

A historical analysis of the policy on intractable diseases in Japan and its peculiarity

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SUMMARY: 1.—Introduction. 2.—Rare diseases as a sociopolitical construct. 3.— Intractable diseases in Japan. 3.1.—The social problem of Subacute Myelo-Optic Neuropathy. 3.2.—From Subacute Myelo-Optic Neuropathy to intractable diseases. 4.—Levels of activities and their separation. 5.—Discussion.

ABSTRACT: This article examines the history of the policy concerning a class of diseases called intractable diseases in Japan with a particular focus on the roles of patient support groups in firstly legitimizing the grouping of such diseases and then shaping the nature of the support that the Japanese Ministry of Health and Welfare provided to the patients and their families affected by them. The Ministry started its policy on intractable diseases in 1972, predating the enactment of the 1983 Orphan Drug Act in the United States, which is known to be one of the most important events for the international rare diseases community. This policy decision was triggered by the emergence of subacute myelo-optic neuropathy (SMON) as a social problem in the country in the late 1960s. The Ministry first made its support available to patients with this particular disease and, as a result of a series of actions from patient support groups and their medical and political supporters, the same support was made available to those considered to be in similarly difficult circumstances. The way in which the support was arranged, however, turned out to be structurally divisive, inviting the patient groups to negotiate with the national and local governments separately depending on subject matters, and for about three decades since the start of the policy, they struggled to present their unified voice in the country. The governmental support for intractable diseases was finally revised in the mid-2000s, but as this article demonstrates, that became possible only after the patient groups came to realize the need of presenting a unified voice in their effort to improve the lives of those affected.

KEYWORDS: Intractable Diseases, Rare Diseases, Patient Support Groups, SMON, Japan.

1. Introduction (*)

In April 2011, the leaders of the European Commission and the US National Institutes of Health made a decision to coordinate their research effort in the area of rare diseases and found an international network called the International Rare Diseases Research Consortium (IRDiRC)¹. The Consortium, being a concerted effort of research funders to develop new diagnostic methods and therapies for rare diseases, was open to new members as long as they demonstrated the scale of their commitment to this area of research. Japan, although it showed its interest in the effort since its beginning², was not able to join it as a full member until 2015, however. The delay was not because the country did not have sufficient research on rare diseases but because its research effort had been organized rather differently, making it difficult for its responsible authority the Ministry of Health, Labour and Welfare (MHLW) to demonstrate its scale. Historically, its research effort has been framed with the concept of intractable diseases, and this article examines the Japanese policy concerning such a class of diseases with a focus on the roles of patient support groups in making and shaping the concept since the late 1960s.

Just as what count as rare diseases are often defined and specified in a policy domain, the concept of intractable diseases is a sociopolitical construct with a historical significance in its local context. Until enactment of the Act of Medical Care for Patients with Intractable Diseases in 2014, the most important policy document in this area had been the Outline of Intractable Diseases Measures³, which was published in 1972 by the Ministry of Health and Welfare, a predecessor of the MHLW. The original document defined intractable diseases as those primarily meeting two criteria: first, they are

(*) This article is based on the work supported by JSPS KAKENHI Grant-in-Aid for Scientific Research (C) No. 18K00252.

1. Alison Abbott, "Rare-disease project has global ambitions," *Nature* 472, no. 7341 (2011): 17, <https://doi.org/10.1038/472017a>
2. Ibid.
3. Mikiko Eto, *Iryo no Seisaku Katei to Jyuekisha: Nambyou Taisaku ni yoru Kanjya Soshiki no Seisaku Sanka* (Tokyo: Shinzansha, 1993); Keiko Horiuchi, *Nambyou Kanjya Fukushi no Keisei* (Tokyo: Jichosha, 2006); Takahiro Kawano, "Establishment of Intractable/Rare Diseases Act and the Present Government Measures to Intractable/Rare Diseases," *Iryo To Shakai* 28, no. 1 (2018): 17-26, <https://doi.org/10.4091/iken.29.026>; Shinji Takemura & Tomofumi Sone, "Research and development on intractable & rare diseases in Japan: Contribution of the National Institute of Public Health to research program management," *Journal of the National Institute of Public Health* 68, no. 1 (2019): 45-54.

diseases of unknown cause and without established treatment, posing a high risk of long-term sequelae; second, being chronic, they impose onerous burdens on patient families due to both financial and caring needs, potentially causing them psychological distress too⁴. A criterion of such diseases being rare was added only in 1997⁵. Although this document confirming the Ministry's awareness of the need for government support to families with such diseases was a significant achievement of patient support groups, they struggled to present their unified voice for about three decades since its publication.

It is this complex relationship between the support to patients and their families that the Ministry promised in the document and the way in which patient support groups organized themselves to address the problems they faced that this article sets to demonstrate through a historical analysis of intractable disease policy in the country. Before examining the historical development of the Japanese policy and related discussion since the late 1960s, the next section reviews briefly the history of rare diseases in the United States and Europe to clarify in what sense the concept can be seen as a sociopolitical construct.

2. Rare diseases as a sociopolitical construct

It is estimated that there are more than 6,000 rare diseases, and many of them are believed to have some genetic components contributing to its occurrence⁶. Because of their rarity, many of them have received little attention in medicine, though that was not always the case historically. In 1902, a British physician Archibald Garrod published a paper describing one of the first inborn errors of metabolism⁷. He then suggested in 1928 in his lecture entitled *The Lessons of Rare Maladies* that studies of rare diseases are as important as those of more common diseases, with reference to a writing of William Harvey, in

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4. The Japanese Ministry of Health and Welfare, "Nanbyou Taisaku Youkou, October 1972," *Japan Intractable Diseases Information Center*, accessed on Dec 1 2021, https://www.nanbyou.or.jp/wp-content/uploads/pdf/nan_youkou.pdf
 5. Ichiro Kanazawa, "Personal proposals toward political management of intractable disease patients," *Journal of the National Institute of Public Health* 60, no. 2 (2011): 84-88.
 6. Abbott, "Rare-disease project," 17.
 7. Archibald Garrod, "The Incidence of Alkaptonuria: A Study in Chemical Individuality," *The Lancet* 160, no. 4137 (1902): 1616-1620, [http://doi.org/10.1016/S0140-6736\(01\)41972-6](http://doi.org/10.1016/S0140-6736(01)41972-6)

which he stated that rare forms of diseases reveal the law of the Nature⁸. However, the rationale for the European Commission and the US National Institutes of Health to establish the international research consortium for rare diseases was not so much to do with their medical significance. It was instead to do with challenges that patients with such diseases tend to face because of their rarity, and equally, if not more importantly, the lack of interest in developing their drugs among pharmaceutical companies⁹.

