

Artificial Intelligence & MDR

Carolina Garcia Vidal

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CLÍNIC
BARCELONA
Hospital Universitari



Cancer patients



Difficult to treat infections



Neutrôfils abs. (analit.)

0.0/BB $10^9/L$

[2.5 - 7.0

NEUTROPENIA FEBRIL



MULTIRESISTANCE

- More antibiotics
- Broad spectrum
- Higher resistance
- More toxicity
- 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

<i>E. coli</i>	24%
CoNS	20%
<i>P. aeruginosa</i>	16%
<i>Enterococcus</i> spp	13%
<i>Klebsiella</i> spp	9%

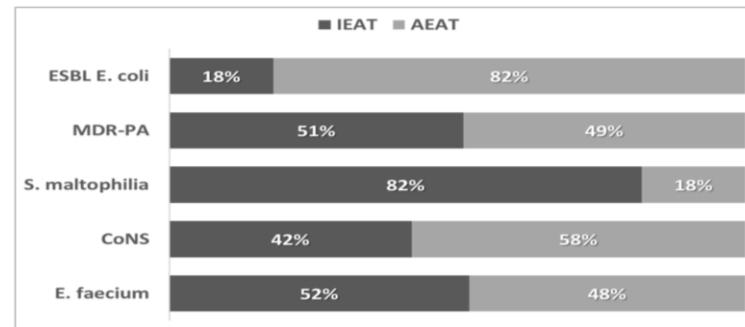
IDSA
recommendations
were followed in 87%
of cases



A total of

24%

received IEAT



Cancer patients



Difficult to treat infections



Neutrophils abs. (analit.)

0.0/BB $10^9/L$

[2.5 - 7.0

NEUTROPENIA FEBRIL



MULTIRESISTANCE

- More antibiotics
- Broad spectrum
- Higher resistance
- More toxicity
- Higher cost

Personalized medicine

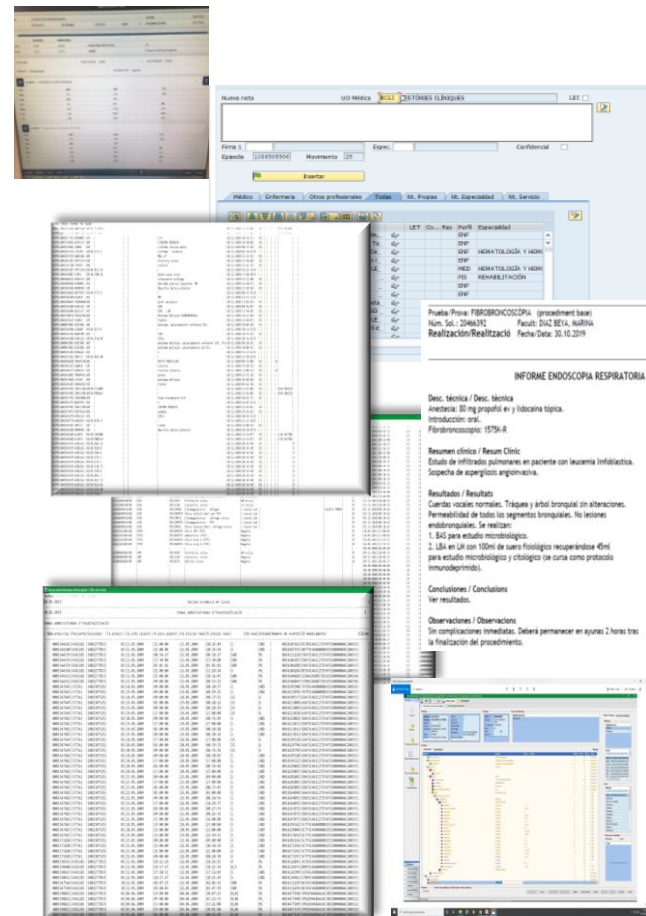
**Can a computer make predictions that help in the
clinical decision-making process?**

-I HAVE DATA

-I'M BETTER WITH PROBABILITY!
No doubt!!!

THAN YOU ARE





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 Total variables = 4488	Structured data in our EHR n (%)	Unstructured data in our EHR 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!

The NEW ENGLAND JOURNAL of MEDICINE

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

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.); Sargis, 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 Mechanical 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 NEJM.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 Buschitzky, Amit N Patel

Summary

Background Hydroxychloroquine or chloroquine, often in combination with a second-generation macrolide, are being widely used for treatment of COVID-19, despite no conclusive evidence of their benefit. Although generally safe when used for approved indications such as autoimmune disease or malaria, the safety and benefit of these treatment regimens are poorly evaluated in COVID-19.

Methods: We did a multinational registry analysis of the use of hydroxychloroquine in patients with and without a macrolide for treatment of COVID-19. The registry comprised data from 671 hospitals in 19 countries. We included all patients hospitalised between Dec 20, 2019, and April 14, 2020, with a positive laboratory test for SARS-CoV-2 and a clinical diagnosis of COVID-19. The treatment groups were patients who received hydroxychloroquine alone, hydroxychloroquine plus a macrolide, or hydroxychloroquine with another macrolide, and patients who received none of these treatments formed the control group. Patients for whom one of the treatments of interest was initiated more than 48 h after diagnosis or when they were on mechanical ventilation, as well as patients who received remdesivir, were excluded. The main outcome of interest was in-hospital mortality and the presence of de-novo ventricular arrhythmia, which was defined as sustained ventricular tachycardia or ventricular fibrillation.

Findings 96,032 patients (message 53.8 years; 46.7% women) were hospitalized during the study period and met the inclusion criteria. Of these, 10,608 patients were in the treatment groups (1868 received chloroquine, 3783 received chloroquine with a macrolide, 3016 received hydroxychloroquine, and 6221 received hydroxychloroquine with a macrolide) and 85,424 patients were in the control group. 10,608 (11.1%) patients died in hospital. After controlling for multiple factors (age, sex, race or ethnicity, body-mass index, underlying cardiovascular disease and its risk factor/diseases, underlying lung disease, smoking, immunosuppressed condition, and baseline disease severity), we compared mortality in the control group (9.3%), hydroxychloroquine (18.0%; hazard ratio 1.35, 95% CI 1.22–1.47), hydroxychloroquine with a macrolide (23.8%; 1.447, 1.368–1.531), chloroquine (16.4%; 1.365, 1.28–1.45), and chloroquine with a macrolide (22.2%; 1.368, 1.273–1.46) were each significantly associated with increased risk of death in hospital after adjusting for other factors. Hydroxychloroquine (18.0%; 1.35, 95% CI 1.22–1.47), hydroxychloroquine with a macrolide (23.8%; 1.447, 1.368–1.531), chloroquine (16.4%; 1.365, 1.28–1.45), and chloroquine with a macrolide (22.2%; 1.368, 1.273–1.46) were each independently associated with an increased risk of de-novo ventricular arrhythmia during hospitalization.

Interpretation: We were unable to confirm a benefit of hydroxychloroquine or chloroquine, when used alone or with a macrolide, on important outcomes for COVID-19. Each of these drug regimens was associated with decreased in-hospital mortality, but also increased frequency of ventricular arrhythmias when used for treatment of COVID-19.

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

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Introduction

The absence of an effective treatment against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has led clinicians to redirect drugs that are known to be effective for other medical conditions to the treatment of COVID-19. Key among these repurposed therapeutic agents are the antimalarial drug chloroquine and its analogue hydroxychloroquine, which is used for the treatment of autoimmune diseases, such as systemic lupus erythematosus and rheumatoid arthritis.^{1,2} These

drugs have been shown in laboratory conditions to have antiviral properties as well as immunomodulatory effects.³⁴ However, the use of this class of drugs for COVID-19 is based on a small number of anecdotal experiences that have shown variable responses in uncontrolled observational analyses, and small, open-label, randomised trials that have largely been inconclusive.³⁵ The combination of hydroxychloroquine with a second-generation macrolide, such as azithromycin (or clarithromycin), has also been advocated.

This online publication has been corrected. The corrected version first appeared at [thelancet.com](https://doi.org/10.1016/S0140-6736(20)31180-6) on May 29, 2020.

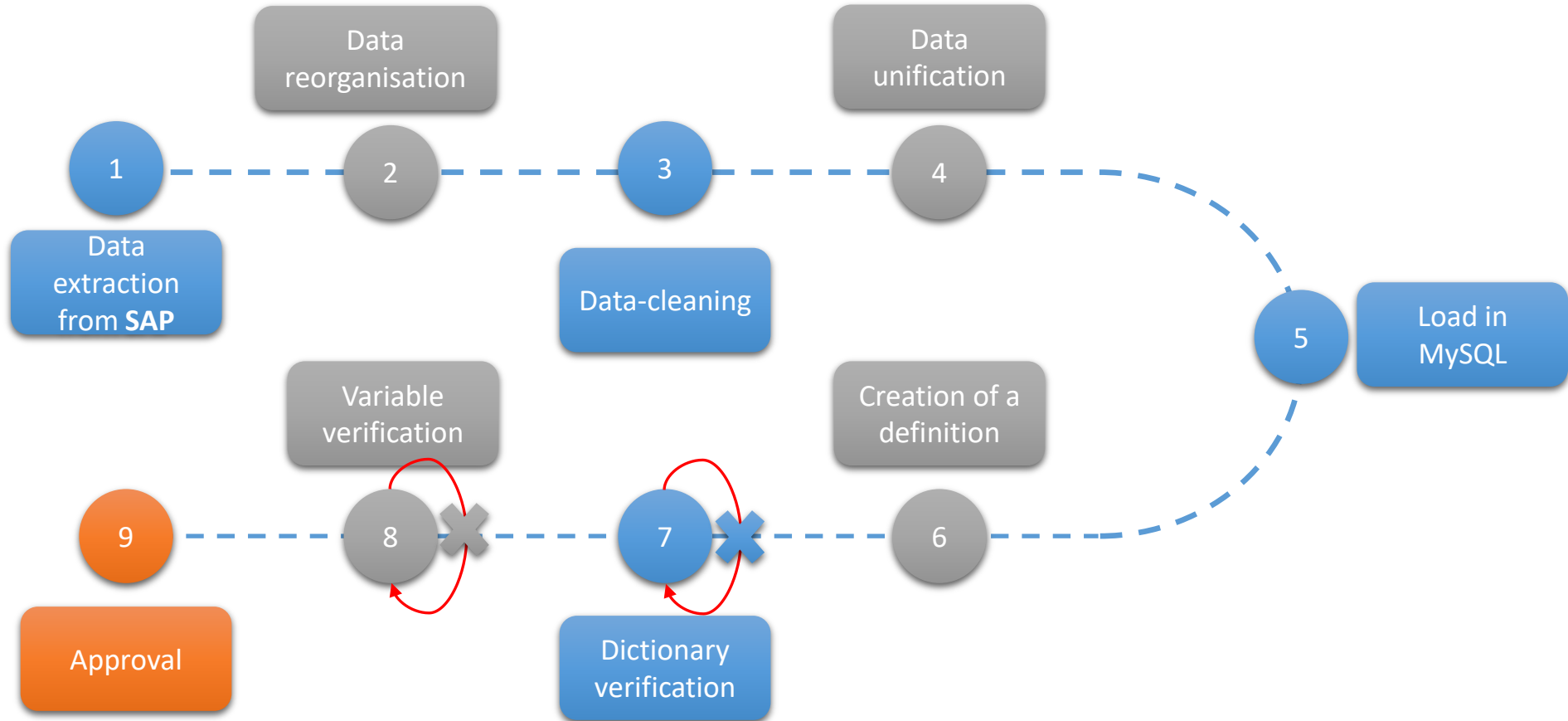
See Online/Comment
[https://doi.org/10.1016/S0140-6736\(20\)31274-0](https://doi.org/10.1016/S0140-6736(20)31274-0)

Brigham and Women's Hospital
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Boston, MA, USA

(Prof M R Mehrara MD); Surgisphere Corporation, Chicago, IL, USA (S S Desai MD); University Heart Center, University Hospital Zurich, Zurich, Switzerland (Prof F Ruschitzka MD); Department of Biomedical Engineering, University of Utah, Salt Lake City, UT, USA (A N Patel MD); and HCA Research Institute, Nashville, TN, USA (A N Patel).

