

References

- Arksey, H., & O'Malley, L. (2005). Scoping studies: Towards a methodological framework. *International Journal of Social Research Methodology*, 8(1), 19–32.
<https://doi.org/10.1080/1364557032000119616>
- Arno, P. S., Bonuck, K., & Davis, M. (1995). Rare diseases, drug development, and AIDS: The impact of the Orphan Drug Act. *The Milbank Quarterly*, 73(2), 231–252.
- Asbury, C. H. (1981). Medical drugs of limited commercial interest: Profit alone is a bitter pill. *International Journal of Health Services*.
<https://doi.org/10.2190/neld-fbm5-ffn3-0flc>
- Asbury, C. H. (1991). The Orphan Drug Act. The first 7 years. *JAMA*, 265(7), 893–897.
- Asbury, C. H. (1992). Evolution and current status of the Orphan Drug Act. *International Journal of Technology Assessment in Health Care*, 8(4), 573–582.
- Aymé, S., Kole, A., & Groft, S. (2008). Empowerment of patients: Lessons from the rare diseases community. *The Lancet*, 371(9629), 2048–2051.
[https://doi.org/10.1016/S0140-6736\(08\)60875-2](https://doi.org/10.1016/S0140-6736(08)60875-2)
- Braun, M. M., Braun, M. M., Farag-El-Massah, S., Farag-El-Massah, S., Xu, K., & Coté, T. R. (2010). Emergence of orphan drugs in the United States: A quantitative assessment of the first 25 years. *Nature Reviews Drug Discovery*
<https://doi.org/10.1038/nrd3160>
- Chan, A. Y. L., Chan, A. Y. L., Li, S. X., Chan, A. Y. L., Chan, V. K. Y., Chan, V. K. Y., Chan, A., Chan, V. K. Y., Olsson, S., Chan, V. K. Y., Olsson, S., Fan, M., Olsson, S., Fan, M., Fan, M., Zhang, S., Gong, M., Fan, M., Jit, M., ... Li, X. (2020). Access and Unmet Needs of Orphan Drugs in 194 Countries and 6 Areas: A Global Policy Review With Content Analysis. *Value in Health*.
<https://doi.org/10.1016/j.jval.2020.06.020>
- Cheng, A., & Xie, Z. (2017). Challenges in orphan drug development and regulatory policy in China. *Orphanet Journal of Rare Diseases*, 12(1), 13.
<https://doi.org/10.1186/s13023-017-0568-6>
- Cheung, R. Y., Cohen, J. C., & Illingworth, P. (2004). Orphan drug policies: Implications for the United States, Canada, and developing countries. *Health Law Journal*, 12, 183–200.
- Clissold, D. B. (1995). Prescription for the Orphan Drug Act: The Impact of the FDA's 1992 Regulations and the Latest Congressional Proposals for Reform. *Food and Drug Law Journal*, 50(1), 125–147.
- Cohen, D., & Raftery, J. (2014). Paying twice: Questions over high cost of cystic fibrosis drug developed with charitable funding. *BMJ (Online)*, 348(February), 10–13.
<https://doi.org/10.1136/bmj.g1445>