This link between the small number of patients affected and the disinterest of pharmaceutical companies was at the heart of the way in which the notion of rare diseases was turned into a sociopolitical construct firstly in the United States and later in Europe¹⁰. The first instance of rare diseases becoming defined legally was the 1984 Amendments to the US Orphan Drug Act of 1983. Due to strict regulation on the drug approval system introduced in the United States in the 1960s, the cost for pharmaceutical companies to put their products on the market increased considerably, giving them little motivation to conduct clinical trials on drugs with little prospect of recovering such cost. Even where university scientists had developed effective drugs, they were still unwilling to take them to the market and make them available to patients if their market size appeared small. Such drugs considered unprofitable became known as “orphan drugs”. The aim of the 1983 legislation was to give pharmaceutical companies incentives, including tax reduction and a seven-year period of exclusive marketing, to adopt such drugs, and that of the 1984 Amendments was to specify which drugs would count as orphans, clarifying who would be eligible for the governmental support. Without the information about the cost and price of drugs being developed, however, the only way that the US Food and Drug Administration could draw the line was based on the size of their potential market, and hence rare diseases became defined in terms of the size of patient population, that is, affecting less than 200,000 individuals in the country¹¹.

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8. Archibald Garrod, “The Lessons of Rare Maladies: The Annual Oration delivered before the Medical Society of London on May 21st, 1928,” *The Lancet* 211, no. 5465 (1928): 1055–1060, [https://doi.org/10.1016/S0140-6736\(00\)99941-0](https://doi.org/10.1016/S0140-6736(00)99941-0)
 9. Abbott, “Rare-disease project,” 17.
 10. Caroline Huyard, “How did uncommon disorders become ‘rare diseases’? History of a boundary object,” *Sociology of Health & Illness* 31, no. 4 (2009): 463–477, <https://doi.org/10.1111/j.1467-9566.2008.01143.x>; Koichi Mikami, “Orphans in the Market: The History of Orphan Drug Policy,” *Social History of Medicine* 32, no. 3 (2019): 609–630, <https://doi.org/10.1093/shm/hkx098>
 11. US Health Promotion and Disease Prevention Amendments of 1984, *Public Law 98-551*, *US Statutes at Large* 98 (1984): 2815–2822.

Although the legislation failed at first to alter the attitude of pharmaceutical companies, the situation changed when some biotechnology firms took advantage of the governmental support to put their products on the market and demonstrated that they could make large profits from supposedly-unprofitable drugs for rare diseases¹². And their success coincided with the formation of a single drug market in Europe. As the European Union was officially founded with the Maastricht Treaty in 1993, its foundation served as an opportunity for companies in the region to have similar policy arrangements¹³. As the rarity of diseases posed challenges to medical research too, rare diseases also emerged as a public health issue that would be better addressed collaboratively by its member states than individually by each of them. These multiple lines of conversation resulted in the introduction of regulation on orphan drugs in the European Union in 2000, defining rare diseases as life-threatening or chronically debilitating conditions affecting not more than five in 10,000¹⁴.

Emphasized in most accounts of these policy movements to promote research and development of drugs for rare diseases is the crucial role that patient support groups played in making them happen. In the United States, a coalition of patient groups demonstrated to the members of the Congress the need for legislative support, and upon passing of the 1983 Orphan Drug Act, they formed the National Organization for Rare Disorders (NORD) to continue their advocacy work¹⁵. Similarly in Europe, the foundation primarily led by French patient groups of the European Organization for Rare Diseases (Eurordis) in 1997 helped to accelerate the policy discussion on orphan drug legislation¹⁶. By forming these coalitions, patient support groups presented

12. Mikami, "Orphans in the Market," 625.

13. Huyard, "uncommon disorders," 473.

14. European Commission, "Commission Regulation (EC) No 847/2000 of 27 April 2000," *Official Journal of the European Communities*, L103 (2000): 5-8.

15. Abbey S. Meyers, *Orphan Drugs: A Global Crusade* (2016), https://www.abbeymeyers.com/pdf/Orphan-Drugs-A-Global-Crusade_Abbey-S-Meyers.pdf; Henry A. Waxman, *The Waxman Report: How Congress Really Works* (New York: Twelve, 2009); Mary Dunkle, "A 30-year Retrospective: National Organization for Rare Disorders, the Orphan Drug Act, and the Role of Rare Disease Patient Advocacy Groups," *Orphan Drugs: Research and Reviews* 4 (2014): 19-27; Mikami, "Orphans in the Market," 620.

16. Huyard, "uncommon disorders," 473; Karim Hamadache & Julienne Brabet, "Rethinking Institutional Entrepreneurship: The Case of the Construction of the Orphan Drug Field in Europe," *Society and Business Review* 9, no. 2 (2014): 139-152, <http://dx.doi.org/10.1108/SBR-02-2014-0005>

the significance not of each rare disease but of rare diseases collectively as a social problem affecting a large number of patients and their families¹⁷. Their actions were critical in drawing policy attention to issues of such diseases, highlighting the existence of unmet medical needs and turning the class of diseases into a defined sociopolitical construct that various stakeholders, including medical scientists, policymakers and pharmaceutical companies, can engage to pursue their own interest, while simultaneously responding to the voice of patients and their needs¹⁸.

Rare diseases became legally defined in Japan in 1993 too as those affecting less than 50,000 individuals in the country. However, that decision was made to devise policy support for local pharmaceutical companies and was little to do with the voice of patient support groups¹⁹. As explained in the following two sections, their main concern since the beginning of the 1970s continued to be about the provision of governmental support to patients and their families. And what made the Japanese history peculiar in contrast to those in the United States and Europe was not so much about their focus *per se* but the reason of them needing to keep their focus on that single agenda for more than thirty years.

