The Burden of Rare Diseases: An Economic Evaluation

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Understanding the cost drivers and economic impact that a lack of available treatments poses for people living with rare diseases is critical for highlighting the unmet needs of the community and how those needs may be addressed. Chiesi Global Rare Diseases, with support from IQVIA, set out to study the direct, indirect, and mortality-related costs for a sample of 24 rare diseases across five therapeutic areas to evaluate the burden of care when treatment is available versus when no treatment exists, and to compare these costs to common mass market diseases. The resulting report provides a benchmark for cost disparities and assesses how the burden of rare diseases is impacted by treatment availability.

Key findings from the study

Rare diseases impose a substantial economic burden that is reduced by treatment availability.

- The burden of rare diseases is approximately 10x higher than mass market diseases on a per patient per year (PPPY) basis.
- A lack of treatment for a rare disease is associated with a 21.2% increase in total costs PPPY.
- The cost for 8.4 million patients in the U.S. impacted by 373 rare diseases considered in this analysis is estimated to be $2.2 trillion per year.
- Based on this estimate, the societal responsibility for all known rare diseases may be in the range of $7.2 trillion to $8.6 trillion per year.

Investment in diagnostic tools, newborn screening, and development of new therapies is justified.

- Empirical studies need to consider many aspects of healthcare costs to gain a full picture of the overall burden of rare diseases.
- Access to therapies for people living with rare diseases generates significant value for society.

Rare diseases overview

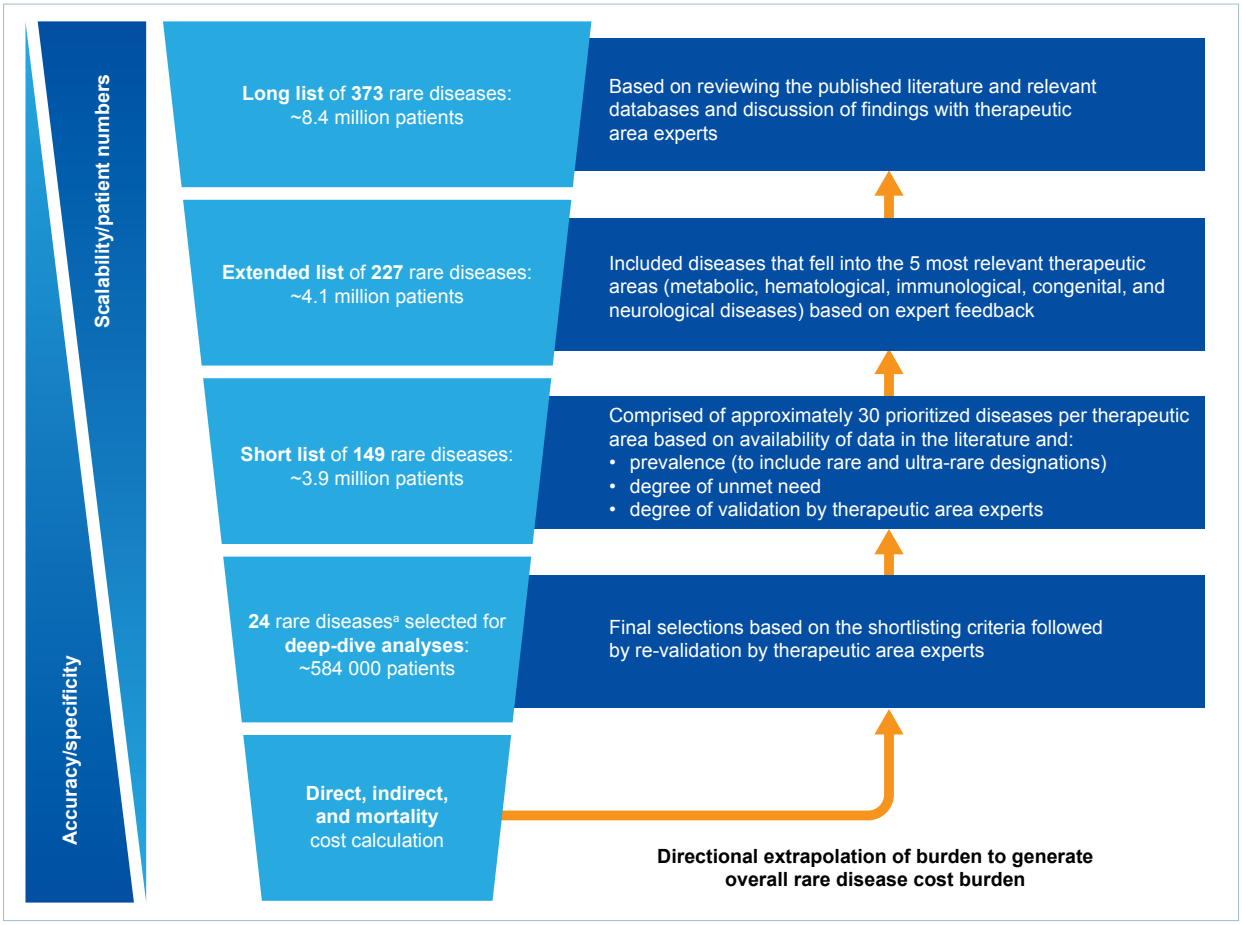
Rare diseases present a societal concern due to difficulties and delays in diagnosis, a lack of treatment availability, difficulty in developing new treatments and the need for favorable regulatory and access conditions. In the U.S., rare diseases are defined as those affecting fewer than 200,000 people.[1] It is estimated that approximately 30 million people in the U.S., half of them children, are affected by more than 7,000 rare diseases.[2] As many as 95% of rare diseases have no specific treatment or curative options. A lack of information on the natural progression of these diseases results in a lack of effective treatments.[3,4] Scarcity of data and disease complexity mean the full extent of the patient, family, and social burden of rare diseases will likely remain undocumented.