- Committee for Orphan Medicinal Products and the European Medicines, Westermark, K., Holm, B. B., Söderholm, M., Llinares-Garcia, J., Rivière, F., Aarum, S., Butlen-Ducuing, F., Tsigkos, S., Wilk-Kachlicka, A., N'Diamoi, C., Borvendég, J., Lyons, D., Sepodes, B., Bloechl-Daum, B., Lhoir, A., Todorova, M., Kkolos, I., Kubáčková, K., ... Belorgey, C. (2011). European regulation on orphan medicinal products: 10 years of experience and future perspectives. *Nature Reviews. Drug Discovery*, 10(5), 341–349.
<https://doi.org/10.1038/nrd3445>
- Côté, A., & Keating, B. (2012). What Is Wrong with Orphan Drug Policies. *Value in Health*.
<https://doi.org/10.1016/j.jval.2012.09.004>
- Daniel, M., Pawlik, T. M., Fader, A. N., Fader, A. N., Fader, A. N. N., Esnaola, N. F., & Makary, M. A. (2016). The Orphan Drug Act: Restoring the Mission to Rare Diseases. *American Journal of Clinical Oncology*.
<https://doi.org/10.1097/coc.0000000000000251>
- Davidson, S. (1996). Orphan drugs: European biotechnology waits for EC act. *Nature Biotechnology*, 14(4), Article 4.
<https://doi.org/10.1038/nbt0496-419b>
- Davies, E. H., Fulton, E., Brook, D., & Hughes, D. A. (2017). Affordable orphan drugs: A role for not-for-profit organizations. *British Journal of Clinical Pharmacology*.
<https://doi.org/10.1111/bcp.13240>
- Dear, J. W., Lilitkarntakul, P., & Webb, D. J. (2006). Are rare diseases still orphans or happily adopted? The challenges of developing and using orphan medicinal products. *British Journal of Clinical Pharmacology*, 62(3), 264–271.
<https://doi.org/10.1111/j.1365-2125.2006.02654.x>
- Dunkle, M., Pines, W., & Saltonstall, P. L. (2010). Advocacy Groups and Their Role in Rare Diseases Research. In M. Posada de la Paz & S. C. Groft (Eds.), *Rare Diseases Epidemiology* (pp. 515–525).
https://doi.org/10.1007/978-90-481-9485-8_28
- Ferreira, C. R. (2019). The burden of rare diseases. *American Journal of Medical Genetics Part A*, 179(6), 885–892.
<https://doi.org/10.1002/ajmg.a.61124>
- Garber, A. M. (1994). Benefits versus profits: Has the orphan drug act gone too far? *PharmacoEconomics*, 5(2), 88–92.
<https://doi.org/10.2165/00019053-199405020-00002>
- Giannuzzi, V., Conte, R., Landi, A., Ottomano, S. A., Bonifazi, D., Baiardi, P., Bonifazi, F., & Ceci, A. (2017). Orphan medicinal products in Europe and United States to cover needs of patients with rare diseases: An increased common effort is to be foreseen. *Orphanet Journal of Rare Diseases*, 12(1), 64.
<https://doi.org/10.1186/s13023-017-0617-1>

- Haffner, M. E. (1991). Orphan Products: Origins, Progress, and Prospects. *Annual Review of Pharmacology and Toxicology*.
<https://doi.org/10.1146/annurev.pa.31.040191.003131>
- Haffner, M. E. (1999). Orphan Drugs: The United States Experience. *Drug Information Journal*, 33(2), 565–568.
<https://doi.org/10.1177/009286159903300226>
- Haffner, M. E. (2003). The Current Environment in Orphan Drug Development. *Drug Information Journal*.
<https://doi.org/10.1177/009286150303700404>
- Haffner, M. E. (2006). Adopting orphan drugs—two dozen years of treating rare diseases. *The New England Journal of Medicine*.
<https://doi.org/10.1056/nejmp058317>
- Haffner, M. E., & Maher, P. D. (2006). The impact of the Orphan Drug Act on drug discovery. *Expert Opinion on Drug Discovery*, 1(6), 521–524.
- Haffner, M. E., Torrent-Farnell, J., & Maher, P. D. (2008). Does orphan drug legislation really answer the needs of patients. *The Lancet*.
[https://doi.org/10.1016/s0140-6736\(08\)60873-9](https://doi.org/10.1016/s0140-6736(08)60873-9)
- Haffner, M. E., Whitley, J., & Moses, M. (2002). Two decades of orphan product development. *Nature Reviews. Drug Discovery*, 1(10), 821–825.
- Heemstra, H. E., Vrueth, R. L. A. de, Weely, S. van, Büller, H. A., Büller, H. A., & Leufkens, H. G. M. (2008). Predictors of orphan drug approval in the European Union. *European Journal of Clinical Pharmacology*.
<https://doi.org/10.1007/s00228-007-0454-6>
- Hendrickx, K., Hendrickx, K., & Dooms, M. (2021). Orphan Drugs, Compounded Medication and Pharmaceutical Commons. *Frontiers in Pharmacology*.
<https://doi.org/10.3389/fphar.2021.738458>
- Herder, M. (2013). When Everyone is an Orphan: Against Adopting a US-Styled Orphan Drug Policy in Canada. *Accountability in Research*.
<https://doi.org/10.1080/08989621.2013.793120>
- Horgan, D., Moss, B., Boccia, S., Genuardi, M., Gajewski, M., Capurso, G., Fenaux, P., Gulbis, B., Pellegrini, M., Mañú Pereira, M. del M., Gutiérrez Valle, V., Gutiérrez Ibarluzea, I., Kent, A., Cattaneo, I., Jagielska, B., Belina, I., Tumiene, B., Ward, A., & Papaluca, M. (2020). Time for Change? The Why, What and How of Promoting Innovation to Tackle Rare Diseases – Is It Time to Update the EU’s Orphan Regulation? And if so, What Should be Changed? *Biomedicine Hub*, 5(2), 1–11.
<https://doi.org/10.1159/000509272>