3. Intractable diseases in Japan

The most significant event that shaped the situation of rare diseases patients in Japan was the publication of the Outline of Intractable Diseases Measures by the Ministry of Health and Welfare in October 1972²⁰. The policy set out in this document reflected the Ministry's struggle with subacute myelo-optic

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17. Vololona Rabeharisoa, Michel Callon, Angela Marques Filipe, Joao Arriscado Nunes, Florence Paterson & Frederic Vergnaud, "From 'politics of numbers' to 'politics of singularization': Patients' activism and engagement in research on rare diseases in France and Portugal," *BioSocieties* 9, no. 2 (2014): 194-217, <https://doi.org/10.1057/biosoc.2014.4>
 18. Helen Crompton, "Mode 2 knowledge production: Evidence from orphan drug networks," *Science and Public Policy* 34, no. 3 (2007): 199-211, <https://doi.org/10.3152/030234207X197066>; Mikami, "Orphans in the Market," 628.
 19. Anonymous, "Dai 4 kai '1993 (Heisei 5) Nen Yakuji-hou Kaisei hoka' Zadankai-Roku," *Iryo To Shakai* 28, no. 4 (2018): 443-472, <http://doi.org/10.4091/iken.28.443>; The Japanese Ministry of Health and Welfare, *Kaisei Yakuji Hou no Kaisetsu: Oufan doraggu hou to korekara no yakumu gyousei* (Tokyo: Chuo Houki Shuppan, 1993), 40.
 20. Eto, *Iryo no Seisaku Katei*, 1; Horiuchi, *Nambyou Kanjya Fukushi*, 13; Kanazawa, "Personal proposals," 86; Takemura & Sone, "Research and development," 47; Saori Watanabe, "The

neuropathy (SMON) between the end of the 1960s and the beginning of the 1970s, and patient support groups certainly played an important role in its making.

3.1. *The social problem of Subacute Myelo-Optic Neuropathy*

SMON, as its name indicates, affects primarily the nervous system, and its cases had been reported as early as the mid-1950s. Its typical symptoms start with stomachache and diarrhoea, and they are followed by minor visual impairment and numbness of the lower body, leading to its paralysis in severe cases. The cases were geographically concentrated forming some hotspots, but their occurrence appeared rather sporadic, and for that reason, they were assumed to do with unknown local conditions. In July 1964, however, the disease came to capture public attention in the country.

Just before the summer that the 1964 Tokyo Olympic Games was held, a number of cases were reported in the city of Toda in Saitama Prefecture, where its boat races were scheduled to take place²¹. With the possibility of this disease being infectious, the Ministry decided to launch its investigation. The investigation lasted for about three years, revealing that the total number of the cases across the country was higher than it was previously thought, with more than 800 cases reported between 1955 and 1966 across the country, and the number had been increasing steadily over the decade²². While the evidence supported the idea that the disease might be infectious, scientists were unable to conclude whether that actually was the case, and the Ministry terminated its investigation in early 1967.

The Ministry then re-launched its investigation in April 1969 with a slightly increased budget²³. As the number of cases reported continued to increase, with recurrent formation of hotspots, the disease re-emerged as

Formative History of Policy for Rare Diseases in Post-War Japan," *Kikan Kakei Keizai Kenkyu* 110 (2016): 55-74.

21. Anonymous, "Mahi no Kibyou Zokuhatsu," *Asahi Newspapers* (Tokyo), Jul 24, 1964: 15; Anonymous, "Shitsumei to Kahanshin-Mahi," *Asahi Newspapers* (Tokyo), Nov 22, 1964: 4.
22. Anonymous, "Densen-sei to Hobo Wakaru," *Asahi Newspapers* (Tokyo), Jan 22, 1966: 15.
23. Anonymous, "Raigetsu, Kenkyu-kai wo Kessei," *Asahi Newspapers* (Tokyo), Mar 2, 1969: 14; Anonymous, "Kenkyu-han Tsukuri Kyumei he," *Mainichi Newspapers* (Tokyo), Mar 2, 1969: 14.

a social problem²⁴. For patients, the diagnosis was devastating. There was no effective treatment, and they had little hope that their condition would recover. The diagnosis meant for them that they now had to carry onerous physical and financial burdens. Furthermore, although it was not confirmed in the earlier investigation, the possibility of the disease being infectious presented the risk of them spreading it to others. Without knowing what caused it, hospitals and local governments had few options to manage its spread, and their desperate attempt to do so in some cases resulted in discriminatory measures against those diagnosed²⁵. Having found themselves suddenly in this tragic and traumatic situation, some patients committed suicide²⁶. It was the seriousness of the problem the disease caused to both patients and their families and hospitals and local governments that forced the Ministry to resume its investigation effort.

At around the same time as the Ministry's new investigation team began its study, patients and their families started organizing a national support group. The fact that SMON patients tended to be geographically concentrated served favourably in this regard, as some hospitals had already initiated informal meet-up sessions for patients who were desperate to know more about their disease²⁷. Such local activities started being linked up with each other when a family of a SMON patient posted a message on a national newspaper in summer 1968. The message invited anyone interested in forming a patient support group to contact him, and the volume of letters that he received in response revealed there was considerable demand for it²⁸. A working group was organized, and a national support group was officially launched in November 1969 with a SMON patient Yoshimitsu Sagara taking up the role of its chairperson²⁹.

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24. Anonymous, "Nennen Fureru SMON Byou," *Mainichi Newspapers* (Tokyo), Jul 14, 1968: 14; Anonymous, "Chiryohou Wakaranu mama," *Asahi Newspapers* (Tokyo), Jul 14, 1969: 2; Anonymous, "Tokeruka SMON no Nazo," *Asahi Newspapers* (Tokyo), Aug 24, 1969: 22; Horiuchi, *Nambyou Kanjya Fukushi*, 53.
 25. Anonymous, "Issho Uramimasu," *Asahi Newspapers* (Tokyo), Mar 9, 1972: 10; Eto, *Iryo no Seisaku Katei*, 88.
 26. Anonymous, "Tsuma ga Anraku-shi Hakaru," *Mainichi Newspapers* (Tokyo), Aug 31, 1968: 8.
 27. Eto, *Iryo no Seisaku Katei*, 102; Horiuchi, *Nambyou Kanjya Fukushi*, 54-55.
 28. Anonymous, "SMON Byou ni Sukuramu," *Mainichi Newspapers* (Tokyo), Aug 17, 1968: 8.
 29. Anonymous, "'Mamoru-kai' de Kouryu he," *Mainichi Newspapers* (Tokyo), Jun 23, 1969: 10.