Correspondence to:
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and Women's Hospital Heart and
Vascular Center and Harvard
Medical School, Boston,
MA 02115, USA
mmehta@bwh.harvard.edu

Data circuit



SILD_03_28_02V2 - Power BI Desktop

Inicio sesión

Archivo Inicio Insertar Modelado Ver Ayuda Formato Datos y detalles Herramientas de tablas Herramientas de columnas

Nombre: id Formato: Número entero Resumen: No resumir Categoría de datos: Sin clasificar

Tipo de datos: Número entero

Estructura Formato Propiedades

Seleccione o arrastre campos para rellenar este objeto visual.

Visualizaciones Campos

Buscar

01 Adminis

Habitaciones sala

Habitaciones UCI

Identificadores del p...

id

NHC

Ingreso

02 Epidem

03 AntPersonales

04 RegClin

05 Analíticas esp...

05 Bioquímica D0...

06 Hematología

07 Micro

08 Tratamientos

09 Pronost

10 Filtros

Página 1

Página 1 de 1

Actualización disponible (clic para descargarla)



MANAGEMENT

The screenshot shows the SPSS Statistics software interface. The main window displays a data view with columns for 'N', 'C', 'D', 'E', 'F', 'G', 'H', 'I', 'J', 'K', 'L', 'M', 'N', 'O', 'P', 'Q', 'R', 'S', 'T', 'U', 'V', 'W', 'X', 'Y', 'Z'. A large red oval with the word 'RESEARCH' is overlaid on the data. The top menu bar includes 'SPSS Statistics', 'Archivo', 'Editar', 'Ver', 'Datos', 'Transformar', 'Analizar', 'Marketing directo', 'Gráficos', 'Utilidades', 'Ampliaciones', 'Ayuda'. The status bar at the bottom shows 'Vista de datos' and 'Vista de variables'.

The screenshot displays the Microsoft Excel interface. The top ribbon shows the 'Inicio' (Home) tab with various formatting options. The main workspace contains a large table of data, likely a dataset for management analysis. A prominent red circle is overlaid on the right side of the image, with the word 'MANAGEMENT' written in large, bold, white capital letters across it. The data table includes columns for dates, times, and various numerical values, with some rows highlighted in yellow. The bottom status bar shows the active cell as 'data for test'.



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EBioMedicine
Published by THE LANCET

Commentary

Artificial intelligence to support clinical decision-making processes



Carolina Garcia-Vidal ^{a,*}, 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

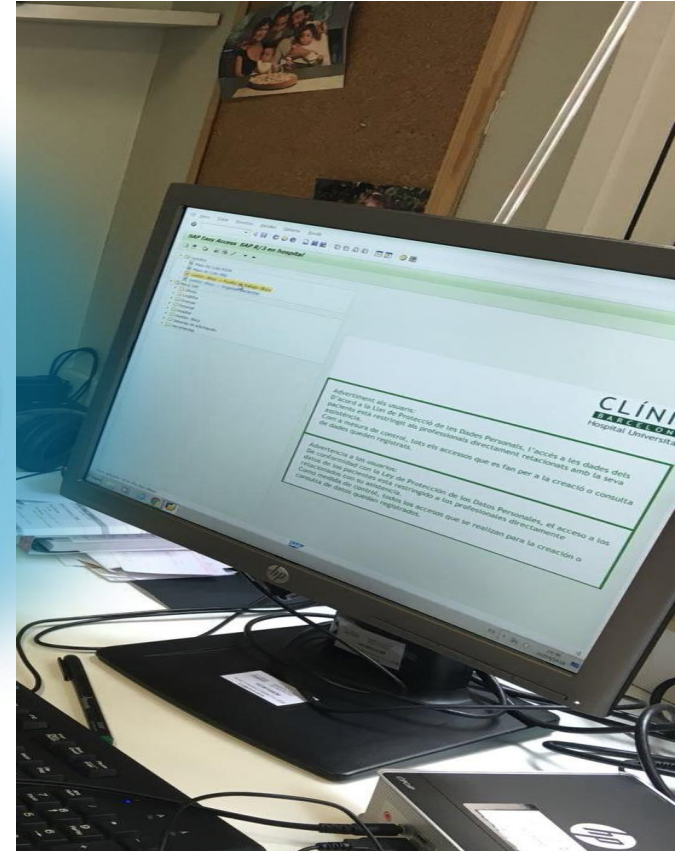
1. Introduction

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.

CAPS



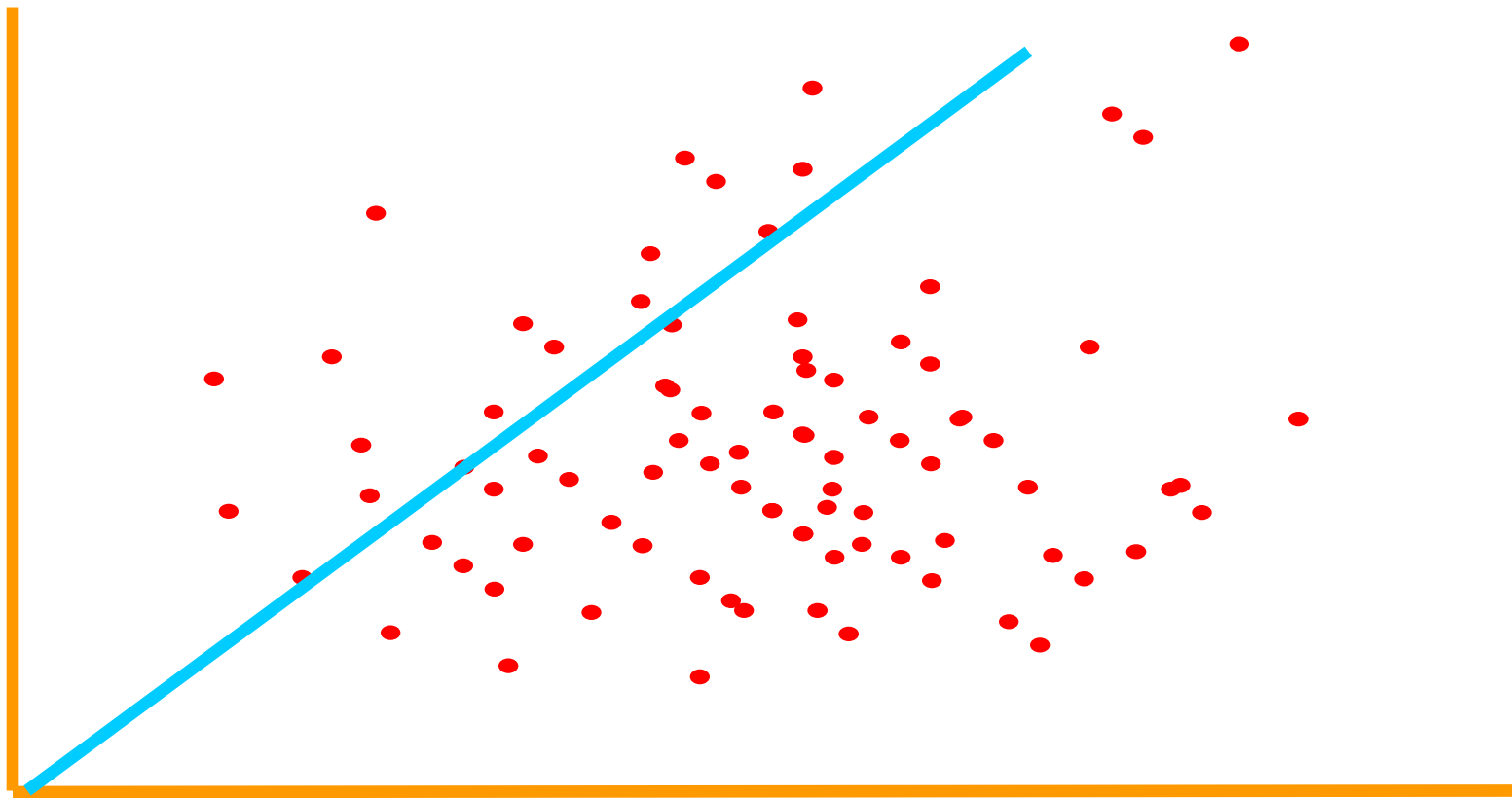


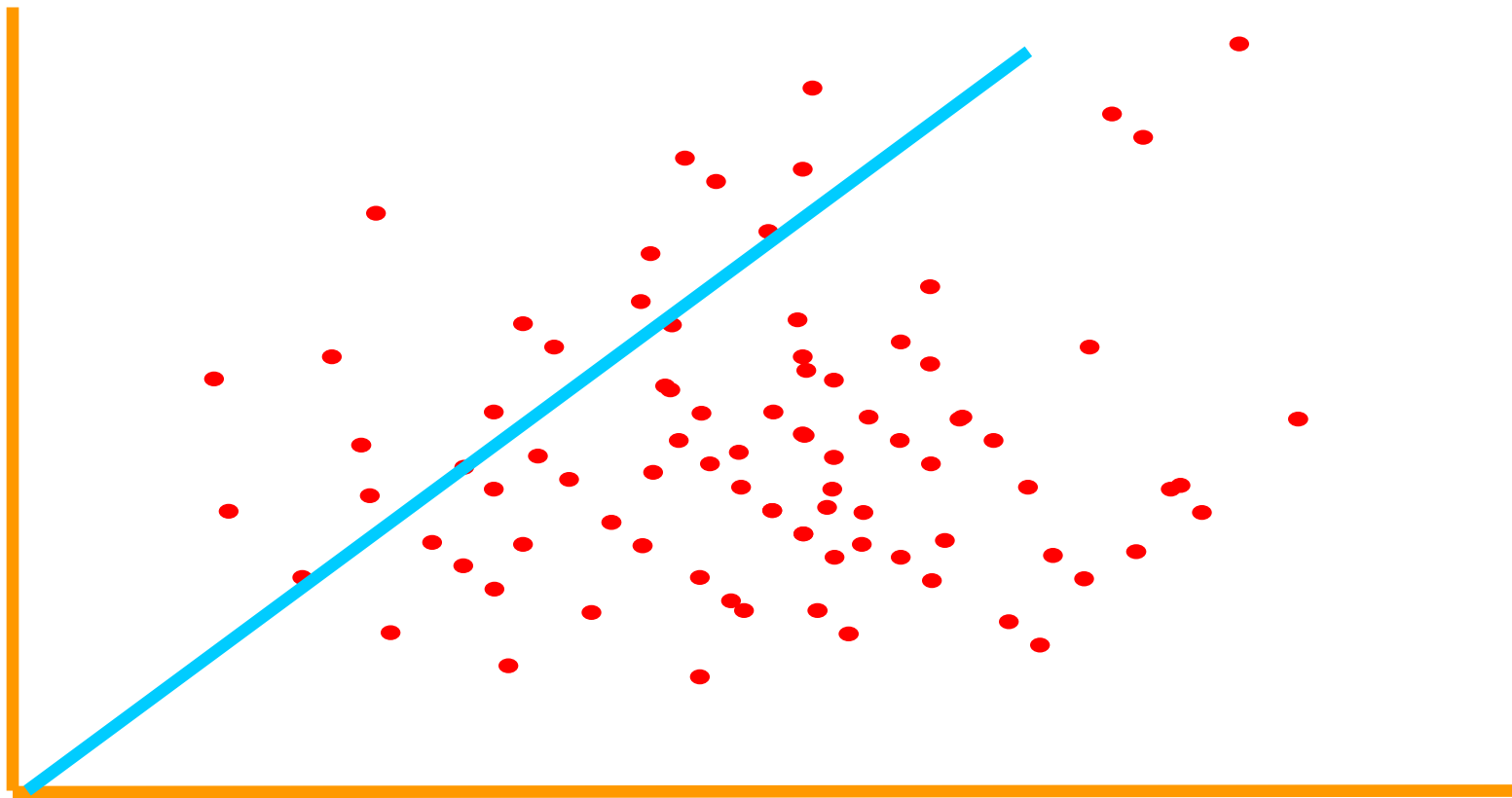
Identification of febrile neutropenia episode

