CASE STUDY: DxGPT (Global)

PILLAR(S): 1 (Patient and family empowerment) & 2 (Equipping Providers)

An AI tool that enables patients and health care providers to accelerate diagnosis for rare disease

Context

The diagnostic journey can be confusing and overwhelming to parents who are wondering whether their child may have a rare disease. Searching the internet for clues based on symptoms is often frustrating and does not necessarily lead to answers or next steps to help get closer to a diagnosis. It can also be challenging for health care providers to diagnose a patient without the right tools and a clear starting point.

Newer technologies and tools, such as artificial intelligence (AI), can potentially revolutionize the field of rare disease diagnosis. The ability to quickly analyze data and identify patterns could improve the accuracy and speed of a diagnosis, reduce costs to the health care system and bring peace of mind to families seeking answers.

DxGPT

Overview of program

Dx29 is a free, AI tool designed for patients/caregivers and providers who suspect a rare disease. The tool supports them in reporting and analyzing symptoms and creating and sharing medical histories in the quest to reach a diagnosis.

Dx29 is the brainchild of Julian Isla, a computer engineer and the father of a child with Dravet's syndrome who was misdiagnosed at a young age with serious health consequences. **Foundation29** is the Spanish non-profit organization that he founded. It is led by activists, scientists, patient advocates, technologists and health care system changemakers devoted to empowering patients to harness the value of their health data to accelerate rare disease diagnosis.

Launched in 2019, Dx29 is an easy-to-use, free of charge digital tool that originally operated as a search engine for providers and later became a valuable resource for patients and caregivers. Dx29 enables users to enter symptoms with simple phrases (e.g., cannot swallow, cannot walk, cannot speak), making it accessible to those who are not familiar with medical terminology.

Users' entries trigger a drop-down menu to help them learn and select the relevant medical terms (e.g., cannot swallow translates to dysphagia). The tool then proposes a list of potential rare diseases, making it possible for patients/caregivers to ask targeted questions of their providers and prompting them to look "beyond the usual suspects" when a case proves difficult to diagnose.

Through streamlining the diagnostic process, the tool helps reduce the time and resources required to reach a diagnosis, potentially improving patient outcomes and reducing health care system costs.

For those who already have a diagnosis, Dx29 can generate a medical history using medical records that the user provides. The AI tool extracts key events from the records, prepares a history in chronological order, provides information on the latest clinical trials and offers resources through links to patient groups. In addition, people who have a diagnosis can upload their data to continuously strengthen Dx29's "intelligence" and ability to diagnose those still searching for answers.

Dx29 not only supports patients and caregivers in reporting and analyzing symptoms but also has the capability to analyze genetic information from Next-Generation Sequencing (NGS) files. This advanced feature enhances the tool's diagnostic capabilities by integrating genetic data into the analysis process. By leveraging datasets and models from various organizations, such as Human Phenotype Ontology, Monarch Initiative, Mondo, and Orphanet, Dx29 can correlate genetic information with phenotypic data, providing a more comprehensive approach to diagnosing rare diseases. This integration results in a more precise identification of potential genetic causes of a patient's symptoms, thereby improving the accuracy and speed of diagnosis.

In November 2022, the emergence of predictive language learning models and generative AI created an exciting opportunity for Dx29 to take a giant leap forward in its ease of use and functionality. **DxGPT** — a 2.0 version of Dx29 — enables users to enter a free-form description of their symptoms and health condition in their own words, eliminating the need for families to decipher medical terms. The open language learning model picks up on key phrases and proposes a more targeted list of differential diagnoses, improving its overall accuracy and providing a more accessible tool. DxGPT utilizes the initial datasets and models and recommends diagnostic methods, tests and treatments, enhancing the overall user experience and providing potential answers even more quickly.

According to a clinical evaluation conducted in July 2024, DxGPT's level of accuracy in diagnosis was similar to that of medical staff from a pediatric hospital in Barcelona for both common and rare diseases. Clinicians participating in this study rated the DxGPT platform highly (3.9/5 overall, 4.1/5 for usefulness, and 4.5/5 for usability), noting that these tools could provide new insights for challenging diagnostic cases such as rare diseases. At this time, DxGPT is a decision support tool designed to assist in the diagnosis of rare diseases under human supervision and cannot be used as a standalone resource to obtain a definitive medical diagnosis.