The Ministry's investigation was led by Reisaku Kono, a medical scientist specialized in virology³⁰. His appointment suggested that the Ministry strongly suspected SMON to be infectious at that time³¹. Although the initial budget for his team was small, the government's decision to put further resources into its work accelerated the research, and by the fall of 1969, it reported some early findings. However, the findings were not exactly what many patients hoped for. While there was no concrete evidence yet, some members of the team reported based on their epidemiological study that the disease was most likely caused by a virus³². This prompted members of the investigation team to search for candidate viruses both in patients' bodies and their living environments, and they came up with some during the following months, reinforcing the idea that SMON was caused by viral infection³³. That also meant that patients ought to be isolated to stop its spread, and hence the social problem became even more serious than it was before³⁴. Mass media reported further incidences of suicides of SMON patients³⁵. The newly established national support group, therefore, was called for research not only to identify the cause of the disease but also to develop its treatment as well as a social welfare scheme to support its patients and their families³⁶.

While the Ministry was willing to respond to the call for further research, it was rather reluctant to set up a scheme to provide SMON patients with financial support for two reasons³⁷. Firstly, the support would cost it more than its budget for the investigation effort. Secondly, providing such support only for SMON patients could be considered unfair to other patients, especially those with lasting health problems like them. However, the situation started to change before long. Triggered that change initially was that a member of the National Diet representing the area known to be

30. Anonymous, "Kenkyu-han Tsukuri Kyumei he"; Anonymous, "Tokeruka SMON no Nazo," *Mainichi Newspapers* (Tokyo), Aug 24, 1969: 22.

31. Eto, *Iryo no Seisaku Katei*, 89.

32. Anonymous, "SMON ha Kansensyosho?" *Asahi Newspapers* (Tokyo), Oct 21, 1969: 14.

33. Anonymous, "SMON Byou: Uirusu Kansensetsu Tsuyomaru," *Asahi Newspapers* (Tokyo), Feb 6, 1970: 1; Anonymous, "SMON no Shin Uirusu Denken Shashin de Kakunin," *Asahi Newspapers* (Tokyo), Jun 26: 1970: 1.

34. Eto, *Iryo no Seisaku Katei*, 106.

35. Anonymous, "SMON byou wo kuni Jisatsu," *Asahi Newspapers* (Tokyo), Oct 31, 1969: 11; Anonymous, "SMON byou de Jisatsu Tsudoku," *Asahi Newspapers* (Tokyo), Nov 3, 1969: 15.

36. Anonymous, "Osoi Yakusho no Torikumi-kata," *Asahi Newspapers* (Tokyo), Feb 6, 1970: 15; Anonymous, "Kansensetsu de Shoku mo Ushinau," *Asahi Newspapers* (Tokyo), Mar 21, 1970: 4.

37. Anonymous, "SMON Byou ni 5 Sen Man En," *Asahi Newspapers* (Tokyo), Jan 30, 1970: 14.

a SMON hotspot showed his interest in tackling the social problem that the disease was causing. At the House of Representatives' committee on social welfare and labor, this politician demanded the then Prime Minister, Eisaku Sato, to set up a new support scheme for SMON patients in March 1970³⁸. A couple of months later, the committee invited both Sagara and Kono to testify, and there, Sagara explained the financial burden that SMON patients and their families had to carry and demanded for public support³⁹. Although the Ministry responded to it by promising that it would consider such support independently from its investigation effort, there was little prospect of any arrangement to be made at least before the beginning of the next fiscal year.

When Sagara and Kono testified at the House of Representative's committee, the view that SMON was caused by viral infection was still prevailing. However, in August 1970, a member of the Ministry's investigation team reported that SMON's symptoms were worsened, rather than improved, by the use of clioquinol as gastrointestinal medicine⁴⁰. It was soon realized that the disease's symptoms resembled its side effects reported abroad⁴¹, and even before the investigation team reached its conclusion, the Ministry discontinued its use immediately in the country⁴². The possibility of the disease being adverse drug reaction, instead of an infectious disease, changed the circumstance dramatically. A local government announced that it would provide financial support to patients in its area⁴³, and several others followed. Some patients soon filed a lawsuit against not only manufacturers of clioquinol products but also hospitals and the national government which failed to protect them from its inadequate use⁴⁴.

In March 1971, the government's budget for the next fiscal year was confirmed, and the Ministry revealed its plan to offer financial support to hospitalized SMON patients as 'rewards' for their participation in its

38. Eto, *Iryo no Seisaku Katei*, 109-111.

39. Anonymous, "Kanjya ha Kyubou Kyusai-saku Hayaku," *Asahi Newspapers* (Tokyo), May 12, 1970: 22.

40. Anonymous, "SMON no Shouzyou Akka ni Seichozai ga Hitoyaku," *Asahi Newspapers* (Tokyo), Aug 7, 1970: 22.

41. Anonymous, "Gaikoku nimo Nita Shouzyou," *Asahi Newspapers* (Tokyo), Sep 4, 1970: 23.

42. Anonymous, "Shiyou Chushi Asu Shimon: Seichozai Kinohorumu," *Asahi Newspapers* (Tokyo), Sep 6, 1970: 1; Anonymous, "Kawari no Kusuri ni Ni-setsu," *Asahi Newspapers* (Tokyo), Sep 8, 1970: 22; Horiuchi, *Nambyou Kanjya Fukushi*, 58.

43. Anonymous, "SMON Kanjya ni Mimaikin 1 Man En," *Asahi Newspapers* (Tokyo), Sep 11, 1970: 23.

44. Anonymous, "Issho Iramimasu," 10; Eto, *Iryo no Seisaku Katei*, 114.

investigation, which was also to be matched by support from their local government⁴⁵. The investigation team remained cautious about concluding clioquinol as the cause of SMON, but as the evidences to support that accumulated, it did so eventually in September 1971⁴⁶.

3.2. *From Subacute Myelo-Optic Neuropathy to intractable diseases*

The success of the Ministry's investigation team in finding SMON's cause after two years of operation was a significant achievement in itself, but the Ministry's handling of the social problem that the disease caused was not particularly commendable, given that when it started its support to the patients, it already knew it was partly responsible for the disease's outbreak, and also because the support was made available only to those who were hospitalized. Despite so, its approach to SMON formed the basis of its new policy for intractable diseases in 1972. To understand how that happened, it is critical to see how other patient support groups responded to this historical event.

