The application of digital health in the diagnosis and management of Gaucher disease

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Disclosures

- Travel, research grants, and honoraria from Sanofi-Genzyme, Takeda, Pfizer
- Advisory board – Takeda, Spur
- The Gaucher Unit receives support from Genzyme/Sanofi for participation in the ICGG Gaucher Registry and from Takeda for the GOS

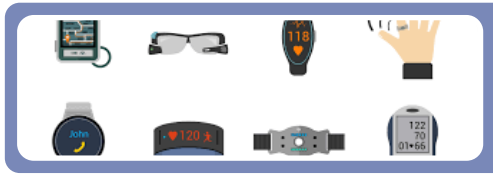
Digital health technologies

Digital technologies aim to enhance the efficiency of healthcare delivery and make medical care more personalized and precise

Telehealth and telemedicine

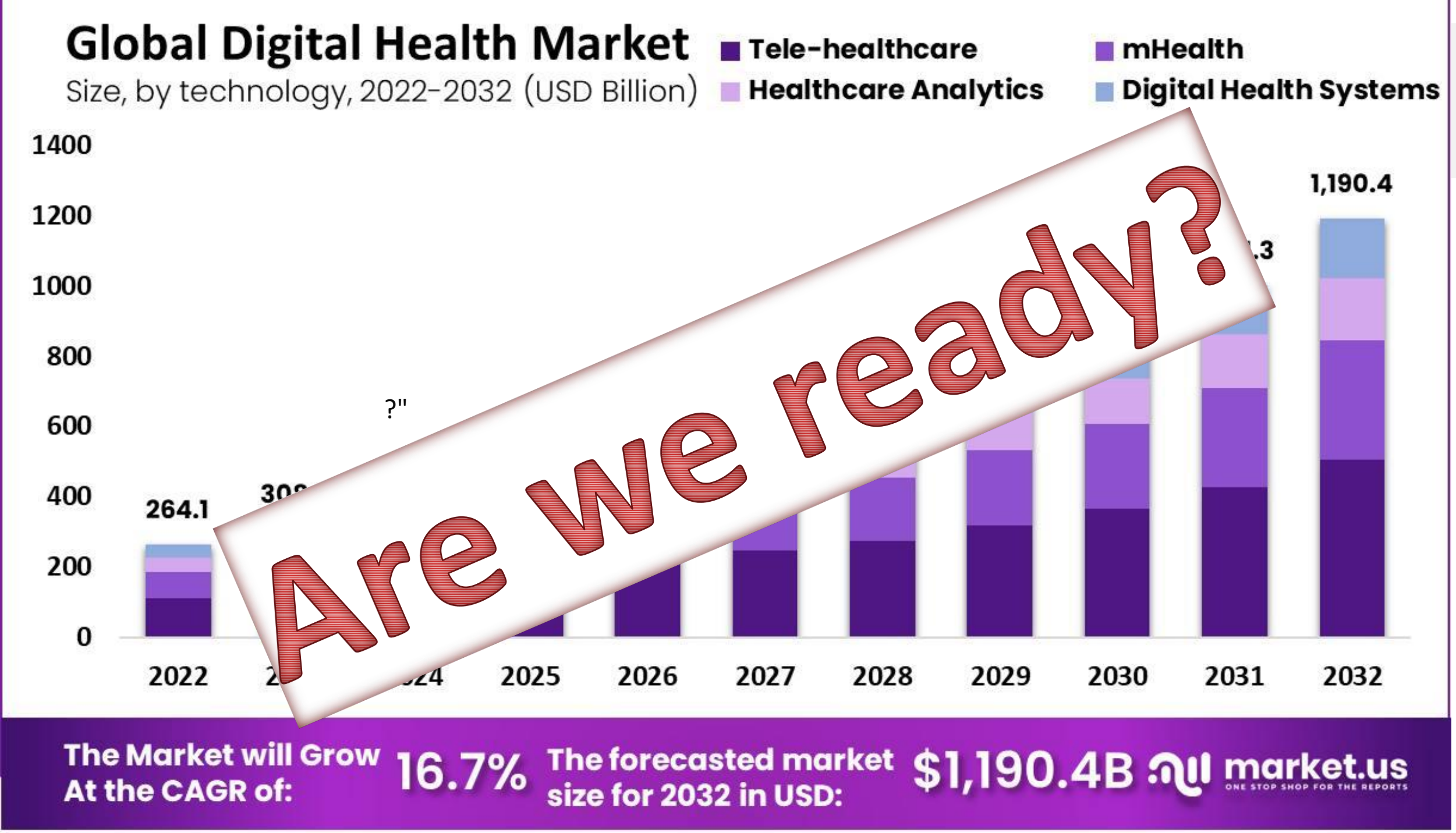
Health information technologies

Mobile health



Wearable devices

Networking


Global Digital Health Market
Size, by technology, 2022-2032 (USD Billion)
Tele-healthcare
mHealth
Healthcare Analytics
Digital Health Systems
1400
1200
1000
800
600
400
200
0
264.1
1,190.4
2022
2025
2026
2027
2028
2029
2030
2031
2032
Are we ready?
The Market will Grow At the CAGR of:
16.7%
The forecasted market size for 2032 in USD:
$1,190.4B
market.us
ONE STOP SHOP FOR THE REPORTS

Top 5 Benefits of Digital Healthcare

Smarter Decisions with Data

Data-driven insights help guide effective treatment choices.

Better Health Outcomes

Real-time monitoring improves patient care and recovery.

Engaged Patients

Health apps keep patients informed and active in care.

Operational Efficiency

Automated systems streamline tasks, saving time and resources.

Cost Savings

There are also concerns around digital health tech...

new tech can be challenging to use

do apps and digital therapies really work?

who has access to my electronic health records and personal data?

is digital health tech properly researched and evaluated?

Getting the need right

”In healthcare, you don’t want to be a technology-driven business; you want to be a needs-based enterprise because healthcare is very slow to change.

Change has to happen from within, as opposed to in the IT world, where it is possible to disrupt established practices simply by coming up with a compelling new technology¨

Rick Altinger, CEO, Glooko Inc.

Glooko_Getting_the_Need_Right_031318.pdf

Unmet needs in Gaucher disease

Improving diagnosis

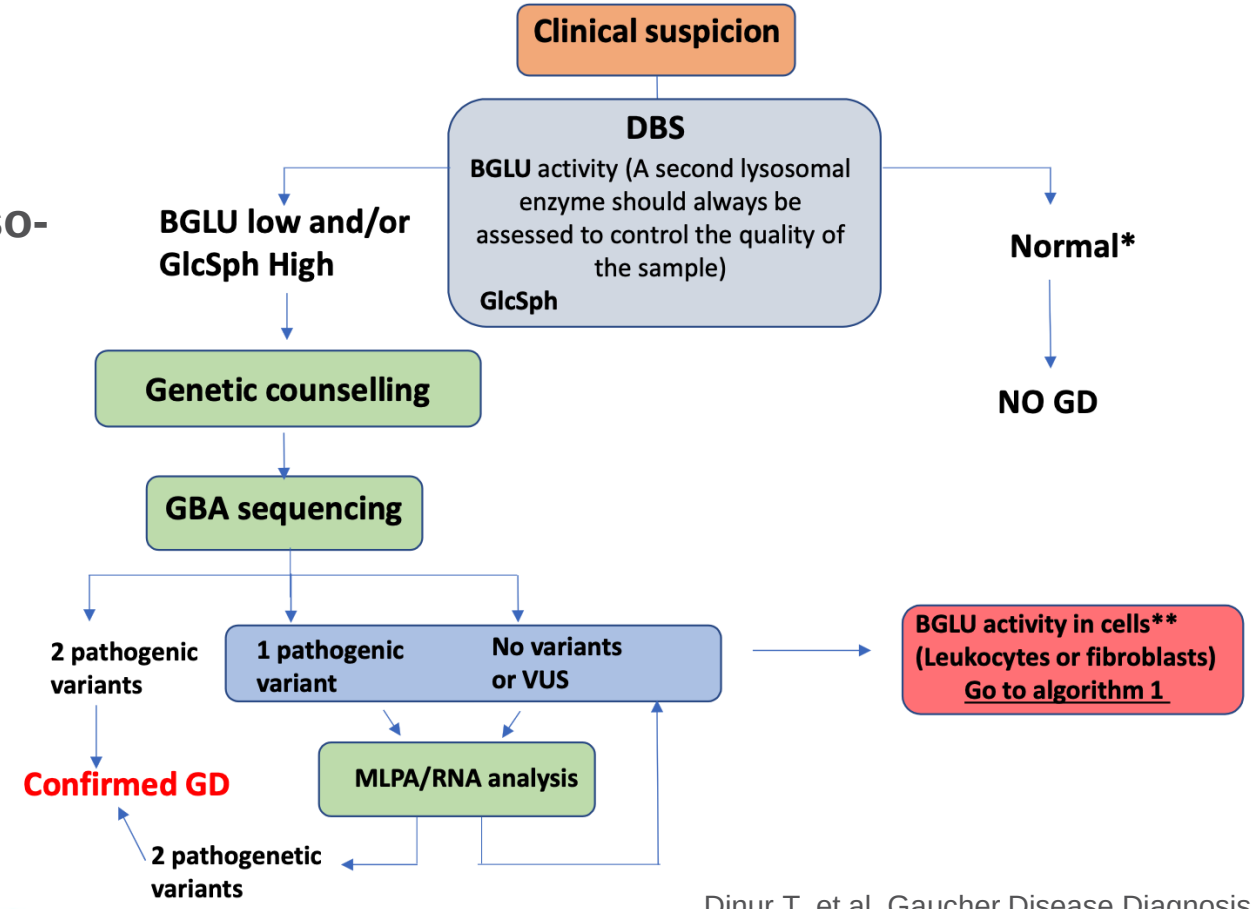
Improving patient care

Improving communication

Diagnosis of Gaucher disease is easy

BGLU – enzyme levels

GlcSph-glycosylsphingosine (Lyso-Gb1)



Dried blood spot (DBS) cards for sample collection[3]

IWGGD The International Working Group on Gaucher Disease

Guideline Activity	Patient centered guidelines for the laboratory diagnosis of Gaucher disease (GD) type 1

Dinur T, et al. Gaucher Disease Diagnosis Using Lyso-Gb1 on Dry Blood Spot Samples: Time to Change the Paradigm? Int J Mol Sci 2022; 23.

Dardis A,, et al. Patient centered guidelines for the laboratory diagnosis of Gaucher disease type 1. Orphanet J Rare Dis 2022; 17: 442.

Misdiagnosis/Delayed diagnosis in GD is a problem

1 in 6 patients were diagnosed **≥ 7 years** after first consulting a doctor (survey of 212 patients)[1]

Up to **8 (mean 3±1.2) different physicians** consulted before final diagnosis (paediatrician, haemato-oncologist, gastroenterologist, geneticist, neurologist)[2]

In the USA, it is estimated that the **currently diagnosed GD patients** (approximately 1800 enrolled in a Gaucher Registry) **account for ≈60% of the total number**[3]

Assuming at least a similar proportion of diagnosed to total GD **we expect 1000-1500 not-yet-diagnosed GD patients in Israel**

Is a prevalence of 1:130,000 in France true?[4]

1. Mehta A, et al. Mol Genet Metab. 2017;122:122–129;
2. Mistry P, et al. Am J Hematol. 2007;82:697–701;
3. Thomas AS, et al. Blood Cells Mol Dis. 2013;50:212–217
4. Camou, et al. Orpha J of Rare Dis. 2025;20:542.

Gaucher disease is a pan ethnic disease (data from newborn screening programs)

Journal of Inherited Metabolic Disease

WILEY

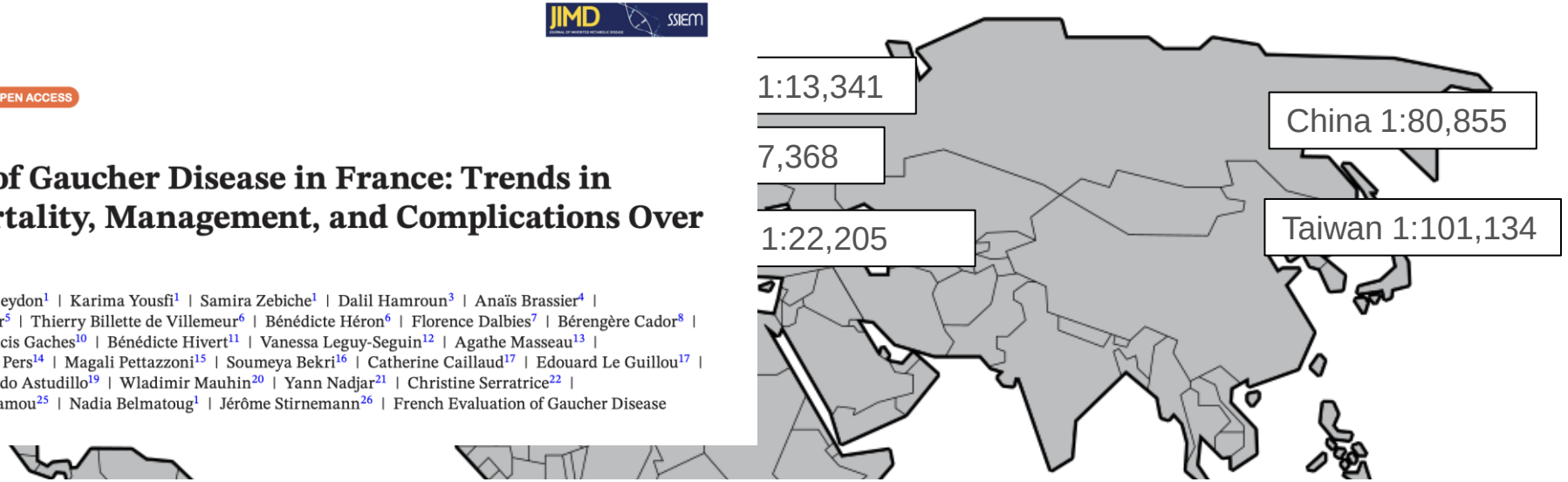
JIMD SSIEM

ORIGINAL ARTICLE OPEN ACCESS

Epidemiology of Gaucher Disease in France: Trends in Incidence, Mortality, Management, and Complications Over Three Decades

Yann Nguyen[1,2] | Maxime Beydon[1] | Karima Yousfi[1] | Samira Zebiche[1] | Dalil Hamroun[3] | Anaïs Brassier[4] | Samia Pichard[4] | Laure Swiader[5] | Thierry Billette de Villemeur[6] | Bénédicte Héron[6] | Florence Dalbies[7] | Bérengère Cador[8] | Anne-Sophie Guemann[9] | Francis Gaches[10] | Bénédicte Hivert[11] | Vanessa Leguy-Seguin[12] | Agathe Masseau[13] | Robin Deshayes[13] | Yves-Marie Pers[14] | Magali Pettazzoni[15] | Soumeya Bekri[16] | Catherine Caillaud[17] | Edouard Le Guillou[17] | Marie Szymanowski[18] | Leonardo Astudillo[19] | Wladimir Mauhin[20] | Yann Nadjar[21] | Christine Serratrice[22] | Marc G. Berger[23,24] | Fabrice Camou[25] | Nadia Belmatoug[1] | Jérôme Stirnemann[26] | French Evaluation of Gaucher Disease Treatment Committee

USA
USA
USA

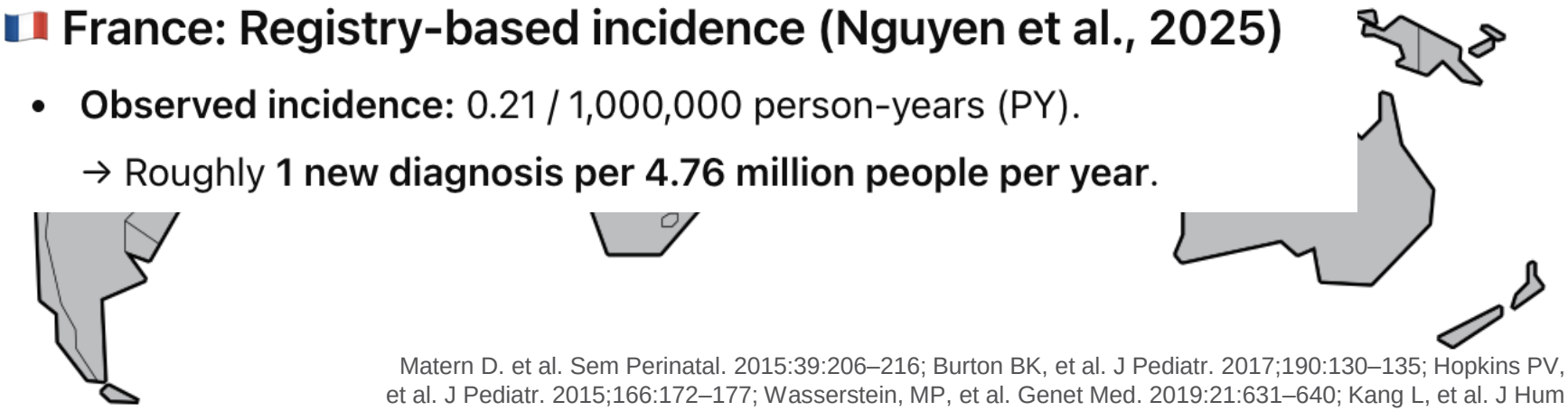


Worldwide incidenc

🇫🇷 France: Registry-based incidence (Nguyen et al., 2025)

- **Observed incidence:** 0.21 / 1,000,000 person-years (PY).

  → Roughly **1 new diagnosis per 4.76 million people per year.**



Matern D. et al. Sem Perinatal. 2015:39:206–216; Burton BK, et al. J Pediatr. 2017;190:130–135; Hopkins PV, et al. J Pediatr. 2015;166:172–177; Wasserstein, MP, et al. Genet Med. 2019:21:631–640; Kang L, et al. J Hum Genet. 2017:62:763–768; Burlina, AB, et al. J Inherit Metab Dis. 2018:41;209–219; Stirnemann J, et al. Int J Mol Sci. 2017:18:441

Gaucher early diagnosis-consensus (GED-C) score

- Delphi consensus process deployed among a global panel of 22 specialists in GD
- A threshold point-scoring system score of 0.82 identified all 14 patients with GD in the analysis set (100% sensitivity) and 27 of 38 patients in the non-GD group (71% specificity)
- Most patients have a score > 6

	Weighting	Clinical sign or co-variable
Major signs and co-variables	3 points	Splenomegaly (≥3× normal)
		Disturbed oculomotor function (slow horizontal saccades with unimpaired vision)
	2 points	Thrombocytopenia, mild or moderate (platelet count, 50–150×10^9/L)
		Bone issues, including pain, crises, avascular necrosis, and fractures
		Family history of Gaucher disease
		Anaemia, mild or moderate (haemoglobin, 95–140 g/L)
		Hyperferritinaemia, mild or moderate (serum ferritin, 300–1000 µg/L)
		Jewish ancestry
		Disturbed motor function (impairment of primary motor development)
		Hepatomegaly, mild or moderate (≤3× normal)
		Myoclonus epilepsy
		Kyphosis
		Gammopathy – monoclonal or polyclonal
	1 point	Anaemia, severe (haemoglobin, <9.5 g/dL)
		Hyperferritinaemia, severe (serum ferritin, >1000 µg/L)
		Hepatomegaly, severe (>3× normal)
		Thrombocytopenia, severe (platelet count, <50×10^9/L)
Minor signs and co-variables	0.5 points	Gallstones
		Bleeding, bruising, or coagulopathy
		Leukopenia
		Cognitive deficit
		Low bone mineral density
		Growth retardation including low body weight
		Asthenia
		Cardiac calcification
		Dyslipidemia
		Elevated angiotensin-converting enzyme levels
		Fatigue
		Pulmonary infiltrates
		Age ≤18 years
		Family history of Parkinson disease
		Blood relative who died of fetal hydrops and/or with diagnosis of neonatal sepsis of uncertain etiology

Mehta, et al. Intern Med J 2019, 49, (5), 578-591; Mehata, et al Intern Med J. 2020 Dec;50(12):1538-1546; Savolainen et al. Mol Genet Metab Rep 2021;27:100725; Revel-Vilk, et al. Int. J. Transl. Med. 2022, 2, 506–514.