- Huyard, C. (2009). How did uncommon disorders become 'rare diseases'? History of a boundary object. *Sociology of Health and Illness*, 31(4), 463–477.
<https://doi.org/10.1111/j.1467-9566.2008.01143.x>
- Joppi, R., Bertele, V., & Garattini, S. (2006). Orphan drug development is progressing too slowly. *British Journal of Clinical Pharmacology*, 61(3), 355–360.
- Joppi, R., Bertele, V., & Garattini, S. (2009). Orphan drug development is not taking off. *British Journal of Clinical Pharmacology*.
<https://doi.org/10.1111/j.1365-2125.2009.03369.x>
- Kanavos, P., & Nicod, E. (2012). What is wrong with orphan drug policies? Suggestions for ways forward. *Value in Health : The Journal of the International Society for Pharmacoeconomics and Outcomes Research*, 15(8), 1182–1184.
- Kesselheim, A. S. (2010). Using Market-Exclusivity Incentives to Promote Pharmaceutical Innovation. *The New England Journal of Medicine*, 363(19), 1862–1855.
<https://doi.org/10.1056/NEJMhle1002961>
- Kesselheim, A. S. (2011). An empirical review of major legislation affecting drug development: Past experiences, effects, and unintended consequences. *Milbank Quarterly*.
<https://doi.org/10.1111/j.1468-0009.2011.00636.x>
- Kesselheim, A. S., Myers, J. A., & Avorn, J. (2011). Characteristics of Clinical Trials to Support Approval of Orphan vs Nonorphan Drugs for Cancer. *JAMA*.
<https://doi.org/10.1001/jama.2011.769>
- Kesselheim, A. S., Myers, J. A., Solomon, D. H., Winkelmayr, W. C., Winkelmayr, W. C., Levin, R., & Avorn, J. (2012). The prevalence and cost of unapproved uses of top-selling orphan drugs. *PLOS ONE*.
<https://doi.org/10.1371/journal.pone.0031894>
- Kesselheim, A. S., Tan, Y. T., & Avorn, J. (2015). The Roles Of Academia, Rare Diseases, And Repurposing In The Development Of The Most Transformative Drugs. *Health Affairs*.
<https://doi.org/10.1377/hlthaff.2014.1038>
- Koay, P. P., & Sharp, R. R. (2013). The Role of Patient Advocacy Organizations in Shaping Genomic Science. *Annual Review of Genomics and Human Genetics*, 14(1), 579–595.
<https://doi.org/10.1146/annurev-genom-091212-153525>
- Liu, B., He, L., He, G., & He, Y. (2010). A cross-national comparative study of orphan drug policies in the United States, the European Union, and Japan: Towards a made-in-China orphan drug policy. *Journal of Public Health Policy*, 31(4), 407–420; discussion 420-421.
<https://doi.org/10.1057/jphp.2010.30>
- Loughnot, D. (2005). Potential Interactions of the Orphan Drug Act and Pharmacogenomics: A Flood of Orphan Drugs and Abuses? *American Journal of Law & Medicine*, 31(2–3), 365–380.
<https://doi.org/10.1177/009885880503100210>