The patient support group that became involved particularly closely in the policy discussion on intractable diseases was that of Behçet disease. Patients with Behçet disease typically suffer from skin and eye disorders, and in severe cases lose sight impacting seriously on their quality of life. Having seen SMON patients forming a national support group to demand the Ministry to allocate more resources in its research and for patient support, two patients decided to set up their own support group with help from their doctors in February 1970⁴⁷. As that was reported in a national newspaper, when SMON was discussed at the House of Representative's committee in March 1970, a politician referred to Behçet disease too, grouping these diseases as "social diseases"⁴⁸. The committee, after it invited Sagara and Kono in May, held a discussion also on Behçet disease, which was then followed by that on a few others like sarcoidosis and muscular dystrophy.

45. Eto, *Iryo no Seisaku Katei*, 111.

46. Anonymous, "Ekigaku Bukai ga Dantei," *Asahi Newspapers* (Tokyo), Oct 1, 1971: 3.

47. Anonymous, "'Behcet no Kai' Kessei he," *Asahi Newspapers* (Tokyo), Jan 17, 1970: 14; Anonymous, "Kanjya-tachi ga 'Tomo no kai'," *Asahi Newspapers* (Tokyo), Feb 6, 1970: 15.

48. Eto, *Iryo no Seisaku Katei*, 108-109.

A major turning point came in early 1971. In February that year, the doctors seeing Behçet disease patients produced a draft legislation concerning what they called “intractable diseases” and made a formal request to the Ministry to consider its introduction⁴⁹. In the draft legislation, intractable diseases were defined as diseases of unknown cause which likely force their patients to abandon ordinary life⁵⁰. Although the decision on what diseases ought to be included in such a class of diseases was left to the Ministry, the doctors demanded that similar arrangements to those made for SMON be done for such other diseases too. The timing of their action was particularly important. As explained above, it was suggested by then that clioquinol was a potential cause of SMON and while the investigation team had not concluded yet, the Ministry had already adopted its precautionary measure to discontinue its use since the summer of 1970. Once the official conclusion was drawn, however, SMON, being an adverse drug reaction, could have been classified differently from other diseases like Behçet disease⁵¹. Their action, therefore, was just in time to endorse legitimately the earlier political gesture that there was a group of diseases deserving political attention and that it included both SMON and Behçet disease⁵².

As long as SMON was part of the discussion, the Ministry, being responsible for the inadequate use of clioquinol in the past, could not easily refuse to consider such a request, but even so, turning the arrangements for SMON into legal requirement for its handling of other diseases did not appear to it to be a pressing issue⁵³. To put further pressure on it, therefore, several actions followed the doctors’ initiative. In March 1971, six patient support groups, including those of SMON and Behçet disease, met up in Tokyo and agreed to form an informal network of patient support groups concerning intractable diseases⁵⁴. The doctors also requested members of the Parliament with an interest in issues of such diseases to form a cross-party group, and this group of politicians organized regular meetings with

49. Anonymous, “Nambyo Kyusai Hou’ Tsukutte,” *Asahi Newspapers* (Tokyo), Feb 10, 1971: 23; Eto, *Iryo no Seisaku Katei*, 117.

50. Anonymous, “Nambyo Kyusai Kihon-hou Genan,” *Asahi Newspapers* (Tokyo), Feb 20, 1971: 4.

51. Eto, *Iryo no Seisaku Katei*, 121.

52. Horiuchi, *Nambyou Kanjya Fukushi*, 63.

53. Anonymous, “Nambyo Kyusai Hou’ Tsukutte,” 23; Anonymous, “Kihon-hou wo Maemuki de Kentou,” *Mainichi Newspapers* (Tokyo), Mar 25, 1971: 17.

54. Anonymous, “Nambyo Kanjya Te wo Tsunagu,” *Asahi Newspapers*, (Tokyo), Mar 31, 1971: 3; Anonymous, “Mina de Katakumi, Chikara Duyoku,” *Mainichi Newspapers* (Tokyo), Mar 31, 1971: 17.

the doctors and the patient groups from May 1971 onwards⁵⁵. Although the Ministry remained cautious about the introduction of the legislation, these collective actions from the doctors, the patient support groups and the politicians made it promise to consider a policy for such diseases in its next year's budget⁵⁶.

By the time when the Ministry's investigation team concluded clioquinol as SMON's cause in that summer, therefore, intractable diseases had already become a politically robust, though not yet official, categorical term to refer to a certain class of diseases. Toward the end of that year, the patient support groups started working towards the formalization of their network as a national liaison council of patient support groups for intractable diseases to negotiate further with the Ministry, which was then planning its budget for the next fiscal year⁵⁷. The Ministry indeed allocated a substantial budget for its effort to tackle diseases of unknown cause and/or those without effective treatments⁵⁸. However, it was still reluctant to introduce a new legislation to turn such effort into legal requirement. That was discussed at the House of Representatives' committee in April 1972, but there some doctors revealed that they too were against such a legislation. They reasoned that once what counted as intractable diseases became legally defined, adding new diseases to them would likely be difficult⁵⁹. While some patient groups kept calling for the legislation, the idea rapidly lost its attraction from that point on.

After consultation with medical professionals over a few months, the Ministry announced its decision to spend its increased budget to set up new research projects for seven intractable diseases — Behçet disease, myasthenia gravis, systemic lupus erythematosus, sarcoidosis, aplastic anemia, multiple sclerosis and intractable hepatitis— in addition to its SMON investigation⁶⁰. It also decided that among these, patients with the first three would be eligible

55. Anonymous, "Nambyou Taisaku Kihon-hou Mezasu," *Mainichi Newspapers* (Tokyo), May 20, 1971: 22; Anonymous, "Nambyou Taisaku no Chotoha Rippou-ka wo Teisho," *Mainichi Newspapers* (Tokyo), Jun 13, 1971: 2; Anonymous, "Wasureruna Nambyou Taisaku," *Mainichi Newspapers* (Tokyo), Jul 18, 1971: 23; Eto, *Iryo no Seisaku Katei*, 118.