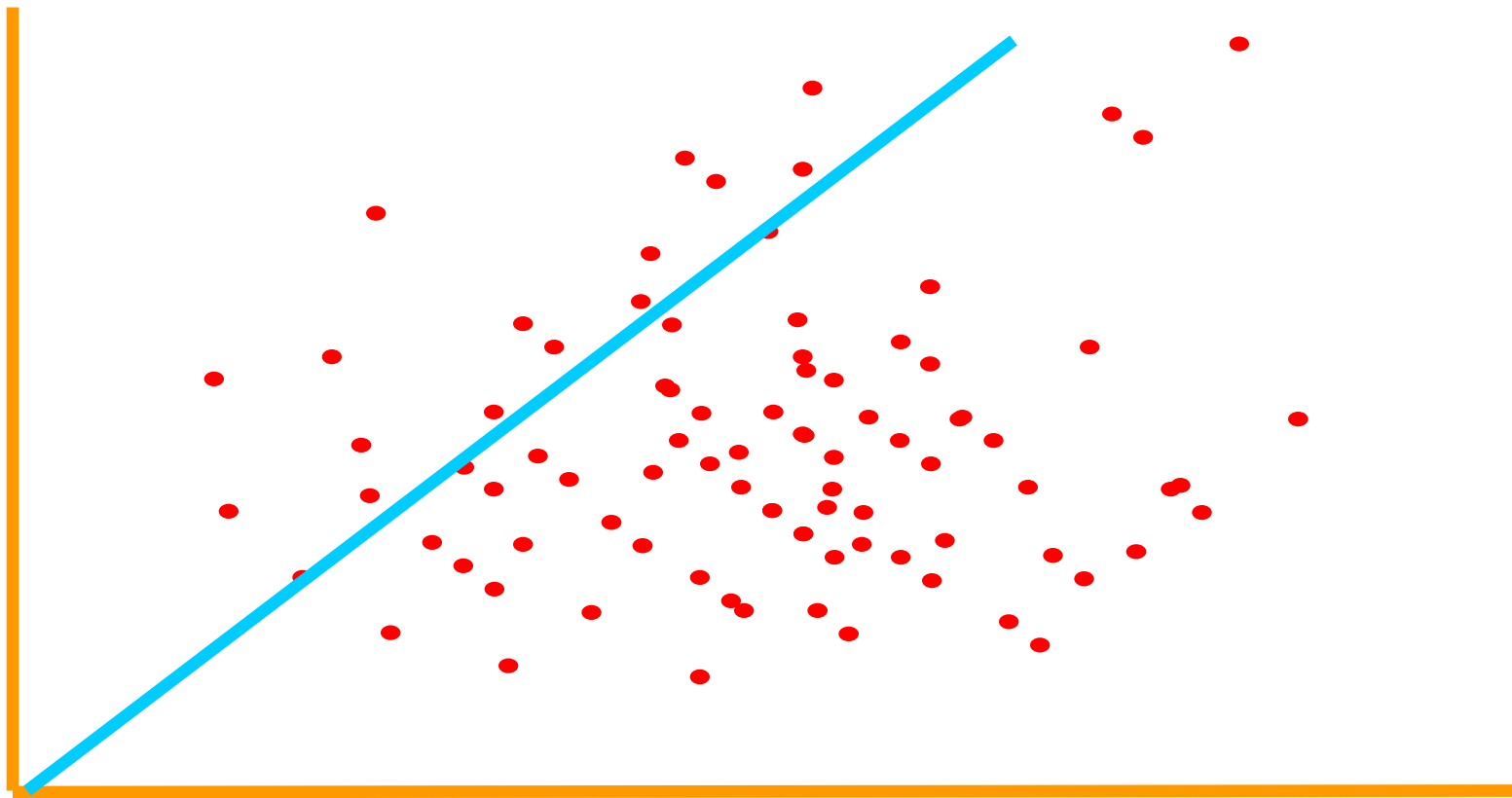
Data retrieved from EHR-> Neuronal network algorithm

