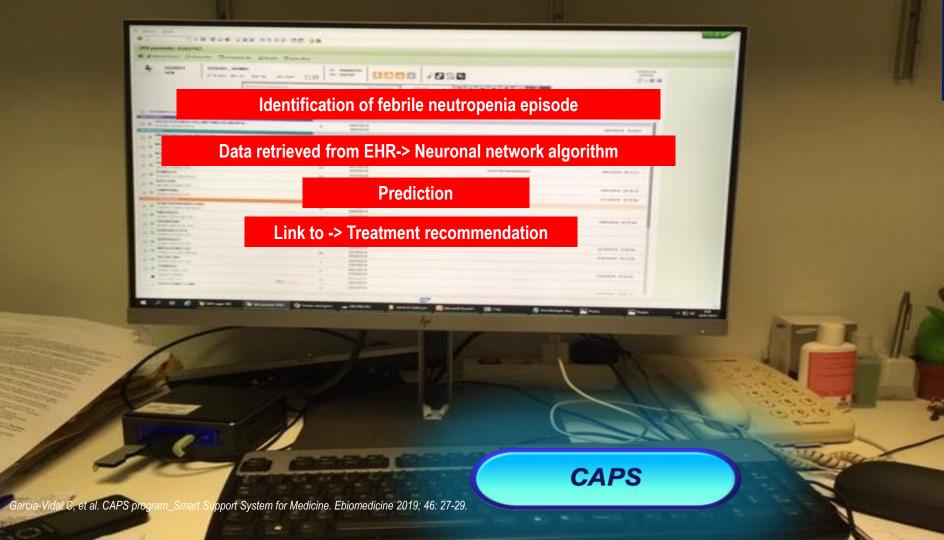
7 million pieces of data	Eigure 1. Main variables in dataset ge Epidemiological data: E.g. Age, sex, co-morbidities, previous admissions or surgeries, venous catheters (days and replacements, if applicable), previous visits to the daytime day care hospital	neration	
	 Data related to underlying disease: Underlying disease: E.g. Type of disease, situation of the underlying diseases, transplant recipient, graft versus host disease Chemotherapx and immunosuppressants: E.g. Previous. CT therapy. number of cycles. type of therapy. corticosteroids. current and accumulative.dose. time.since. treatment 		
	 Data related to the episode: Clinical variables: E.g., days of fever., I.T., mucositis. GVHD Analysis: E.g., RCP., neutrophils., screatininglons Initial evolutions E.g., need for serum therapy., need for vasoactive drugs., need for ICU 		ASSIGN RISK OF MDR- GNB FOR EMPIRICAL TREATMENT COVERAGE IN HRFN
	 Microbiological data: From the patient: E.g. Previous isolations, previous MDR isolates From the unit: E.g. Previous isolations, MDR % the previous months, MDR % at that time From other areas of patient action: E.g. Previous isolations in the units visited by the patient, patients treated by shared nurses and/or doctors 		
	Data related with ATB treatment: E.g., Previous ATB consumption, type of ATB, time and doses consumed, ATB at the time of the episode]]	

Garcia-Vidal C, et al. Machine learning to assess the risk of multidrug-resistant Gramnegative bacilli infections in febrile neutropenic haematological patients. *Infectious Diseases and Therapy*, 2021.

Table 2. Metrics of ML models to predict the need of MDR-GNB coverage in HRFN

patients.

					Negative	Positive
Models	AUC	F1_Score	Sensitivity	Specificity	Predictive Value	Predictive Value
GBM	0.7872	0.9705	0.4583	0.9988	0.9438	0.9778
XGBoost	0.7945	0.9670	0.4895	0.9886	0.9464	0.8246
<u>Random</u>						
Forest	0.7896	0.9711	0.4583	1.00	0.9439	1.0
GLM	0.7827	0.9716	0.4687	1.00	0.9449	1.0





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WE ACHIEVED MORE THAN 3 TRILLION PIECES OF HIGH QUALITY

OF DATA FROM PATIENTS WITH COVID-19 IN FOUR MONTHS

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deticled around the world with more rown a meanin warew detifit. A next analysis of 44415 confirmed care in China throughout the EU on 1 July 2020, Initial circuit and any account debts. A ment analysis of 44415 common contract of throughout bettom 1 and 2000 million and an analysis of the debt of bits were symptomatic or mill. Like were seen to do mit demonstrated the superiority of medical in 1 and the superiority of medical in 1 and the debt of the superiority of medical in 1 and the superiority of the debt of the superiority of medical in 1 and the superiority of the debt of the superiority of the debt decible tod sit were appropriate within overall motify of 23%. Among discussion intervenient of day 12° or at day 11° however, C Die Authoriti 2021. Published by Oxford University Press on behalf of the British Society for Antimicrobid Chemistherapy. All rights reserved.