Revel-Vilk *et al.*
Orphanet Journal of Rare Diseases (2024) 19:71
https://doi.org/10.1186/s13023-024-03042-y

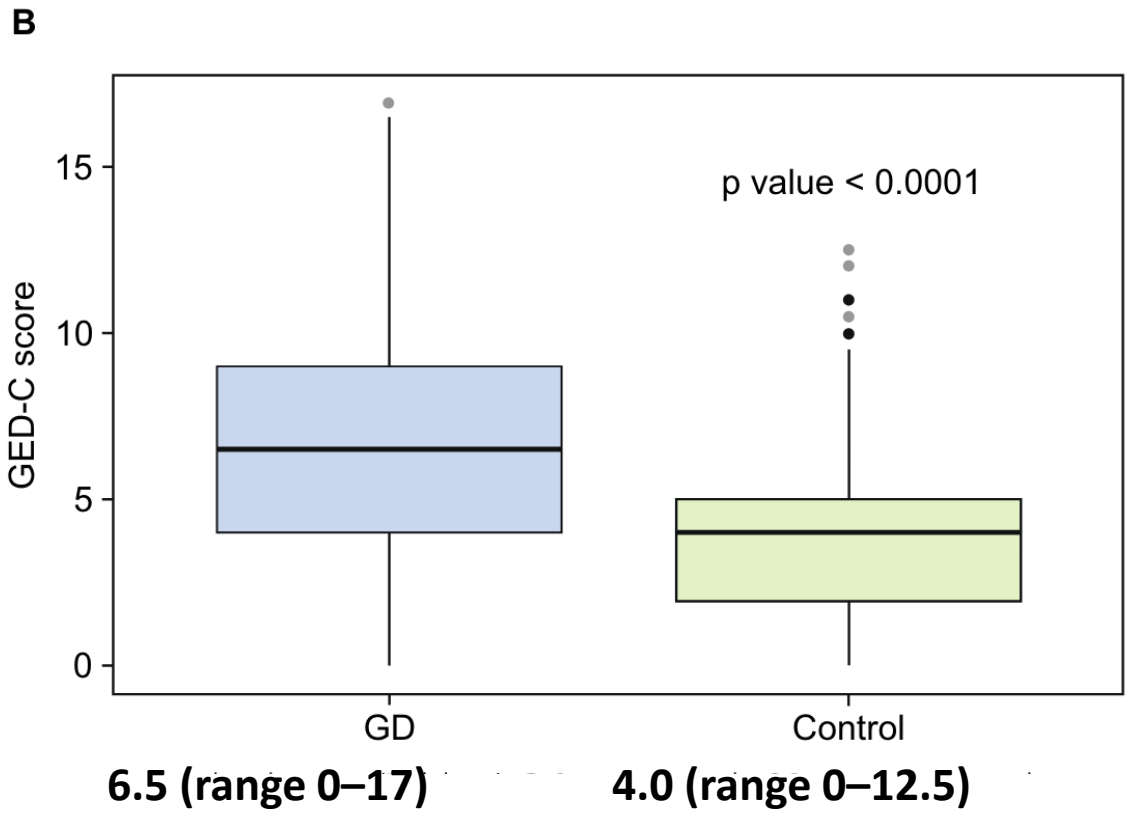
Orphanet Journal of
Rare Diseases

RESEARCH Open Access

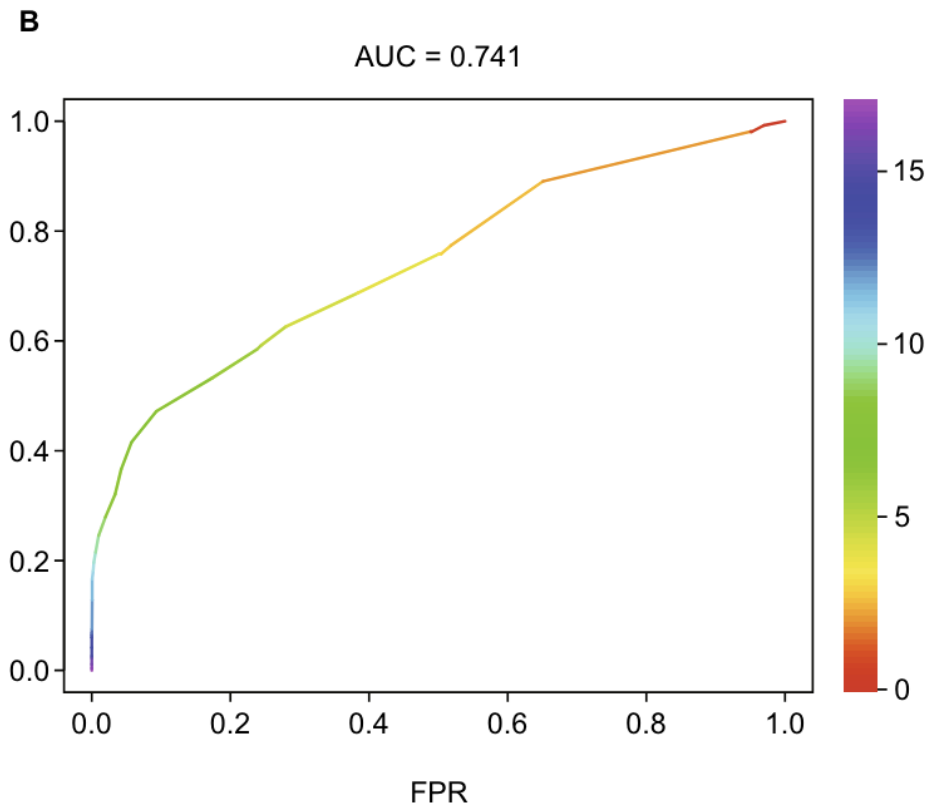
Assessing the diagnostic utility of the Gaucher Earlier Diagnosis Consensus (GED-C) scoring system using real-world data

Shoshana Revel-Vilk[1,2,3*], Varda Shalev[4], Aidan Gill[5], Ora Paltiel[2,3,6], Orly Manor[3], Avraham Tenenbaum[4], Liat Azani[7] and Gabriel Chodick[4,7]

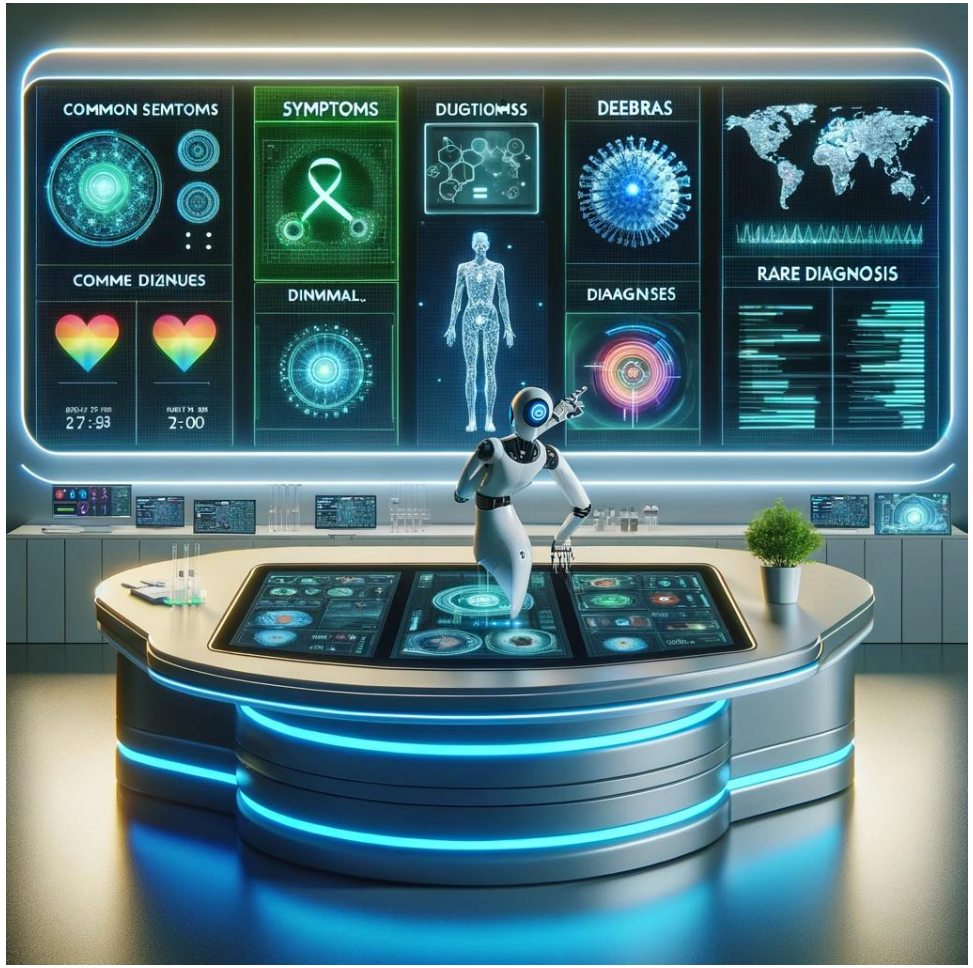
Figure 2. ROC curve for GED-C scoring of patients with GD versus controls



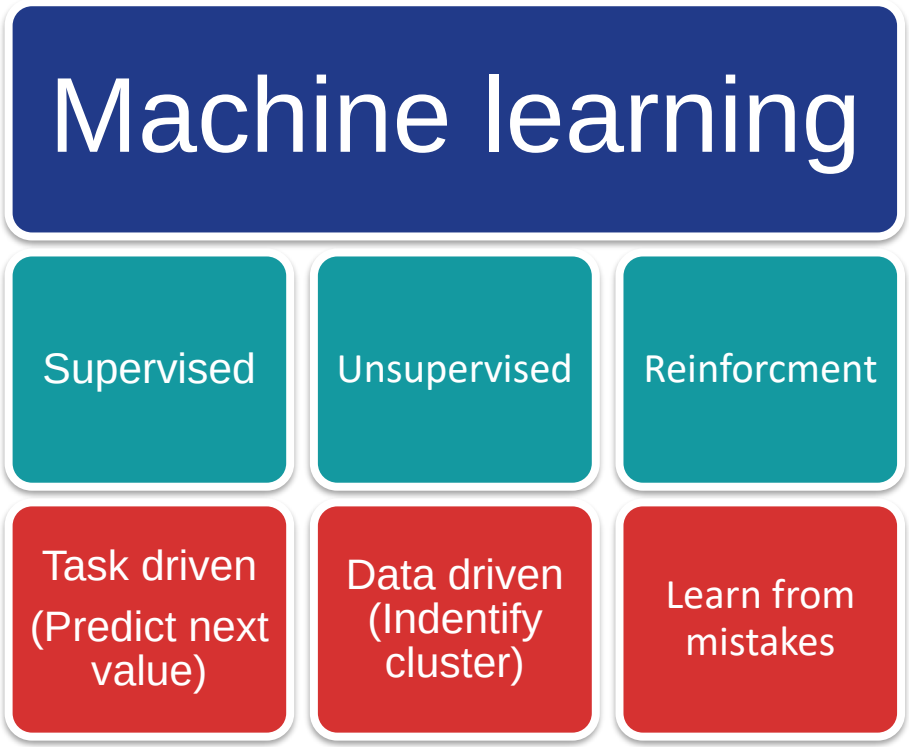
6.5 (range 0–17) **4.0 (range 0–12.5)**



Can the machine be better than us?



Created with assistance from ChatGPT.



Wilson *et al.*
Orphanet Journal of Rare Diseases (2023) 18:280
https://doi.org/10.1186/s13023-023-02868-2

Orphanet Journal of
Rare Diseases

RESEARCH Open Access

Development of a rare disease algorithm to identify persons at risk of Gaucher disease using electronic health records in the United States

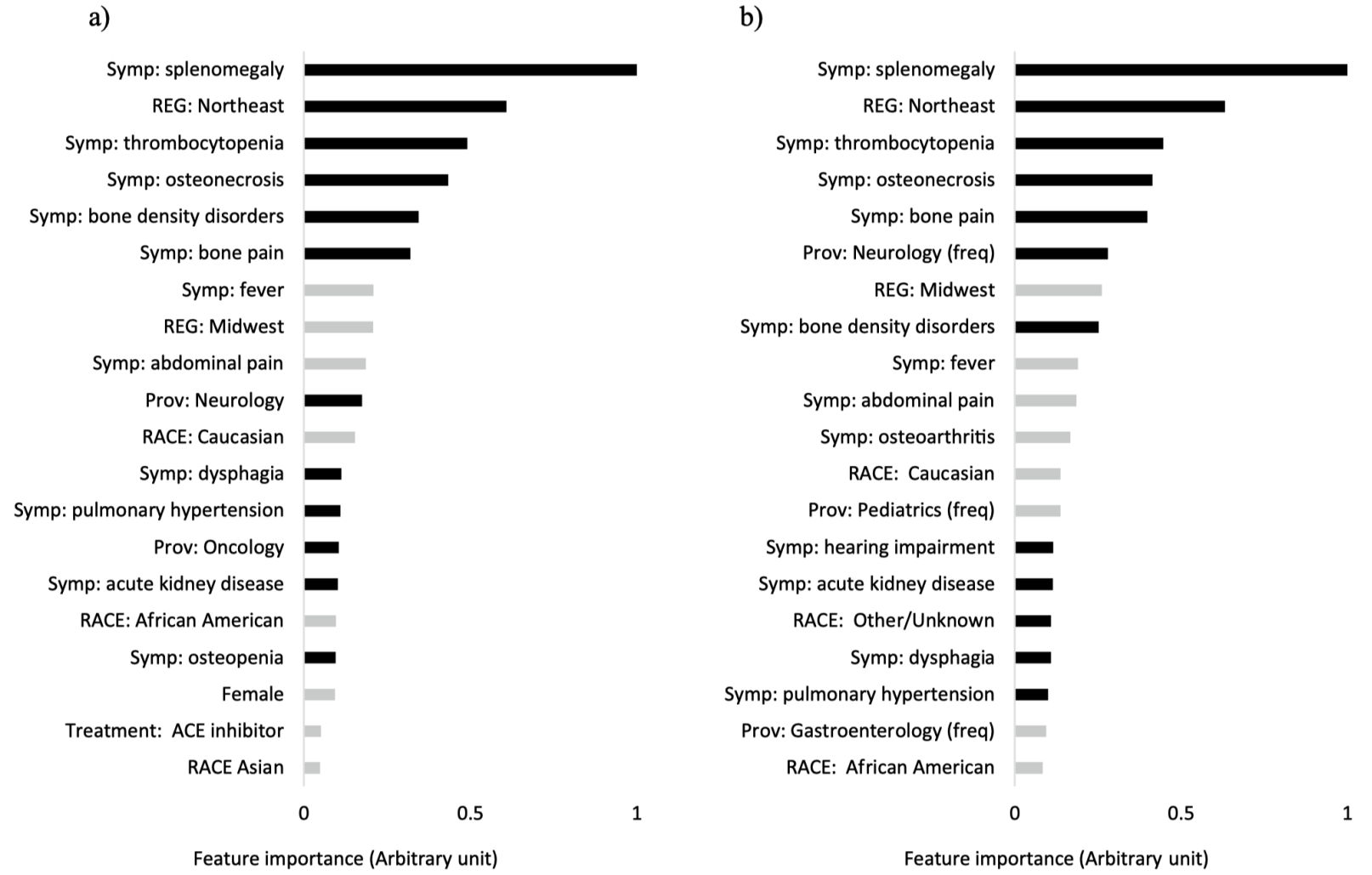
Amanda Wilson[1], Alexandra Chiorean[2], Mario Aguiar[3], Davorka Sekulic[3], Patrick Pavlick[4], Neha Shah[5], Lisa Sniderman King[4], Marie Génin[2], Mélissa Rollot[2], Margot Blanchon[2], Simon Gosset[2], Martin Montmerle[2], Cliona Molony[6] and Alexandra Dumitriu[7*]

Methods

- Optum ® Integrated database includes> 700 hospitals and > 7000 clinics, treating > 102 million patients
- The GD cohort was defined as patients with at least two instances of GD diagnoses (ICD-10 code E75.22) or at least one record of a GD-specific treatment (Table S1) in the integrated database
- A total of 756 patients with GD were matched with 328,000 controls (500 controls for 1 patient with GD)
- LightGBM method used
  - age-based algorithm - encoding defined by age at first occurrence
  - prevalence-based algorithm - encoding was binary (presence/absence)

Wilson, et al. *Orphanet J Rare Dis* **2023,** 18, (1), 280.

Feature importance



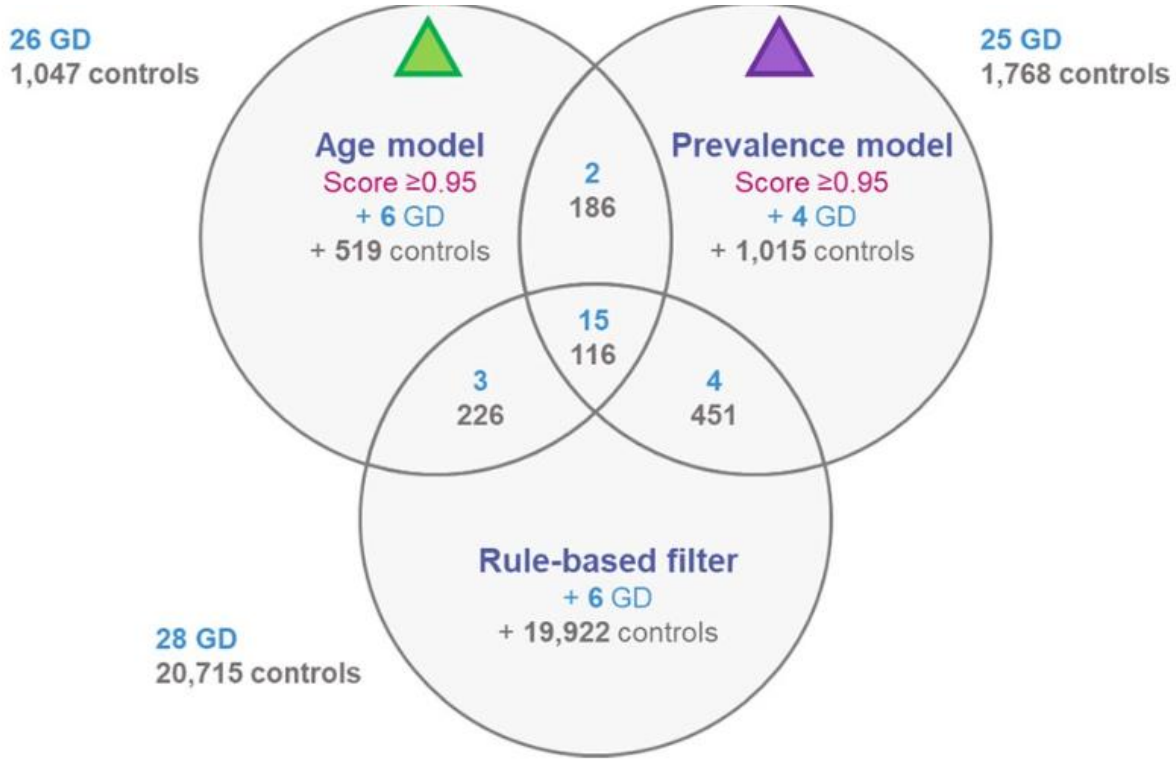
Black = features that had a posive influence towards the GD diagnosis; grey = features that had a negave influence on GD diagnosis

Assessing algorithm performance

- The number of patients to be assessed to identify 28 patients with GD

  - **1204 age-based algorithm**
  - **2862 prevalence-based algorithm**
  - **20,743 clinical diagnostic algorithm**

Both the **age-based** and **prevalence-based** algorithms achieved an **AUPRC of 0.66**



AUPRC (Area Under the Precision-Recall Curve):

ELSEVIER

Journal of Clinical Epidemiology 175 (2024) 111517

Journal of Clinical Epidemiology

ORIGINAL RESEARCH

A machine learning model for early diagnosis of type 1 Gaucher disease using real-life data

Avraham Tenenbaum[a,1], Shoshana Revel-Vilk[b,c,d,1,*], Sivan Gazit[e], Michael Roimi[f], Aidan Gill[g,2], Dafna Gilboa[h,2], Ora Paltiel[c,d], Orly Manor[d], Varda Shalev[a], Gabriel Chodick[a,e]

