Mount Sinai Health Hackathon

Creating Novel Technology Solutions For Healthcare

Rare Diseases

Problem Statement

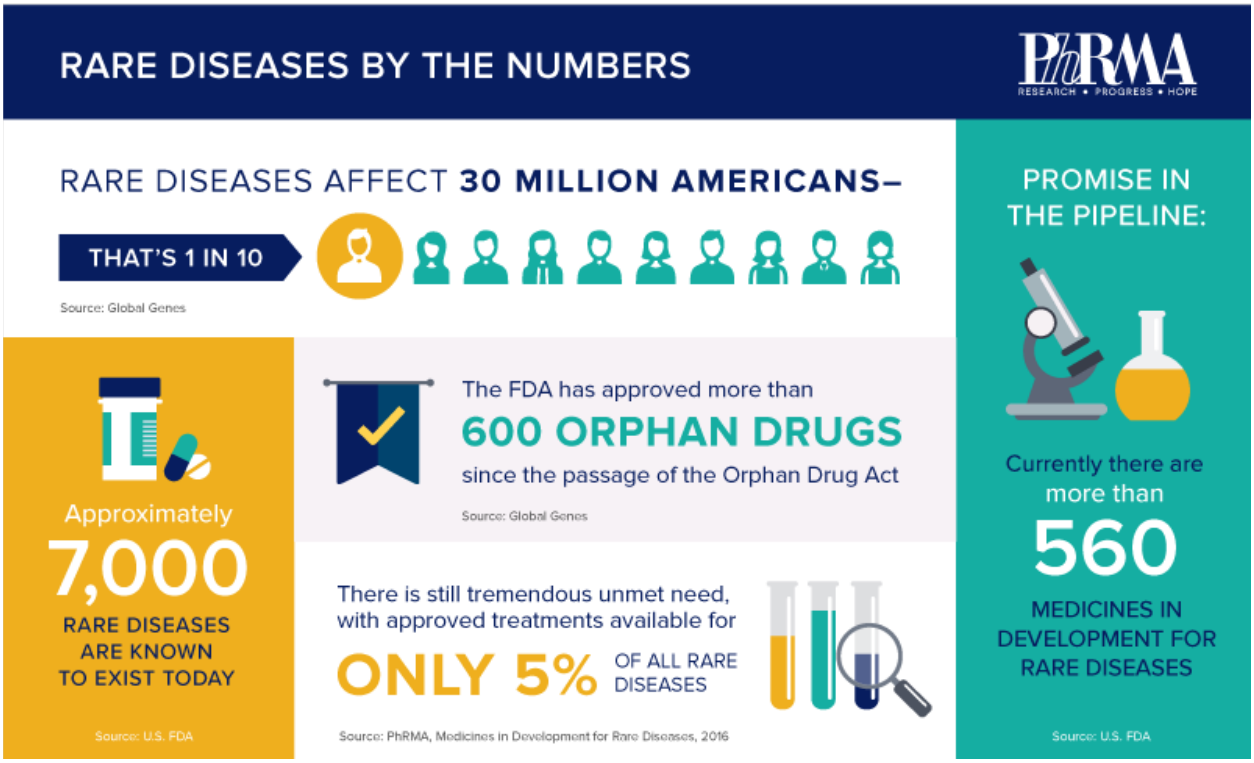
There are more than 7,000 rare diseases identified[6] and there are 300 million people affected. Only a fraction of these conditions have an approved treatment and statistics for the number of people seeking care with disorders of unknown/or unclear etiology (i.e. undiagnosed rare disease patients) are not defined[1].

As the National Organization for rare diseases states, in its latest compelling video, Rare Diseases are not so rare, comes in all ages, shapes and sizes, ethnicities and race; there is a compelling need to advance the outlook of patients with rare diseases and to find novel technology solutions to address the needs of this community.