powers was require inoppositions, even are rule or rule and son and mortality are around 20%. ² * On 1 May 2020, remdesivin Up to April 2001, more than 140 million cases of severe acute in-received. TDA emergency: use acutevation for hepitalized Up to April 2011, more than 1 vari manan cares in where a war in gradient syndrome connaisma 2 (WAG Care 2) election had been patients with COVID-19 and war difficulty approved on 22 Obdate ignatory syndrome counciend. / UNIXO Like Line relation values in the State St

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Bockground: The use of remdesive has demonstrated a significant reduction in the time to recovery in patients exemptions: me and or remained near one particle or approximate execution rate to memory exponents with COVID-19. However, the impact on monitory is still controlensist. Therefore, it is necessary to evolution with Unity in nowner, the impact on invitianty is the construment, internet, is a neurosity in analysi whether there is a specific subgrady of potients in whom an active antiwed therapy data reduces the mantaly. Methods: Resents admitted for H&R in our hospital for a SARS Car 2 confirmed or suspected election from nconset, manual variante variante na na na na varia varia varia variante variante variante en exercitaria tradi Relatory 2010 ta February 2011 were relatorated very andyted. The primary automated the study was mantality

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pliembers are listed in the Acknowledgements section.

+Contributed equally.

Conesponding author, E-mail: asoriano@clinic.cat

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"Department of Infectious Diseases, Harpital Clinic of Bacelone 2018APS, University of Bacelone, Bacelone, Spain-"Department of separment of infectous useaux, natybas ume of parcelona scalars, unvensity of parcelona, source vary supervision Monbiologi, Hapita Cunic of Barelana, University of Barelana, Barelana, Scant, Tushake for Gobal Heath (NGubal, Barelana,

Sergio Prieto-Gonzalez", Alex Almuedo-Tiera 🐨 ", Josep Mensa", José Antonio Mertinez", Gerema Sonjuan ", J. M. Nicolos", A. del Rio, José Nunoz ", Jordi Via-3", Felipe Garcia" and Alex Soriano 🎯 * on behalf of the

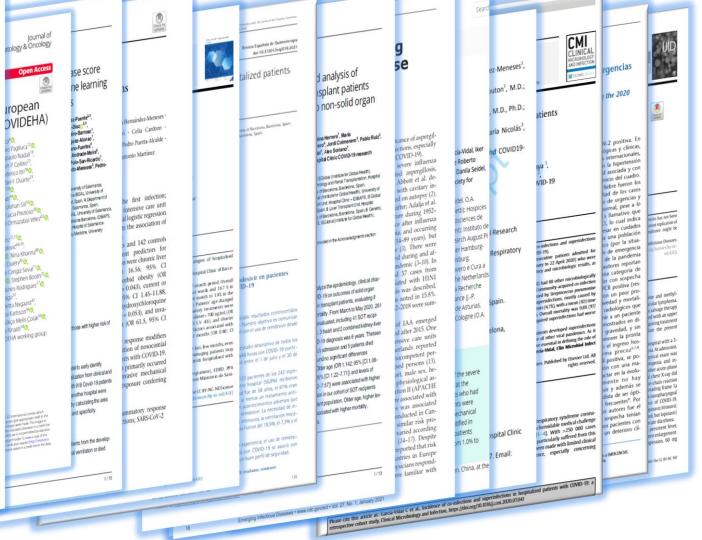
Carolina Garcia-Vidal¹t, Rodrigo Alonso¹t, Ana M. Camon¹, Celia Cardoza¹, Lala Albiach¹, Dalana Agüero¹, ureano unicar vinue 1, novergo narosev (, novera, camori, xero varose, varoseno, varoseno, varoseno paga M. Angeles Marcoy J. Juan Ambresioni J. Marta Bodro', Mariang Chambite', Loyena de la Marci, in, Angens Marcas''', Auan Amoresoni', Marta Booro', Marana Chumbra', Lorena de la Mora', Nicole Garcia Pauton', Gerard Datens @ ; Marta Hennadez-Menster, Alexy Inciarte ; Genareve Cuesto @ 1, Standard Marta Standard and Standard and Hennadez Alexandra (Alexy Inciarte ; Genareve Cuesto @ 1, Nicole Garcia-Pourani , Gerard Duenos (g. ; Marta Nernander-Seneses , Auny Incure , Genovera Lueno (g. Fernanda Nelle (g. 1 Luero Marcta', Pedro Puerto Alcade (g. 1 Sobbro Henero , Mantie Tuset , Pedro Castro , fernanda Meira © ', Laura Marata', Peano Puerto-Accasa ₪ ', Sabina hemera', Annae Iuset', Peano Castra Sergio Printo-Ganzález[®] Alex Almuedo Riera © ^{1,1} Josep Menso[®], Asia Antonio Martinez[®] Germin Sonjuni I.