[a]*School of Medicine, Tel Aviv University, Tel Aviv, Israel*
[b]*Gaucher Unit, The Eisenberg R&D Authority, Shaare Zedek Medical Center, Jerusalem, Israel*
[c]*Faculty of Medicine, Hebrew University, Jerusalem, Israel*
[d]*Braun School of Public Health and Community Medicine, Hebrew University, Jerusalem, Israel*
[e]*MaccabiTech, Maccabi Healthcare Services, Tel Aviv, Israel*
[f]*Intensive Care Unit, Rambam Health Care Campus, Haifa, Israel*
[g]*Takeda Pharmaceuticals International AG, Zurich, Switzerland*
[h]*Takeda Israel Ltd, Petah Tikva, Israel*

Accepted 2 September 2024; Published online 6 September 2024

Research support

– Takeda Pharmaceutical

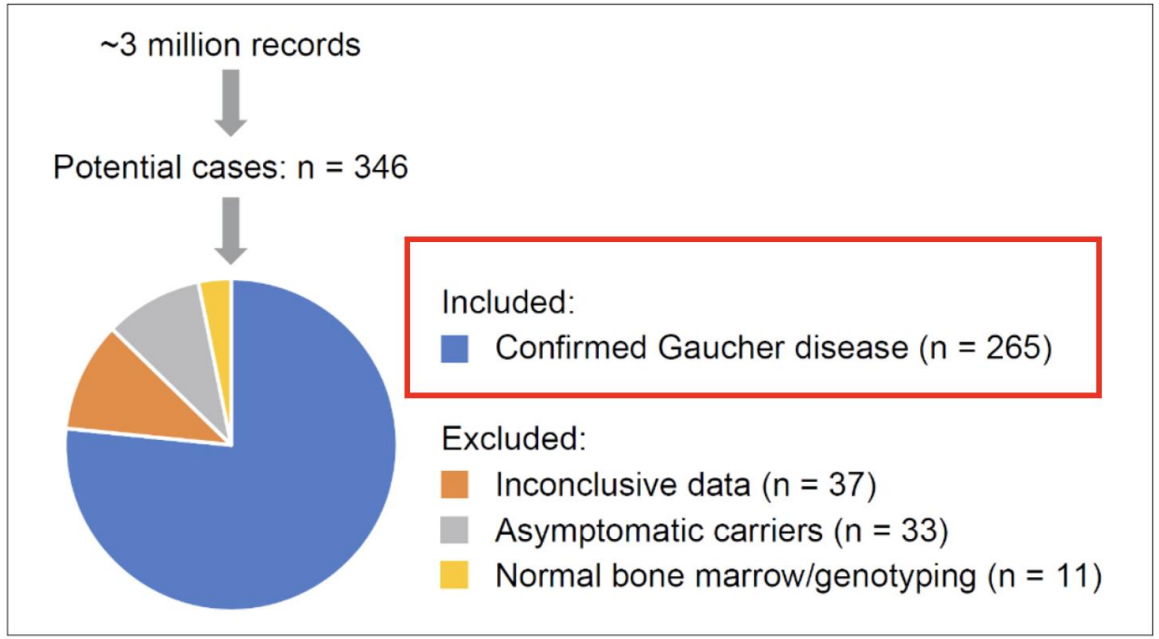
Methods: Data source

- The study utilized electronic records from the Maccabi Healthcare Service (MHS)
  - ~ 3 million health records from 25% of the Israeli population
  - Fully computerized
  - Integrated with central laboratory, digitized imaging, and pharmacy purchase data

Revel-Vilk S, et al. *Int J Transl Med* 2022, 2, 506-514;
Revel-Vilk S, et al. *Orphanet Journal of Rare Diseases*, 2024;19:71;
Tenenbaum A, Revel-Vilk S, et al. *J Clin Epidemiol* 2024; 175: 111517

Methods: Identification of cases and controls

- MHS was scanned for diagnosis code of GD (Y71156)



Cases excluded:

- No notes confirming GD diagnosis or disease-specific treatment
- recognized as a "Gaucher carrier"
- notes indicating negative GD testing

- 13 randomly selected controls for each GD patient- matched for year of birth, sex, socioeconomic status (n= 3445)

Revel-Vilk S, et al. *Int J Transl Med* 2022, 2, 506-514;

Lesson #1: Get the Case Definitions Correct

Misclassified cases lead to misleading algorithms

Data extraction

From the first record available until 1 year after the first documentation of GD

Demographics, body measurements (wt, ht)

ICD9 codes, surgical and fracture history

Imaging tests (referrals)

Purchased medications

Laboratroy data

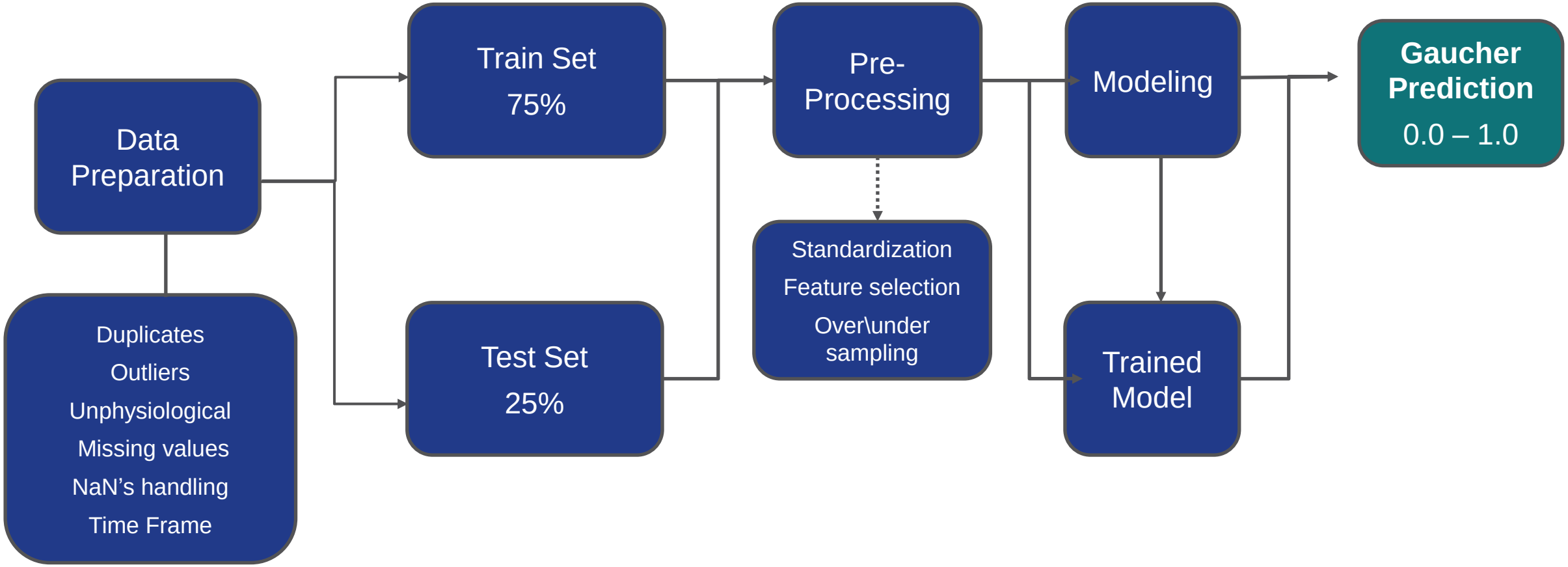
Registries (osteoporosis, diabetes mellitus, cancer, myocardial infarction, stroke)

Tenenbaum A, Revel-Vilk S, et al. *J Clin Epidemiol* 2024; 175: 111517

Lesson #2: Data Quality Matters

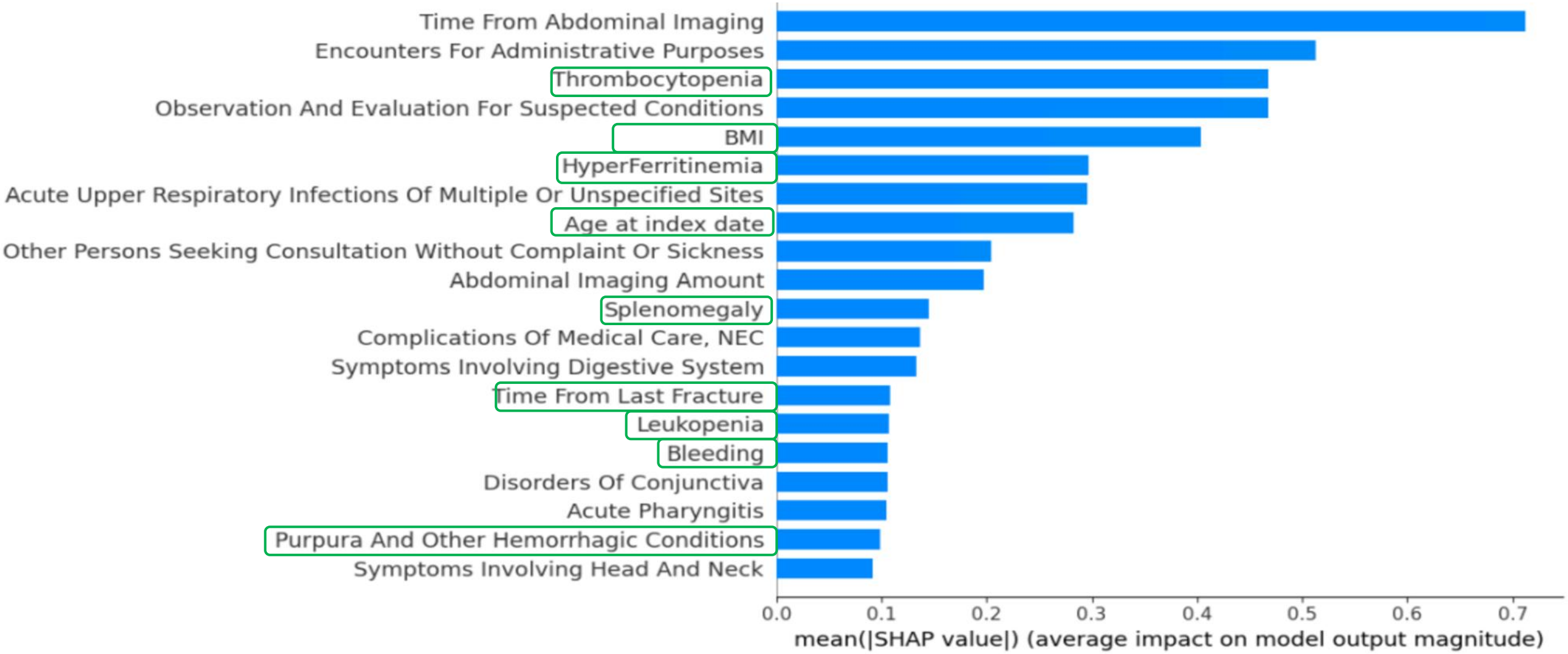
Real-world data is messy, often incomplete, or entered incorrectly, and requires careful cleaning and validation to ensure model reliability

Model development

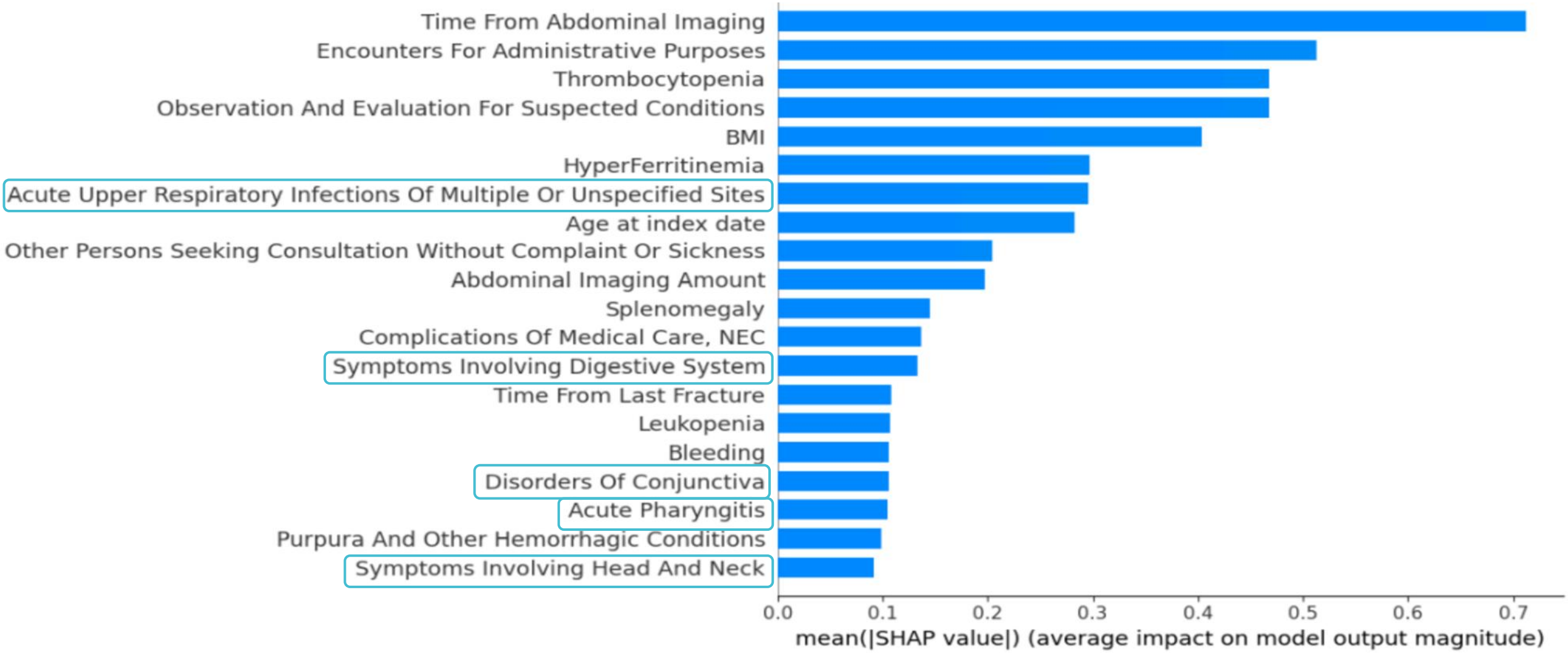


Tenenbaum A, Revel-Vilk S, et al. *J Clin Epidemiol* 2024; 175: 111517

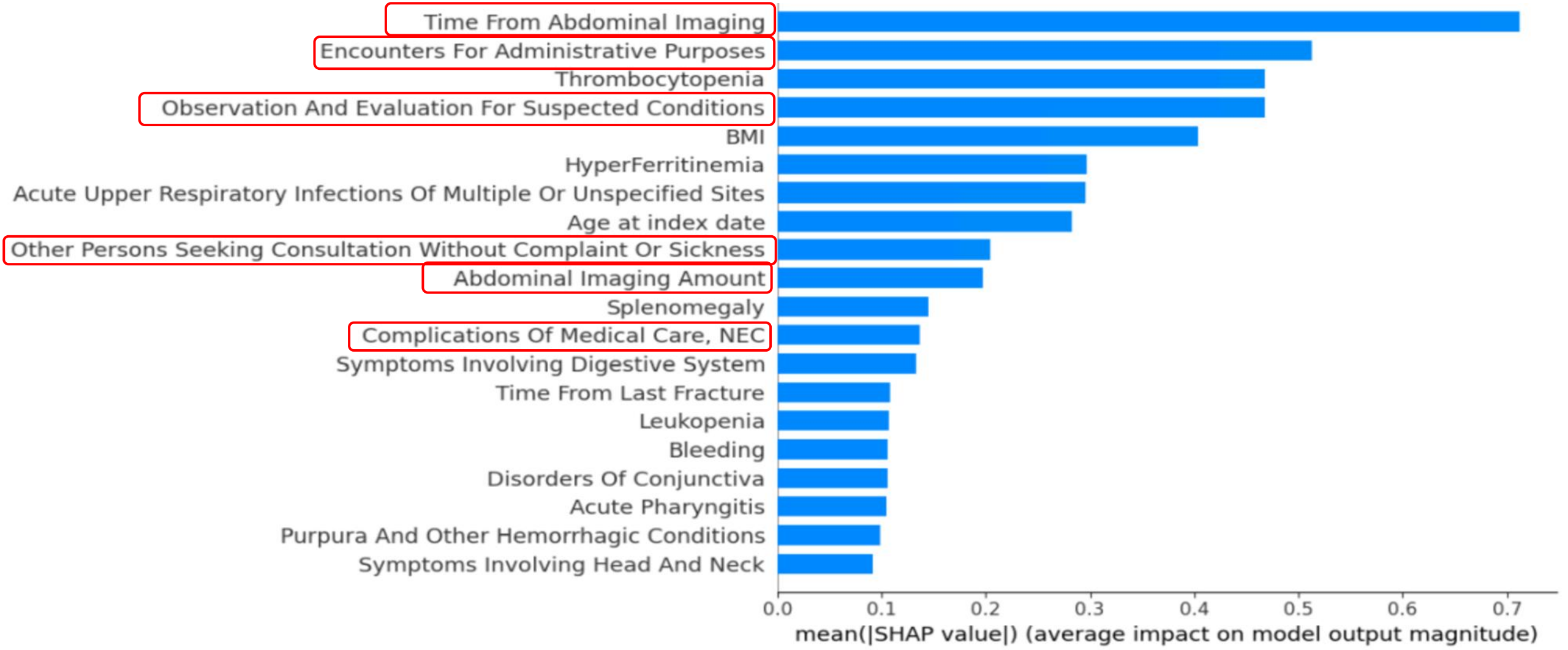
Feature importance – GD related



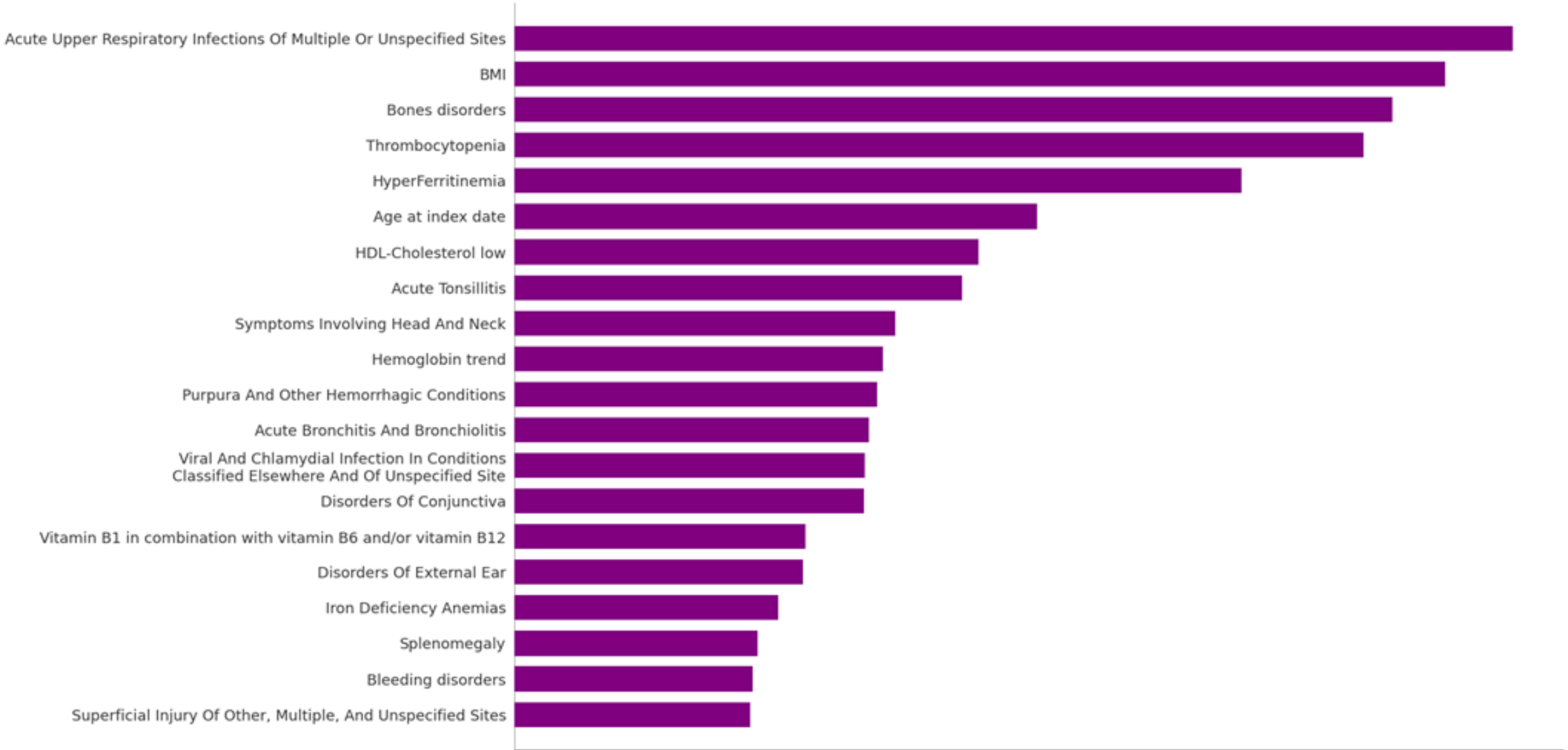
Feature importance – clinical non-GD realted



