Striking a high note in representation of rare disease publications

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Plain Language Summary

In 1983, the US government started a program to motivate companies to make new drugs for rare diseases. This is important because 4% to 6% of people worldwide live with a rare disease. This study evaluated if how quickly the number of rare disease publications increased over time was similar to how quickly the number of publications in broader areas of medicine increased over time. We found that between 1980 and 2024, fewer than 1% of medical publications covered rare diseases. Rare disease publications increased from 0.2% of publications in 1982 to 0.9% of publications in 2022. The percent of rare disease publications increased over time within each area of medicine studied. The number of combined rare disease publications grew almost twice as fast as overall publications. However, overall publication growth slowed down, especially in the last 10-15 years, and there are now fewer new publications each year than the year before it. For rare disease publications, the speed of this decline was faster. Rare diseases are underrepresented in medical publications because other sources report that 11.5% of clinical trials study rare diseases. It is important for rare disease publication professionals to publish articles conveying their core medical messages. They should also consider strategies to maximize how many people use each publication.

Objective

- Rare diseases are defined by the number of people they affect, ranging regionally from 5 to 76 per 100,000 people [1]
- There are >6,172 rare diseases, with 262.9 to 446.2 million people worldwide (~3.5 to 5.9%) living with a rare disease [1]
- To increase available treatments for rare diseases, the US Congress passed the 1983 Orphan Drug Law Act, offering financial incentives to pharmaceutical companies [2]
- Diagnosis of rare diseases and identification of novel rare diseases has improved since the early 2000s with advances in genetic sequencing [3] and artificial intelligence [4]
- As of 2012, 11.5% of clinical trials in the United States evaluated rare diseases [5]
- The annual number of clinical trial publications, although recently plateauing, increased twofold between 2000 and 2020 [6]
- **We evaluated if the growth rate of rare disease publications was similar to the growth rate of publications in broader therapeutic areas**

Research Design + Methods

- PubMed searches were conducted in January 2025 for six therapeutic areas (neurology, oncology, respiratory, metabolic and endocrine, immunology, and pediatrics) using medical subject heading and title/abstract terms (Table 1). Searches were performed with and without rare disease terms, for a total of 12 searches
- The following filters were applied in PubMed before exporting results: years 1980-2024, case report, clinical trial, meta-analysis, observational study, randomized controlled trial, review, systematic review, English, and exclude preprints
- Five-year rolling averages of annual growth rates ([Year2-Year1]/Year1*100) were calculated to smooth the data and evaluate sustained trends
- Year-over-year changes in growth rates were calculated by linear regression in Microsoft Excel

Table 1. PubMed search strings

Neurology	"Neurology"[M] OR "Nervous System Diseases"[M] OR "neurol* disease"[T/A] OR "neurol* disorder"[T/A] OR "brain disease"[T/A] OR "brain disorder"[T/A]
Oncology	"Neoplasms"[M] OR "cancer"[T/A] OR "oncol*"[T/A] OR "neoplasm"[T/A] OR "tumor"[T/A] OR "malign*"[T/A]
Respiratory	"Respiratory Tract Diseases"[M] OR "Respiratory Disease"[T/A] OR "Respiratory Disorder"[T/A] OR "Lung Disease"[T/A] OR "Lung Disorder"[T/A] OR "pulmonary disease"[T/A] OR "pulmonary disorder"[T/A]
Metabolic + Endocrine	"Metabolic Diseases"[M] OR "Endocrine System Diseases"[M] OR "metabol* disease"[T/A] OR "metabol* disorder"[T/A] OR "Endocrine System Diseases" [T/A] OR "Endocrine Diseases"[T/A] OR "Endocrine Disorders"[T/A]
Immunology	"Immune System Diseases"[M] OR "Immunity"[M] OR "Immunol*"[T/A] OR "autoimmune disease"[T/A] OR "autoimmune disorder"[T/A] OR "immune system disease"[T/A] OR "immune system disorder"[T/A]
Pediatrics	"Congenital, Hereditary, and Neonatal Diseases and Abnormalities"[M] OR "Congenital Disease"[T/A] OR "Hereditary Disease"[T/A] OR "Neonatal Disease"[T/A] OR "Congenital Disorder"[T/A] OR "Hereditary Disorder"[T/A] OR "Neonatal Disorder"[T/A]
With or without	
Rare diseases	"Rare Diseases"[M] OR "rare disease"[T/A] OR "rare disorder"[T/A] or "orphan disease"[T/A]

A, abstract; M, medical subject heading; T, title.

Limitations

- Publications were limited to those which were indexed on PubMed
- Six therapeutic areas were chosen to narrow results to clinically-relevant publications. This selection is not random, may count individual publications more than once because of potential overlap in search terms, and may not be representative of all clinically-relevant literature
- Rare disease classification used "rare disease" or a related term, rather than individual disease names, which may underestimate the number of publications
- Individual publications were not assessed for relevance

Results

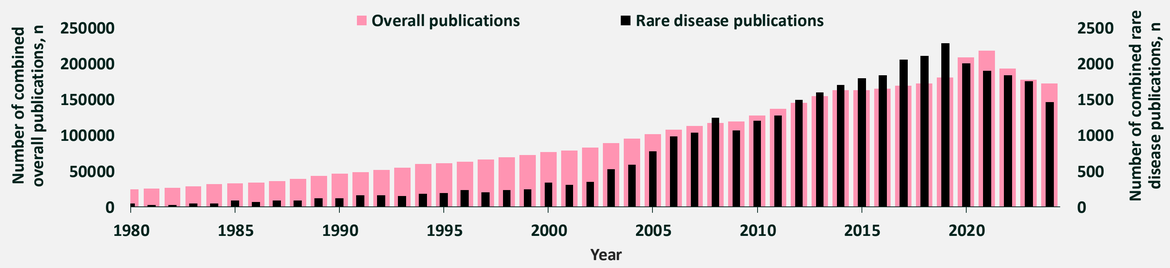
- Overall, 0.8% of publications covered rare diseases (Table 2)