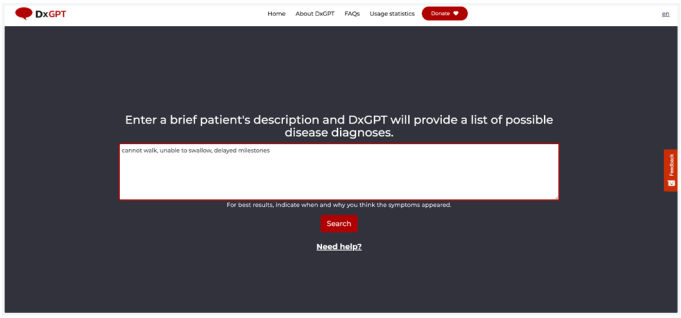


Figure 1: Homepage allowing freeform typing

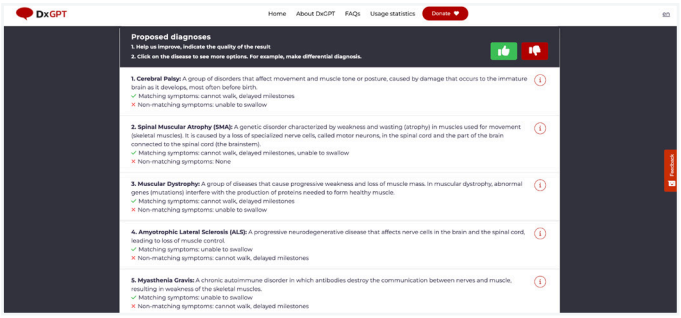


Figure 2: Proposed list of diagnoses once search function is enabled

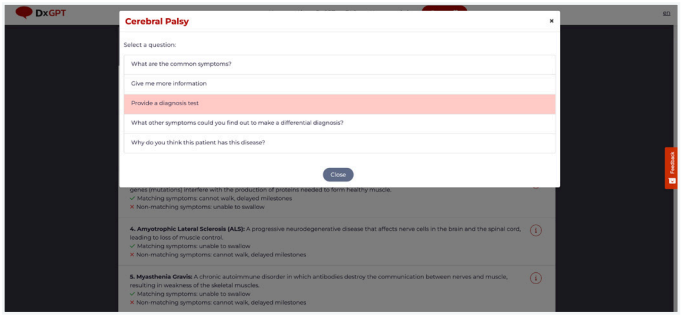


Figure 3: Additional tabs when clicking on each disease

Figure 4: Pop up window for suggested diagnostic test under cerebral palsy

Key advantages of using the DxGPT tool when looking for a diagnosis include:

Patient empowerment

While the interface currently operates in Spanish, French and English, patients or caregivers can enter their symptoms in nearly any language and receive responses in that language through the search engine-like feature. As a result, they can tell their story using their own words and share information with their physician.

Better patient-provider communication

The tool generates comprehensive medical histories, helping patients and caregivers become more informed and adept at communicating with health care providers faster because their symptoms are arranged in chronological order.

Advanced analytics

As a tailored "search engine," the tool analyzes data using a state-of-the-art algorithm to predict a rare disease diagnosis, saving significant time and resources.

Results

DxGPT is experiencing growing popularity, with more than 62,000 new users in the past year and currently more than 450 daily users from across the world. Eighty percent of users are from the U.S., Spain, India and the UK.

DxGPT is producing impressive results in pinpointing diagnoses. In nearly 60% of cases, the first suggested diagnosis matched the actual/confirmed diagnosis, and the right diagnosis was among the top five suggestions in nearly 65% of cases.

Madrid's health care system recently integrated a branded version of DxGPT (called SermasGPT) into the electronic medical record system across all primary care settings to help patients obtain a rare disease diagnosis much faster. At present, more than 30 physicians are actively using SermasGPT (which has its own data storage guidelines) every day, and 20 cases have been diagnosed thus far. The Ministry of Health in Spain has expressed interest in expanding SermasGPT beyond Madrid; adoption has already begun in the Catalonia region.

The Foundation29 team has made their code open source, allowing any health system or other third party to use it. Sponsorships have made it possible for DxGPT to be available at no cost to patients, their caregivers and providers globally — fulfilling the goal of making the diagnostic journey easier to navigate and obtaining a faster, more accurate diagnosis.

Learnings

- **Innovation can empower patients:** DxGPT puts the power of technology in the hands of those seeking answers for their child's disease, enabling patients and their caregivers to come to medical appointments with informed questions, facilitating a meaningful conversation with their care team and prompting providers to think about rare diseases sooner.
- **Integrating feedback leads to a better user experience:** To keep the tool responsive to users' needs and improve their experience, the team was committed to requesting feedback and adapting the tool to provide what users wanted. Since the release of DxGPT, the team has been collecting user feedback in various ways on the platform and has noted high user satisfaction.