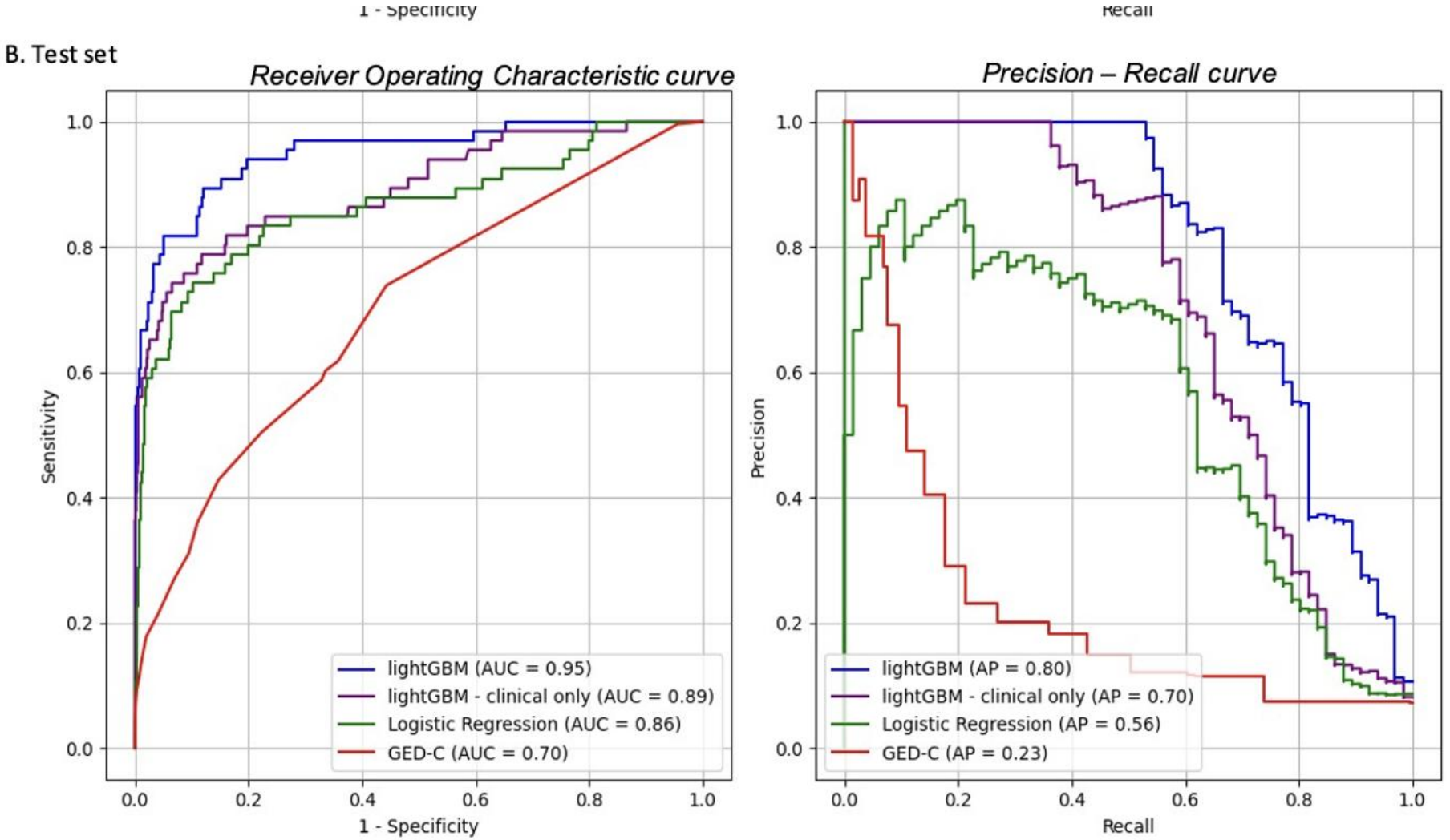
Feature importance – administrative



Clinical only model
[excluding administrative data]



Model evaluation

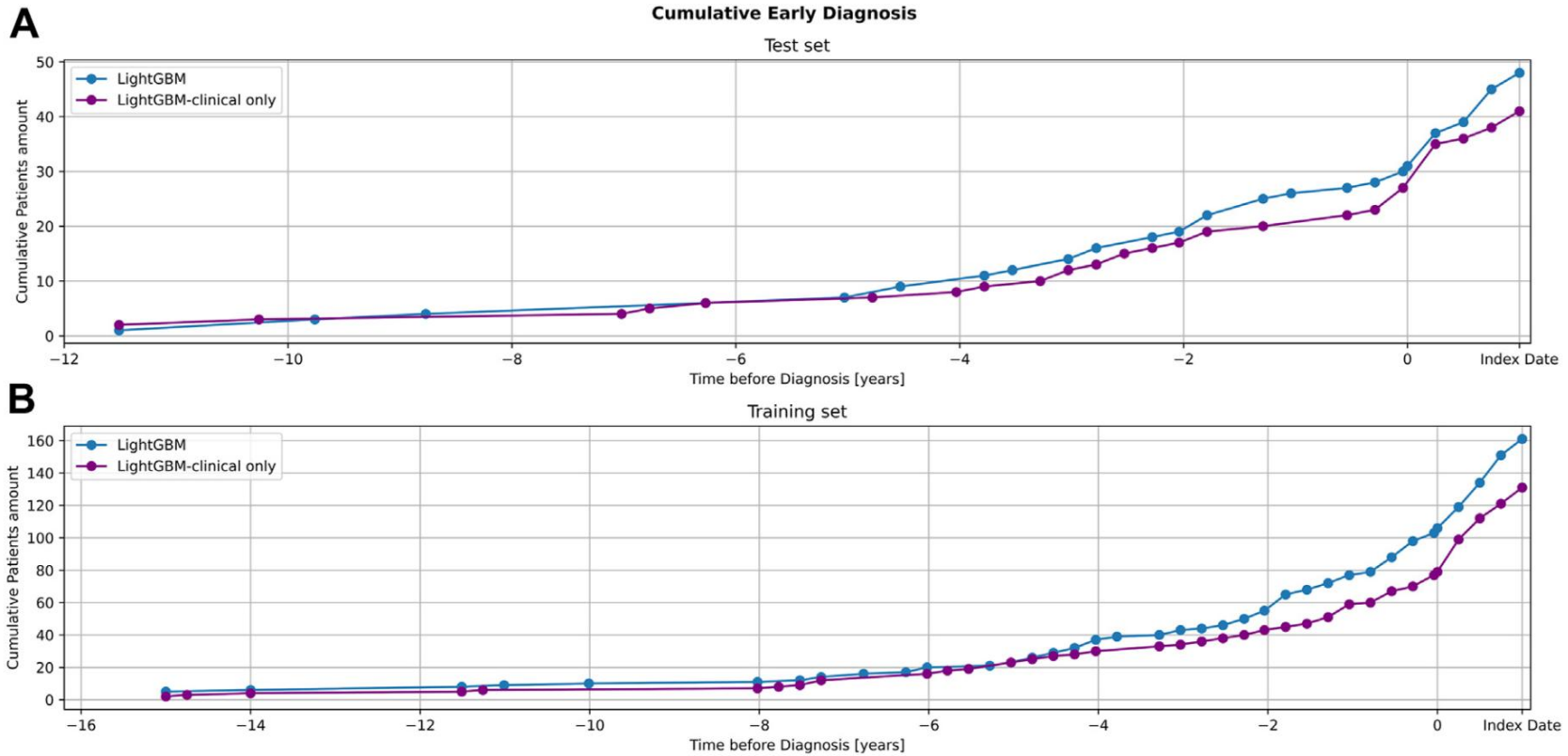


GED-C- Gaucher early diagnosis- consensus [see Mehta, et al. Intern Med J 2019, 49, (5), 578-591.] LightGBM- light gradient-boosting machine, AUC- area under the curve

Tenenbaum A, Revel-Vilk S, et al. *J Clin Epidemiol* 2024; 175: 111517

Timing of GD diagnosis detected by the model

The median (25th-75th percentile) time of early detection was 2.78 (1.29-4.53) years



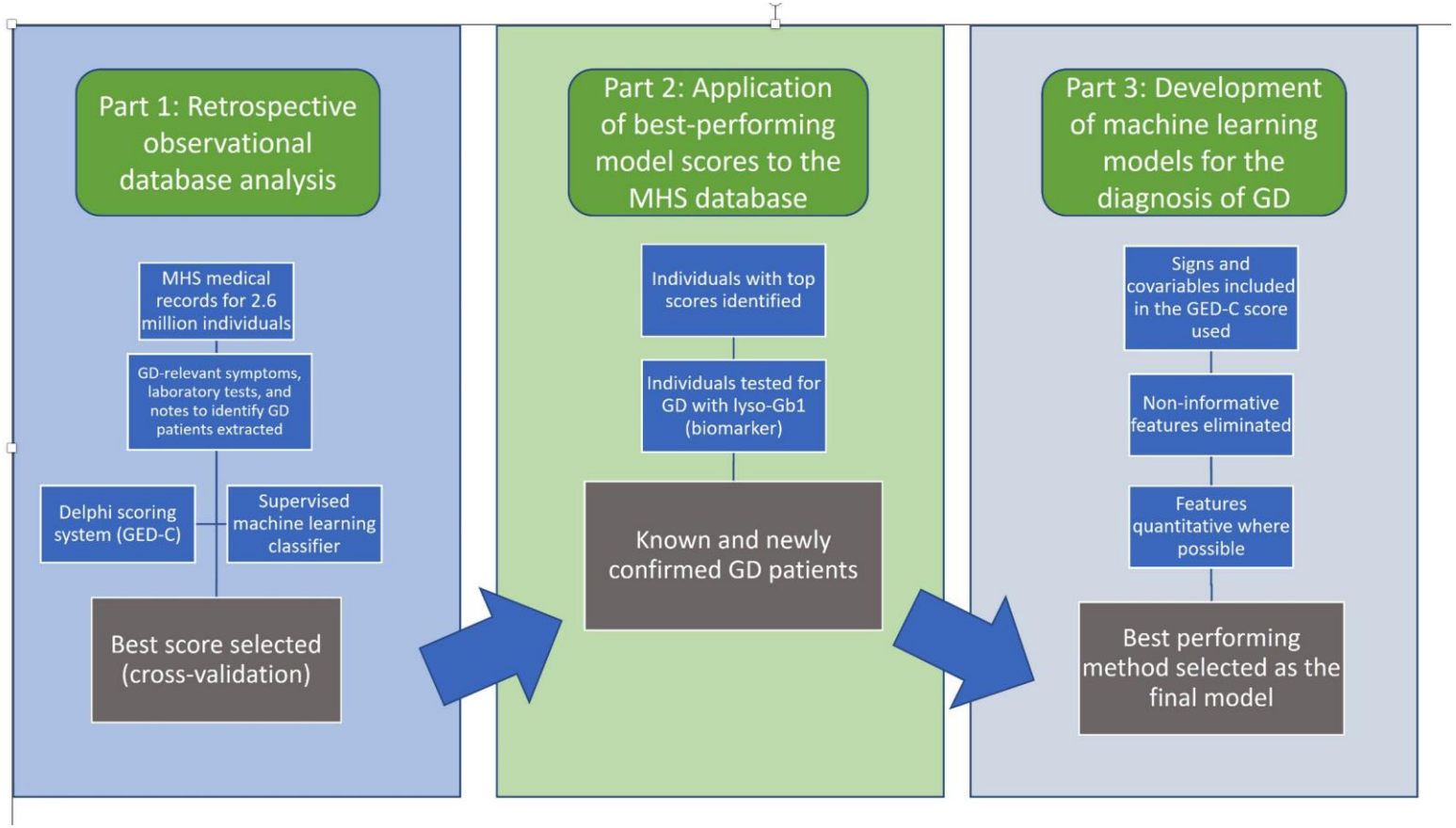
Tenenbaum A, Revel-Vilk S, et al. *J Clin Epidemiol* 2024; 175: 111517

Lesson #3: Models Uncover Hidden Clinical Signals

Unexpected features—clinical or administrative—may emerge, offering insights into diagnostic processes or comorbidities

Next steps

- Internal validation
- External validation

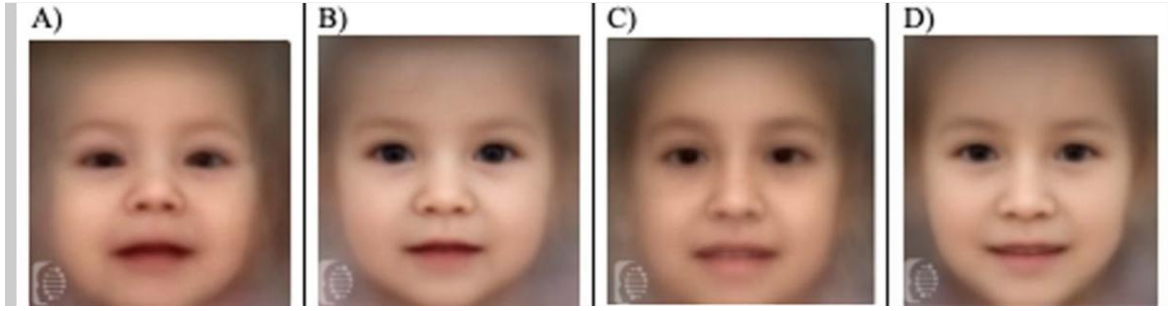


Facial recognition technology for nGD

- 47 children with GD2
- 86 children with GD3

		Predicted		
		TYPE 3	TYPE 2	CONTROLS GD3
Actual	TYPE 3	0.67	0.17	0.16
	TYPE 2	0.18	0.80	0.02
	CONTROLS GD3	0.15	0.02	0.83

Mean Accuracy: 76.64% Standard Deviation: 3.45% Random Chance for Comparison: 37.24%



Emily Daykin, Nicole Fleischer, Magy Abdelwahab, Nehal Hassib, Raphael Schiffmann, Emory Ryan, Ellen Sidransky,. Investigation of a dysmorphic facial phenotype in patients with Gaucher disease types 2 and 3, Molecular Genetics and Metabolism, 2021;134(3):274-280.

FACE2GENE
Smart Phenotyping. Better Genetics.

Unmet needs in Gaucher disease

Improving diagnosis

Improving patient care

Improving communication

nGD

Individualized treatment approaches

Cost and accessibility of treatment

Comorbidities

Skeletal complications

Spanish registry data

Andrade-Campos *et al. Orphanet Journal of Rare Diseases* (2020) 15:256
https://doi.org/10.1186/s13023-020-01520-7

Orphanet Journal of Rare Diseases

RESEARCH Open Access

Identification of risk features for complication in Gaucher's disease patients: a machine learning analysis of the Spanish registry of Gaucher disease

Marcio M. Andrade-Campos[1,2,3], Laura López de Frutos[1,3,4], Jorge J. Cebolla[4,5], Irene Serrano-Gonzalo[3,4], Blanca Medrano-Engay[3,4], Mercedes Roca-Espiau[3,6], Beatriz Gomez-Barrera[7], Jorge Pérez-Heredia[8], David Iniguez[7,8] and Pilar Giraldo[1,3,4*]

- 340 patients with type 1 GD
- Predictive models for long-term complications using decision trees

Correlation network between variables

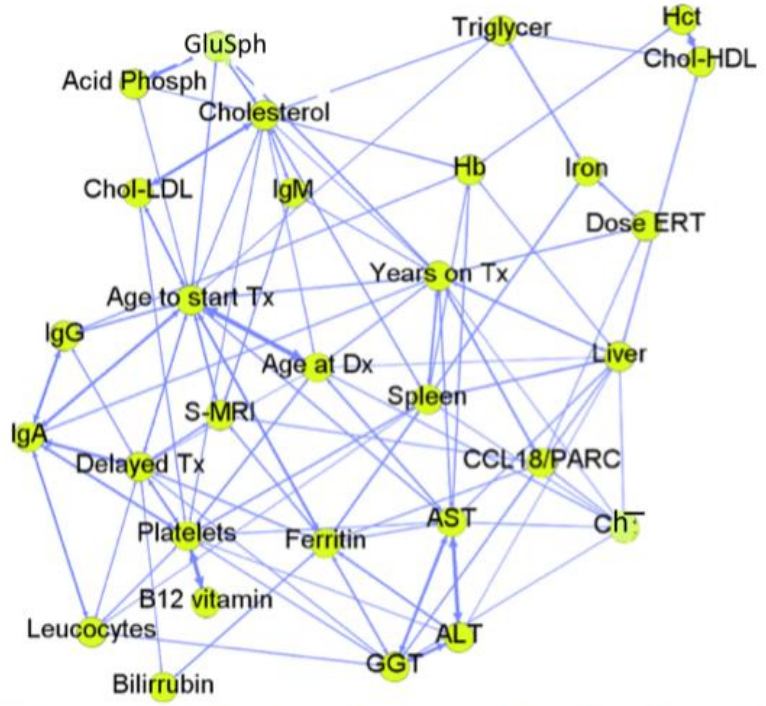


Fig. 1 Correlation network between numerical variables. Nodes are the variables and a link is established between them if correlation is statistically significant (p-value ≤0.05). Those nodes that are joined by stronger links are placed closer, while those that are unrelated are further away. GluSph: Lyso-glucosylsphingosine; Triglycer: serum triglycerides; Hct: hematocrit; Acid Phosphatase; Chol-HDL: cholesterol HDL, Chol-LDL serum concentration: cholesterol LDL serum concentration; IgM: immunoglobuline M serum concentration; Tx: therapy; Delay Tx: time since diagnosis to start of therapy

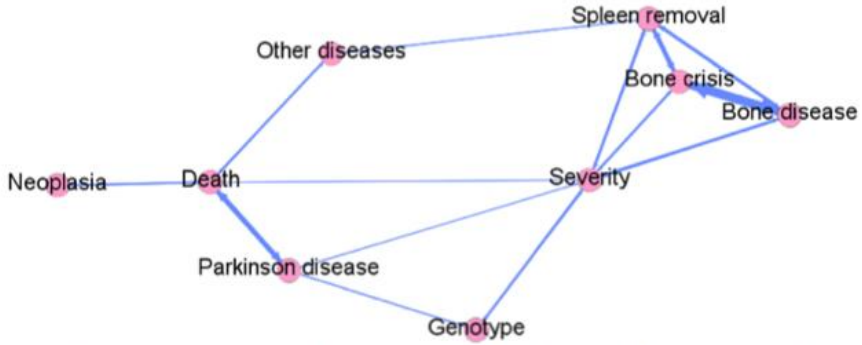
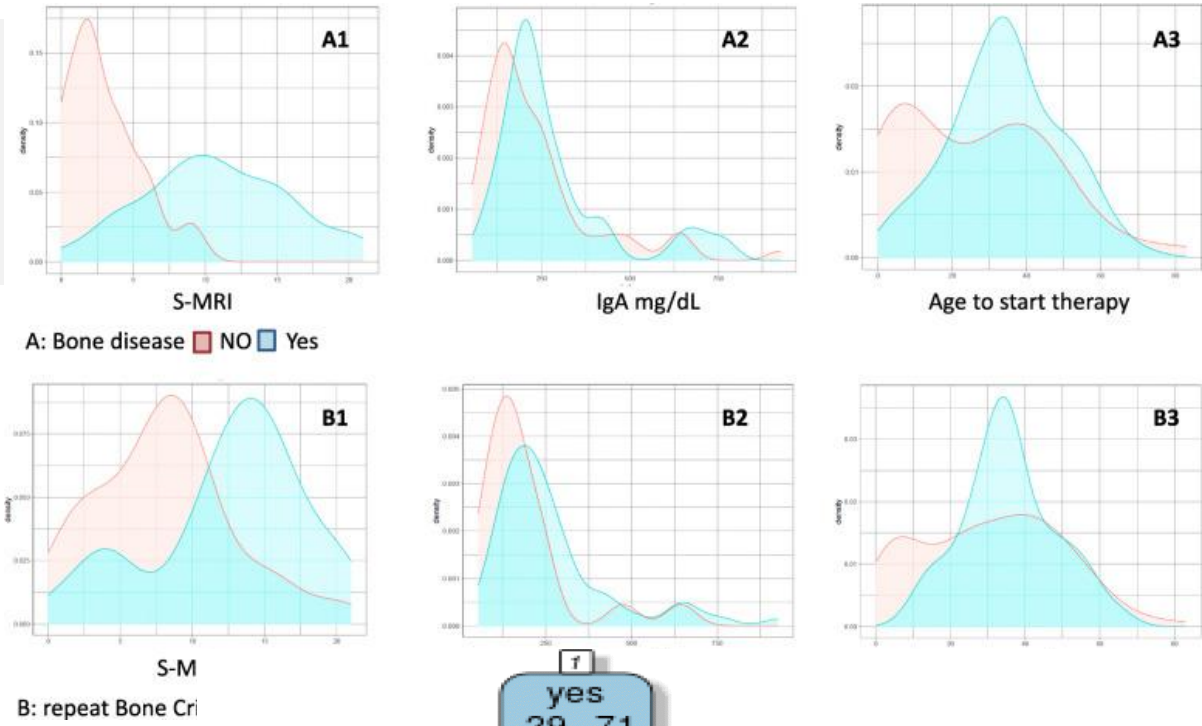