Building a database of priority therapeutic areas

We generated a database of 373 rare diseases covering approximately 8.4 million patients in the United States to serve as the basis for this analysis. The rare diseases were selected following a review of more than 500 published articles and lists from sources including Orphanet, the Genetic and Rare Diseases Information Center, the National Organization for Rare Diseases (NORD), and the National Institutes of Health. The selections were discussed with IQVIA experts, several patient advocacy groups including the EveryLife Foundation for Rare Diseases and Global Genes, and therapy area experts from 15 international institutions.

Next, we discussed with physicians and experts to identify top priority therapeutic areas among rare diseases. This focused our research to metabolic, neurological, congenital, hematological, and immunological rare diseases encompassing 227 well-documented rare diseases. Further discussions with patient advocacy groups and physicians led to the selection of the 24 most relevant rare diseases in the priority therapeutic areas based on several criteria, including the degree of unmet need, relative importance to patient advocacy groups, interest in the scientific community, prevalence, and apparent burden of disease. Together these 24 rare diseases impact approximately 584,000 people in the U.S.

Overview of process to determine rare disease burden



Selected rare diseases across therapeutic areas

Metabolic disorders	Hematologic disorders	Immunological disorders	Congenital disorders	Neurological disorders
• Fabry disease	• Acquired aplastic anemia	• Autoimmune encephalitis	• Angelman syndrome	• Amyotrophic lateral sclerosis
• Gaucher disease type I	• Acute intermittent porphyria	• Common variable immune deficiency	• Christianson syndrome	• Ataxia telangiectasia
• Mucopolysaccharidosis (Hunter, Hurler)	• Atypical hemolytic uremic syndrome	• Juvenile idiopathic arthritis	• Deletion 5p	• Duchenne muscular dystrophy
• Ornithine transcarbamylase deficiency	• Beta thalassemia major	• Myasthenia gravis	• Fragile X syndrome	• Early onset familial Alzheimer's disease
• Phenylketonuria	• Sickle cell disease	• Pemphigus vulgaris		• Spinal muscular atrophy type I (proximal)

Evaluating healthcare costs

Costs of care associated with the selected 24 rare diseases were explored with published data, patient advocacy groups, key opinion leaders, and data from the U.S. Bureau of Labor Statistics and Medi-Span Price Rx. The overall cost burden was evaluated across three categories:

- **Direct costs** including the cost of treatment, medical procedures, hospitalizations, physician visits, home healthcare, and other medical costs.
- **Indirect costs** including patient and caregiver productivity loss, work loss, home changes, traveling and accommodation for medical visits.
- **Mortality costs** based on value of statistical life (VSL) and the difference between average life expectancy and that for people with a rare disease.