Rare diseases are characterized by several unmet needs and one of the most important is the difficulty in making a timely and accurate diagnosis. Delays in diagnosis can have significant life-changing or life-shortening consequences for patients, delaying proper disease management.

Other challenges faced by developing interventions and diagnostics for Orphan/rare diseases, is that the diseases are so rare that sponsors are reluctant to develop them under normal marketing conditions. Over the last couple of decades, there have been regulatory adjustments such as expedited priority review and extended market exclusivity, made by the FDA in order to incentivize the development of improved treatments for serious diseases. If a drug meets certain criteria, it may qualify for orphan designation and therefore also for various developmental incentives. The Rare Pediatric Disease Priority Review Voucher, allows a sponsor/manufacturer who receives an approval for a drug or biologic for a 'rare pediatric disease', to qualify for a voucher that will allow for priority (accelerated) FDA review for a different product. This voucher is transferable and may be sold for financial returns (multimillions of dollars). (ref. 7)

- In recent years, groundbreaking therapies include:
  - First treatments directed at treating the underlying causes of cystic fibrosis
  - New medicines that can prevent or slow the impact of devastating conditions including pulmonary hypertension, hereditary angioedema and Gaucher disease
  - First therapies are available to treat rare pediatric diseases e.g. Hypophatasia, lysosomal acid lipase deficiency and neuroblastoma



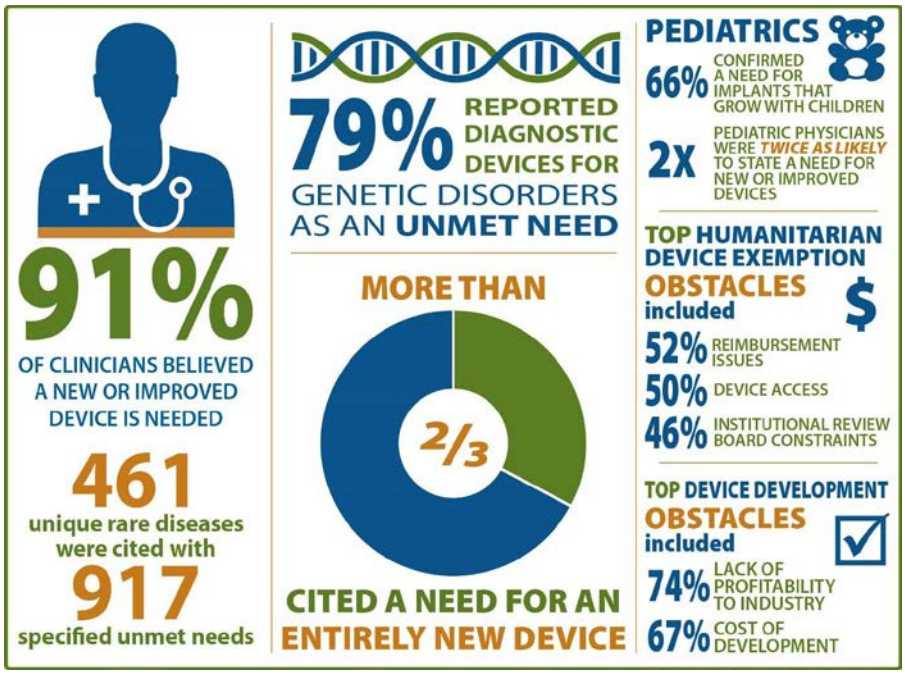
(ref.8)

Legislation regarding medical devices for rare diseases is also in place and offers an expedited route to approval (Humanitarian Device Exemption (HDE) [3]. HDE has provided a helpful pathway for bringing devices to market; however, considerable challenges remain concerning reimbursement, patient access and institutional review board (IRB) constraints. A recent survey conducted by NCATS in partnership with the FDA in 2017[4] described a number of specific unmet needs regarding devices for rare diseases, including:

- Development of new or improved medical devices for diagnosing and treating rare diseases
- Creation of diagnostic devices for inherited genetic disorders
- Construction of new prototypes rather than modifications or repurposing of currently available devices, which are often inadequate and of limited value in diagnosing or treating rare diseases

The above survey also highlighted several impediments to the development process of new devices for rare diseases which included significant costs and the perceived lack of return on investment and profitability for industry.