Impact of remdesivir according to the pre-admission symptom duration in patients with COVID-19

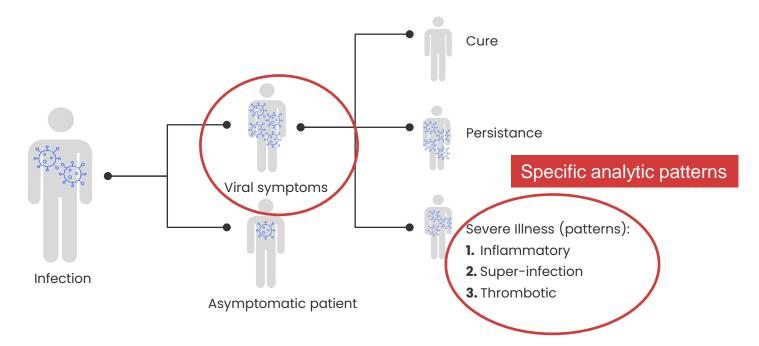
J Antimicrob Chemother

doi:10.1093/jac/dkab321

Journal of Antimicrobia Chemotherapy



Garcia-Vidal C, et al.Personalized therapy approach for hospitalized patients with COVID-19. Clinical Infectious Disease 2020; doi: 10.1093







SUBJECTIVE Dyspnea, fever, cougth, ...



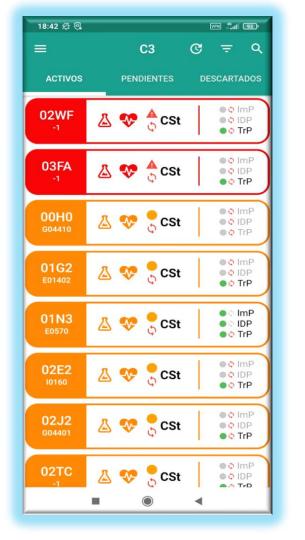
	Days from symptoms onset CT-PCT Lymphocite count	C-RP Ferritin LDH	Procalcitonin/ Cr Urinary antigen Sputum culture	Dimer-D CT scan Troponin	Others
	Virus	Inflammation	Co-infection	Thrombopaty	Others
Pacient 1	x x	x			
Pacient 2	X	x x	x		
Pacient 3		x	x	x	
	Remdesivir Plasma Monoclonal antibodies Paxlovid Molnupinavir	Tocilizumab Dexametasona Anakinra Baricitinib 	Antibiotics Antifungals	Anticoagulation	Others

EIT health award 2020

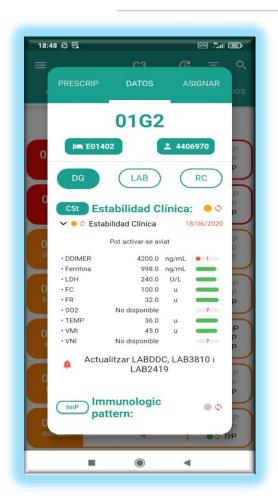
(European Union-Innovative Technology Department)!!!!