Estimates of the total cost burden associated with 24 chronic mass-market diseases (including diabetes, cardiovascular, Alzheimer's disease, arthritis and back pain, cancers, and others) were used for the purpose of benchmark comparisons with the rare disease burden.[5] Data on direct and indirect costs were obtained from the 2018 Milken Institute report on the cost of chronic conditions, and mortality costs were estimated using VSL, as for the calculation of mortality costs for rare diseases.

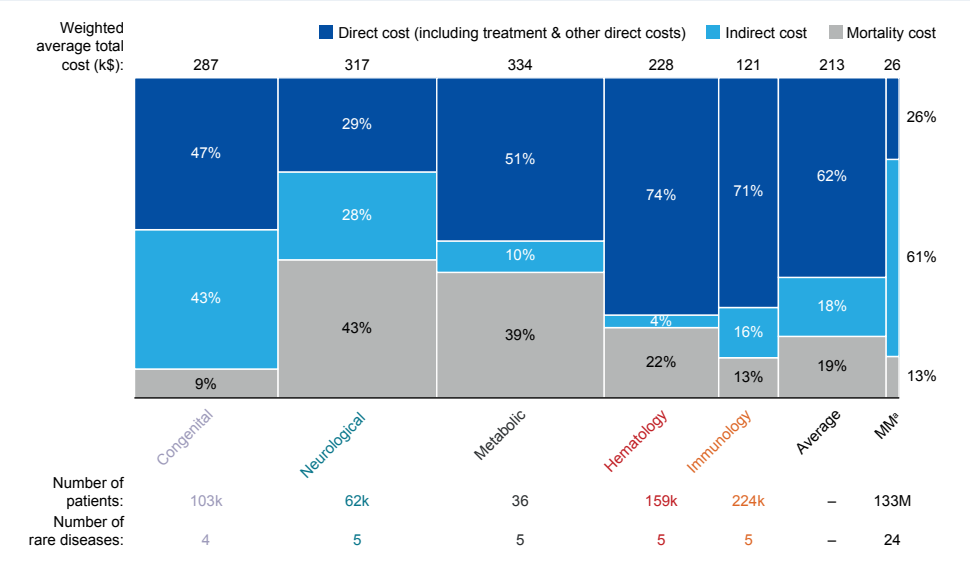
Cost sources included in this analysis

Direct costs	Indirect costs	Mortality costs
• Prescription drugs • Medical products • Hospitalization: inpatient • Hospitalization: outpatient • Home healthcare • Professional services (e.g., nurse visit) • Administration	• Productivity cost: patient & caregiver • Work loss • Home changes • Cost of secondary treatments • Traveling & accommodation	• Value of statistical life ($130,000 per year; $10.3 million for 79-year average lifespan in the U.S.)

Results of the analysis

This study revealed that for 24 rare diseases selected for a deep-dive analysis **the total cost to society is approximately $125 billion** with an **overall economic burden PPPY ranging from $121,000 to $334,000** (average overall cost of $266,000 PPPY), which is approximately **10x the cost associated with mass market diseases** ($26,000 PPPY). Overall, burden was generally driven by direct and mortality costs. Indirect costs, while substantial, represent the smallest proportion of cost burden for rare diseases. The overall burden was highest for metabolic ($334,000 PPPY) and neurological disorders ($317,000 PPPY).

Average burden of rare disease therapeutic areas PPPY across 24 rare diseases



Mean total costs based on a weighted average (by number of patients) of the top five diseases across neurological, metabolic, hematology and immunology diseases, top four congenital diseases and 24 comparator MM diseases. Column widths are weighted based on the average total cost per group.

[a]MM diseases included diabetes, cardiovascular, Alzheimer's disease, arthritis and back pain, cancers and others.