Children are commonly affected by rare diseases and are the largest population at risk. Unique challenges for the construction of devices of benefit for children with rare diseases include the variation in sizes of specific devices needed over time, as a child ages and the need for devices and implants, in some instances, to grow along with the child, in order to remain useful.



Other issues to consider in the development of new devices including wearables for rare diseases were highlighted in a recent report on Orphan diseases[5] and include:

- Lack of readily available access to data and knowledgeable management tools regarding specific rare disease that are actionable to increase the evidenced based delivery and efficiency of care. Data and information is dispersed through a range of range of primary sources, surveys, trials, publications such as scientific articles, real-world data from organized sources (electronic health records, pharmacovigilance data, and care management databases), and unorganized sources like the Internet and social media. No integrated resource is available rending access to information feasible in a timely and integrated fashion.
- Clinical trial recruitment challenges in rare diseases remain abundant and under resourced.

Case Example - Spinal Muscular Atrophy (SMA)

SMA is a hereditary neurodegenerative disease that can affect movement, breathing, and swallowing. Mutations of the SMN1 gene are responsible for the disorder and cause a deficiency of SMN protein. This leads to degeneration of neurons in the brain and spinal cord, and progressive muscle weakness throughout the body.[6]

Below are some examples of the different angles with which this condition is managed or treated.

Therapeutics

- The first FDA-approved drug for kids and adults with SMA (2016) nusinersen.
- Gene therapy: in 2017, the FDA designated Single-dose Gene Replacement therapy for SMA as a breakthrough therapy based on the strength of the early trial results.

Wearables

- A wearable robotic hand to improve hand control for manual functions in patients with SMA https://smanewstoday.com/2017/01/27/wearable-robot-hand-give-sma-patients-better-hand-control/
- Roche to use wearable sensors to monitor infants in clinical trial (2/3/2017)

  "Drugmaker Roche will use Great Lakes NeuroTechnologies' BioRadio wireless, wearable data acquisition system to monitor infants' respiratory and pulmonary function in near real time in a clinical trial for a spinal muscular atrophy treatment. Roche will also use Vivonoetics' VivoSense data analysis software, which works with BioRadio, to measure chest and abdominal wall movement."
- Exoskeletons

Devices

- http://www.curesma.org/support-care/living-with-SMA/medical-issues/equipment/
  - Strollers, bath chairs, vests

Digital Health Apps

- Smartphone and tablet devices to facilitate communication and overcome challenges around routine tasks:
  - https://globalgenes.org/raredaily/ipad/
  - Eye-tracking (http://www.umoove.me/)
- Voice recognition such as Siri or Alexa
- Child development and special needs-aware entertainment apps
  - https://itunes.apple.com/gb/app/reactickles-magic/id491691985?mt=8

References

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2. https://www.rarediseaseday.org/videos

3. https://blogs.fda.gov/fdavoice/index.php/2018/02/taking-new-steps-to-meet-the-challenges-of-rare-diseases-fda-marks-the-11th-rare-disease-day/

4. "Unmet medical device needs for Patients with Rare diseases", Results of Survey, NCATS/ORDR & FDA, 2017. https://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/DesignatingHumanitarianUseDevicesHUDS/ucm596177.htm

5. Highlights from the Orphan Drugs & Rare Diseases Global Congress in London, March 2018, Alessio Brunello, MSc, GlobalData Neurology & Ophthalmology Analyst

6. https://www.fda.gov/forindustry/developingproductsforrarediseasesconditions/default.htm
7. https://catalyst.phrma.org/rare-disease-day-unmet-need-inspires-innovation