56. Anonymous, "Nambyou Taisaku ni Madoguchi," *Asahi Newspapers* (Tokyo), Sep 5, 1971: 3.

57. Horiuchi, *Nambyou Kanjya Fukushi*, 63.

58. Anonymous, "Nambyou Taisaku Shitsu wo Secchi," *Asahi Newspapers* (Tokyo), Jan 13, 1972: 19.

59. Eto, *Iryo no Seisaku Katei*, 118.

60. Anonymous, "Chiimu de Chosa Kenkyu," *Asahi Newspapers* (Tokyo), Jul 4, 1972: 2; Anonymous, "Yattsu no Nambyou ni Kenkyu-han," *Asahi Newspapers* (Tokyo), Sep 17, 1972: 3; Anonymous, "Yattsu ni Shibori Honkaku Chosa," *Mainichi Newspapers* (Tokyo), Jul 4, 1972: 2; Anonymous, "Nambyou Kyumei ni Yaku 2 Oku En," *Mainichi Newspapers* (Tokyo), Sep 17, 1972: 2.

for the financial arrangement that had been available for SMON patients since 1971, again as the reward for their participation in research. Following this announcement, the Ministry organized a new administrative section to coordinate its effort concerning intractable diseases, and in October 1972 published the policy document the Outline of Intractable Diseases Measures summarizing the nature of the effort. It was this document that gave the concept of intractable diseases not legal but political legitimacy.

Along with its publication, the Ministry announced its plan to add further twelve diseases to its list of intractable diseases and start research projects on them in the next year⁶¹. It was assumed that by expanding the scale of the effort to a total of twenty diseases, its policy should cover most of intractable diseases in the country⁶². The financial support was made available for patients with aplastic anemia and sarcoidosis too. The fact that the newly elected Prime Minister Kakuei Tanaka was supportive of the Ministry's policy assisted its plan⁶³, and it was realized in April 1973 with the approval of a substantially increased budget⁶⁴. The condition for the Ministry's financial support of having to be hospitalized was also removed, making all patients with the six diseases eligible for it⁶⁵. Soon the Ministry came to the view that it needed to expand the scope even further by adding ten more diseases to its list and also making its financial support available to patients with four other diseases⁶⁶.

Thus, as a result of the concerted effort from the doctors, the patient groups and the policymakers, the arrangements combining coordination of a research project and provision of financial support that the Ministry initially made for SMON formed the basis of its intractable diseases policy in 1972. The close working of patient support groups in particular was important in giving legitimacy to the concept of intractable diseases and in the re-organization of the Ministry's effort in accordance with it. And once it was formalized in the form of the Outline of Intractable Diseases Measures,

61. Anonymous, "Roku Shikkan ni Kouhi Futan," *Asahi Newspapers* (Tokyo), Oct 3, 1972: 1.

62. *Ibid.*

63. Anonymous, "Nambyo Chiryuu, Kuni ga Sekinin," *Asahi Newspapers* (Tokyo), Oct 28, 1972: 2.

64. Anonymous, "Nambyo Yosan, Baizo he," *Asahi Newspapers* (Tokyo), Jan 6, 1973: 2; Anonymous, "Shitei 'Nambyou' ni 12 Shikkan wo Tsuika," *Asahi Newspapers* (Tokyo), Apr 24, 1973: 3.

65. Anonymous, "Jyubun na Iryo koso Senketsu," *Asahi Newspaper* (Tokyo), Jan 20, 1973: 8.

66. Anonymous, "Arata ni 10 Shikkan Shitei," *Asahi Newspapers* (Tokyo), Sep 2, 1973: 1; Anonymous, "Nambyou' ha Youkyu Douri," *Asahi Newspapers* (Tokyo), Dec 27, 1973, 1; Anonymous, "Nambyou ni 10 Shikkan Tsuika," *Asahi Newspapers* (Tokyo), May 5, 1974, 3.

the Ministry expanded its scope by adding new diseases to the list of such diseases. The history of intractable diseases policy, however, revealed that these arrangements were structurally divisive, and for nearly three decades patient support groups remained unable to unify their voice to turn their diseases into a social problem again.

4. Levels of activities and their separation

Patient support groups were aware that the conflict of interest among them could undermine their cooperation. An aim of setting up the national liaison council of patient support groups for intractable diseases, or the national intractable diseases council for short, in early 1972 was to prevent them from competing against each other for political attention and resources that the Ministry was to allocate to its effort. Once the effort was formalized, however, the council had little incentive to sustain its level of activities. Since its first general meeting was held upon its launch in April 1972⁶⁷, a general meeting was not organized for four years⁶⁸. By then, the SMON national support group, which was central to the council's foundation, had withdrawn from the cooperation. Being aware of its political significance, it was at the beginning highly motivated to work with other groups to improve the healthcare system in the country⁶⁹. Yet the confirmation of cloquinol as the cause of the disease and the series of lawsuits against pharmaceutical companies, hospitals and the government followed that changed its priority. Despite the investigation team's conclusion that cloquinol did cause SMON, it took seven years before the parties came to agree on a settlement. The long-lasting legal dispute posed challenges to running the national support group⁷⁰.

The significance of national-level cooperation of patient groups was downplayed also by the establishment of regional-scale liaison councils. The first regional council was formed in Toyama Prefecture in March 1972, which predated the publication of the Ministry's policy document on intractable diseases. Toyama Prefecture was where itai itai disease, the well-known case

67. Anonymous, "Genin Kyumei, Rikai wo," *Mainichi Newspapers* (Tokyo), Apr 11, 1972: 17.

68. Hiroshi Osa, *Kanjya Undou* (Tokyo: Keiso Shobo, 1978), 181.

69. Horiuchi, *Nambyou Kanjya Fukushi*, 68.

70. *Ibid.*, 85.

of mass cadmium poisoning, broke out, and families affected were still in the legal battle against the company that polluted the local river with the toxic substance. The circumstance invited the prompt local reaction to the rapidly changing policy situation at the national level. The formalization of the Ministry's effort then encouraged patient support groups in other areas to follow its lead. Seven regional councils, including those in Tokyo and Osaka, were formed within a year, and the number increased to fourteen by the end of 1975⁷¹. Some regional councils then recognized the potential advantage of working together in their negotiation with local as well as national governments and tried to strengthen their tie by organizing joint executive meetings. Representatives from seven regional councils attended the first such meeting in March 1975, and nine of them did the second which was held half a year later⁷². Only a few years after the foundation of the national liaison council, therefore, the network of regional councils was being formed in parallel.