- Luzzatto, L., Hollak, C. E. M., Cox, T. M., Schieppati, A., Licht, C., Kääriäinen, H., Merlini, G., Schaefer, F., Simoens, S., Pani, L., Garattini, S., & Remuzzi, G. (2015). Rare diseases and effective treatments: Are we delivering? *The Lancet*, 385(9970), 750–752.
[https://doi.org/10.1016/S0140-6736\(15\)60297-5](https://doi.org/10.1016/S0140-6736(15)60297-5)
- McCabe, C., Stafinski, T., & Menon, D. (2010). Is it time to revisit orphan drug policies. *BMJ*.
<https://doi.org/10.1136/bmj.c4777>
- Meekings, K. N., Williams, C. S. M., & Arrowsmith, J. E. (2012). Orphan drug development: An economically viable strategy for biopharma R&D. *Drug Discovery Today*, 17(13), 660–664.
- Menon, D., Stafinski, T., Dunn, A., & Wong-Rieger, D. (2015). Developing a Patient-Directed Policy Framework for Managing Orphan and Ultra-Orphan Drugs Throughout Their Lifecycle. *The Patient - Patient-Centered Outcomes Research*, 8(1), 103–117.
<https://doi.org/10.1007/s40271-014-0108-6>
- Mestre-Ferrandiz, J., Palaska, C., Kelly, T., Hutchings, A., & Parnaby, A. (2019). An analysis of orphan medicine expenditure in Europe: Is it sustainable? *Orphanet Journal of Rare Diseases*, 14(1), 287.
<https://doi.org/10.1186/s13023-019-1246-7>
- Mikami, K. (2017). Orphans in the Market: The History of Orphan Drug Policy. *Social History of Medicine*.
<https://doi.org/10.1093/shm/hkx098>
- Mikami, K., & Sturdy, S. (2017). Patient organization involvement and the challenge of securing access to treatments for rare diseases: Report of a policy engagement workshop. *Research Involvement and Engagement*, 3(1), 14.
<https://doi.org/10.1186/s40900-017-0065-z>
- Miller, K. L. (2017). Do investors value the FDA orphan drug designation? *Orphanet Journal of Rare Diseases*, 12(1), 114.
<https://doi.org/10.1186/s13023-017-0665-6>
- Miller, K. L., Kraft, S., Ipe, A., & Fermaglich, L. (2022). Drugs and biologics receiving FDA orphan drug designation: An analysis of the most frequently designated products and their repositioning strategies. *Expert Opinion on Orphan Drugs*, 9(11–12), 265–272.
<https://doi.org/10.1080/21678707.2021.2047021>
- Murakami, M., & Narukawa, M. (2016). Matched analysis on orphan drug designations and approvals: Cross regional analysis in the United States, the European Union, and Japan. *Drug Discovery Today*, 21(4), 544–549.
- Novas, C. (2009). Orphan Drugs, Patient Activism and Contemporary Healthcare. *Quaderni*.
<https://doi.org/10.4000/quaderni.262>

- Padula, W. V., Parasrampur, S., Socal, M. P., Conti, R. M., & Anderson, G. F. (2020). Market Exclusivity for Drugs with Multiple Orphan Approvals (1983-2017) and Associated Budget Impact in the US. *PharmacoEconomics*.
<https://doi.org/10.1007/s40273-020-00934-2>
- Penington, R. C., Penington, R., & Stubbings, J. A. (2016). Evaluation of Specialty Drug Price Trends Using Data from Retrospective Pharmacy Sales Transactions. *Journal of Managed Care Pharmacy*.
<https://doi.org/10.18553/jmcp.2016.22.9.1010>
- Provost, G. P. (1968). “Homeless” or “Orphan” Drugs. *American Journal of Hospital Pharmacy*, 25(11), 609.
<https://doi.org/10.1093/ajhp/25.11.609>
- Rollet, P., Lemoine, A., & Dunoyer, M. (2013). Sustainable rare diseases business and drug access: No time for misconceptions. *Orphanet Journal of Rare Diseases*. <https://doi.org/10.1186/1750-1172-8-109>
- Sarpawari, A., Beall, R. F., Abdurrob, A., He, M., He, M., & Kesselheim, A. S. (2018). Evaluating The Impact Of The Orphan Drug Act’s Seven-Year Market Exclusivity Period. *Health Affairs*.
<https://doi.org/10.1377/hlthaff.2017.1179>
- Sarpawari, A., & Kesselheim, A. S. (2019). Reforming the Orphan Drug Act for the 21st Century. *New England Journal of Medicine*, 381(2), 104–106.
[https://doi.org/DOI: 10.1056/NEJMp1902943](https://doi.org/DOI:10.1056/NEJMp1902943)
- Seoane-Vazquez, E., Rodriguez-Monguio, R., Szeinbach, S. L., & Visaria, J. (2008). Incentives for orphan drug research and development in the United States. *Orphanet Journal of Rare Diseases*.
<https://doi.org/10.1186/1750-1172-3-33>
- Shiragami, M., & Nakai, K. (2000a). Development of Orphan Drugs in Japan: Characteristics of Orphan Drugs Developed in Japan. *Drug Information Journal*, 34(3), 839–846.
<https://doi.org/10.1177/009286150003400320>
- Shiragami, M., & Nakai, K. (2000b). Development of Orphan Drugs in Japan: Effects of a Support System for Development of Orphan Drugs in Japan. *Drug Information Journal*, 34(3), 829–837.
<https://doi.org/10.1177/009286150003400319>
- Shulman, S. R., & Manocchia, M. (1997). The US orphan drug programme 1983-1995. *PharmacoEconomics*, 12(3), 312–326.
- Song, P., Tang, W., & Kokudo, N. (2013). Rare diseases and orphan drugs in Japan: Developing multiple strategies of regulation and research. *Expert Opinion on Orphan Drugs*, 1(9), 681–683.
<https://doi.org/10.1517/21678707.2013.832201>