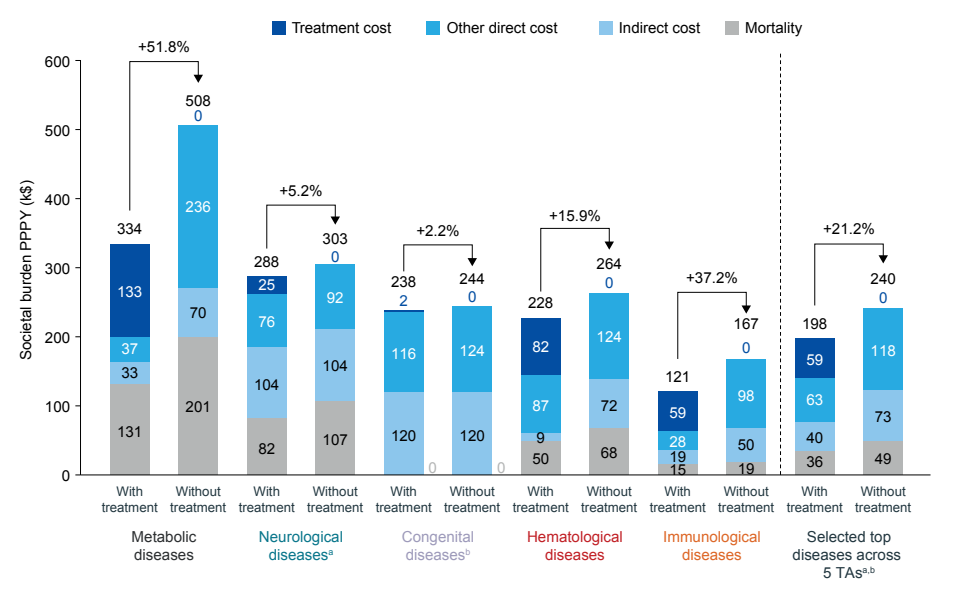
A scenario analysis was conducted to assess the average cost if treatments were not available and found that **a lack of treatment was associated with a 21.2% increase in total costs PPPY.** The percentage increases ranged from a 2.2% increase for congenital diseases to 51.8% for metabolic diseases.

- **Direct costs:** $63,000 PPPY with treatment vs. $118,000 PPPY without treatment
- **Indirect costs:** $40,000 PPPY with treatment vs. $73,000 PPPY without treatment
- **Mortality costs:** $36,000 PPPY with treatment vs. $49,000 PPPY without treatment

Importantly, across all the therapeutic areas assessed, access to treatment effectively shifts burden relating to indirect and mortality costs into direct costs (treatment and other direct costs). These costs are more likely to be financed by private and public payers.

Value of treatment is further demonstrated by decreases in PPPY indirect costs. When no treatments were available, the range for productivity loss was approximately $33,000 to $61,000 for patients and $25,000 to $61,000 for caregivers, compared with approximately $3,000 to $22,000 for patients and $4,000 to $5,000 for caregivers when treatments were available. These findings highlight that providing access to rare disease treatments generally generates substantial value for society because it lowers the associated economic burden on patients and caregivers.

Burden of disease PPPY across rare diseases with and without treatment and value assessment