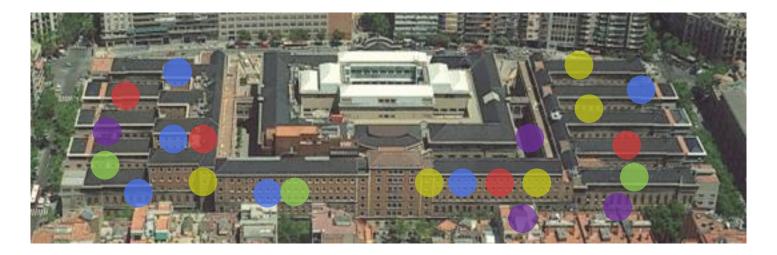


APP COVID 19





COVID-19 Central Control (C3)



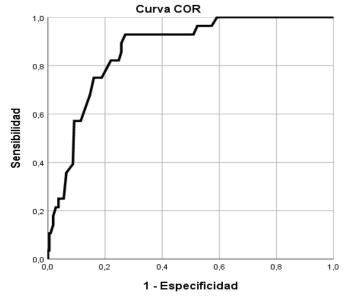
Co-infection

Patients with suspiction of thrombotic diseases

Ready for hospital discharge!

Antiinflammatory Treatment

Garcia-Vidal C, et al.Personalized therapy approach for hospitalized patients with COVID-19. Clinical Infectious Disease 2020; doi: 10.1093



Los segmentos de diagonal se generan mediante empates.

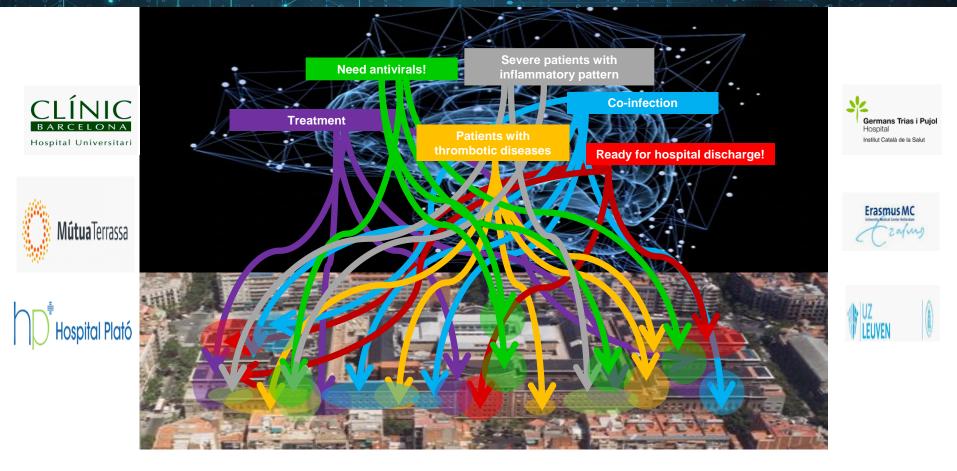
▶ Multivariate analyses showed that personalized therapy was independently associated with decreased early mortality (OR 0.144; 95% confidence interval [CI], 0.03–0.686; p=0.015).

 Increasing age (OR 1.06; 95% CI, 1.003-1.121; p=0.038) and therapeutic effort limitation (OR 9.684; 95% CI, 2.934-31.959; p<0.001) were found as independent factors associated with higher mortality.
 The goodness of fit of the model -> Hosmer-Lemeshow test (p=0.275).

The discriminatory power of the model had an AUC of 0.907 (95% CI,

0.847–0.967), demonstrating an excellent ability to predict mortality.

COVID-19 Central Control (C₃)



naftali
harris
$$\beta = (x^{\tau}x)^{-1}x^{\tau}y$$

Blog About Contact I'm Feeling Lucky

Visualizing K-Means Clustering

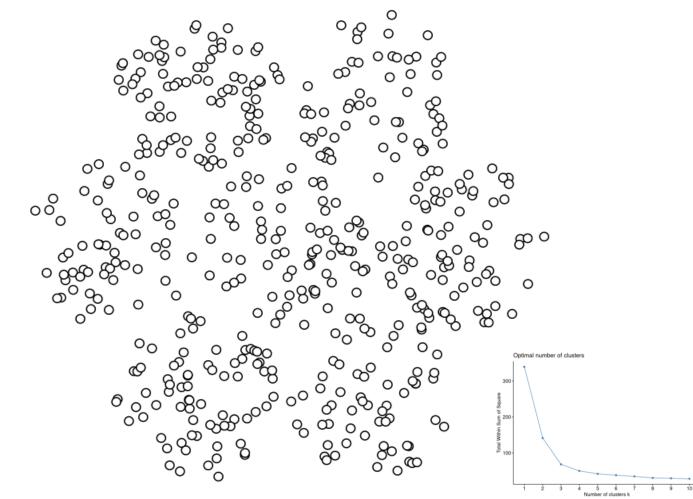
January 19, 2014

Suppose you plotted the screen width and height of all the devices accessing this website. You'd probably find that the points form three clumps: one clump with small dimensions, (smartphones), one with moderate dimensions, (tablets), and one with large dimensions, (laptops and desktops). Getting an algorithm to recognize these clumps of points without help is called *clustering*. To gain insight into how common clustering techniques work (and don't work), I've been making some visualizations that illustrate three fundamentally different approaches. This post, the first in this series of three, covers the k-means algorithm. To begin, click an initialization strategy below:

How to pick the initial centroids?