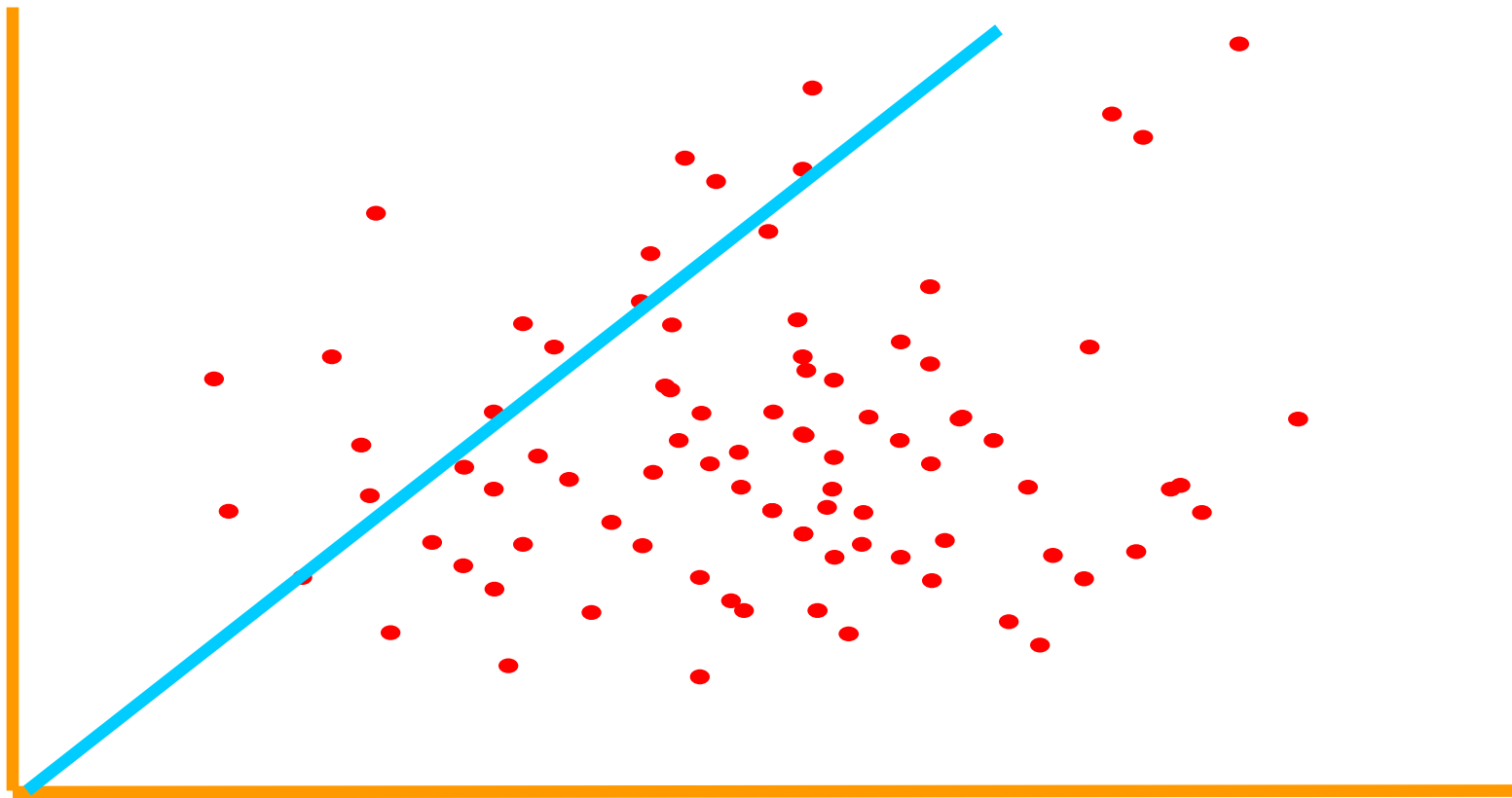
Prediction

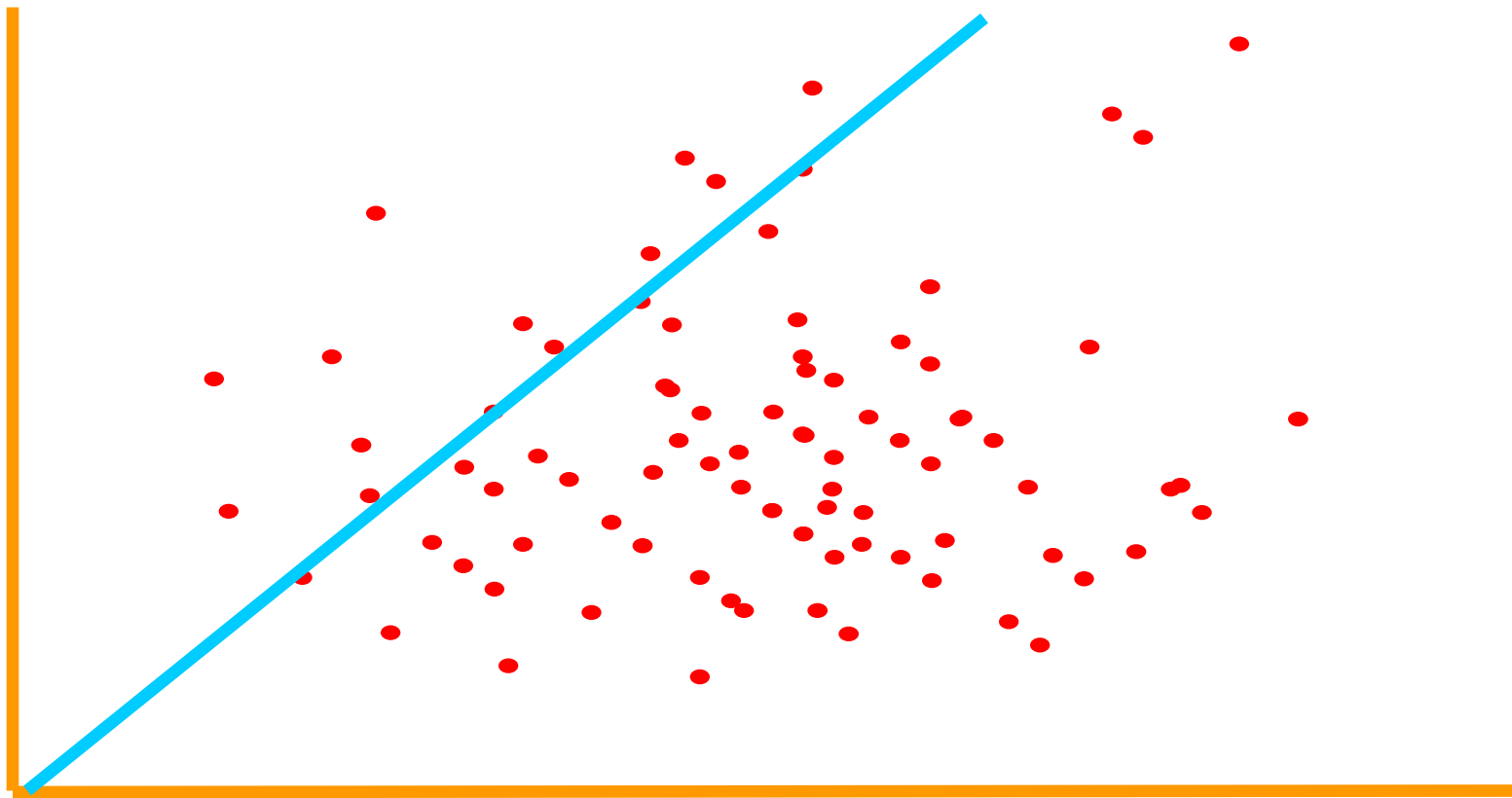
CAPS

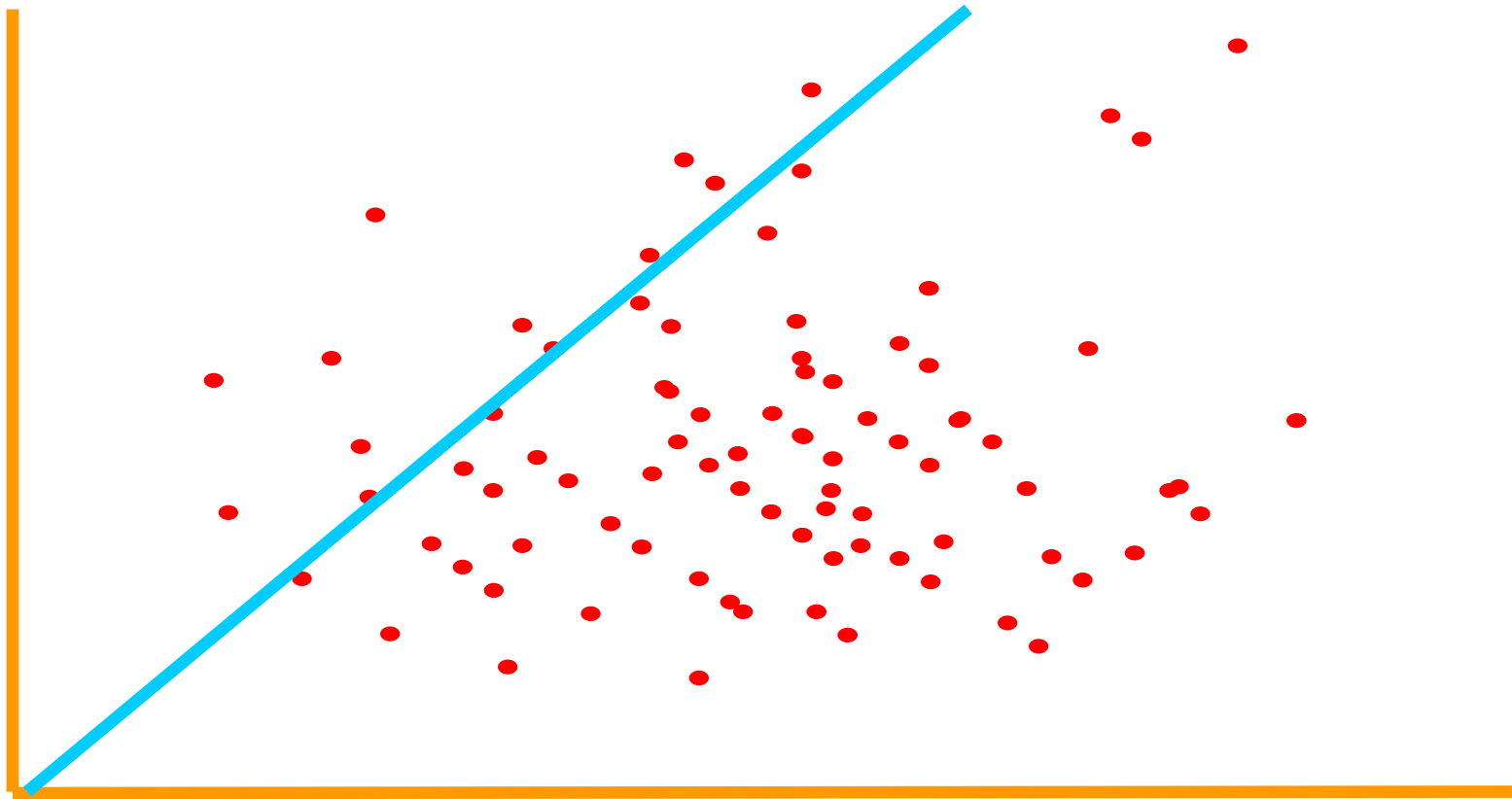


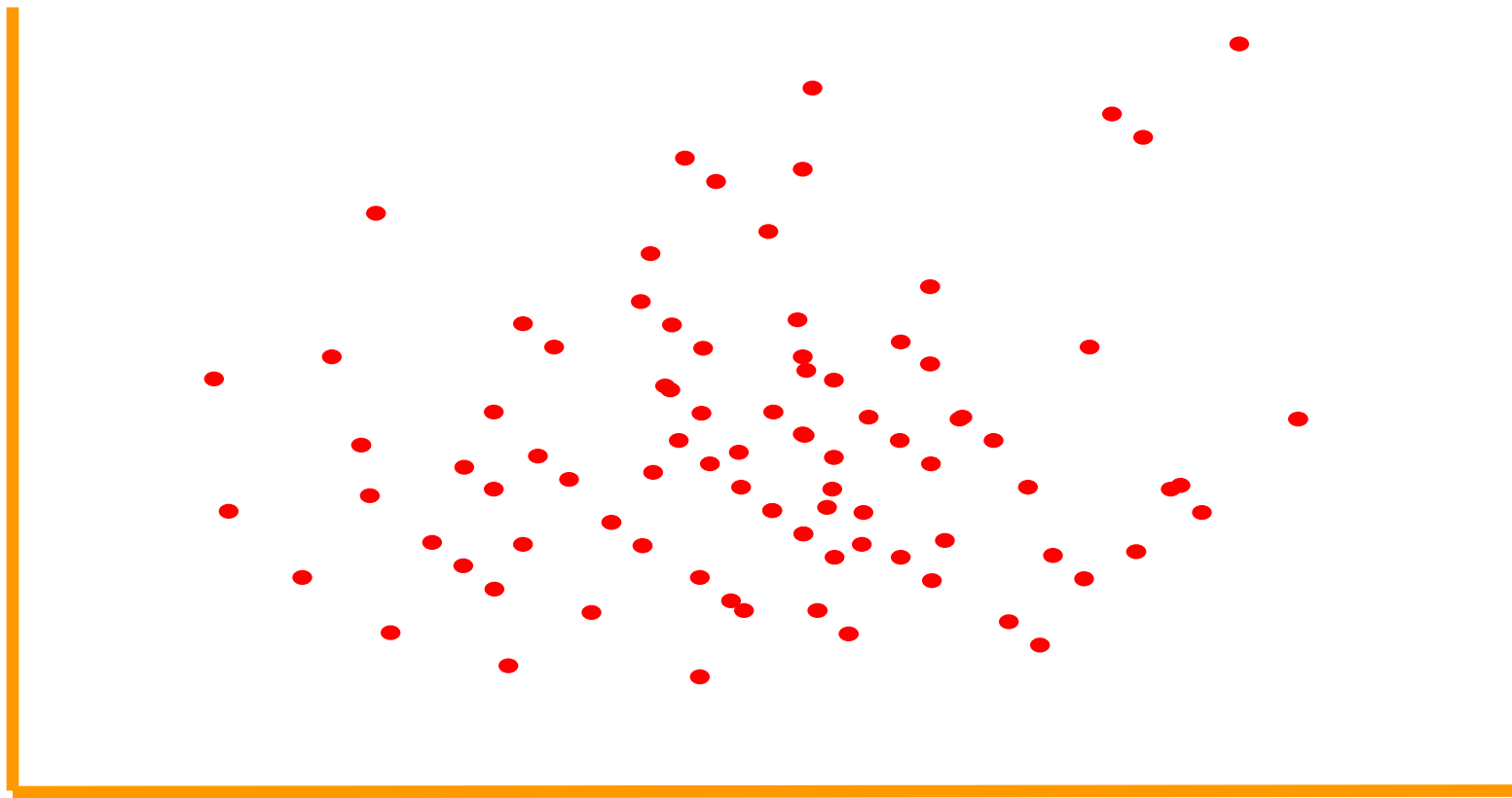


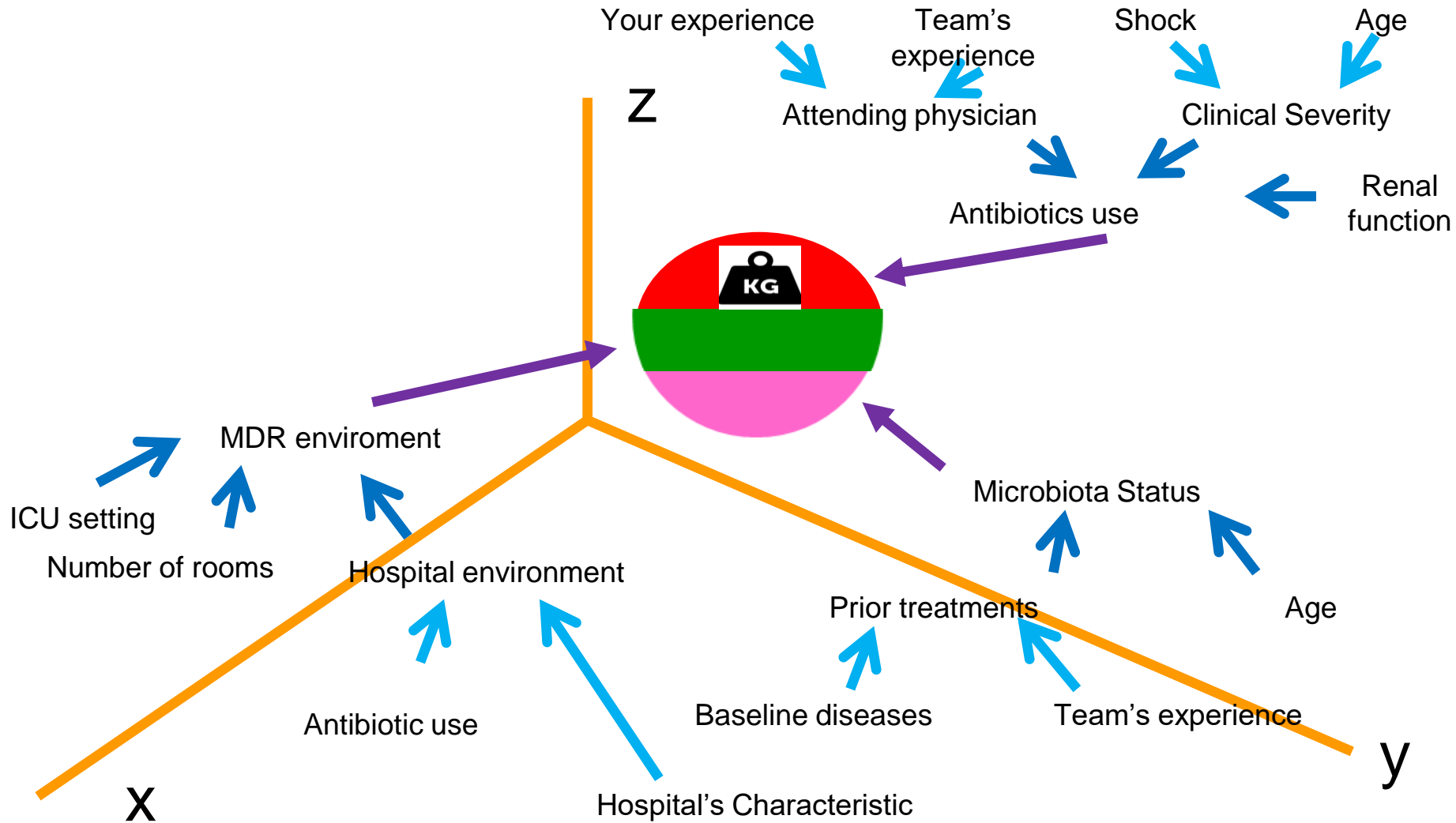


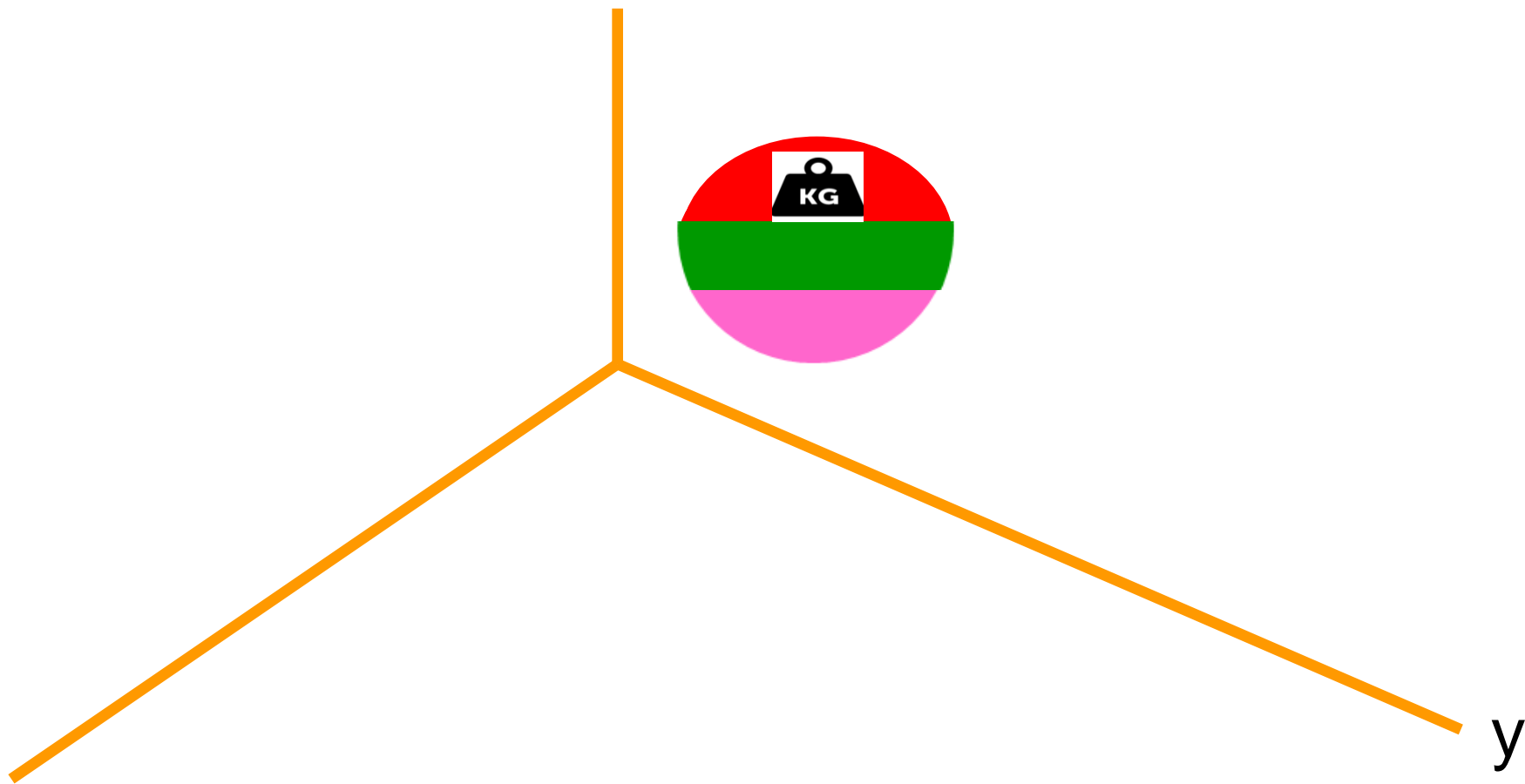




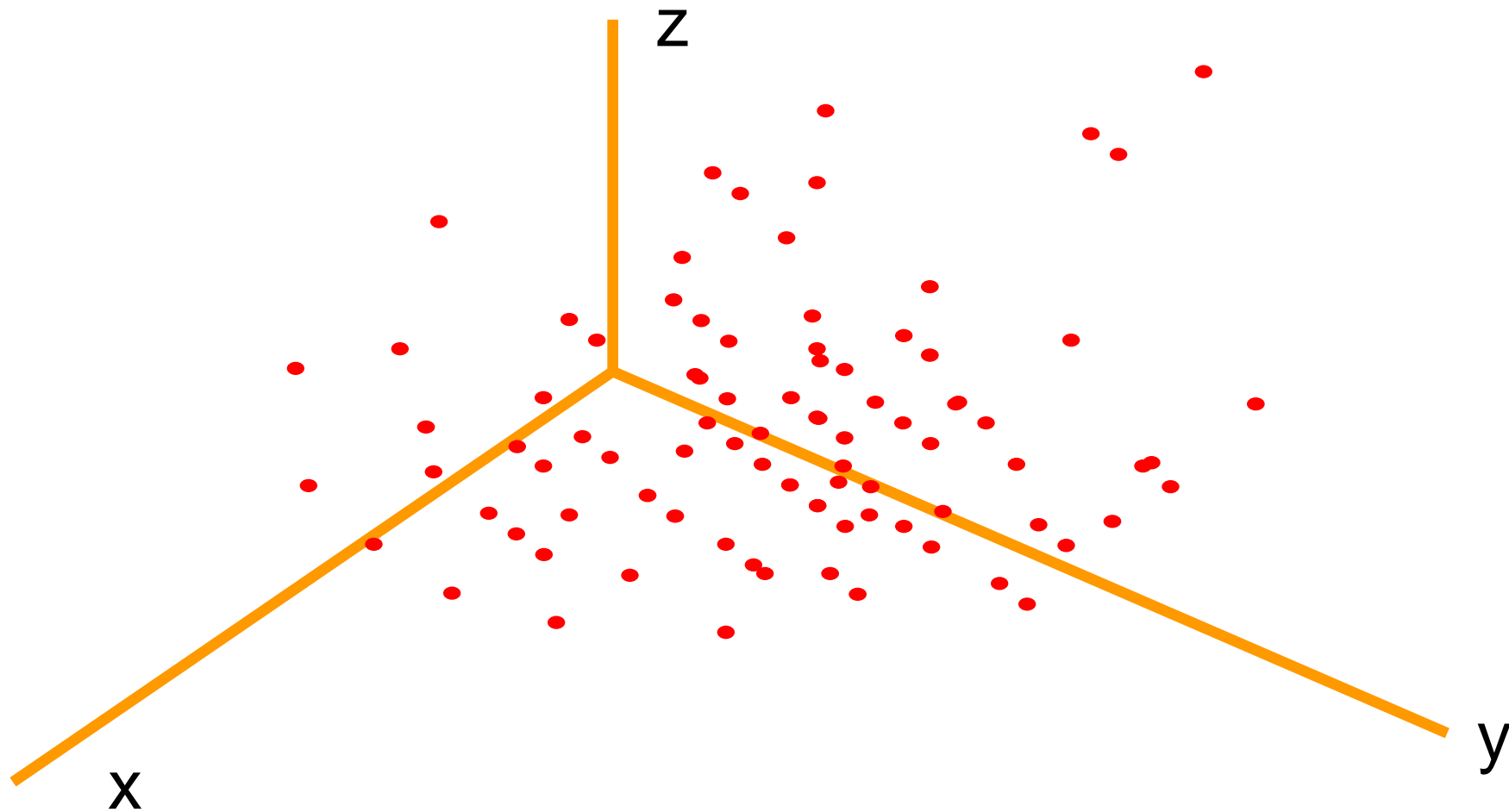


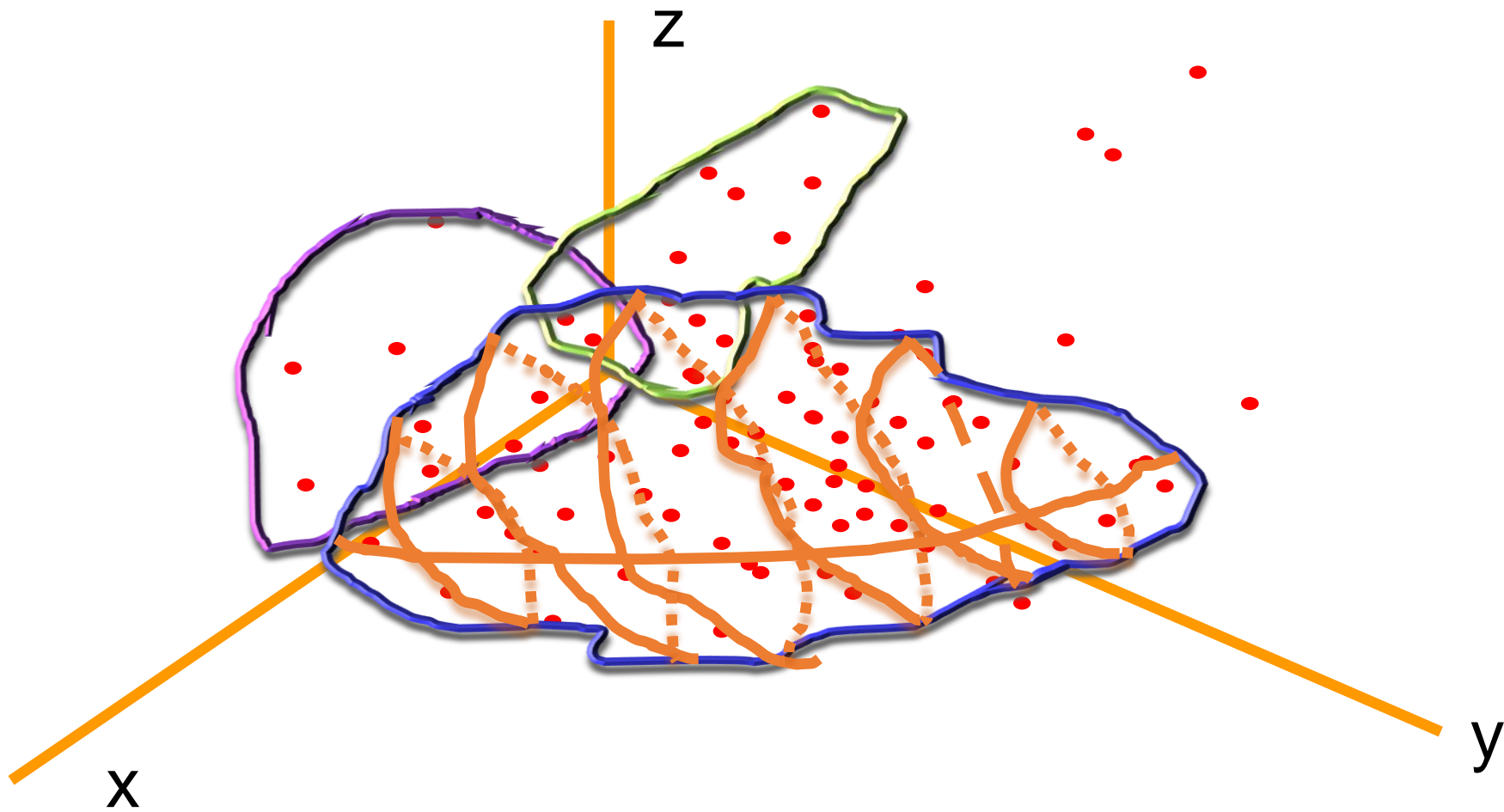






Análisis en tres dimensiones

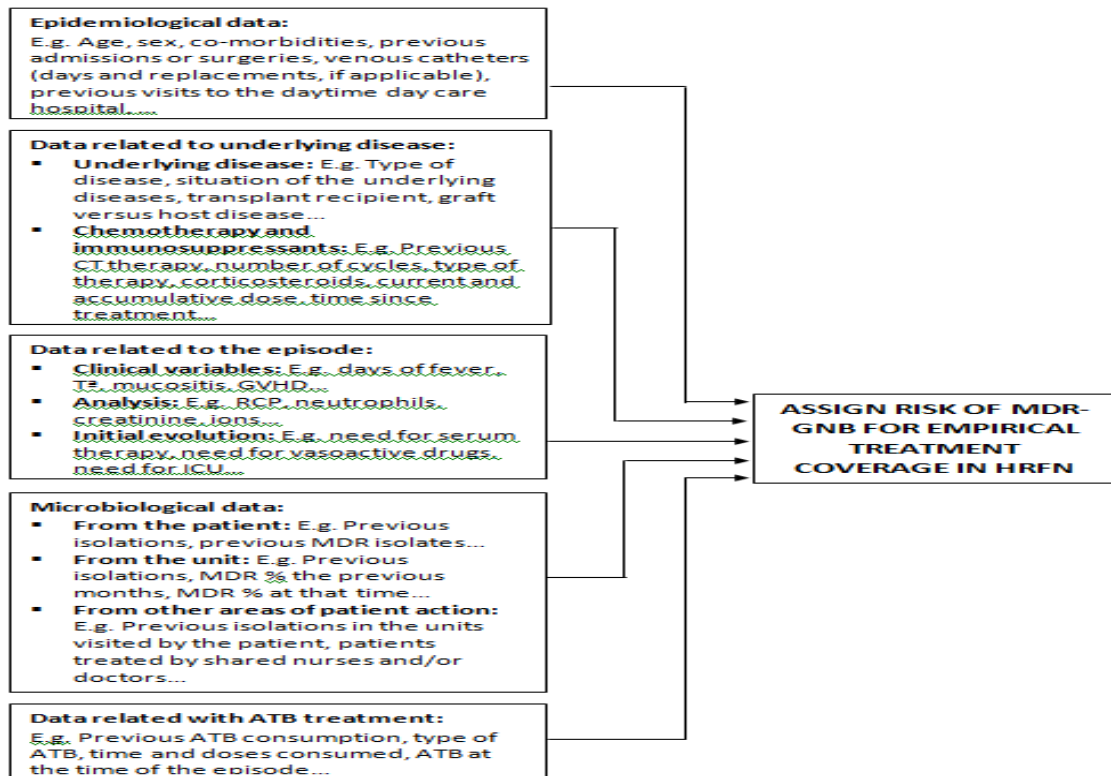




Garcia-Vidal C, et al. Machine learning to assess the risk of multidrug-resistant Gram-negative bacilli infections in febrile neutropenic haematological patients. Infectious Diseases and Therapy, 2021.

7 million pieces of data

Figure 1. Main variables in dataset generation



Garcia-Vidal C, et al. Machine learning to assess the risk of multidrug-resistant Gram-negative 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.

<u>Models</u>	<u>AUC</u>	<u>F1_Score</u>	<u>Sensitivity</u>	<u>Specificity</u>	<u>Negative Predictive Value</u>	<u>Positive Predictive Value</u>
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