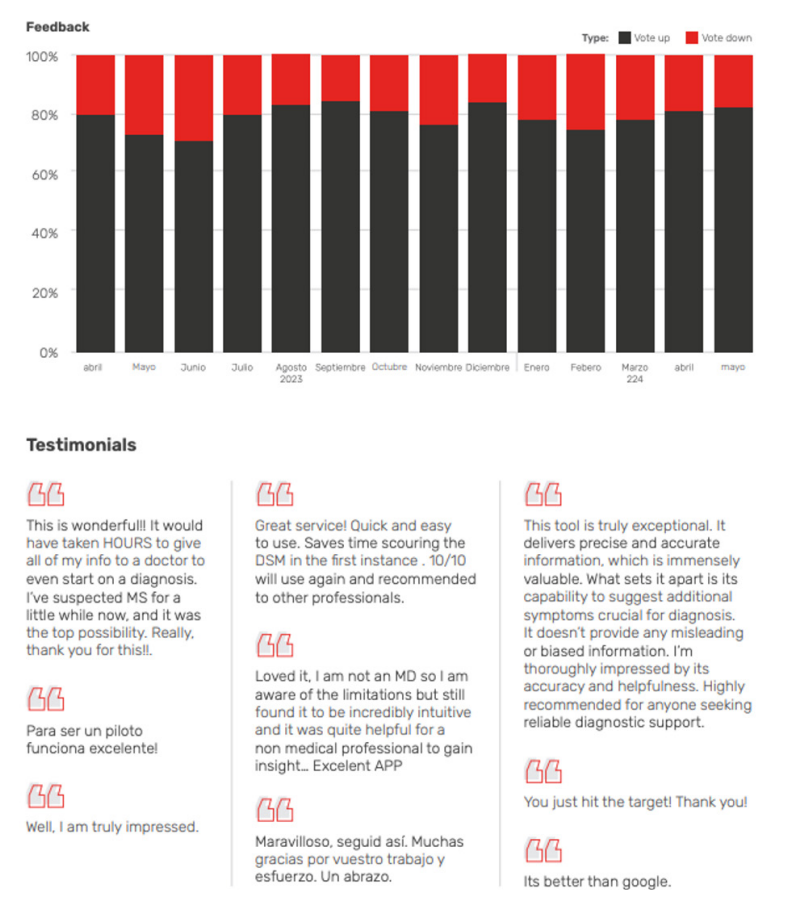


Figure 6: DxGPT user testimonials and feedback

Learnings

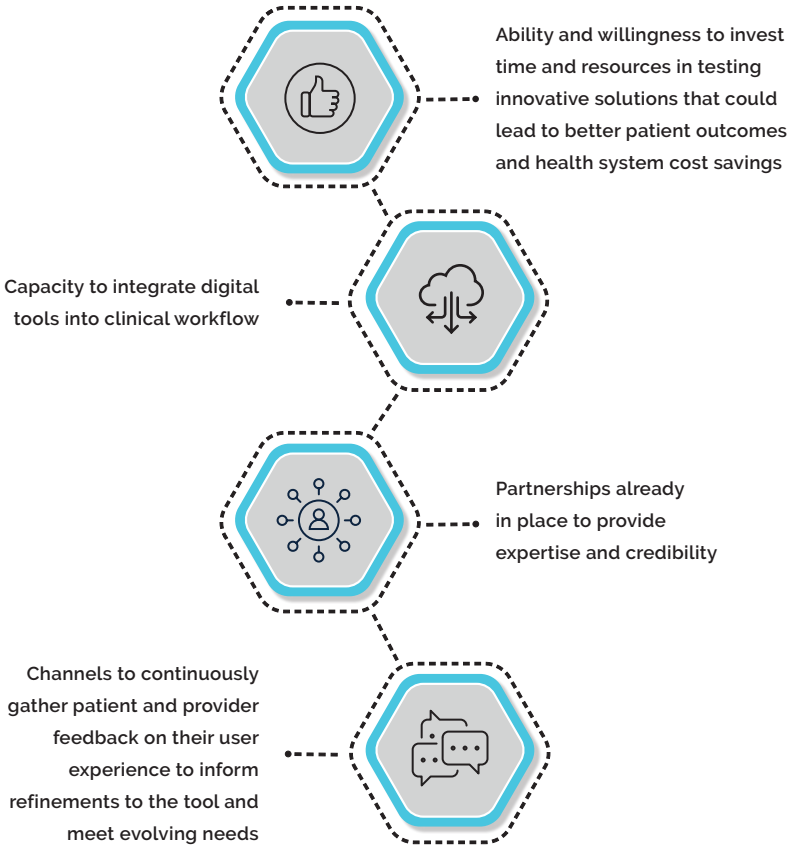
- **Accumulated expertise:** The success of these tools is rooted in Foundation29's years of experience and dedication to rare disease diagnosis. The team's accumulated know-how contributed to the development of a robust database integrating multiple reputable sources, continuous refinement of the tool based on user feedback, and an understanding of both patient and health care provider needs. This expertise enabled Foundation29 to create a tool that not only leveraged cutting-edge technology but also addressed real-world needs in the rare disease community.
- **Innovation must respond to user needs:** The evolution from Dx29 to DxGPT demonstrates Foundation29's commitment to continuous improvement. By staying abreast of technological advancements and actively seeking user feedback, the team has been able to enhance the tool's capabilities and user experience over time. Because the developers had been testing Dx29 for a few years, they understood its users and their needs. As a result, the team was able to rapidly leverage new technology to evolve the tool — into DxGPT — to better serve patients and families who find it easy to use.
- **The right partners and expertise are necessary to achieve goals:** Strategic partnerships and collaborations that provided the necessary resources, expertise and credibility enhanced the development and success of these tools. Microsoft provided technical support, patient associations were valuable in ensuring that patient and family needs were considered when designing this tool, Takeda and Sanofi provided financial grant support, members of the Global Commission offered guidance on how to strengthen the tool for physicians to use in their practices, and the team integrated datasets from organizations like Human Phenotype Ontology and Orphanet.
- **Word travels:** Without a formal communications strategy, DxGPT has experienced organic growth through patient and provider networks, with users increasing exponentially and sharing the tool as a key resource in their communities. As a result, DxGPT has gained global attention, and the developers secured a partnership with Google which launched a sponsored marketing campaign to promote DxGPT when users are looking for rare disease resources.
- **Data privacy and protection are essential to attract users:** By prioritizing user data protection and offering the tool at no cost, the team removed potential barriers to adoption and built trust within the user community. Only users can share their data — Foundation 29 does not share this information. To ensure providers, patients and their families feel confident in sharing personal information, data privacy protection has been an important element in encouraging them to use the tool. To comply with General Data Protection Regulations, DxGPT does not store patient data and has an automated process that detects and deletes personal information that the user may have added accidentally. In the future, additional functionality will enable patients to store their data on their own hardware.