- Sunyoto, T., Potet, J., & Boelaert, M. (2018). Why miltefosine—A life-saving drug for leishmaniasis—Is unavailable to people who need it the most. *BMJ Global Health*.
<https://doi.org/10.1136/bmjgh-2018-000709>
- Tambuyzer, E. (2010). Rare diseases, orphan drugs and their regulation: Questions and misconceptions. *Nature Reviews. Drug Discovery*, 9(12), 921–929.
<https://doi.org/10.1038/nrd3275>
- Thamer, M., Brennan, N., & Semansky, R. (1998). A cross-national comparison of orphan drug policies: Implications for the U.S. Orphan Drug Act. *Journal of Health Politics, Policy and Law*, 23(2), 265–290.
<https://doi.org/10.1215/03616878-23-2-265>
- Towse, A., & Kettler, H. (2005). A review of IP and non-IP incentives for R&D for diseases of poverty. What type of innovation is required and how can we incentivise the private sector to deliver it? *Innovation and Public Health*
- Trouiller, P., Olliaro, P., Olliaro, P., Torreele, E., Torreele, E., Orbinski, J., Laing, R., & Ford, N. (2002). Drug development for neglected diseases: A deficient market and a public-health policy failure. *The Lancet*.
[https://doi.org/10.1016/s0140-6736\(02\)09096-7](https://doi.org/10.1016/s0140-6736(02)09096-7)
- Uchida, K. (1996). Orphan Drugs in Japan. *Drug Information Journal*, 30(1), 171–175.
<https://doi.org/10.1177/009286159603000119>
- Valverde, A. M., Reed, S. D., & Schulman, K. A. (2012). Proposed ‘Grant-And-Access’ Program With Price Caps Could Stimulate Development Of Drugs For Very Rare Diseases. *Health Affairs*.
<https://doi.org/10.1377/hlthaff.2012.0235>
- Van Woert, M. H. (1978). Profitable and Nonprofitable Drugs. *New England Journal of Medicine*, 298(16), 903–906.
<https://doi.org/10.1056/NEJM197804202981608>
- Wellman-Labadie, O., & Zhou, Y. (2010). The US Orphan Drug Act: Rare disease research stimulator or commercial opportunity? *Health Policy*.
<https://doi.org/10.1016/j.healthpol.2009.12.001>
- Wolinsky, H. (2017). Charities and the lure of capitalism: Philanthropies dedicated to finding cures for rare diseases explore new models for funding and cooperation to accelerate research and drug development. *EMBO Reports*.
<https://doi.org/10.15252/embr.201744065>
- Yin, W. (2008). Market incentives and pharmaceutical innovation. *Journal of Health Economics*.
<https://doi.org/10.1016/j.jhealeco.2008.01.002>
- Yin, W. (2009). R&D policy, agency costs and innovation in personalized medicine. *Journal of Health Economics*.
<https://doi.org/10.1016/j.jhealeco.2009.06.011>

Zhang, L., & Wang, J. (2021). Incentives to promote the US pharmaceutical innovation: Empirical research based on the case of Epogen. *Drug Development and Industrial Pharmacy*.
<https://doi.org/10.1080/03639045.2021.1935997>