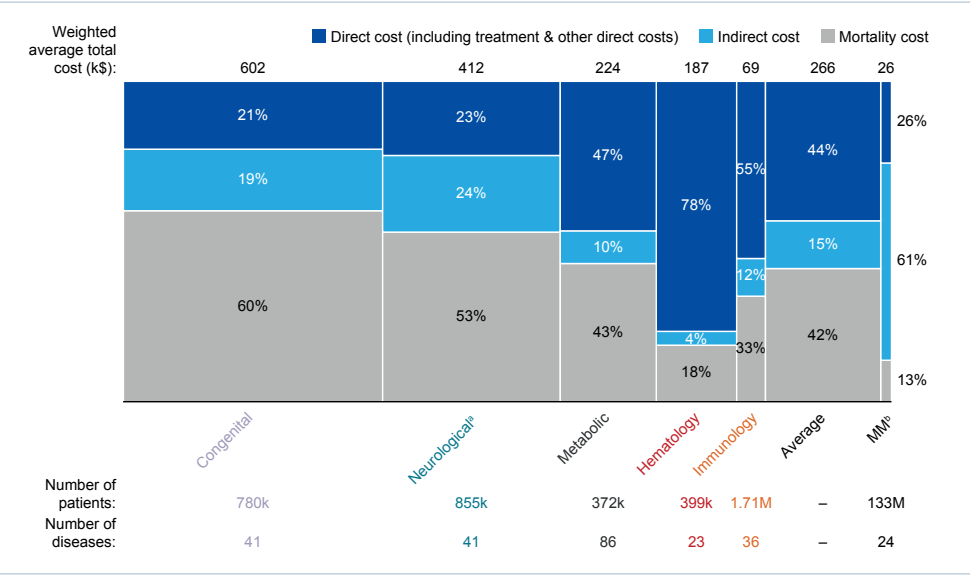
Bars show the average burden PPPY (broken down by cost driver) associated with TAs as well as the average of selected diseases across the TAs.

[a]Excludes spinal muscular atrophy because it was an outlier in this space.

[b]From the selected top diseases in congenital TA; Christianson and Deletion 5P were excluded because no treatment exists for these diseases; hence, no difference in cost magnitude.

When these results were extrapolated to 227 rare diseases belonging to the five priority therapeutic areas, similar results were obtained. The average cost of rare diseases was again approximately 10x higher than for mass market diseases. If extrapolated again to the total of 8.4 million people in the U.S. impacted by the 373 rare diseases in this analysis, **the overall cost of rare diseases in the U.S. is estimated to be $2.2 trillion per year** compared with $3.4 trillion per year for 133 million patients with mass market diseases.

Extrapolated average burden of rare disease therapeutic areas PPPY across 227 rare diseases



Mean total costs based on a weighted average (by number of patients) of the 227 included diseases across neurological, metabolic, hematology, immunology, and congenital TAs and 24 comparator MM diseases.

[a]Spinal muscular atrophy was excluded from the weighted average of representative disease to determine the average % of direct and indirect costs because it is an outlier, since it has a curative treatment.

[b]MM diseases included diabetes, cardiovascular, Alzheimer's disease, arthritis and back pain, cancers, and others.

These overall findings may represent an underestimate because social costs (including impact on health-related quality of life) were not part of this analysis. A previous systematic literature review of qualitative research suggested that living with a rare disease is associated with a substantial psychological and social impact. These observations highlight the need to consider as many aspects of healthcare costs as possible to gain a full picture of the overall burden of rare diseases.

An economic tool for further analysis of the impact of rare diseases

A major strength of this study is that it presents an economic tool for analysis of the positive impact of rare disease treatments. It also provides scenarios so that policymakers can understand the benefit of investing in innovation and policy reforms to accelerate the availability of, and access to, rare disease treatments.

These results highlight the need for policymakers to nurture and sustain innovation based on the positive economic return from rare disease therapies and justify an increased governmental investment in diagnosis and newborn screening to ensure wider patient access to therapies. Incentives for drug development, particularly restoring the Orphan Drug Tax Credit to 50% and maintaining its current applicability to multi-indications, encourage investment and have led to progress in rare disease drug approvals.

These findings also support other reports that show the substantial economic burden that rare diseases represent in the US.[6,7,8,9,10] Economic burden remains high even when treatments are made available, but the cost composition shifts towards medical care and away from indirect and mortality costs. To the extent that new treatments provide clinical benefit for patients and their families, these shifts in burden are likely productive. These findings support the view that the development of safe and effective treatments for rare diseases generates substantial value for society.

Policy makers must recognize the distinct characteristics of developing and commercializing rare disease treatments and that the value assessment for rare disease treatments greatly differ from mass market diseases.[11,12] Policy changes should be specific to the unique nature of rare disease drug development. Emphasis on a patient centric approach, accelerated progress in diagnostic methods for early treatment, as well as promoting an ecosystem providing incentives and supporting the development of rare disease treatment options should be considered by lawmakers.

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