I'll Choose	Randomly	Farthest Point
-------------	----------	----------------

https://www.naftaliharris.com/blog/visualizing-k-means-clustering/



Data provided by the author for educational purposes.

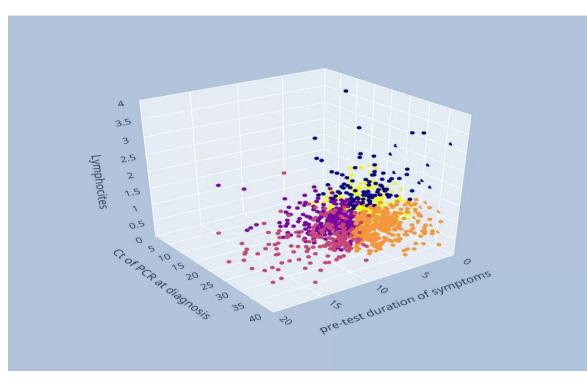
How to pick the initial centroids?



Restart

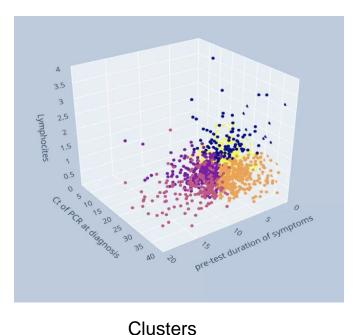
K-Means Algorithm

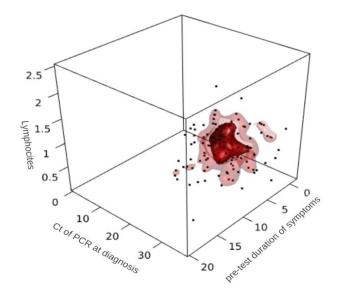
Garcia-Vidal C, et al. Clustering and validation of clinical phenotypes of hospitalized patients with COVID-19 and their various responses to remdesivir . Submitted



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Garcia-Vidal C, et al. Clustering and validation of clinical phenotypes of hospitalized patients with COVID-19 and their various responses to remdesivir . Submitted





Mortality

Data provided by the author for educational purposes.

Garcia-Vidal C, et al. Clustering and validation of clinical phenotypes of hospitalized patients with COVID-19 and their various responses to remdesivir . Submitted

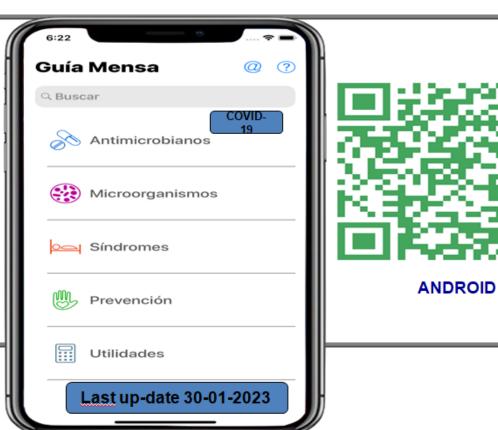
K-means cluster		Median Ct (IQR)	Median days of pre-test duration of symptoms (IQR)	Median lymphocyte count (IQR)	60-d mortality (%)	60-d mortality/ pts receiving remdesivir (%)	60-d mortality/ pts who did not receive remdesivir (%)	p value
Cluster 1	Derivation cohort n=100	26 (23-30)	5 (3-7)	1.7 (1.5-2)	2	ο	2.4	0.53
Cluster 2	Derivation cohort n=273	24 (22-26)	8 (7-9)	0.8 (0.6-1)	11	0	11	0.34
Cluster 3	Derivation cohort n=183	31 (28-34)	11 (10-13)	0.8 (0.6-1.1)	8.2	NA	8.2	NA
Cluster 4	Derivation cohort n=318	31 (29-33)	5 (4-7)	0.8 (0.6-1)	10.4	2.9	11.3	0.13
Cluster 5	Derivation cohort n=284	21 (17-23)	3 (1-4)	0.7 (0.5-0.9)	29.7	10.5	36.7	< 0.001

