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SUFFERING IN SILENCE: ASSESSING RARE DISEASE AWARENESS AND MANAGEMENT IN ASIA-PACIFIC

Sponsored by:

CSL Behring

Contents

- 3 Executive summary**
- 6** About the research
- 7 Section I. An introduction to rare diseases in Asia-Pacific**
- 7** Rare diseases move up the health policy agenda
- 8** Measuring up: The size of the rare disease challenge
- 10 Section II. Overarching challenges in managing rare diseases**
- 10** United in diversity: To what extent do rare diseases constitute a coherent category?
- 14** Box 1: Which diseases count?
- 15** Inconsistent care quality
- 17** Limited knowledge and experience
- 18** Making the necessary knowledge available at the right time
- 20** Box 2: Efforts to improve diagnosis in South Korea and Japan
- 22 Section III. Prioritising the response in Asia-Pacific**
- 22** Difficulties in diagnosis
- 24** The broader financial burden
- 25** Looking at the person beyond the disease
- 26** Box 3: Taiwan's comprehensive approach
- 28 Conclusions: Raising the profile of rare diseases in Asia-Pacific**

Executive summary

The collective challenge of rare diseases has risen up the policy agenda in both the Asia-Pacific region and globally. Various new and revised health and social system measures in Australia, China, Japan, South Korea and Taiwan—along with the 2018 Asia-Pacific Economic Co-operation (APEC) Rare Disease Action Plan—reflect a growing recognition of the need to act.

As the region begins to get to grips with rare diseases, it will need to address significant challenges, some of which are still emerging. Health and social systems are making progress in many of these areas, but finding solutions remains a work in progress.

This Economist Intelligence Unit study, sponsored by CSL Behring, looks at the nature of the rare disease challenge in the region, how prepared five of its economies are to face it, and reviews the initiatives aiming to provide better care. It draws on a substantial survey of over 500 clinicians, interviews with 16 academic, medical, government and patient experts, and extensive desk research.

Our research identified several overarching challenges and three high-profile priorities in Asia-Pacific:

Overarching challenges

1. The lack of a unified definition for rare diseases can interfere with common understanding, but an inflexible approach is impractical based on the diversity of rare conditions

- “Rarity” is not an objective medical concept. As such, the definition of the rare disease burden can vary greatly depending on who is describing it. The true burden of many rare diseases in Asia-Pacific is not yet defined.

This has important consequences for those deciding the design of research programmes, care packages and forming health policy.

- There are between 6,000 and 7,000 unique rare conditions, each with causes, symptoms, treatment options and outcomes that may have little in common beyond their rarity. Underneath this diversity, there are commonalities which make it sensible to address rare diseases collectively. These include common problems for patients and families around interacting with the health system as well as similar financial and social needs arising from the debilitating nature of many of these conditions.

2. Only a minority of patients receive the best available evidence-based care

- Inconsistency and inequity in care is a challenge for rare disease patients in Asia-Pacific. Our survey respondents report that only a third of their rare disease patients receive best available evidence-based care. When asked how well their health systems performed overall on diagnosis, treatment, and quality of care, the responses indicate adequate, but not excellent, care.
- Our experts explain that the current situation is nuanced. The more common rare diseases, especially where treated by multi-disciplinary teams, can receive excellent treatment. Care for those with rarer conditions, those who live in rural areas away from large medical centres or those whose disease goes unrecognised are more likely to have only adequate provision or worse (see Page 16 of this report).

3. Knowledge of many rare diseases is scant, as are reliable data

- Knowledge of rare diseases among healthcare professionals in our survey is limited. Ranking their peers' knowledge of rare disease on a scale of "very poor" (1) to "very good" (5), respondents on average gave a middling score (3.1). Knowledge gaps in our survey respondents were common: 34% did not know if their country had a unified definition of "rare disease" and 35% were unsure whether a rare disease policy existed at all.
- This may simply reflect a lack of contact with patients: respondents saw a median of one new rare disease case per year and rarely encountered the same disorder more than a few times in an entire career.
- There is a need to improve general background knowledge through education; analyse where expertise exists in the health system; collect and analyse data; and better integrate information for use at point-of-care (see Page 18 of this report).

High-profile priorities

1. Reaching a correct diagnosis often involves a lengthy journey through the health system

- Our respondents rated diagnosis as the greatest challenge in the rare disease field. The issue includes both getting it right and getting it done quickly. Too often, patients wait years and see multiple doctors before they are diagnosed.

- National undiagnosed disease programmes are becoming more common in the Asia-Pacific region. Examples in Korea and Japan show that a combination of multi-disciplinary teams, advanced DNA sequencing techniques, use of clinical databases, and networking among domestic and international experts can facilitate accurate diagnoses for around a third of difficult cases (see Page 20 of this report).