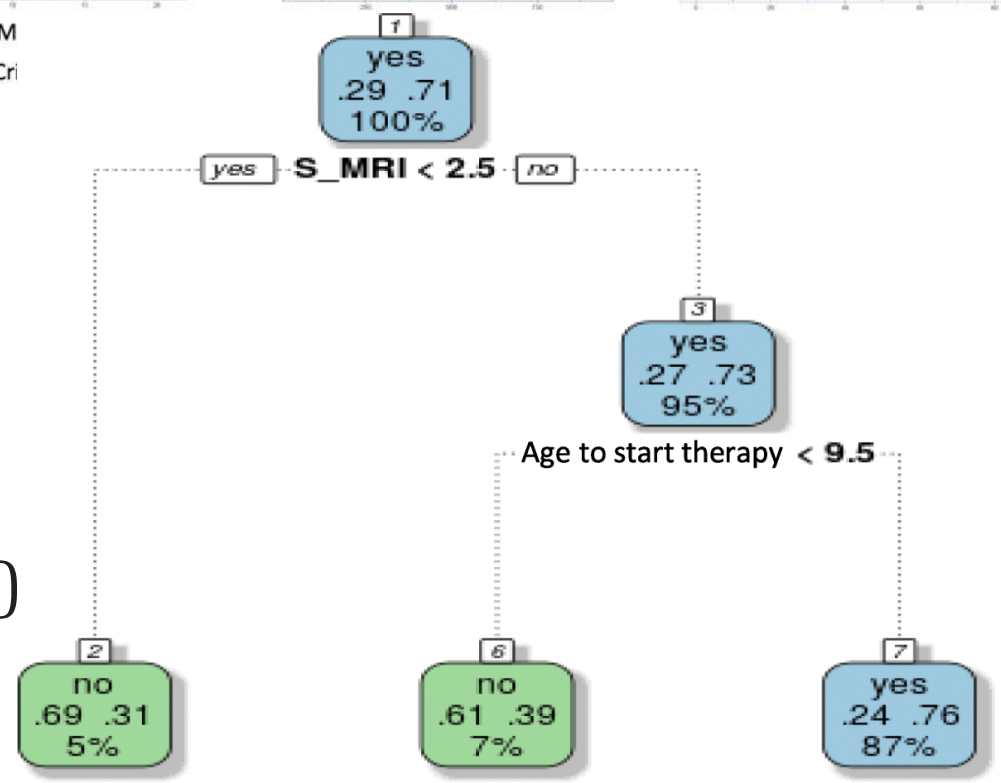
Fig. 2 Correlation network between categorical variables, where the nodes are the different variables and a link is established between two of them if the correlation calculated between them is statistically significant (p-value ≤0.05). Those nodes that are joined by stronger links are placed closer, while those that are unrelated are further apart

Andrade-Campos MM, et al. Orphanet J Rare Dis. 2020;15:256

Severe bone disease



- Previous splenectomy (p = 0.005)
- Spanish MRI score (S-MRI) ($U_n = 0.98$, $p < 0.01$)
- IgA levels ($U_n = 0.93$, $p = 0.01$),
- Ferritin levels ($U_n = 0.85$, $p = 0.06$)
- Triglyceride levels ($U_n = 0.75$, $p < 0.01$)
- Diagnosis > 9.5 years ($p < 0.001$)
- Years between Dx and treatment ($U_n = 0.67$, $p = 0.01$)
- Delayed age of initiation of ERT ($U_n = 0.61$, $p = 0.01$)



Andrade-Campos MM, et al. Orphanet J Rare Dis. 2020;15:256

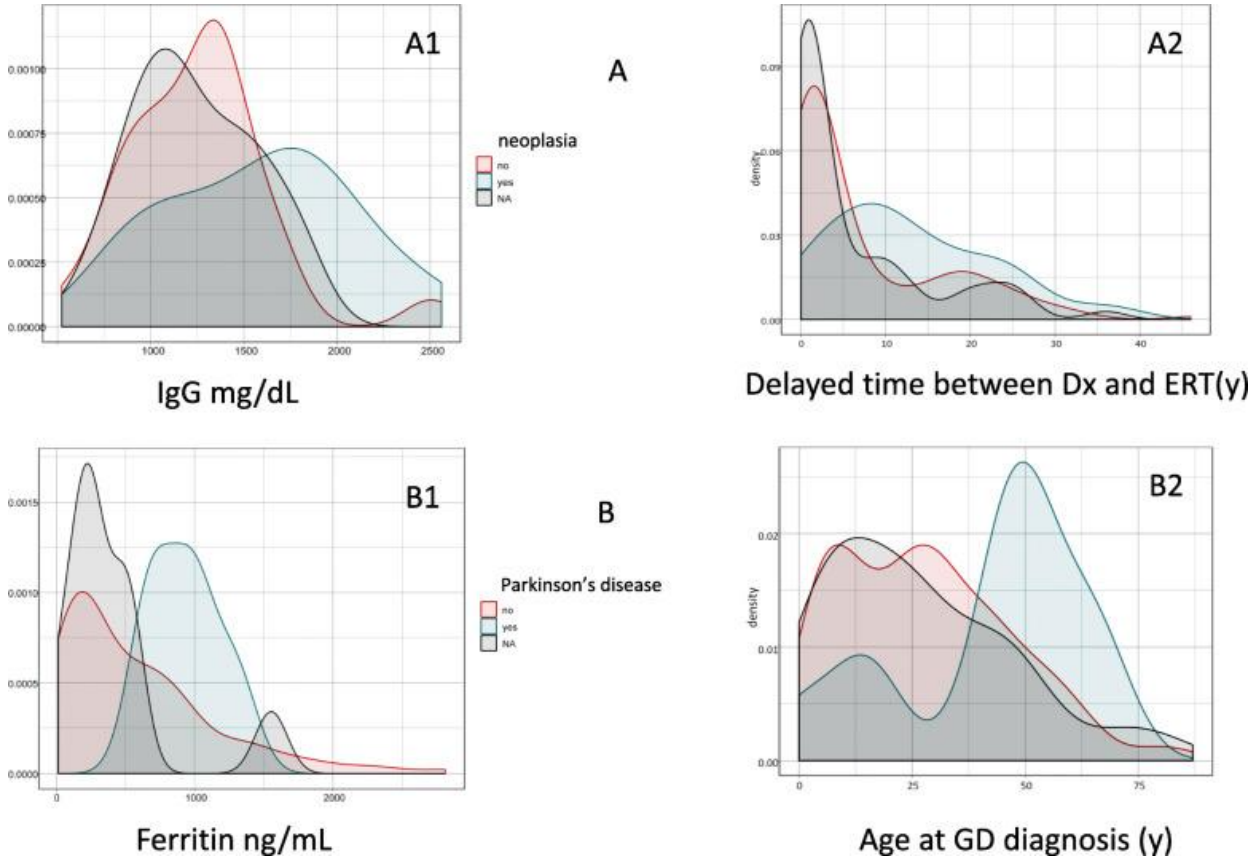
Risk for comorbidities

Cancer

- High levels of IgG ($U_n = 0.91$, $p = 0.01$)
- Delayed Tx time ($U_n = 0.70$, $p = 0.00$)

Parkinson disease

- Ferritin levels ($U_n = 0.92$, $p = 0.04$)
- Age at Dx ($U_n = 0.45$, $p = 0.01$)

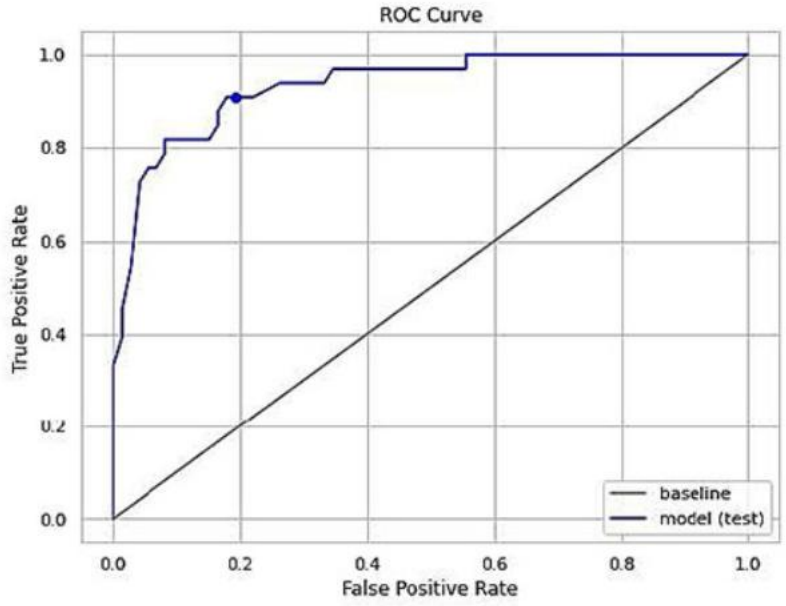


Andrade-Campos MM, et al. Orphanet J Rare Dis. 2020;15:256

Advantages of digital technology in the assessment of bone marrow involvement in Gaucher's disease

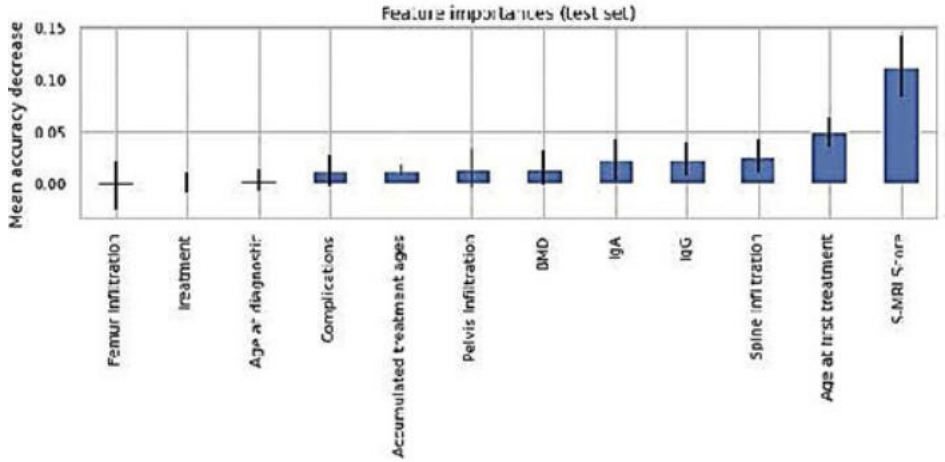
Esther Valero-Tena [1,2], Mercedes Roca-Espiau [2], Jose Verdú-Díaz [3], Jordi Diaz-Manera [3], Marcio Andrade-Campos [2,4,5] and Pilar Giraldo [2,4]*

[1]Departamento de Medicina Interna y Reumatología, Hospital MAZ, Zaragoza, Spain, [2]Fundación Española para el Estudio y Terapéutica de la Enfermedad de Gaucher y otras Lisosomales (FEETEG), Zaragoza, Spain, [3]John Walton Muscular Dystrophy Research Center, Newcastle University, Newcastle upon Tyne, United Kingdom, [4]Grupo Español de Enfermedades de Depósito Lisosomal de la SEHH (GEEDL), Madrid, Spain, [5]Grupo de Investigación en Hematología, Instituto de Investigación Hospital del Mar, IMIM-Parc de Salut Mar, Barcelona, Spain



Severe bone disease was associated with -

- bone marrow infiltration degree
- age at the start of therapy
- femur infiltration



Front Med (Lausanne) 2023 May 12:10:1098472

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biannual
meeting
2024

No.19

Deep learning-based quantification of osteonecrosis using magnetic resonance images in Gaucher disease

Patrick Deegan, Boliang Yu, Tristan Whitmarsh, Philipp Reide, Scott McDonald, Joshua Kaggie, Timothy Cox, Kenneth Poole

Department of Medicine, University of Cambridge, Cambridge, UK; Department of Astronomy, University of Cambridge, Cambridge, UK; Department of Radiology, University of Cambridge, Cambridge, UK.

Osteonecrosis (ON) is a principal clinical manifestation of Gaucher disease and often leads to joint collapse and fractures. T1-weighted (T1w) modality in MRI is widely used to assess bone involvement in Gaucher disease. However, objective and quantitative methods for assessing osteonecrosis are limited. Here, we present a deep learning-based quantification approach for the segmentation of osteonecrosis and the extraction of characteristic parameters. We constructed two independent U-net models to segment osteonecrosis and bone marrow unaffected by osteonecrosis (UBM) in spine and femur respectively, based on T1w images from patients in the national GAUCHERITE study. We manually segmented osteonecrosis and UBM from 364 T1w images (176 for spine, 188 for femur) as the learning datasets, and the trained models were then applied to all 917 T1w images in the database. To quantify the segmentation, we calculated volume of ON, volume of UBM, and the fraction of total marrow occupied by ON (ON.F). We assessed whether clinical factors, known to be linked with risk of ON, were also associated with the quantitative measure of ON. Prior splenectomy was closely associated with the fractional volume of ON, especially in the spine (Mann-Whitney, $p<0.001$ for spine and $p< 0.05$ for femur). Applying a cut-off value of 0.001 to the ON.F to establish a binary diagnosis of ON, we also found a strong association between splenectomy and the presence of ON (Chi-square $p< 0.001$ for spine and $p<0.05$ for femur). Similarly, we found a relationship between interval from age at first symptom to age of onset of treatment with ON.F (Mann-Whitney, $p<0.001$ each for spine and femur). We propose this as an efficient tool for assessing the presence and extent of osteonecrosis in MR images. The particularly close association between splenectomy and ON of the spine merits close attention.

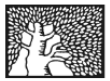
Prior splenectomy →

Interval to strart Tx →

No.51

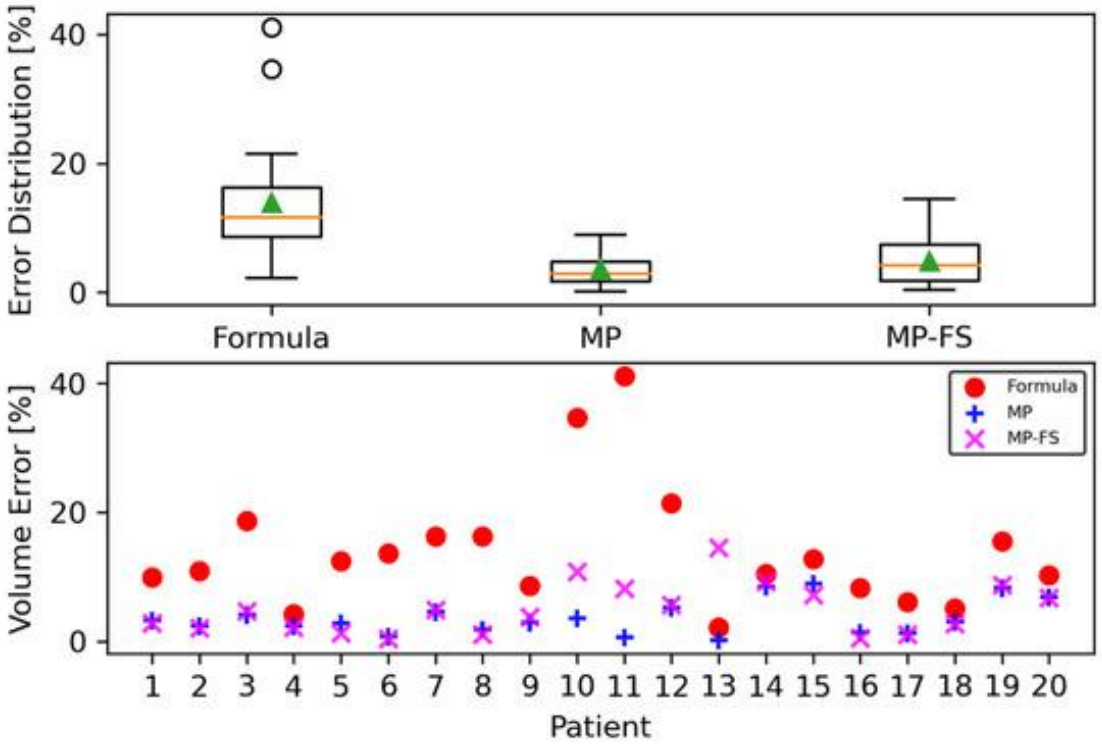
A Deep-Learning Approach to Spleen Volume Estimation in Patients with Gaucher Disease

Majdolen Istaiti[1], Ido Azuri[2], Ameer Wattad[3], Keren Peri-Hanania[4], Tamar Kashti[4], Ronnie Rosen[4], Yaron Caspi[4], Makram Wattad[3], Yaakov Applbaum[2,5], Ari Zimran[1,5], Shoshana Revel-Vilk[1,5], Yonina C.Eldar[4]



מכון ויצמן למדע
WEIZMANN INSTITUTE OF SCIENCE
Department of Computer Science and Applied Mathematics

- Aim: Develop a precise and reliable alternative for spleen volume assessment by radiologists
- 30 abdominal MRIs
- Group truth – spleen volume as reported by the radiologists
- Modeling had significantly less volume error compared to formula calculation
- Need to be updated and re-trained to account for changes in MRI data and to work with different MRI machines



Azuri, I., et al. 2023, J Clin Med **12**(16).

AI-Driven personalized treatment strategies

Journal of
Clinical Medicine

MDPI

Article

A Feasibility Open-Labeled Clinical Trial Using a Second-Generation Artificial-Intelligence-Based Therapeutic Regimen in Patients with Gaucher Disease Treated with Enzyme Replacement Therapy

Noa Hurvitz [1], Tama Dinur [2], Shoshana Revel-Vilk [2,3], Samuel Agus [4], Marc Berg [4,5], Ari Zimran [2,3,†] and Yaron Ilan [1,3,*,†]

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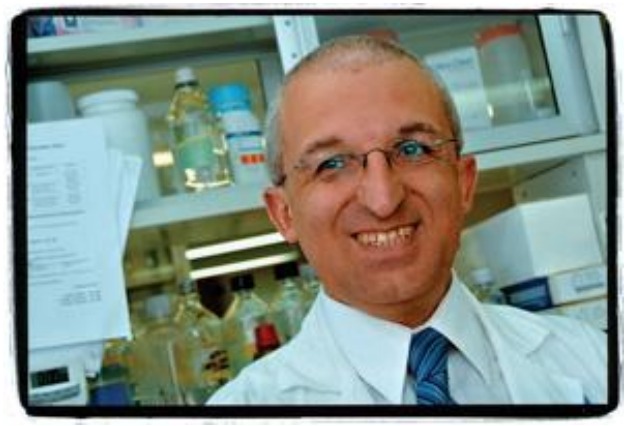
[2] Gaucher Unit, The Eisenberg R&D Authority, Shaare Zedek Medical Center, Jerusalem 9103102, Israel; dinurtama@gmail.com (T.D.); srevelvilk@gmail.com (S.R.-V.); azimran@gmail.com (A.Z.)
[3] Faculty of Medicine, Hebrew University, Jerusalem 9112001, Israel
[4] Oberon Sciences and Area 9 Innovation, Chestnut Hill, MA 02467, USA; sam.agus@samagus.com (S.A.); marc@area9.dk (M.B.)
[5] Stanford University, Palo Alto, CA 94305, USA
* Correspondence: ilan@hadassah.org.il; Tel.: +972-2-6778511
† These authors contributed equally to this work.