Random 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



Identification of febrile neutropenia episode

Data retrieved from EHR-> Neuronal network algorithm

Prediction

Link to -> Treatment recommendation

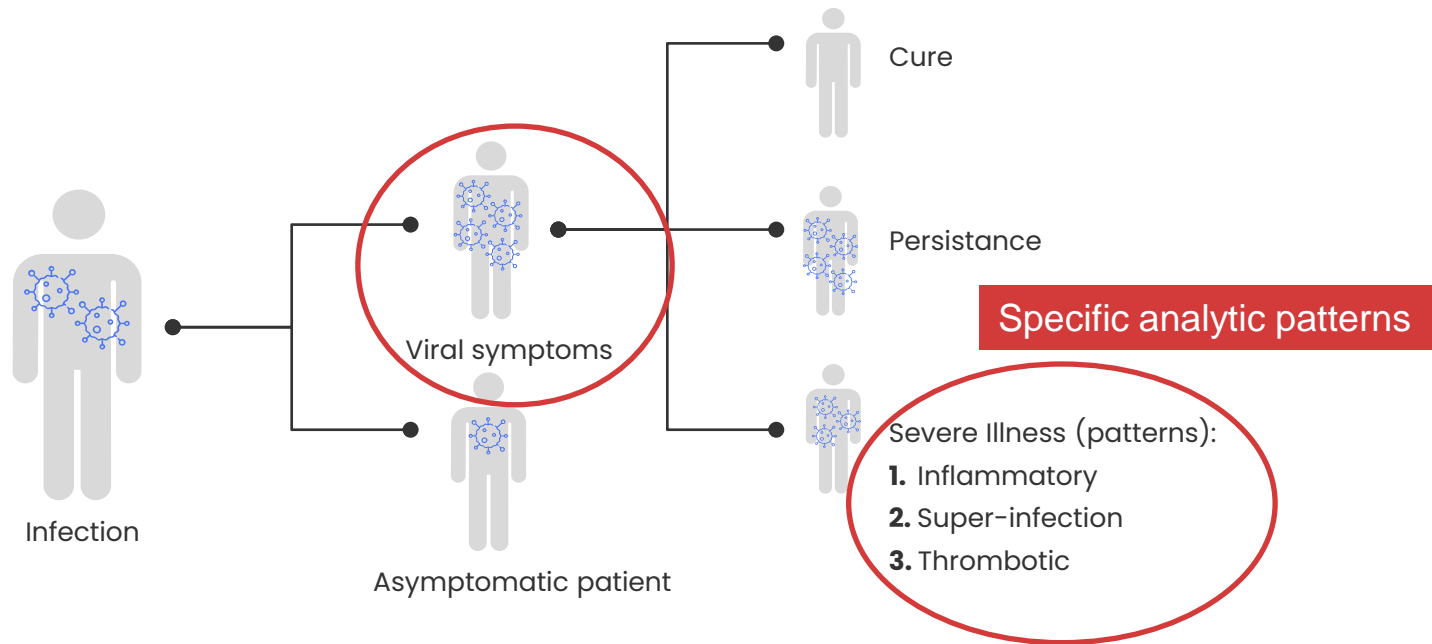
CAPS



[illegible]

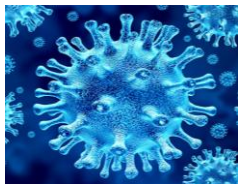
**WE ACHIEVED MORE THAN 3 TRILLION PIECES OF HIGH QUALITY
OF DATA FROM PATIENTS WITH COVID-19 IN FOUR MONTHS**

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



DAY 0

DAY 3-5



Dyspnea, fever, cough, ...



SUBJECTIVE

Day 1

Day 2

OBJECTIVE



Days from
symptoms onset
CT-PCT
Lymphocyte count

C-RP
Ferritin
LDH

Procalcitonin/ Cr
Urinary antigen
Sputum culture

Dimer-D
CT scan
Troponin

Others

Virus

Inflammation

Co-infection

Thrombopathy

Others

Patient 1

x x

x

Patient 2

x

x x

x

Patient 3

x

x

x

...

Remdesivir
Plasma
Monoclonal antibodies
Paxlovid
Molnupinavir

Tocilizumab
Dexametasona
Anakinra
Baricitinib
...

Antibiotics
Antifungals

Anticoagulation

Others

C3

 EN