In the mid-1970s, these regional councils became more active than the national liaison council. The Ministry in its policy identified advances in medical research, provision of medical facilities and reduction of medical cost as three pillars of its intractable diseases measures⁷³. Having been united with the goal of making the Ministry's arrangements for SMON available for other intractable diseases, the national council already achieved its most important goal when the Outline of Intractable Diseases Measures was produced. Furthermore, the Ministry began rolling out the arrangements to the diseases that the original member groups of the national council were concerned about⁷⁴. This by no means meant that these patient groups were concerned only about their diseases, and just like the SMON group, they hoped that their action would improve the country's healthcare system as a whole. Yet, it appeared to them as if they had made good progress on that front too, as the list of intractable diseases continued to expand and an increased number of patients became eligible for the Ministry's financial support in the first few years⁷⁵.

71. Osa, *Kanjya Undou*, 190

72. Teizou Katsuragi, *Nambyou Kanjya Undou* (Tokyo: Seikatsu Shoin, 2019), 23.

73. Eto, *Iryo no Seisaku Katei*, 127; The Ministry of Health and Welfare, "Nambyou Taisaku Youkou."

74. Anonymous, "Roku Shikkan ni Kouhi Futan," 1; Anonymous, "Nambyo Yoson, Baizo he," 2.

75. Anonymous, "5 Shikkan ni Iryo Hojo," *Asahi Newspapers* (Tokyo), May 4, 1975, 3; Anonymous, "Nambyou no Josei Sarani 2 Byou," *Asahi Newspapers* (Tokyo), Sep 30, 1976, 20.

Despite the Ministry's new policy, however, patients' struggle continued. The three pillars of the Ministry's measures were important but were not sufficient to change their lives beyond relieving them from the medical cost. Particularly problematic was that social welfare services were not included in its scope⁷⁶. The nature of services, such as compensation for unemployment, educational support for children with special needs and nursing care for bedridden patients at home, was left to the decision of local governments. Tateo Ito, who initiated the establishment of a regional council in Hokkaido Prefecture, made it clear in his statement in March 1973 that many patients and their families still felt socially excluded without sufficient support⁷⁷. And the 1973 Oil Crisis made the situation even worse as both the national and local governments cut their budget for social welfare services, and that in turn stimulated activities of regional councils in the mid-1970s.

The cut of the government expenditure on social welfare services served as a wake-up call not only for patient support groups concerning intractable diseases but for others too. In 1975, eight large patient support groups focusing on diseases and conditions other than intractable diseases founded a national liaison council⁷⁸. The national intractable diseases liaison council too was revived under the leadership of a patient support group for kidney diseases⁷⁹. Despite such re-activation of national-level cooperation among patient groups, however, the economic crisis continued to affect the Ministry's effort on intractable diseases. The increase in the number of diseases eligible for its financial support slowed down to the pace of a disease a year after it reached eighteen in 1976. That disappointed patients who had been waiting for their turn⁸⁰. Recognizing that strong advocacy from patients was needed urgently, the network of regional councils invited the two national liaison councils to work with it to organize a national conference⁸¹. The national conference of patients and their families to improve medical and social welfare services was held in 1978 successfully with 773 attendees from 52 patient groups⁸². The success was encouraging for the national councils, but

76. Eto, *Iryo no Seisaku Katei*, 164.

77. Osa, *Kanjya Undou*, 188-189.

78. Osa, *Kanjya Undou*, 183.

79. *Ibid.*, 181.

80. Anonymous, "Nambyou Chiryu-hi Shibomu," *Mainichi Newspapers* (Tokyo), Jan 13, 1977: 9; Anonymous, "Pakinson Byou Tsuika," *Mainichi Newspapers* (Tokyo), Jun 18, 1978: 3.

81. Osa, *Kanjya Undou*, 202.

82. Katsuragi, *Nambyou Kanjya Undou*, 29.

regional councils, which were not able to coordinate their effort as much, faced internal criticisms that they ought to shift their focus back to local activities⁸³.

The parallel existence of the two national liaison councils and the network of regional councils continued until the establishment of a new national-level organization called the Japan Patient Council in 1986. This organization was a result of the merger between the network of regional councils and the national council concerning non-intractable diseases. Since the 1978 conference, national-level activities of regional councils lessened, but some members revitalized them toward the International Year of Disabled Persons in 1981⁸⁴. The network of regional councils, in order to sustain its national-level activities, proposed to the two national liaison councils in 1984 the organization of another national event with a future prospect of merger⁸⁵. Discussion took place among them, and after some coordinated actions, they almost agreed on a three-party merger. Yet the national intractable diseases liaison council pulled out at the last minute for an unknown reason, leaving the other two to form the new organization⁸⁶.

Active advocacy work by the Japan Patient Council led to the addition of the fourth pillar of improvement and coordination of regional medical and social welfare services to the Ministry's measures for intractable diseases in 1989⁸⁷. Based on that, local health centres were made legally responsible for the provision of support for patients with intractable diseases and their families in their area. That was the first instance since the Ministry formalized its intractable diseases policy in 1972 that support for patients with such diseases became a legal requirement, though it was not for the Ministry but for local governments. Furthermore, in 1995, the Japan Patient Council's request to improve measures for intractable diseases in the country was adopted in the National Diet⁸⁸. Following that, the fifth pillar of promotion of social welfare policies to improve the quality of life of patients was added to the Ministry's policy in 1996, resulting its new support schemes for patients being cared at home⁸⁹.

83. *Ibid.*, 28.

84. *Ibid.*, 31-32.