Constrained disorder principle (CDP)

- Living systems need variability to stay healthy
  - heart rate, glucose levels, immune system

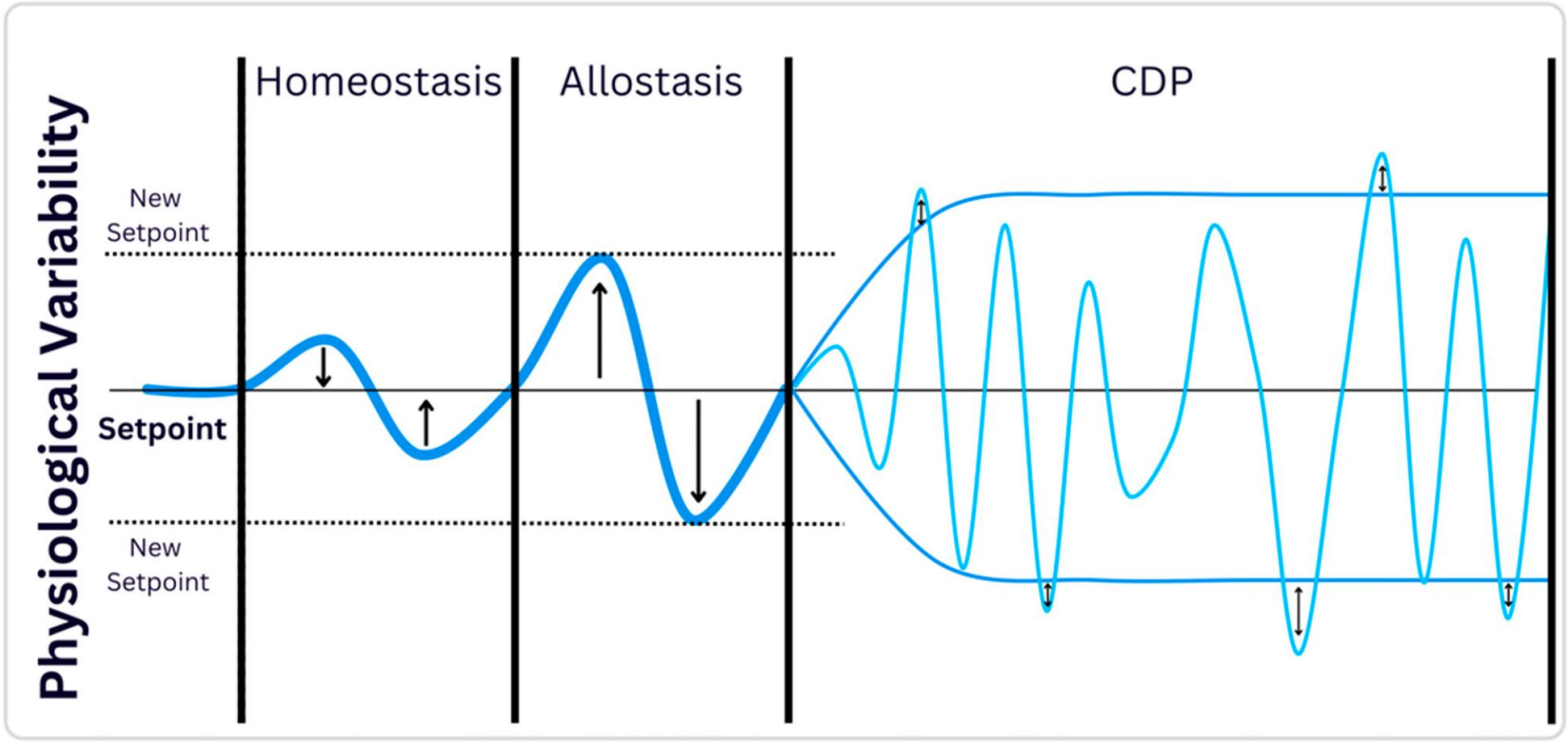
- Disease = loss of constrained disorder
  - variability is lost
    - flat heart rate variability → heart failure
  - variability becomes uncontrolled
    - uncontrolled glucose swings → diabetes complications
    - uncontrolled immune system → autoimmune disease

Constrained disorder principle (CDP)

Body’s attempt to keep things stable around a fixed set point

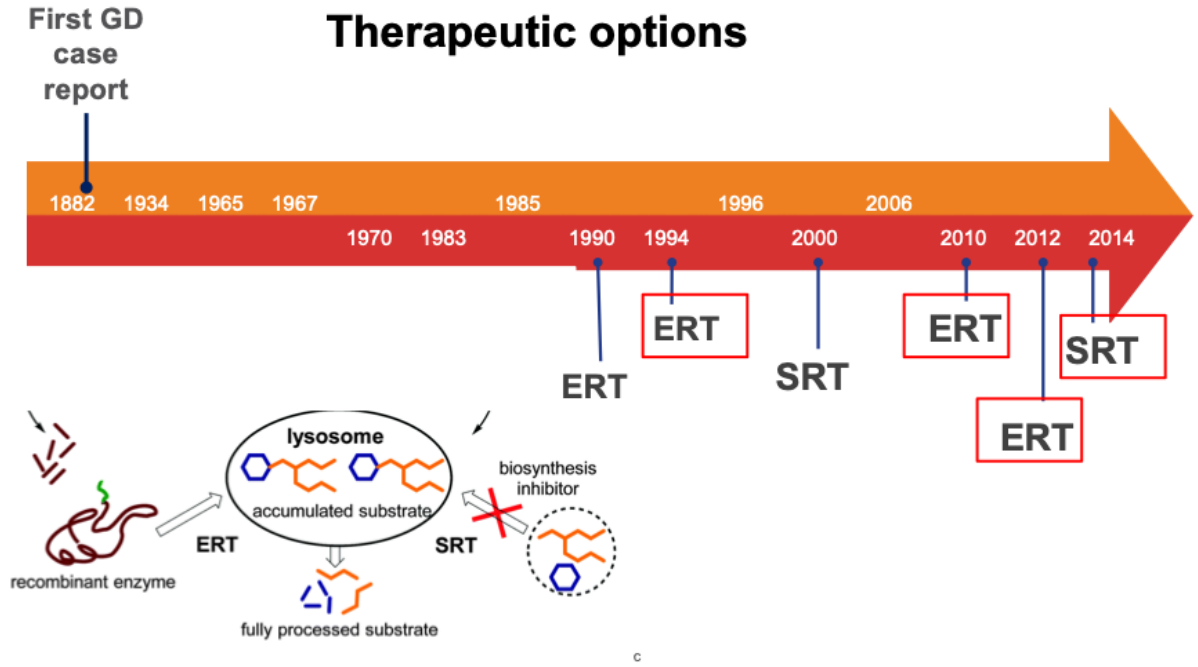
The body adjusts to new set points stress or illness. These shifts still require energy

The system functions within dynamic limits, adapting over time based on the environment



Background for study in Gaucher disease

- **>10% of patients** show incomplete or diminishing response to current Gaucher disease therapies



- Applying **AI-driven adaptive dosing can** tailor treatment patterns and potentially improve GD-related therapy effectiveness

Methods

- **Design:** 6-month, open-label, single-center, proof-of-concept study
- **Participants:** 5 adults with GD1 on stable ERT (30–60 U/kg/month)
- **Platform:** *Altus Care*™ mobile app
- Randomized ERT **dosage** and **administration intervals**
  - Dosing interval: **10–18 days** (vs. standard 14).
  - Randomized infusion time: **7 a.m.–2 p.m.**

Table 2. An example of drug administration based on the randomization algorithm for one of the subjects in the study.

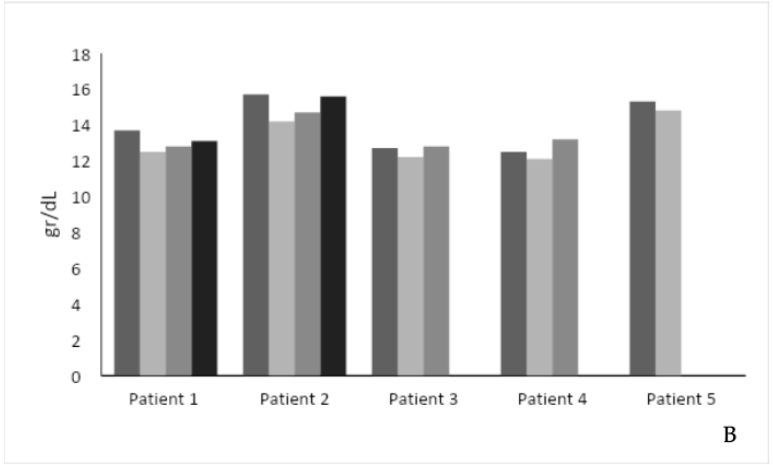
Administration time: Days since recruitment	1	14	31	45	62	74	91	104	121	135	149	165
Dosage	3200	2000	4400	800	1200	4000	800	4400	3600	1600	2000	3200
Administration time—hour	8:30	9:45	8:45	9:00	9:30	8:15	7:15	7:00	9:00	7:45	9:00	8:45

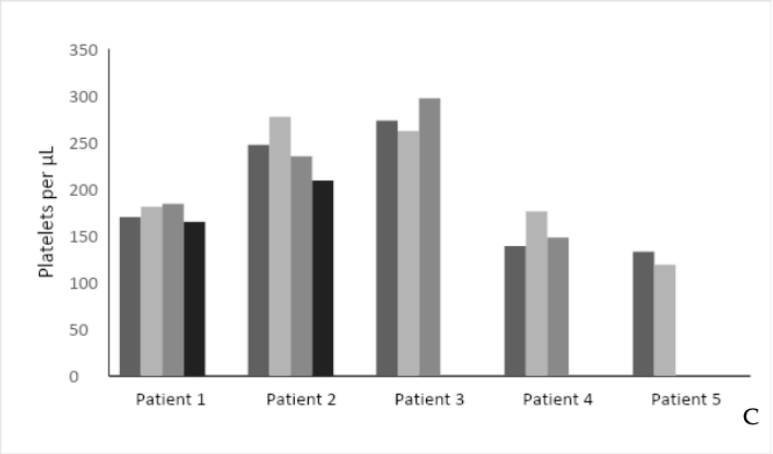
Hurvitz, N., et al. J. Clin. Med. 2024, 13, 3325.

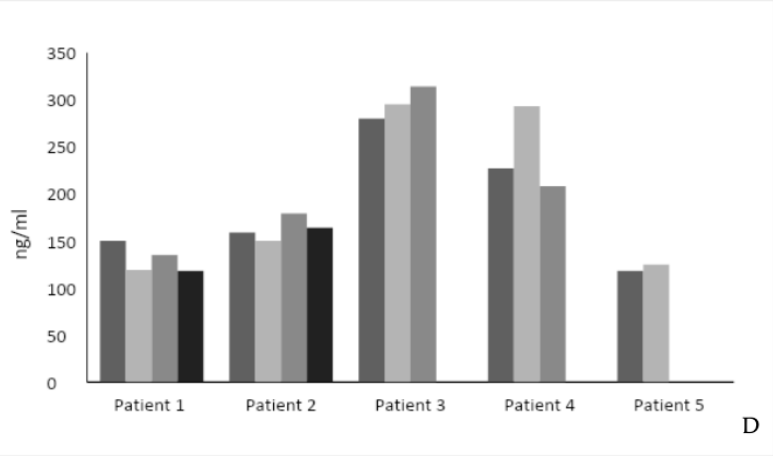
Results

- **Completion:** 5/5 patients completed 6 months; no adverse events
- **Adherence:** 100% engagement through the Altus Care™ app

- **Quality of Life (SF-36):** ↑ in 1, stable in 3, slight ↓ in 1
- **Hemoglobin:** Stable in 4, ↑ in 1 (Δ +0.7 g/dL)
- **Platelets:** ↑ in 2, ↓ in 2, stable in 1.
- **Lyso-Gb1:** ↓ in 2 patients (mean –25 ng/mL)







Hurvitz, N., et al. J. Clin. Med. 2024, 13, 3325.

Unmet needs in Gaucher disease

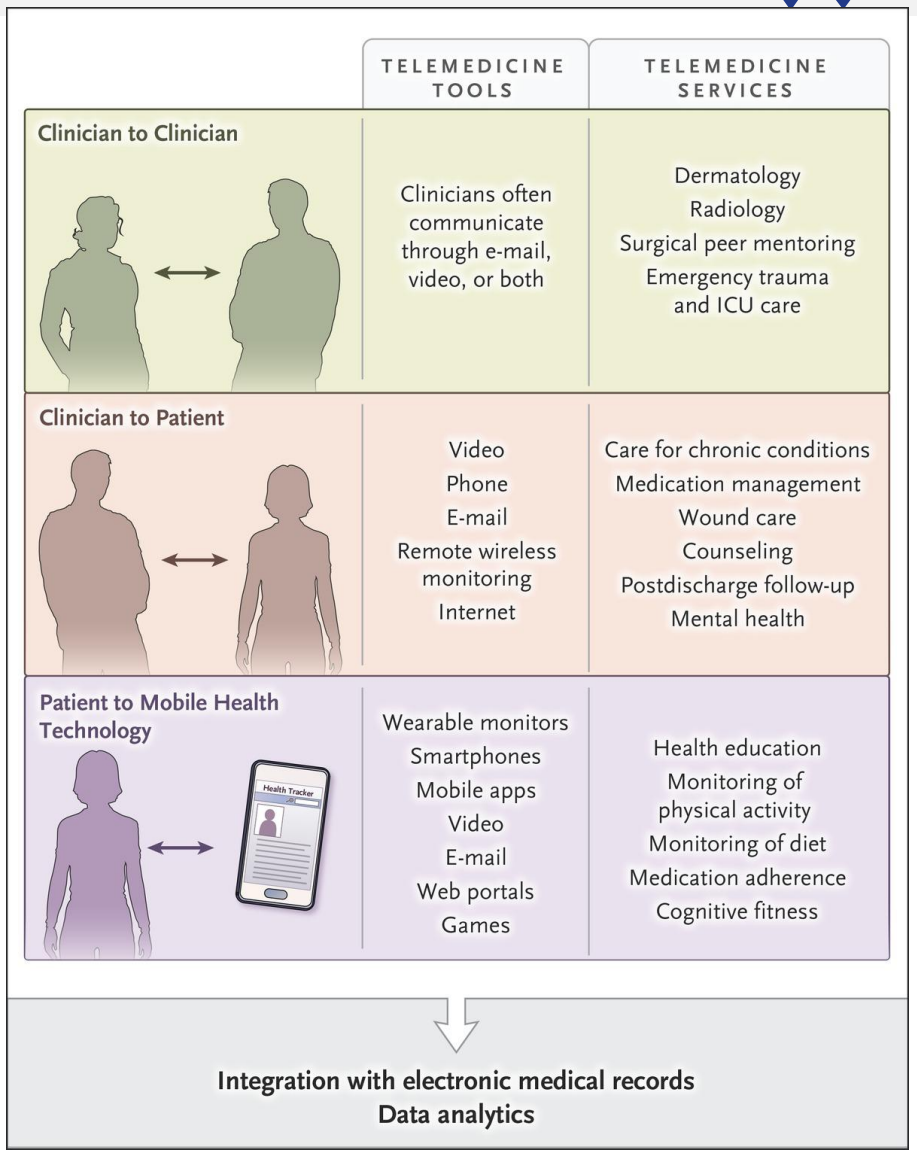
Improving diagnosis

Improving patient care

Improving communication

Telemedicine tools

- Consultation/services to physicians or other practitioners
- Direct care for patients using face-to-face videoconferencing, with or without peripheral devices
- Remote patient monitoring tools to manage chronic illnesses to supplement in-person care



ICU, intensive care unit

Tuckson RV, et al. N Engl J Med. 2017;377:1585–1592

J Parkinsons Dis. 2020 Jun 8. doi: 10.3233/JPD-202109. Online ahead of print.

Care, Convenience, Comfort, Confidentiality, and Contagion: The 5 C's That Will Shape the Future of Telemedicine

E Ray Dorsey [1], Michael S Okun [2], Bastiaan R Bloem [3]

Affiliations + expand

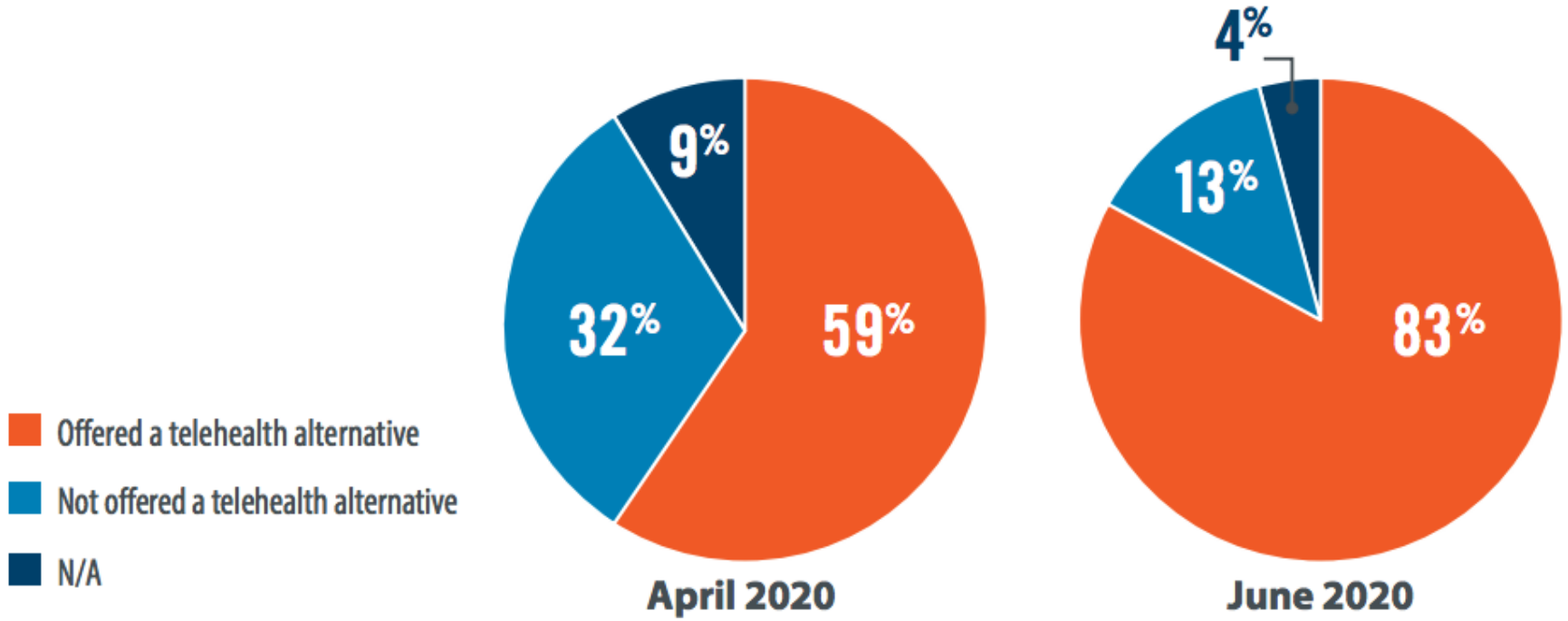
PMID: 32538870 DOI: 10.3233/JPD-202109

- Accessible **C**are
- Increased **C**onvenience
- Enhanced **C**omfort
- Greater **C**onfidentiality to patients and families
- Reduced risk of **C**ontagion

- Inability to perform parts of the physical examination
- Technologies related to laboratory testing, imaging
- Deliver care to patients from sub-specialties (physiotherapists, dieticians, social workers, etc.)
- Ethical issues

Telemedicine in GD during COVID pandemic

For people with rare diseases, access to telemedicine has increased since the start of the COVID-19 pandemic.



https://rarediseases.org/wp-content/uploads/2020/11/NRD-2061-RareInsights-CV19-Report-2_FNL.pdf