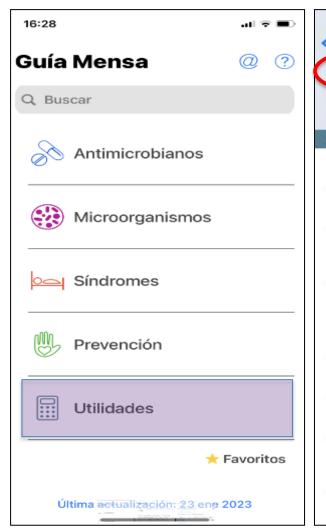
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Antimicrobial book



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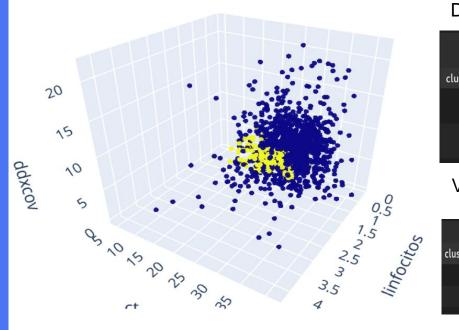




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Utilidades	
Calculadoras Scores Tablas	
Q Buscar en calculadoras	
Calculadoras	
Agua corporal total	>
Anión gap	>
Calcio corregido por albúmina o pro- teínas	>
Concentración sérica de un β-lactá- mico administrado en "bolus", infu- sión extendida o infusión continua	>
Déficit de agua libre	>
Excreción fraccional de sodio	>
Filtrado glomerular (Cockcroft- Gault)	>
Filtrado glomerular estimado (MDRD	>

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Administració	n de antibiót 😽
Cmin (valle (antibiótico libr % tiempo > CII	
Antibiótico	Amoxicilina >
CIM	8 mg/L
Dosis	2 g
Tiempo de infusió	n 2 h
Intervalo de admir	nistración
4h 6h 8	8 h 12 h 24 h
Peso	61 kg
* Vd normal: C	0,30 L/kg — +
2	\$

Garcia-Vidal C, et al. Artificial intelligence with deep learning identify patients hospitalised with COVID-19 in whom remdesivir decreased mortality. Work in process



Derivation cohort

	n	%	n Remde	n No Remde	% Death Remde	% Death No Remde	% Death	pvalue
cluster								
1	972	84.6	87	885	4 (4.6%)	98 (11.1%)	102 (10.5%)	0.060124
2	177	15.4	45	132	5 (11.1%)	57 (43.2%)	62 (35.0%)	0.000077

Validation cohort

	n	%	n Remde	n No Remde	% Death Remde	% Death No Remde	% Death	pvalue
cluster								
1	895	91.2	94	801	7 (7.4%)	73 (9.1%)	80 (8.9%)	0.592543
2	86	8.8	24	62	4 (16.7%)	26 (41.9%)	30 (34.9%)	0.027466

Garcia-Vidal C, et al. Trends in mortality of hospitalized COVID-19 patients: A single centre observational cohort study from Spain. The Lancet Regional Health 2021

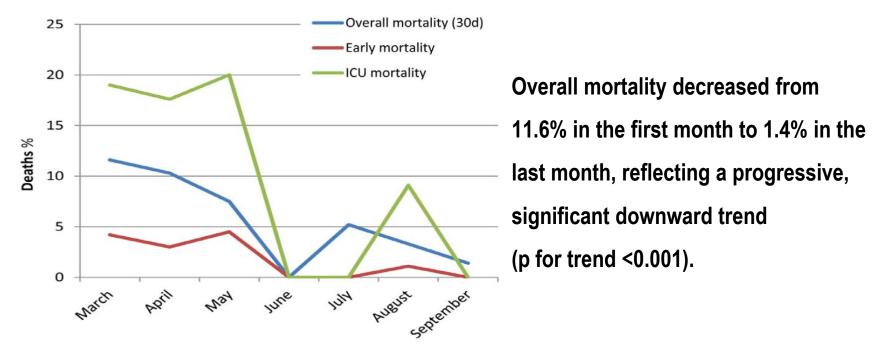


Fig. 1. Overall mortality trends for patients admitted with COVID-19 (distribution by months).



Thanks for you attention

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