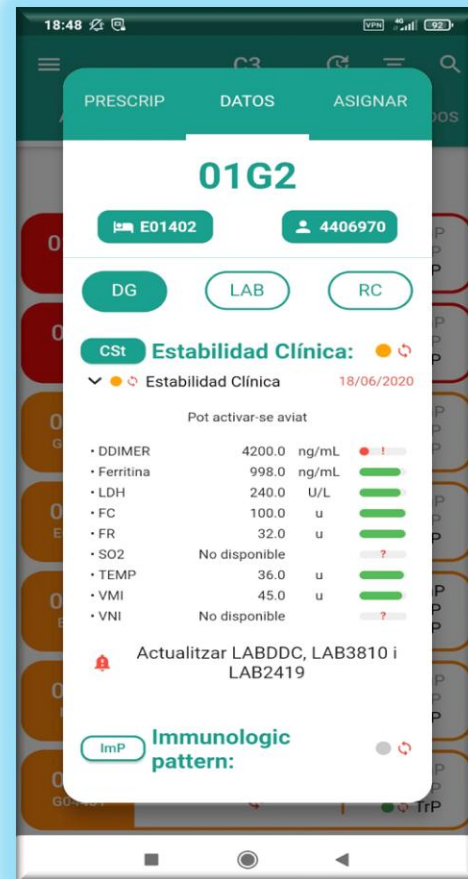
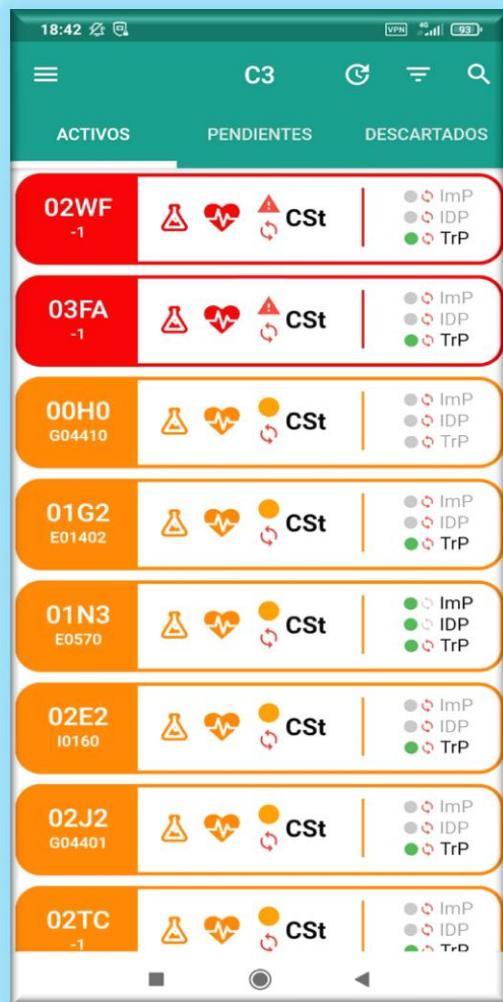
INFORMATION

HOSPITAL STATE	
Active cases	122
- My patients	0
- 🕒 25 days (Detec.)	34
- ⚙️ 25 days (Detec.)	88
Pending cases	0
Rejected cases	25
PHENOTYPE	
[CSt] Clinical Stability	4
[CoIP] Co-infection Pattern	1
[InP] Inflammatory Pattern	4
[TrP] Trombotic Pattern	3
[VP] Viral pattern	0
WARDS	
PLATO	0
General care ward	18
Semi-critical unit	4

Active cases with COVID

3DWA <small>G092121</small>		VP	CoIP	InP	TrP		⬆
3ALB <small>G111012</small>		VP	CoIP	InP	TrP	> G111	⬆
3CCA <small>G111072</small>		VP	CoIP	InP	TrP	> G111	⬆
3CWF <small>I092061</small>		VP	CoIP	InP	TrP	- Empty	⬆
3ER9 <small>I092081</small>		VP	CoIP	InP	TrP	- Empty	⬆
3DM0 <small>I092091</small>		VP	CoIP	InP	TrP	- Empty	⬆
40G1 <small>I092101</small>		VP	CoIP	InP	TrP	- Empty	⬆
41I9 <small>E073013</small>		VP	CoIP	InP	TrP	> E073	⬆
3DM2 <small>G044022</small>		VP	CoIP	InP	TrP	> G044	⬆

🔍 Patient
Last Update: 2021/09/03, 10:05:34



COVID-19 Central Control (C3)



Co-infection



Ready for hospital discharge!