Molecular Genetics and Metabolism Reports 28 (2021) 100788

Contents lists available at ScienceDirect

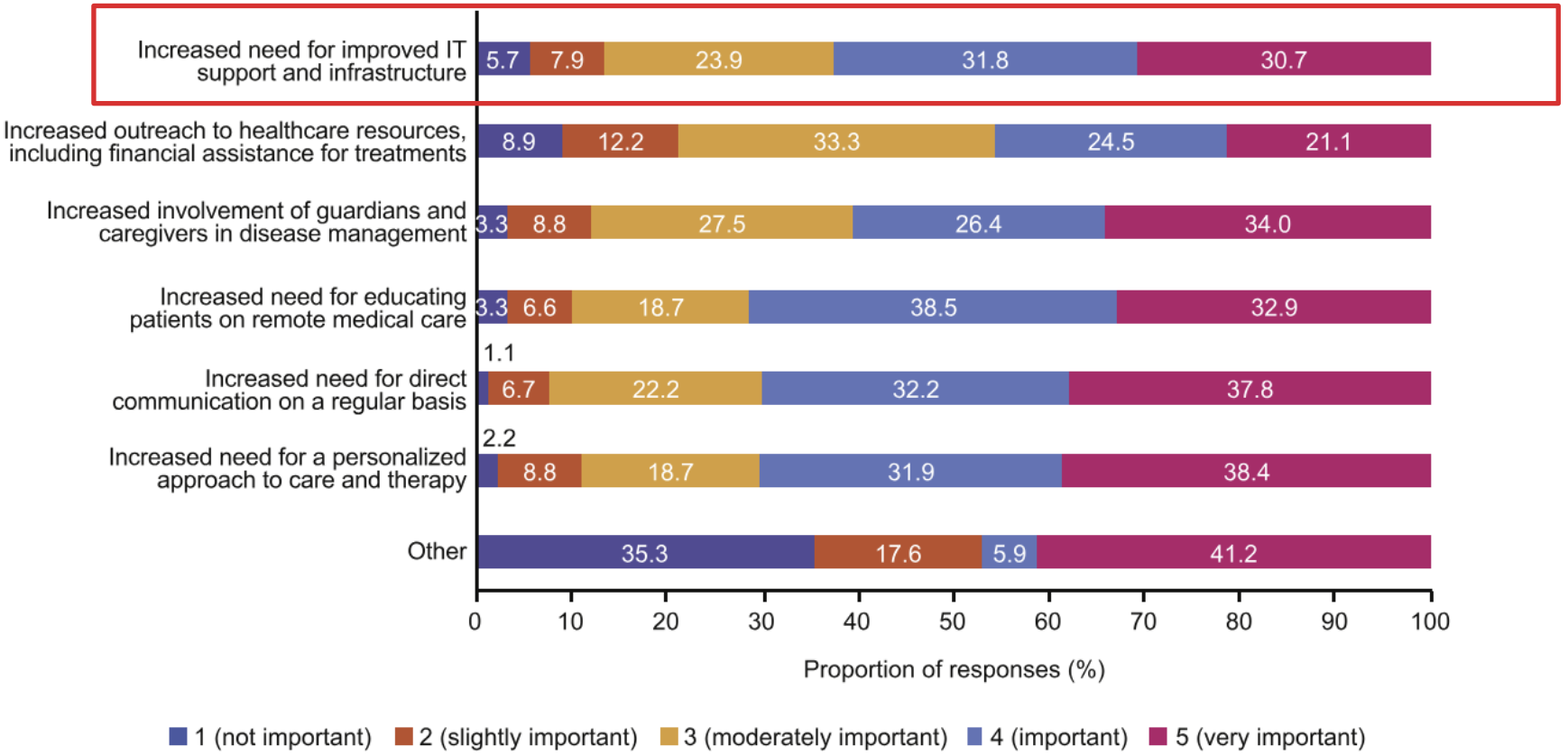
Molecular Genetics and Metabolism Reports

journal homepage: www.elsevier.com/locate/ymgmr

Short Communication

Impact of the COVID-19 pandemic on the standard of care for patients with lysosomal storage diseases: A survey of healthcare professionals in the Fabry, Gaucher, and Hunter Outcome Survey registries

Deborah Elstein [a,*], Roberto Giugliani [b], Joseph Muenzer [c], Jörn Schenk [d], Ida V.D. Schwartz [b], Christina Anagnostopoulou [d]



Wearables and mobile app.

Collected: step counts, events (e.g., bone pain, sleep), PROs (CHU9D, PedsQL Fatigue, Sleep & Stress Scales)

Donald et al. Orphanet Journal of Rare Diseases (2019) 14:212
https://doi.org/10.1186/s13023-019-1182-6

aparito

RESEARCH Open Access

Measuring disease activity and patient experience remotely using wearable technology and a mobile phone app: outcomes from a pilot study in Gaucher disease

Aimee Donald[1], Huseyin Cizer[2], Niamh Finnegan[3], Tanya Collin-Histed[4], Derralynn A. Hughes[3] and Elin Haf Davies[2*]

. 2019;14:212

Table 1 Summary Demographics of patients enrolled in wearable activity monitoring study

	ALL ($n = 21$)	nGD ($n = 16$)	GD1 ($n = 5$)
Age (yr)	Mean: 22.3 (5–48)	Mean: 21 (5–48)	Mean: 24.8 (13–42)
Sex (M:F)	6:15	2:14	4:1
Genotype		75% L444P/L444P (others mutations include: D409H, R463C, RecNcil, E233D)	Mutations: L444P, N370S, F397S, 55bpdel, 2x large deletions
mSST	Mean: 4.76 (0–17)	Mean: 6.06 (0.5–17)	Mean: 0.6 (0–3)
6MWT ($n = 15$)		($n = 12$); the mean distance was 391 m (median 377 m; SD 122.707)	($n = 3$); the mean distance was 475.67 m (age range: 18-42 yrs);
6MWT Z score		−5.57 (age range: 18-42 yrs);	−3.99 (age range 6-42 yrs)

6-minute walk test (6MWT)

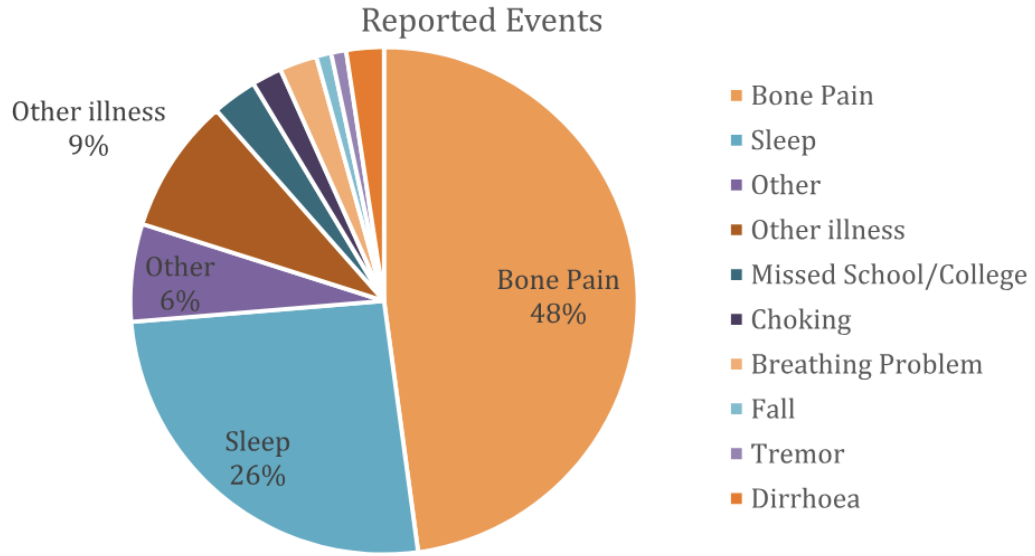


Fig. 1 Frequency of reported events via the phone app. Legend: Pie chart showing reported events, colour coded by frequency as percentage and colour coded to depict bone pain, sleep, other event, other illness, missed school, choking, breathing, fall, tremor, diarrhoea

Event reporting

Patient-reported outcomes (PROs)

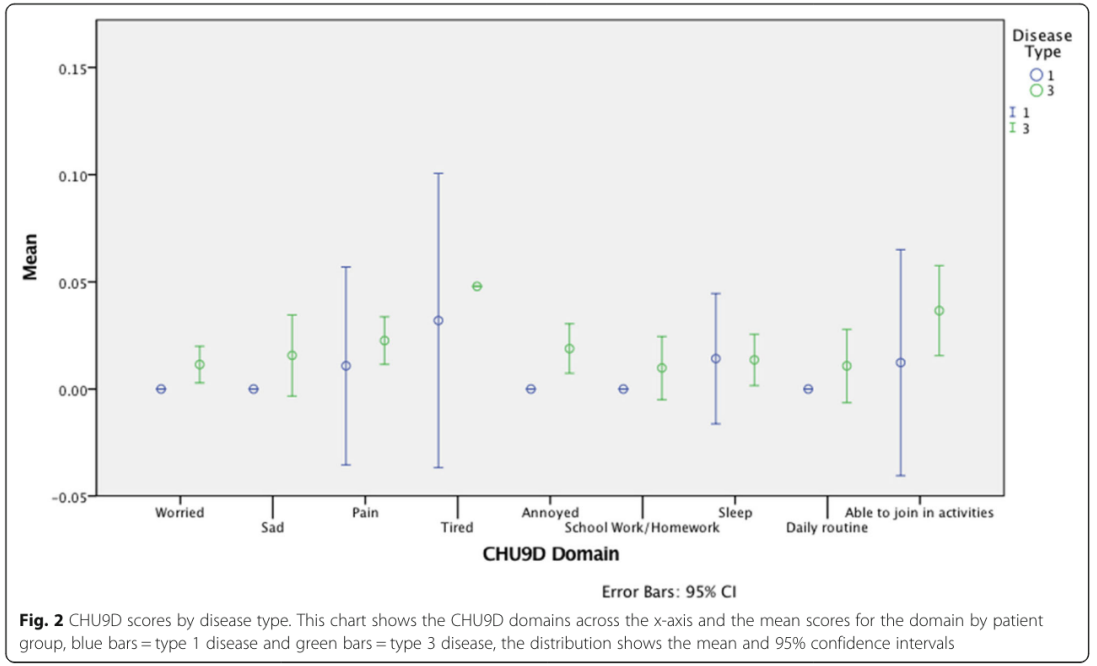


Fig. 2 CHU9D scores by disease type. This chart shows the CHU9D domains across the x-axis and the mean scores for the domain by patient group, blue bars = type 1 disease and green bars = type 3 disease, the distribution shows the mean and 95% confidence intervals

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2024c

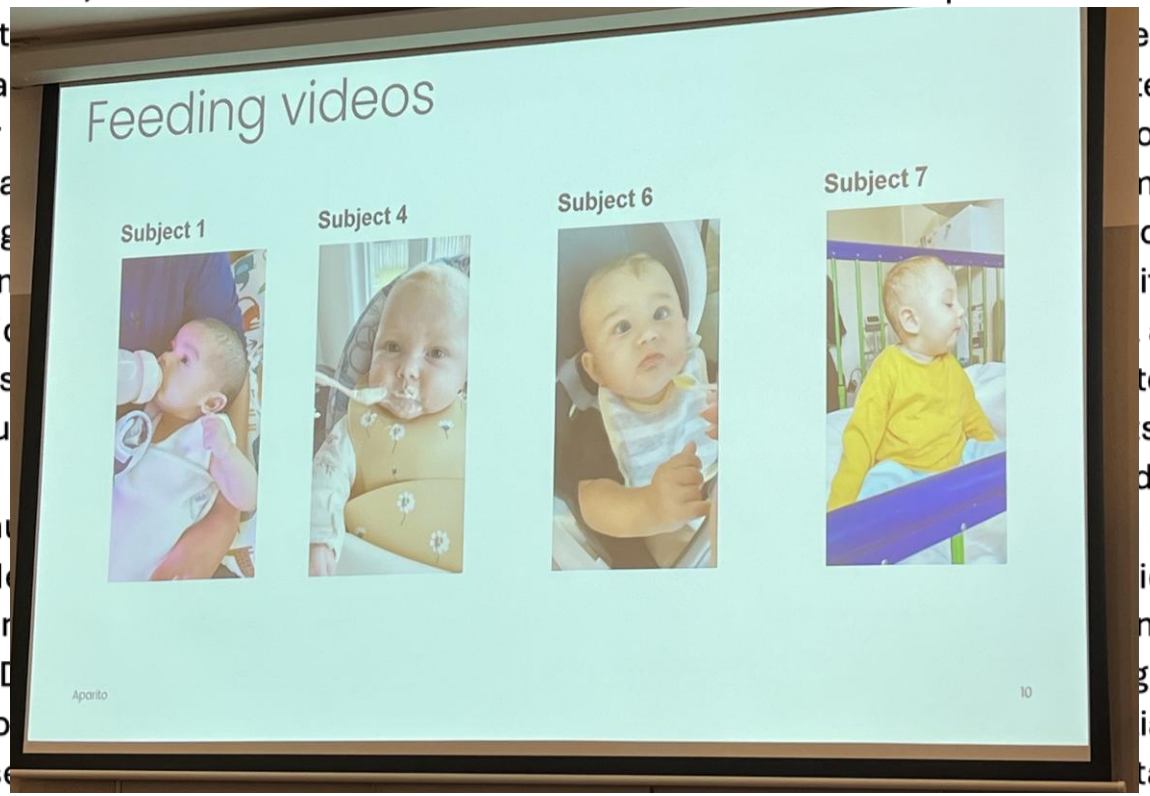
No.3

Assessing paediatric feeding in neuronopathic GD using remote smartphone video technology

Elin Haf Davies, Navdeep Sahota, Marilyn Richard, Sarah Neuhaus, Daniel Hatch, Yael Beckerman, Paul Tamburri, Rebecca Howarth

Aparito Limited, Royal Manchester Children's Hospital, Prevail Therapeutics (a Lilly company)

Paediatric feeding disorders are common, with 25% of children reported to present with some form of feeding disorder; this number increases to 80% in children with developmental delay, such as neuronopat e multifactorial including fa ted development, and distress for optic endoscopic evaluation a npliance rate. Children with feeding optimally in their regular (hon ity of parent/caregiver captured vi assessment. Up to 20 participants to achieve at least 50 video captu s with mild dysphagia (at least 5). ded. Video data of at least 2-minu by parents/caregivers and upload ideos are performed by two indepen mely, International Dysphagia D g, coughing, alterations in breath so iability analysis of clinical asse tal Questionnaire responses. A proportion of videos that are of sufficient quality to make each of the clinical assessments will also be reported. Home based video capture of eating/feeding skills via study specific mobile phone app has the potential to provide important insight and reduce patient burden.



PROTOCOL OF A TELEREHABILITATION EXERCISE PROGRAM FOR THE IMPROVEMENT OF OSTEOPOROSIS IN PATIENTS WITH GAUCHER DISEASE

European Working Group on Gaucher Disease 14th EWGGD MEETING

López Royo MP[1,2,3] Valero-Tena E[3], Roca-Espiau M[3,5,6], Giraldo P[3,6]

[1]Grupo de Investigación iPhysio. Universidad San Jorge. Villanueva de Gállego, Zaragoza, Spain.
[2] Universidad de Zaragoza. Facultad de Ciencias de la Salud y del Deporte. Zaragoza, Spain.
[3] Traslational Research Unit GIIS-012. IIS Aragón. Zaragoza Spain.
[4] Department of Rheumatology, Hospital MAZ Zaragoza, Av., Zaragoza, Spain.
[5] Radiology Center Cemedi. Zaragoza. Spain
[6] Fundación Española para el Estudio y Terapéutica Enfermedad de Gaucher y otras Lisosomales (FEETEG). Zaragoza, Spain.

MATERIAL & METHODS

This is a pilot study in which, the intervention will be performed on adult GD patients who have a BMD t-score equal or lower than -1.

INTERVENTION: Patients will receive through the application (Héfora App).

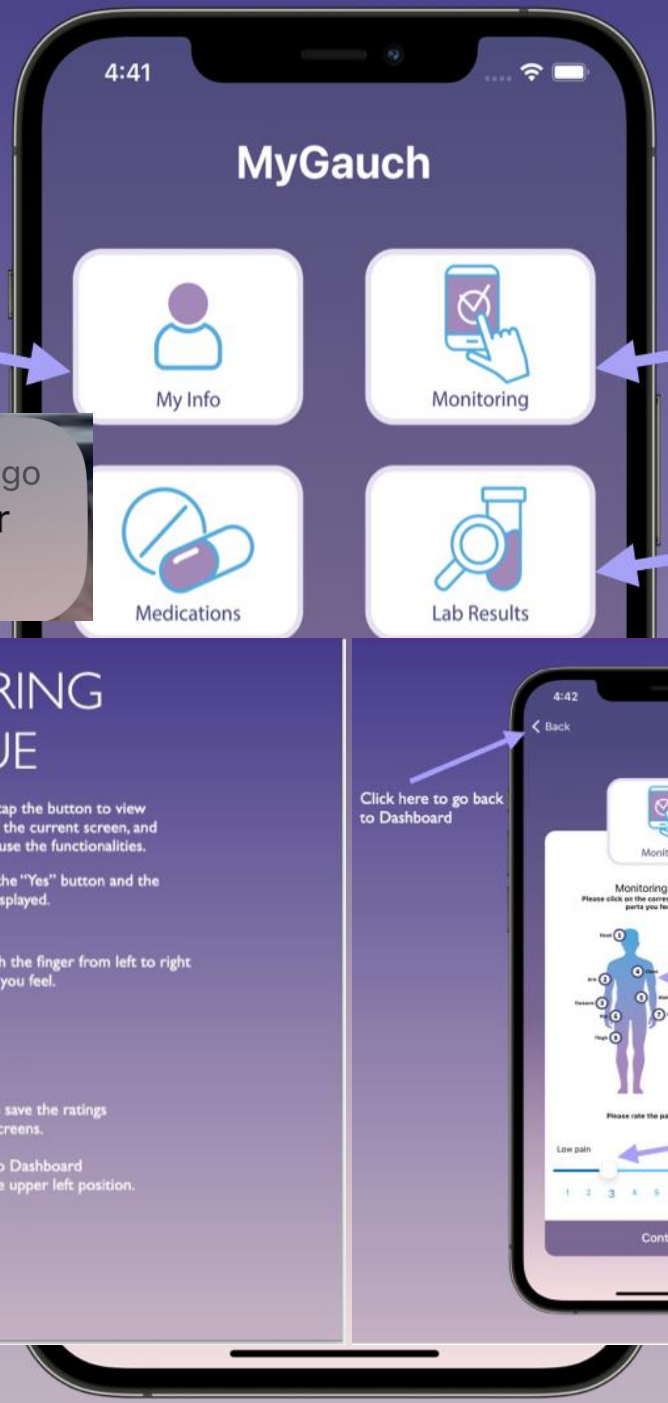
A specific exercise protocol for strength, balance and aerobic training will be developed, carried out 3 times a week for 6 months in 50-minute sessions.

This application allows subjects to have a schedule with daily notifications with the exercises they must perform, as well as watch videos, obtain explanations and daily contact with the physiotherapist.

EVALUATION: Measurements will be made to know the BMD of the patients with a densitometry, as well as their quality of life with SF-36 questionnaire, the functional capacity with six minutes walking test and the balance with Tinetti Scale.

These assessments will be registered at the beginning (day 1), at 3 months and at the end of the study (6 months).