Table 2. Number of publications retrieved

Therapeutic Area	Number of overall publications, n	Number of rare disease publications, n	Proportion of rare disease publications, %
Combined	4,457,737	36,214	0.8
Neurology	904,867	5,754	0.6
Oncology	1,431,240	11,282	0.8
Respiratory	494,744	3,653	0.7
Metabolic + endocrine	544,138	4,983	0.9
Immunology	630,493	4,043	0.6
Pediatrics	452,255	6,499	1.4

- Between 1980 and 2024, annual rare disease publications exhibited a sigmoidal curve before declining (Figure 1)
- The proportion of annual combined rare disease publications to overall publications increased from 0.2% in 1982 to 0.9% in 2022
- Annual combined rare disease and overall publications declined following peaks in 2019 and 2021, respectively

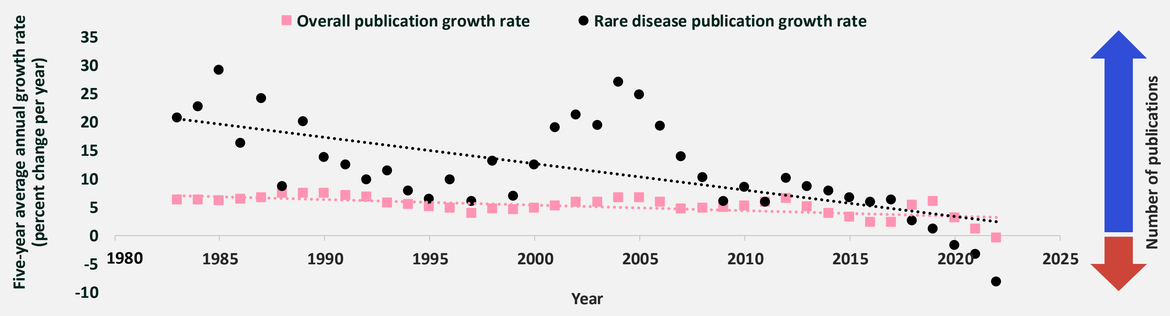
Figure 1. Number of annual publications



5-year average	1982	1992	2002	2012	2022
Overall publications, n	27,692	52,673	84,748	145,743	194,156
Rare disease publications, n	43.8	160	426	1,456	1,794
Proportion, %	0.2	0.3	0.5	1.0	0.9

- Median (range) 5-year average growth rate was 9.9% (–8.3%, 29.0%) per year for rare disease publications and 5.3% (–0.5%, 7.3%) per year overall
- The 5-year average growth rate of rare disease publications was variable, and highest between 1985 to 1990 and 2000 to 2005, while the overall publication growth rate was more consistent (Figure 2)
- Change in growth rate was −0.46% year-over-year for rare disease publications and −0.10% year-over-year for overall publications

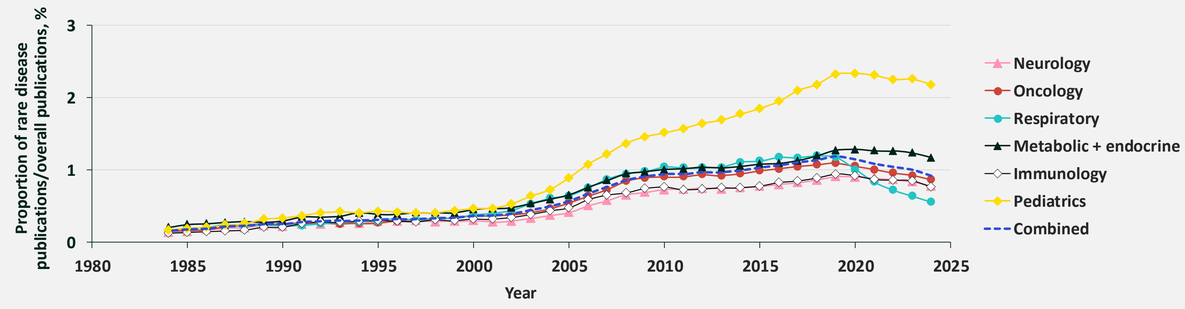
Figure 2. Five-year average annual growth rate of publications



	Change in growth rate, % year-over-year	Fit (R^2)
Overall publications	y = –0.0986x + 202.49	0.4576
Rare disease publications	y = –0.4629x + 938.35	0.4187

- While the proportion of rare disease publications to overall publications increased within each therapeutic area, individual therapeutic areas exhibited differences in growth patterns (Figure 3)

Figure 3. Proportion of annual publications that cover rare diseases by therapeutic area



Conclusions

- The representation of rare diseases in publications has increased since the 1980s
- Despite this, the proportion of rare disease publications (≤1%) is lower than the proportion of rare disease clinical trials (11.5% in 2012), and rare disease publication growth is declining faster than that for overall publications
- As this analysis is correlative, it is unclear what is driving the recent decline in publications, if this effect will be sustained, and why rare disease publications are more impacted
- Rare disease publication professionals should emphasize publishing articles conveying their core medical messages and consider strategies to maximize educational impact (eg, extenders)

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Disclosures
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