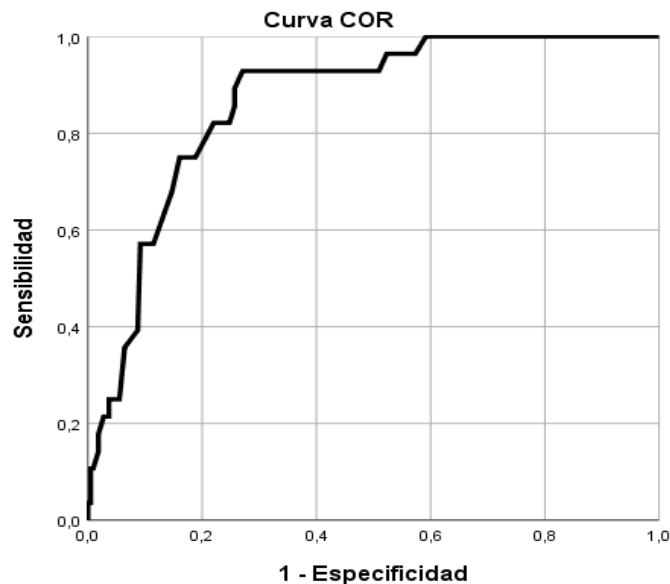


Patients with suspicion of thrombotic diseases



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.

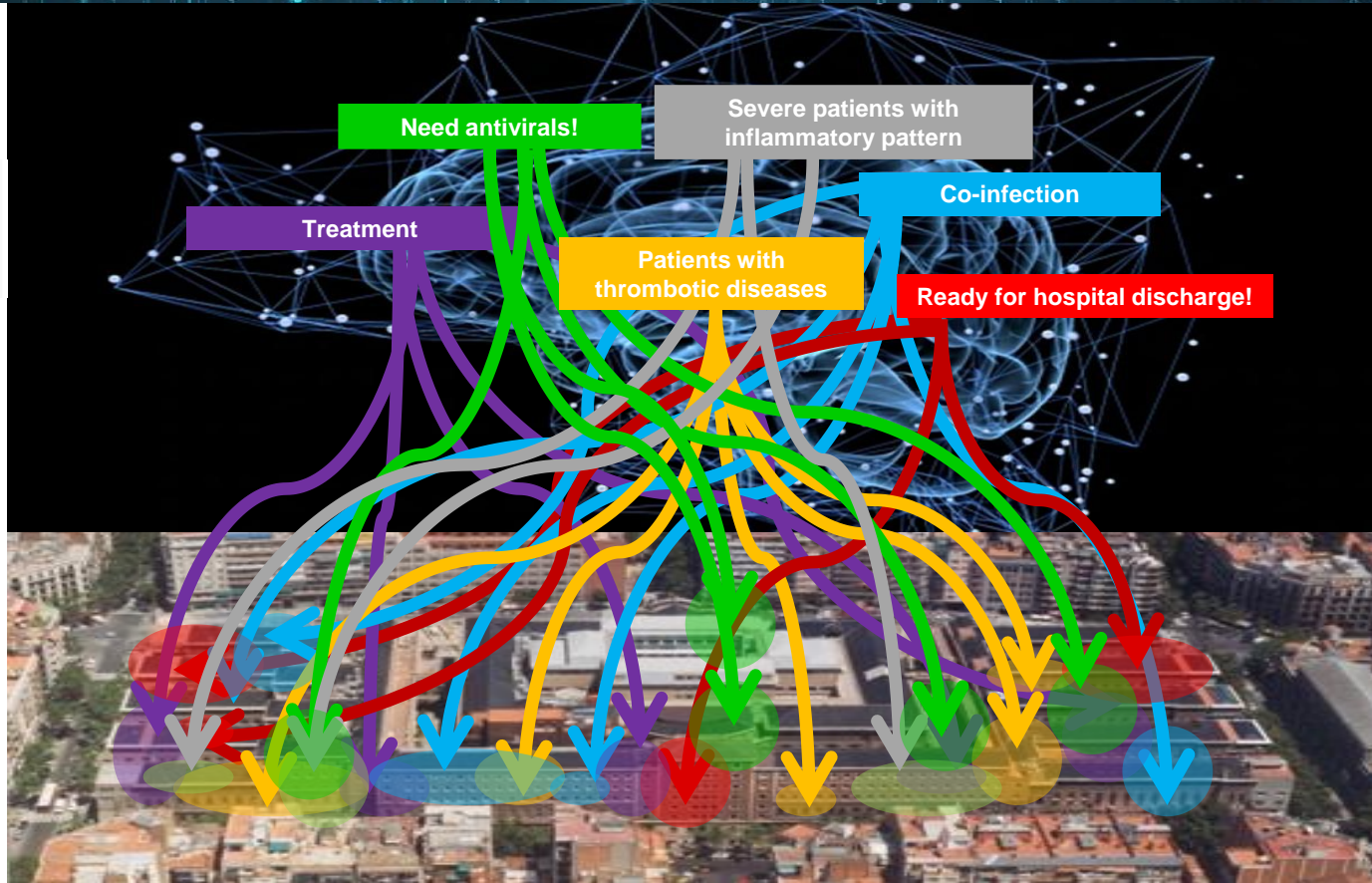
➡ Multivariate analyses showed that **personalized therapy** was independently associated with **decreased early mortality** (OR 0.144; 95% confidence interval [CI], 0.03–0.686; $p=0.015$).

➡ **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)



CLÍNICA
BARCELONA
Hospital Universitari

 **MútuaTerrassa**

 **Hospital Plató**


Germans Trias i Pujol
Hospital
Institut Català de la Salut

Erasmus MC
University Medical Center Rotterdam


 **UZ LEUVEN**

Visualizing K-Means Clustering

January 19, 2014

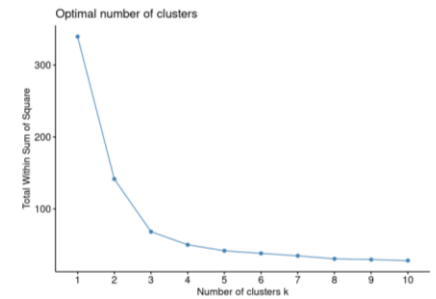
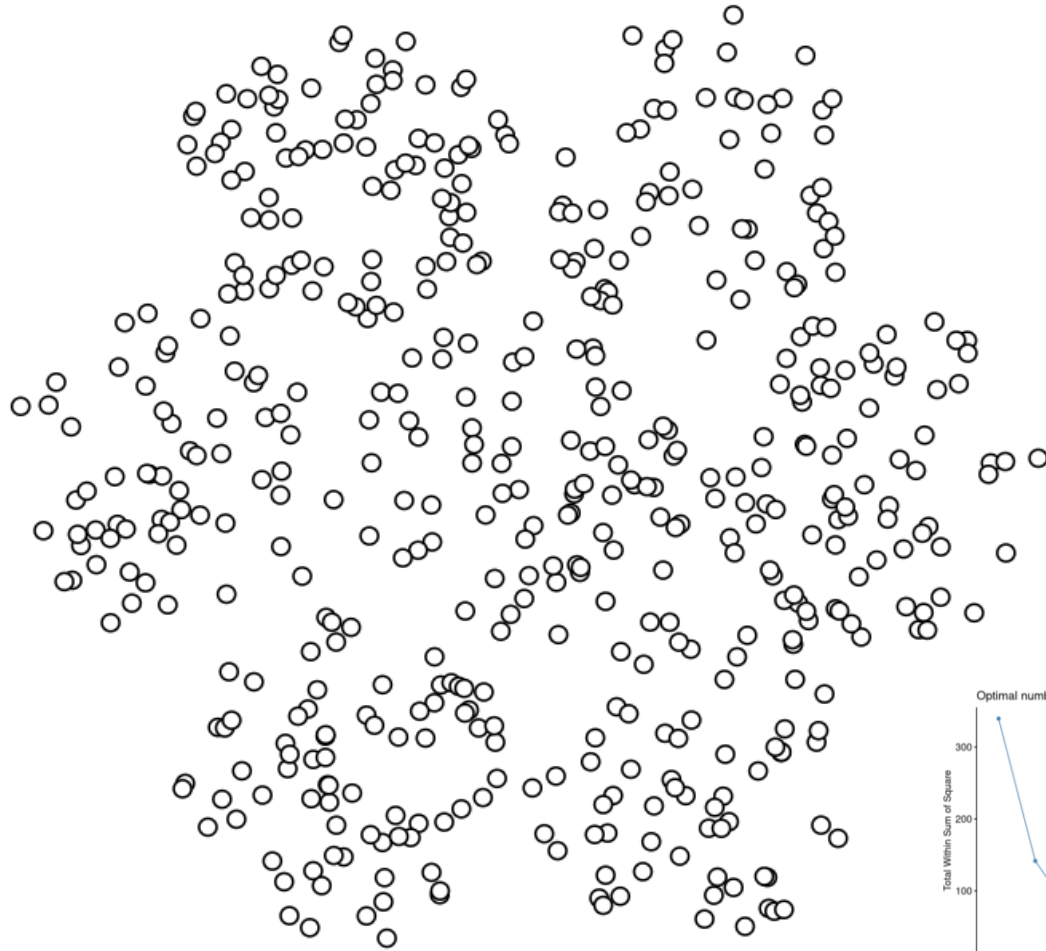
Suppose you plotted the screen width and height of all the devices accessing this website. You'd probably find that the points form three clumps: one clump with small dimensions, (smartphones), one with moderate dimensions, (tablets), and one with large dimensions, (laptops and desktops). Getting an 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



Data provided by the author for educational purposes.

How to pick the initial centroids?