Goals & next steps

Looking ahead, the Foundation 29 team aims to:

- **Scale in collaboration with governments outside of Spain:** The tool has captured the attention of other countries, with France and Germany reaching out to assess potentially using the tool.
- **Facilitate smoother patient navigation:** Foundation29 is working towards integrating **a virtual personal health assistant** with DxGPT to improve the patient experience by facilitating coordination between different levels of care, from primary care to hospital specialists.
- **Improve the accuracy of the existing model continuously:** The team aims to increase the diagnostic accuracy and response speed of DxGPT through its most recent upgrade to OpenAI's language model, GPT-4o. This effort will also include minor changes to the interface and checking symptoms through a visual reference.
- **Take advantage of evolving technology:** Learning language models (LLM) show potential for sustaining and growing the tool. The team's goal is to develop DxGPT at the same speed that current LLMs are evolving to ensure that Foundation29 fully explores the potential of new AI models.
- **Build path toward greater adoption:** Foundation29 aims to foster adoption of the tool among organizations, institutions and public and private health care providers. In addition, the team is exploring the possibility of going through a regulatory pathway and obtaining a medical device certification which would lead to more widespread adoption.

Considerations in adopting an AI tool



References

1. Human Phenotype Ontology: Provides a standardized vocabulary of phenotypic abnormalities encountered in human disease
2. Monarch Initiative: Integrative data and analytic platform connecting phenotypes to genotypes across species, bridging basic and applied research with semantics-based analysis
3. Mondo: Provides a hierarchical structure which can be used for classification of diseases to higher level groupings and mappings to other disease resources
4. Orphanet: Provides high-quality information on rare diseases, and maintains the Orphanet rare disease nomenclature
5. Alvarez-Estape, Marina & Cano, Ivan & Pino, Rosa & Grado, Carla & Aldemira-Liz, Andrea & Gonzálvez-Ortuño, Javier & Olmo, Juanjo & Logroño, Javier & Martínez, Marcelo & Mascías, Carlos & Isla, Julián & Roldán, Jordi & Launes, Cristian & Garcia-Cuyas, Francesc & Esteller-Cucala, Paula. (2024). Evaluation of the Clinical Utility of DxGPT, a GPT-4 Based Large Language Model, through an Analysis of Diagnostic Accuracy and User Experience. 10.1101/2024.07.23.24310847.
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