85. Horiuchi, *Nambyou Kanjya Fukushi*, 93.

86. Katsuragi, *Nambyou Kanjya Undou*, 40.

87. Horiuchi, *Nambyou Kanjya Fukushi*, 94.

88. Katsuragi, *Nambyou Kanjya Undou*, 43.

89. Horiuchi, *Nambyou Kanjya Fukushi*, 95.

The late 1990s, however, turned out to be a challenging time for patient groups as a series of discussions to revise the Ministry's policy for intractable diseases took place. Such discussions were provoked by the amendment of the Pharmaceutical Affairs Law, specifically its inclusion of a new clause on orphan drugs. In Japan, the demand for the clause was put forward by pharmaceutical companies, rather than patients and their families, inspired by the 1983 US Orphan Drug Act and the success of biotechnology companies in taking advantage of it⁹⁰. When the Law was amended, rare diseases eligible for its orphan-drug tax exemption scheme was defined as those with less than 50,000 patients in the country. This decision led to a discussion within the Ministry about if the limit should also be applied to its support for patients with intractable diseases, and that resulted in the addition of a new criterion that intractable diseases ought to be rare to the Ministry's Outline in 1997. This addition then provoked the question of what happens to a disease listed if its patient population exceeds the limit. Although it was not considered as a strict cut-off line, the fact that no disease had been taken off the list since the start of the policy in 1972 came to the Ministry's attention. Estimation in the West that there could be more than 6,000 rare diseases too caused a considerable concern that its arrangements for intractable diseases could go unmanageable soon. It was therefore concluded that diseases could be removed from the list if they no more meet the criteria for intractable diseases⁹¹. It was also decided in 1998 that patients should pay part of their medical cost, which had been fully covered by the Ministry over the past twenty-five years.

These changes reflected predominantly the Ministry's budgetary concern in the context of the prolonged national economic crises since the start of the 1990s⁹². It continued the discussion to revise its intractable disease policy into the 2000s, inviting both the Japan Patients Council and the national intractable diseases liaison council. It was around that time when they came to the decision that it was high time for them to merge. Appealing against the Ministry's gesture to slim down its arrangements was part of its motivation, but more problematic from their perspective was its unwillingness to deal

90. Anonymous, "Yakuji-hou Kaisei, 445; Ministry of Health and Welfare, *Kaisei Yakuji Hou no Kaisetsu*, 40.

91. Horiuchi, *Nambyou Kanjya Fukushi*, 96.

92. Ichiro Kanazawa, "Waga Kuni-no Nambyou Seisaku ni tsuite," *No to Hattatsu* 44, no.3 (2012): 185-189, <https://doi.org/10.11251/ojjsncn.44.185>

with issues with access to social welfare services at regional levels for which it delegated legal responsibility to local governments⁹³. Patient groups came to recognize that separating their national and regional activities only allowed a loophole in the policymaking. The Japan Patients Association was formed in May 2005 and finally began to present a unified voice of patients and their families in the country.

5. Discussion

The peculiarity of this Japanese history cannot be reduced to its unique concept of intractable diseases. The policy that the Ministry of Health and Welfare introduced for such a group of diseases more than a decade prior to the enactment of the 1983 US Orphan Drug Act combined the organization of a research project and the provision of patient support. That was how it approached to the emerging social problem of SMON at the beginning of the 1970s, and in responding to the pressure from a group of patient support groups and their medical and political supporters, it made the same arrangements available for other intractable diseases. The patient groups then attempted to consolidate their cooperation by forming a national liaison council, just as the NORD was established in the United States in 1983.

The patient support groups in Japan, unlike those in the United States and Europe, did not need to aggregate the numbers of patients and their families affected by the diseases to demonstrate the social significance of their problems, owing to the social problem of SMON already recognized nationally in the early 1970s. However, the dependence on SMON resulted in the policy which turned out to be structurally divisive. Because support to patients was made available in the form of rewards for their participation in research activities, it became necessary for patients that they have a group of medical scientists interested in studying their disease even to hope that they become eligible for such support. Furthermore, in its policy, the Ministry only dealt with the areas of medicine that it had direct control of. The need to negotiate separately with local governments about social welfare services prompted patients and their families to engage in regional activities more since the mid-1970s. Regional councils were founded in various areas, and

93. Katsuragi, *Nambyou Kanjya Undou*, 43-45.

soon their national network was formed. It was this parallel existence of the national liaison council and the network of regional councils that also characterized the country's history.

At the beginning of the 1990s, the network of regional councils through its advocacy work as a new national-level patient organization gradually made social welfare services a part of the Ministry's measures for intractable diseases. Such change in its scope in turn united different levels of actions from patient support groups and enabled them to present their unified voice finally in the mid-2000s. The Ministry's attempt to superimpose the condition for its support for orphan drug development onto the concept of intractable diseases also contributed to their realization of the need for a unified voice. Once that happened and with the formation of the Japan Patient Association, the policy for intractable diseases in the country began to undergo a dramatic revision leading to the enactment of the legislation concerning intractable diseases in 2014⁹⁴. Under this legislation, intractable diseases became defined differently from rare diseases and as affecting roughly less than 0.1 per cent of the entire population. The Ministry also produced a new list of such diseases for the purpose specifically of its financial support with more than 300 diseases listed by 2018⁹⁵.

This separation of the Ministry's financial support from its research activities also gives patients with rarer forms of disease a better chance of being eligible for the support than previously. In contrast to the diseases like SMON and Behçet disease, which were at one point in the history considered by politicians as "social diseases," those affecting only ten or so in the country have been given little attention. Although a patient support group on such diseases was founded in 1977⁹⁶, patients with them had little hope of their diseases being added to the Ministry's list of intractable diseases because that required their research project to be launched. Yet, it is important to note that the new policy still maintains the listing system. Although the number of the diseases listed increased significantly, it is not difficult to imagine that there still exist numbers of patients without adequate support, if one compares the figure of 300 odd diseases listed in Japan to the scale of rare

94. Tateo Ito, "Patient Groups' Advocacy Activity and Nanbyo Act (The Iatric Services to Patients Suffering from Intractable Disease): From the View Point of Patient Groups," *Iryo To Shakai* 28, no. 1 (2018): 27-36, <https://doi.org/10.4091/iken.29.027>

95. Kawano, "Establishment of Intractable/Rare Disease Act,"

96. Anonymous, "Kishou Namyou Kanjya ga Rentai," *Asahi Newspapers* (Tokyo), Jan 13, 1978: 3.

diseases suggested to exist, though many of the diseases listed are defined rather broadly and are more inclusive than the number may appear. As it was suggested back in the early 1970s, having a legal basis could potentially make adding new diseases to the list more difficult than otherwise, and the time will tell if this actually is the case.

The Intractable Diseases Act of 2014, which separated the Ministry's research effort from its financial support, was a major step in the history of rare diseases in Japan, enabling the country to partake in the international research consortium in 2015. The hope now is that increased interactions with the rare diseases community abroad would help it to finally put the historical peculiarity described in this article behind, and allow the local concept of intractable diseases to serve as a focal point for multiple stakeholders to advance their effort and respond to the unified voice of patients, just as that of rare diseases does in the West. ■

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