I'll Choose

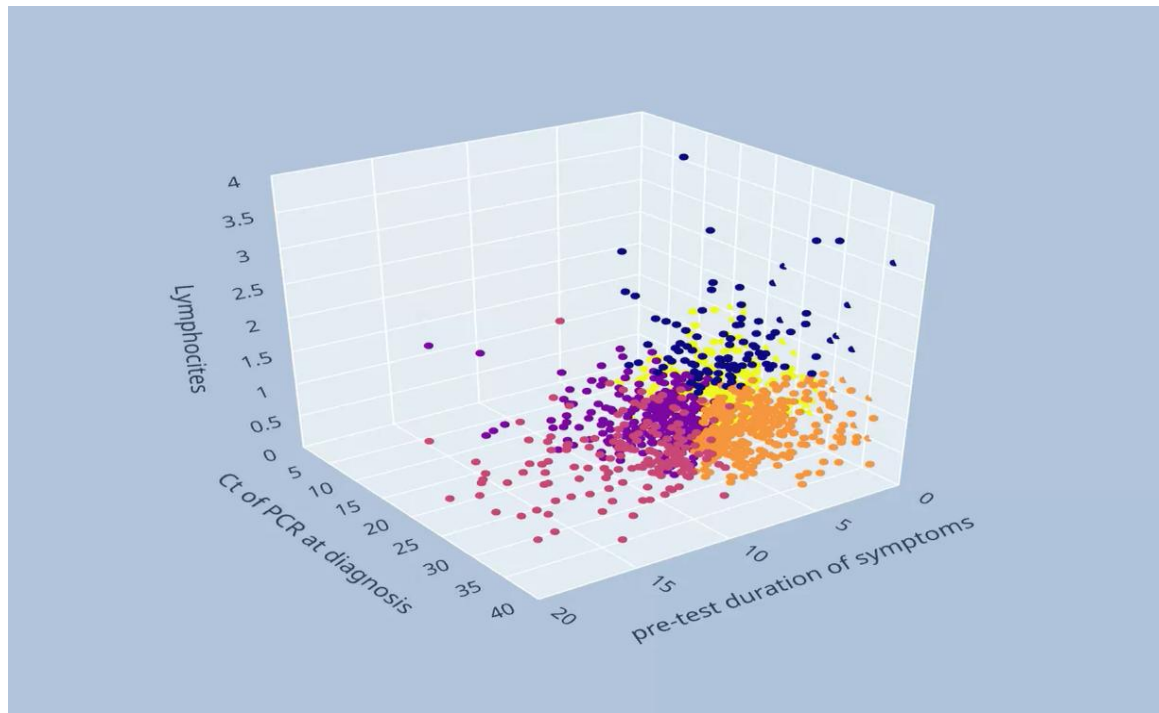
Randomly

Farthest Point

Restart

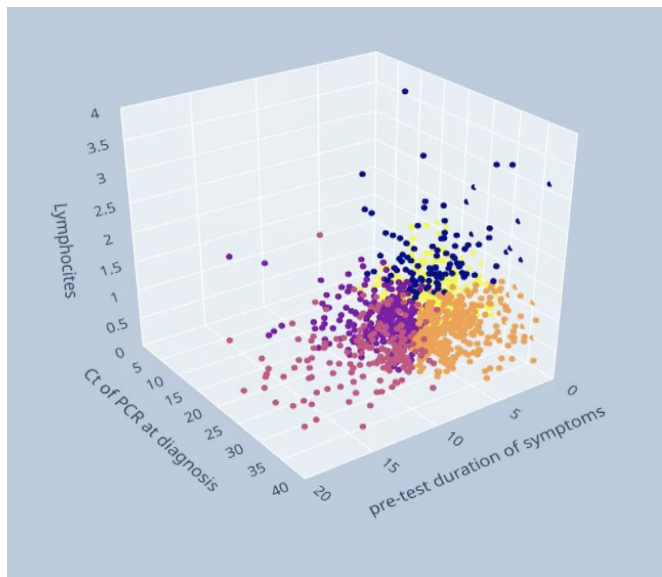
K-Means Algorithm

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

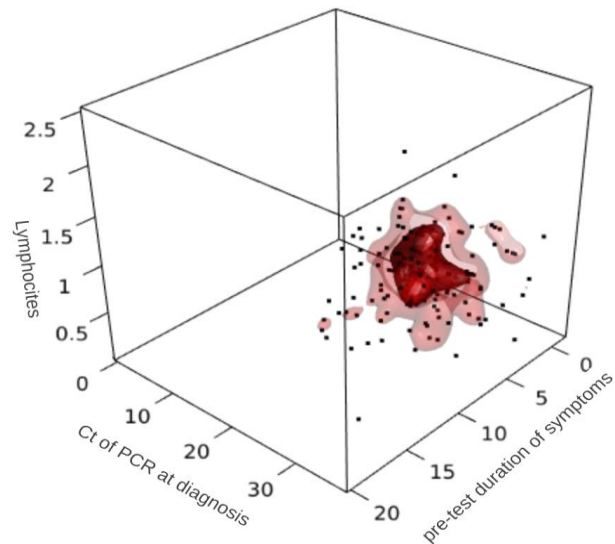


Data provided by the author for educational purposes.

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



Clusters



Mortality

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	0	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

Antimicrobial book



IOS



ANDROID

16:28



Guía Mensa



Antimicrobianos



Microorganismos



Síndromes



Prevención



Utilidades

★ Favoritos

Última actualización: 23 ene 2023

16:28



Utilidades

Calculadoras

Scores

Tablas

Calculadoras

Agua corporal total >

Anión gap >

Calcio corregido por albúmina o proteínas >

Concentración sérica de un β -lactámico administrado en "bolus", infusión extendida o infusión continua >

Déficit de agua libre >

Excreción fraccional de sodio >

Filtrado glomerular (Cockcroft-Gault) >

Filtrado glomerular estimado (MDRD) >

16:29



Administración de antibiót...

C_{min} (valle): **3 mg/L**
(antibiótico libre)
% tiempo > CIM: **74 %**



■ Antibiótico

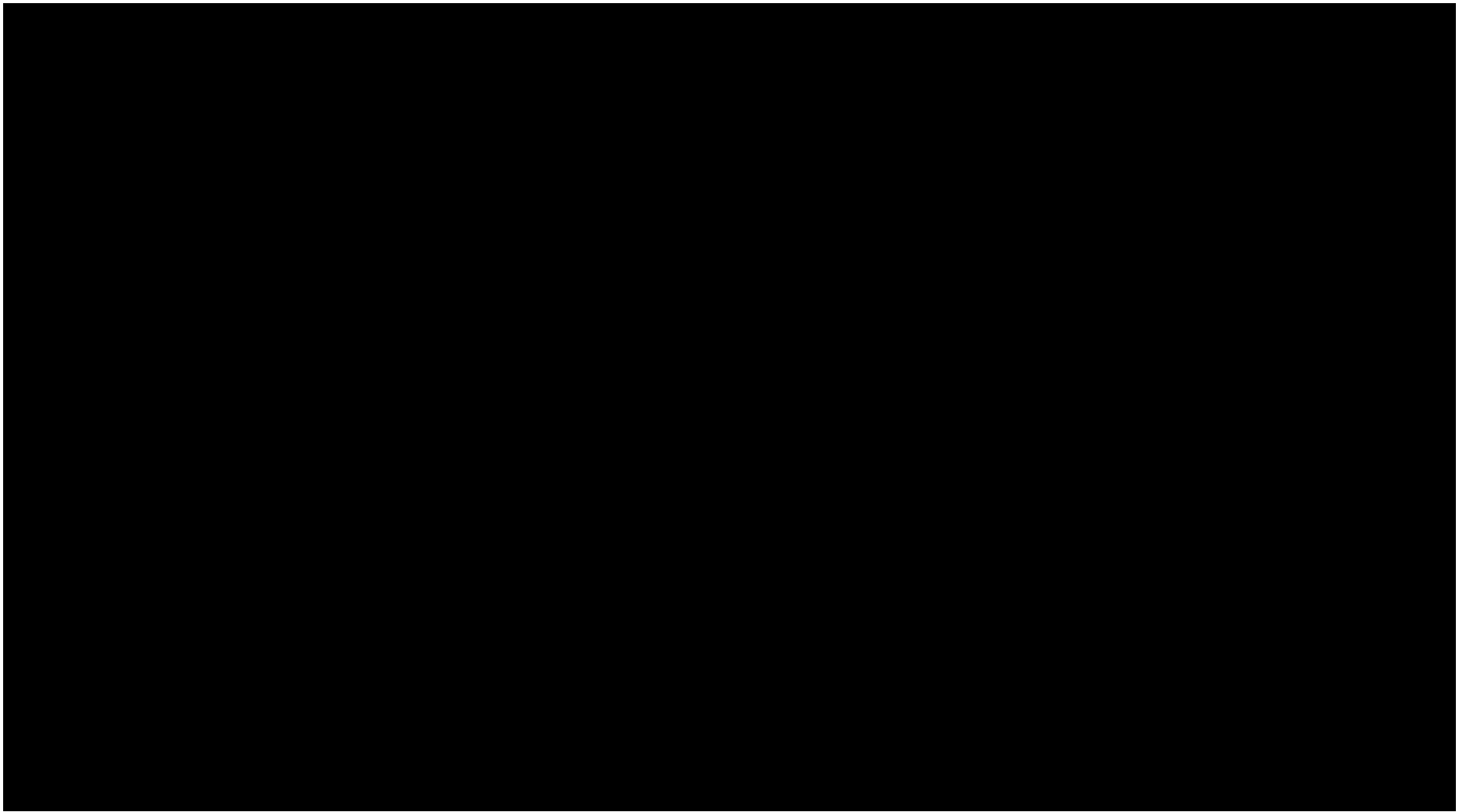
Amoxicilina >

■ CIM **8 mg/L**■ Dosis **2 g**■ Tiempo de infusión **2 h**

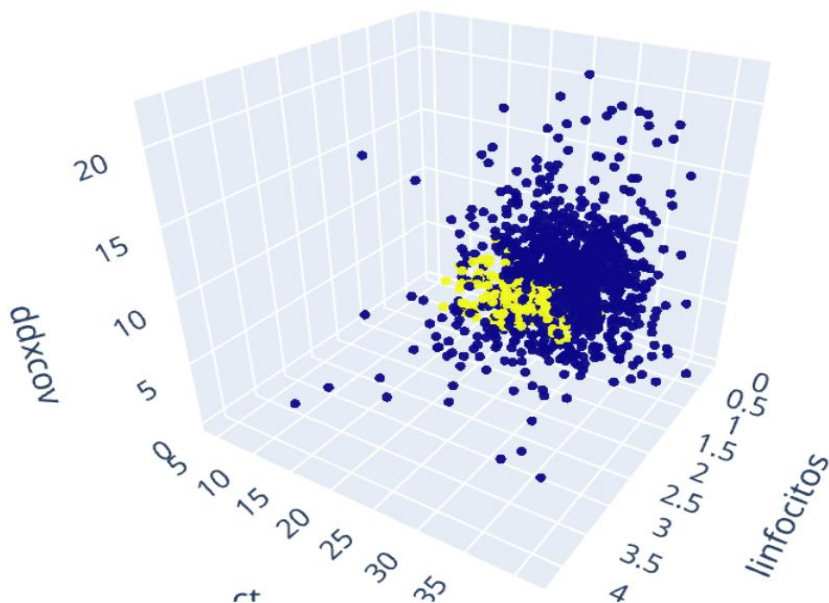
■ Intervalo de administración

4 h 6 h 8 h 12 h 24 h

■ Peso **61 kg*** Vd normal: **0,30 L/kg** - +



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



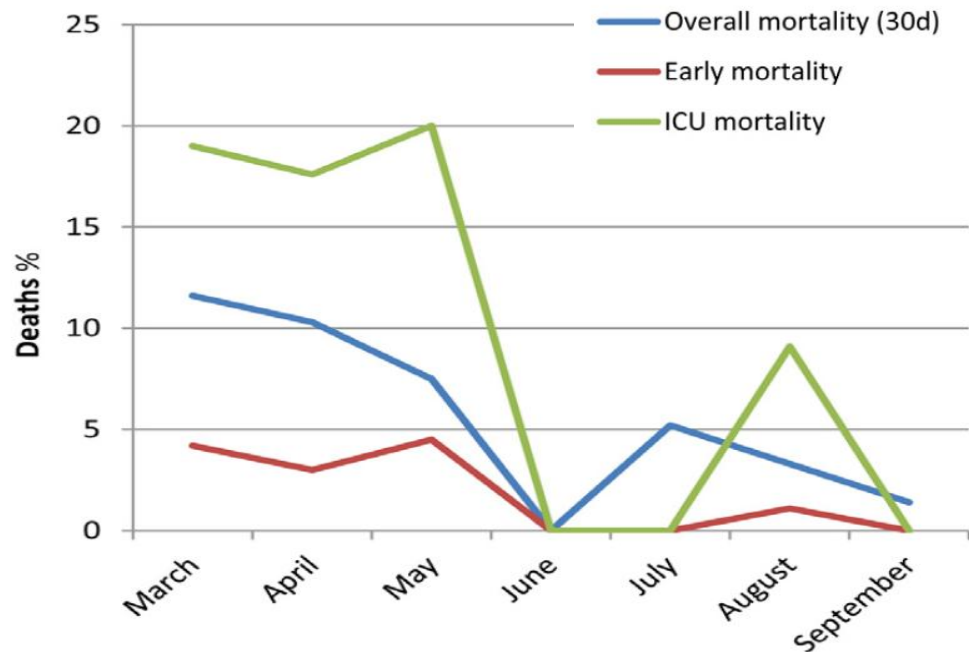
Derivation cohort

	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



Overall mortality decreased from 11.6% in the first month to 1.4% in the last month, reflecting a progressive, significant downward trend (p for trend <0.001).

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



Thanks for you attention

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