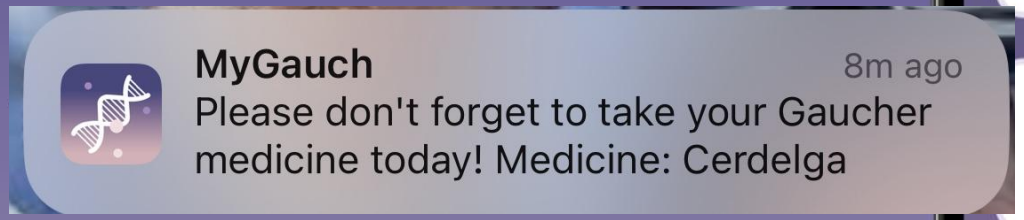
López Royo MP, et al. Poster presented at the 14th EWGGD Meeting, 12–13 October 2020 (virtual). With permission

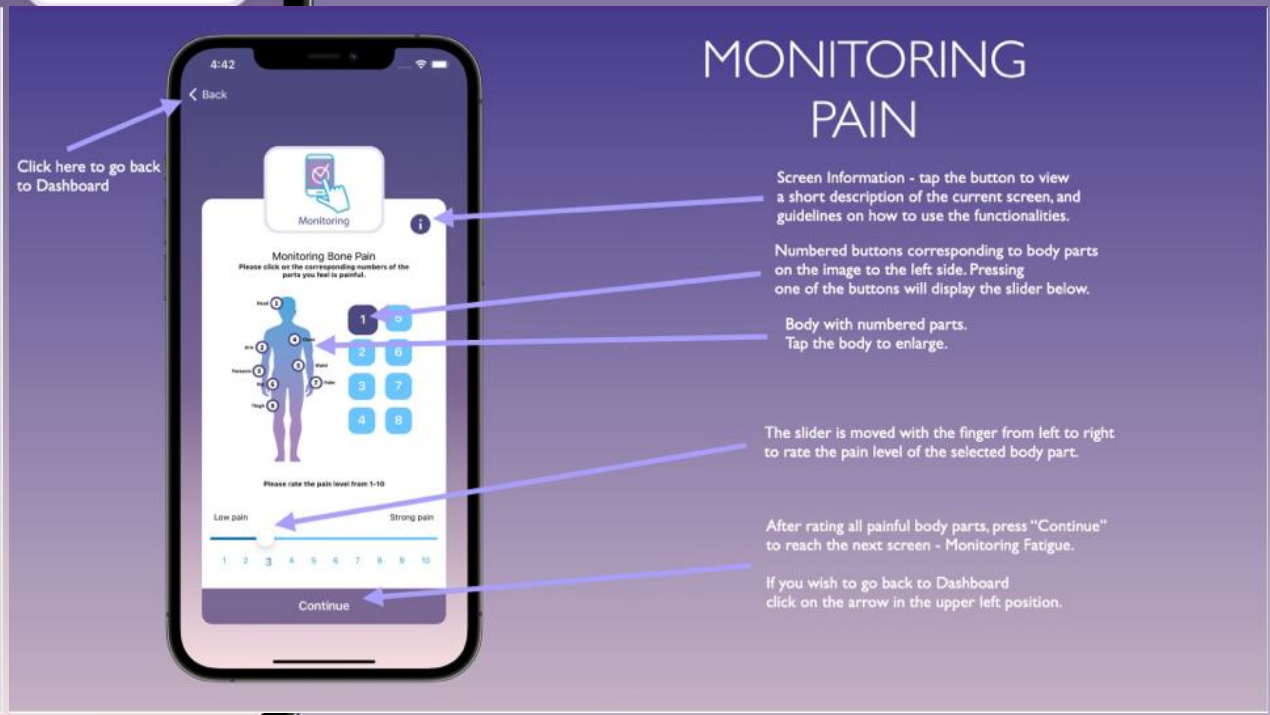


Patient information - The phone number can be changed here if necessary

Monitoring pain and fatigue

A list of the latest lab results



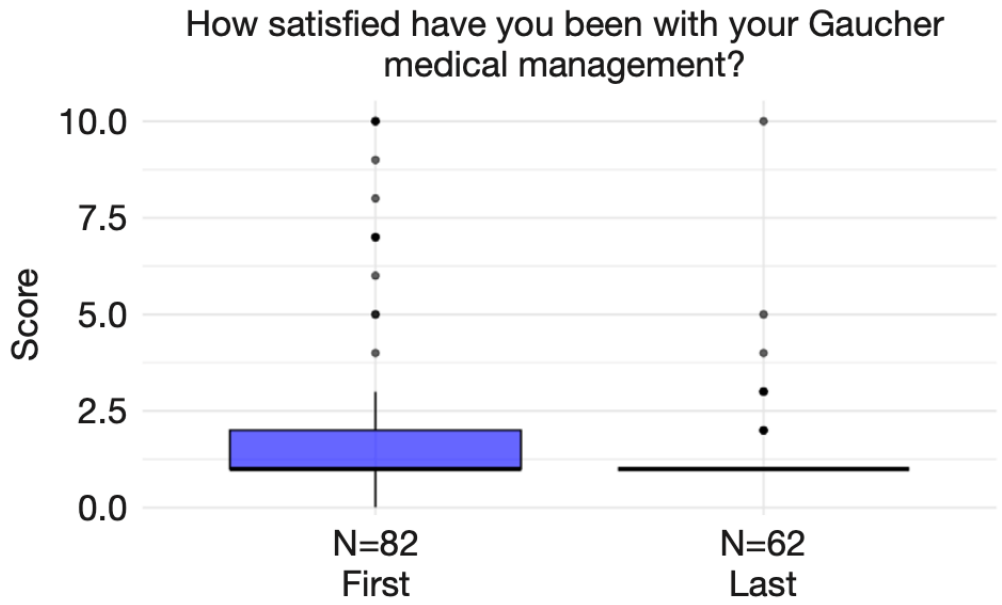


Original Article

MyGauch™: a patient-centered digital health app for Gaucher disease

Majdolen Istaiti[1], Elena Shulman[1], Tama Dinur[1], Dafna Frydman[1], Linda Harnevo[2], Moshe Farin[2], Ari Zimran[1,3], Shoshana Revel-Vilk[1,3,4]^

mHealth 2025 | https://dx.doi.org/10.21037/mhealth-24-100



The lower the better

Table 2 Reasons for non-participation in the study

Reason	Number
Not interested	35
No specific reason	30
Doesn't want to be reminded about Gaucher	3
Too many applications	1
Concern from data protection	1
Barriers	48
No access to smart phone/computer	26
Language (Russian/Arabic)	10
Older age (not good with technologies)	11
Parkinson's disease (cannot use his phone)	1

SANOFI

Next step- 2nd MyGauch global version

My Gaucher

Track symptoms, your quality of life, and manage your condition more effectively

Symptoms 23 May >

1 reported

Featured articles

Gaucher Disease Type 1

Gaucher Disease Type 3

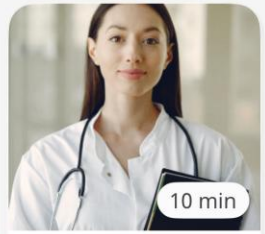
Home | Learn | Medications | My Health | My profile

Learn

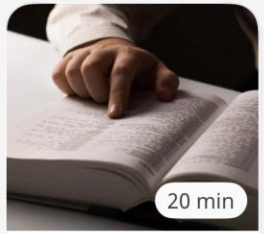
This section is dedicated to learn about GD and a little more on how to improve your day to day.

Managing Gaucher Show all

Pre-Clinic Forms



Understanding Gaucher



Essential Glossary: Clear...

Laboratory Moni-toring in Gauch...

Home | Learn | Medications | My Health | My profile

Select view

Medication list | Medication log

Imiglucerase (Cerezyme)

2400 units
Every 14 days, 1 time a day
Reminders: On
Weekly adherence is 0%

Edit

About

Enter all your medications here to easily remember all of and to share them with your care-team. Use the Edit button to keep this list up to date. Keeping an updated list of medications is an important part of your care.

Add medication

Home | Learn | Medications | My Health | My profile

Your Files

This is your file suitcase, where you can upload your chosen files to keep your most recent test results.

Your Image Studies >

-- response(s)

Blood Tests >

-- response(s)

Questionnaires

Your GD Questionnaire 15 Aug >

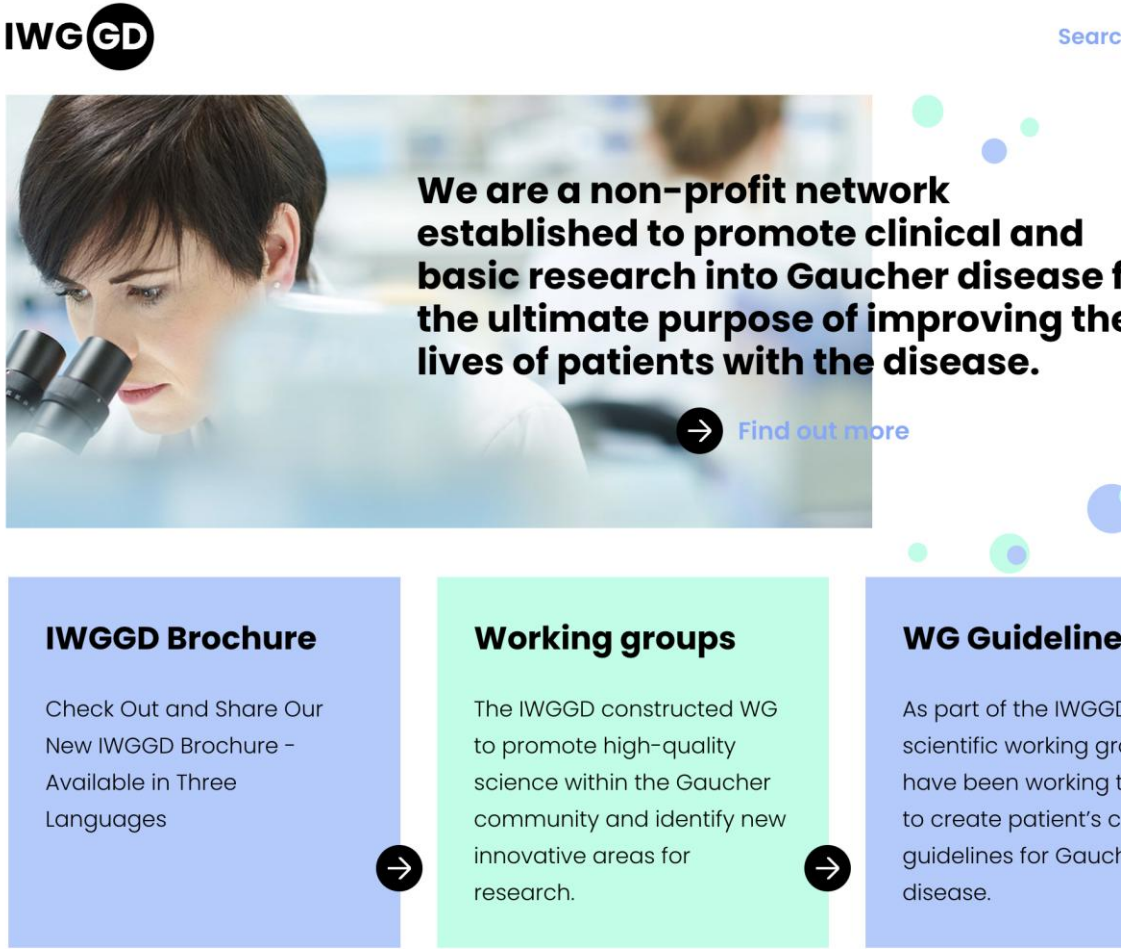
29 response(s)

Developed by the IGA and IWGGD

IWGGD

IGA

Networking



https://iwggd.com/

https://gaucheralliance.org/

Maybe a ChAT bot would be better to capture PRO

XOLTAR: Reinventing the Patient Support Experience in Healthcare

What does Chat GP has to say on digital health in Gaucher disease

ChatGPT

Summary

1. **Telemedicine**
   - **Remote Consultations**: Telemedicine allows patients to consult with specialists without the need for travel, which is particularly beneficial for those living in remote areas or with limited access to healthcare facilities.
   - **Regular Monitoring**: Patients can have regular check-ups and monitoring of their condition through virtual visits, reducing the frequency of in-person appointments.
2. **Mobile Health Apps**
   - **Symptom Tracking**: Mobile apps can help patients track their symptoms, medication adherence, and overall health status. This data can be shared with healthcare providers to optimize treatment plans.
   - **Patient Education**: Apps can provide educational resources about Gaucher disease, treatment options, and lifestyle recommendations.
3. **Wearable Devices**
   - **Health Monitoring**: Wearable devices can continuously monitor vital signs, physical activity, and other health parameters. This real-time data can alert patients and healthcare providers to potential issues before they become serious.
   - **Data Integration**: Data from wearables can be integrated into electronic health records (EHRs), providing a comprehensive view of the patient's health.

Summary

What does Chat GP has to say on digital health in Gaucher disease

ChatGPT

4. Artificial Intelligence and Machine Learning

- **Predictive Analytics**: AI can analyze large datasets to develop diagnostic algorithms, predict disease progression and treatment outcomes, helping clinicians make more informed decisions.
- **Virtual Assistants**: AI-powered virtual assistants can help patients manage their daily health routines, answer questions about their condition, and provide medication reminders.

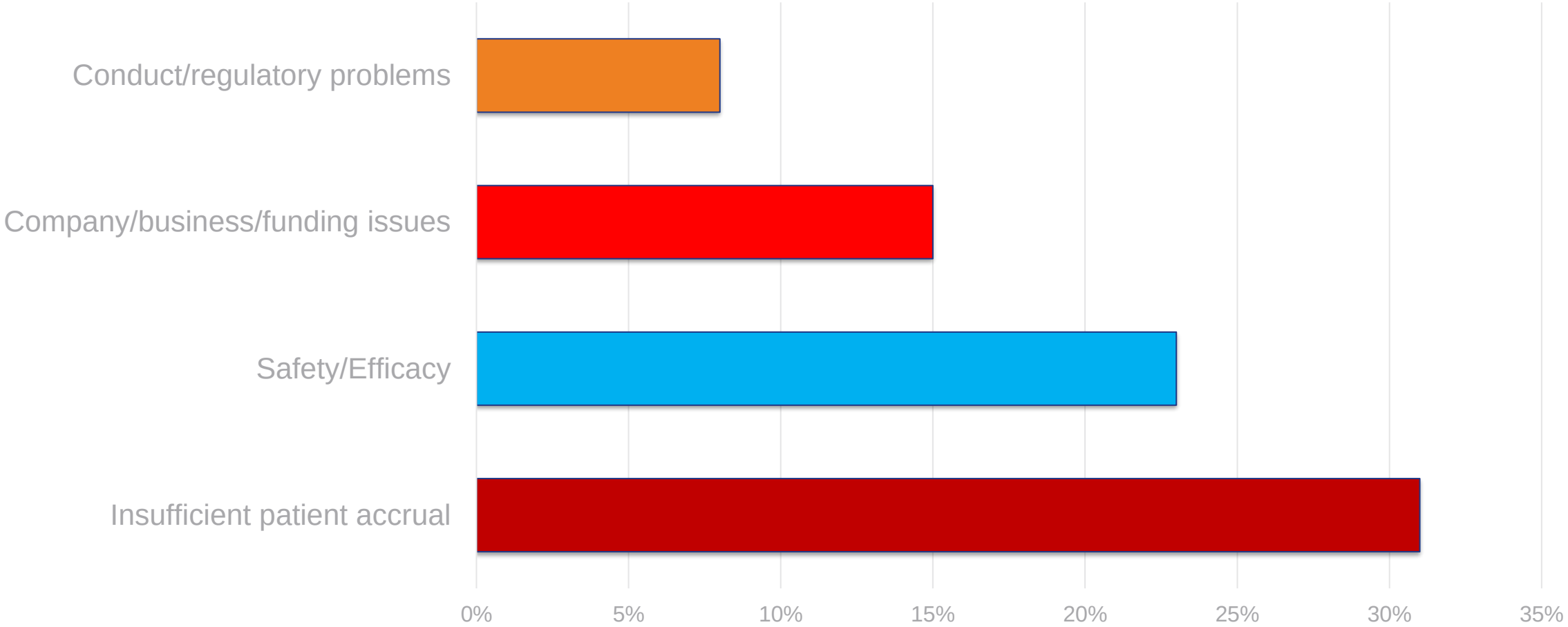
5. Patient Support Communities

- **Online Forums and Support Groups**: Digital platforms can connect patients and families affected by Gaucher disease, providing emotional support, shared experiences, and practical advice.
- **Research Participation**: Patients can participate in clinical trials and research studies via digital platforms, advancing the understanding and treatment of Gaucher disease.

6. Genomic and Personalized Medicine

- **Genetic Testing**: Advances in genomic technologies can facilitate early and accurate diagnosis of Gaucher disease. Genetic information can also guide personalized treatment plans.
- **Biomarker Identification**: Digital health tools can help identify biomarkers of disease progression and treatment response, enabling more targeted and effective therapies.

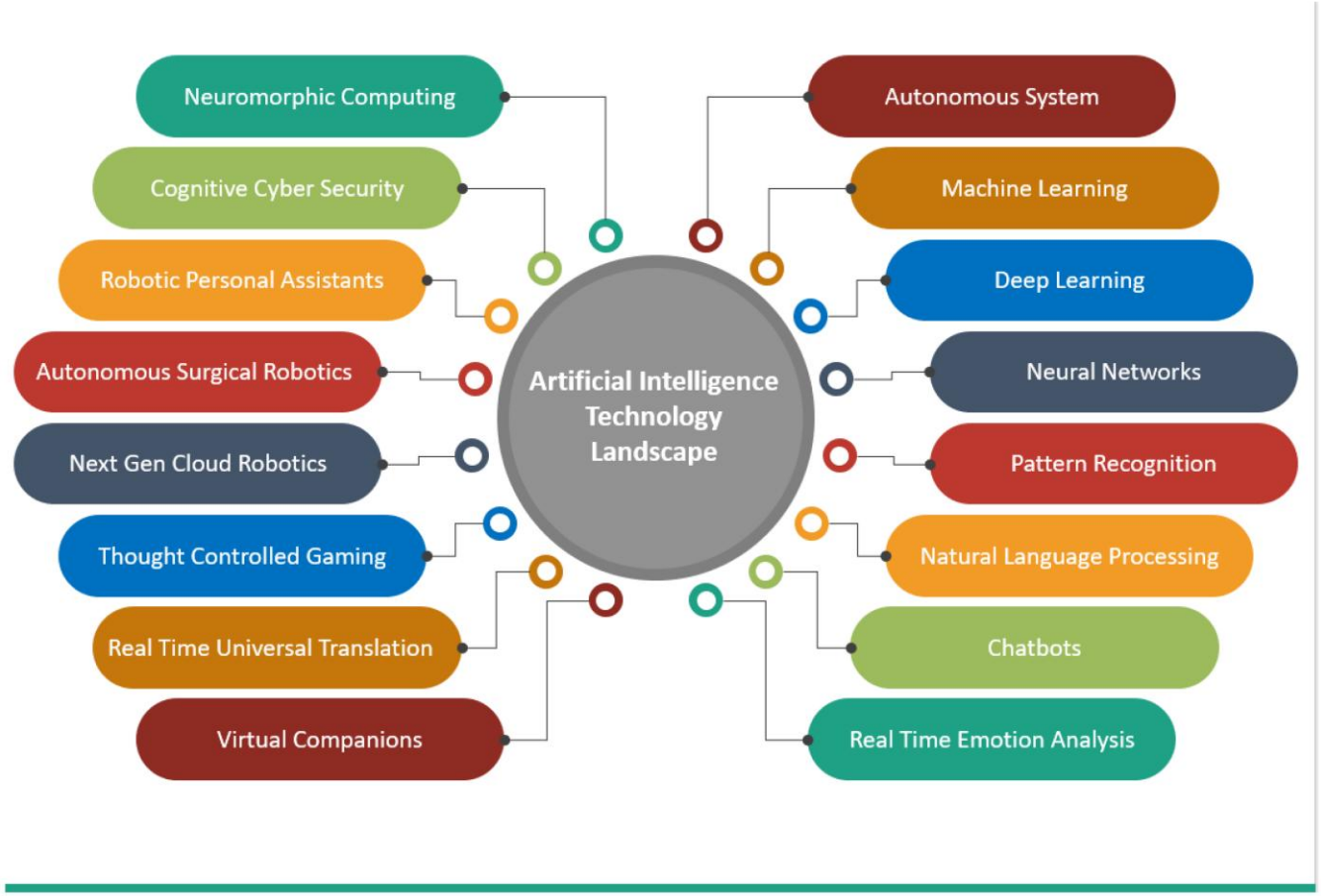
Leading Causes of Failure in Rare Disease



Rees C, et al. PLoS Medicine, 2019; Schoenen S, et al. Orphanet Journal of Rare Diseases, 2024

Integration of AI in clinical trails

- Patient recruitment and screening
- Clinical trial design and feasibility
- Data capture, monitoring, and analysis



Aldoseri A, Al-Khalifa KN, & Hamouda AM (2023). *Applied Sciences*, *13*(12), 7082.

Successful implementation of digital health

- **Stakeholder Involvement**- patients, caregivers, and healthcare professionals
- **Collaboration-** Promote data sharing among healthcare providers, researchers, and institutions
- **Training and Support**
- **Regulatory Compliance**
- **Continuous Improvement**- Implement feedback mechanisms and regularly update based on user feedback and performance data
- **Accessibility and affordability-** Develop cost-effective solutions to make digital health affordable for a wider population

Thanks for your attention !

SZMC Gaucher Unit

IWGGD The International Working Group on Gaucher Disease

Supportive care working group

Subwork working on Digital Health

Please contact me if interested in joining

Srevelvilk@gmail.com