2. The financial burden can be substantial

- When our respondents were asked which single action would most help those living with rare diseases, nearly half (47%) mentioned improvements to financial support. The economic burden of rare diseases for patients and families is substantial. In China, for example, the drugs themselves are unaffordable for patients. Although other markets provide some support for such costs, not every condition is covered equally. Out-of-pocket expenses beyond medical costs can become substantial for patients across the region (see Page 24 of this report).

3. Requirements of those living with rare diseases include financial and social care needs, not just medical assistance

- When asked how well government systems provided for the different needs of those living with a rare disease, our respondents ranked them lowest overall at supporting quality of life. With 94% of rare diseases lacking any approved medical treatment, this is also the area in which policy can have the most immediate impact in many cases.

- The multi-faceted needs of those with rare diseases make wider social care imperative. As patients often have difficulty accessing employment or education, assistance in these areas is an essential part of their overall care (see Page 25 of this report).

Responding to the challenge: Co-ordinated policies can address the diverse needs of those living with rare diseases

Despite the numerous challenges identified in this study, there has been slow but steady progress towards co-ordinated, integrated care for rare disease patients across the region. There are several currently-achievable or near-term goals that policy-makers could prioritise to make further improvements. These include better collection and use of data, enhanced education, broader dissemination of available knowledge and the integration of social care through partnerships with patient representatives (see conclusions of this report for more details).

About the research

In November-December 2019, The Economist Intelligence Unit surveyed 503 healthcare professionals across five Asia-Pacific markets to gauge their understanding of rare diseases and identify the challenges faced by national health systems. Respondents comprised currently-practising specialist physicians (n=172), general practitioners (n=229), nurses (n=40) and pharmacists (n=62). Markets included were Australia (n=103), China (n=100), Japan (n=100), South Korea (n=100) and Taiwan (n=100).

In addition, in-depth contextualising interviews were conducted with 16 expert representatives of clinical practice and patient organisations to inform our research programme and this report. Our sincerest thanks go to the following for their time and insight:

Takeya Adachi, program officer, Agency for Medical Research and Development, Japan

Younjhin Ahn, Division of Rare Diseases, Korean National Institute of Health Centre for Biomedical Sciences, South Korea

Matthew Bellgard, professor and director of eResearch, Queensland University of Technology, Australia and chair of the Asia Pacific Economic Cooperation (APEC) Rare Disease Network, Australia

Gareth Baynam, clinical geneticist and director of the Undiagnosed Diseases Program Genetic Services of Western Australia, Australia

Dong Dong, research assistant professor, Chinese University of Hong Kong, Hong Kong SAR

Elizabeth Elliott, professor of Paediatrics and Child Health, University of Sydney, Australia

Kevin Huang, founder, Chinese Organization for Rare Disorders, China

Ritu Jain, president, Asia-Pacific Alliance of Rare Disease Organisation, Singapore

Sonoko Misawa, associate professor, Chiba University Graduate School of Medicine, Japan

Yukiko Nishimura, founder and president, NPO ASrid (Advocacy Service for Rare and Intractable Diseases' Multi-Stakeholders in Japan)

Min-Chieh Tseng, co-founder, Taiwan Foundation for Rare Diseases, Taiwan

Gregory Vijayendran, chair, Rainbow Across Borders

Richard Vines, chair, Rare Cancers Australia, Australia

Jiaan-Der Wang, director of the Centre for Rare Diseases and Haemophilia, Taichung Veterans General Hospital, Taiwan

Yí'ou Wang, secretary-general, Illness Challenge Foundation, China

Chao-Chun Wu, deputy director general, Health Promotion Administration Taiwan

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March 2020.

Section I. An introduction to rare diseases in Asia-Pacific

Rare diseases move up the health policy agenda

Rare diseases in Asia-Pacific have seen “an increase in focus” and “are getting more and more attention” notes Matthew Bellgard, chair of the Asia-Pacific Economic Co-operation (APEC) Rare Disease Network, as well as professor and director of eResearch, Queensland University of Technology, Australia. Gregory Vijayendran, chair of Rainbow Across Borders—an Asia-Pacific rare disease patient umbrella group based in Singapore—agrees: “Awareness has slowly but significantly improved over the past five years.”

Both experts consider there to be a variety of factors behind this recent shift. Dr Bellgard points to health system-related changes, believing that the broader drive toward universal health coverage has called attention to the inadequate provision of care to under-served groups, including those with rare diseases. In addition, he notes that an increasing emphasis on patient-centred care is creating an environment in which the multi-faceted needs of rare disease patients can be more effectively met. Mr Vijayendran, meanwhile, points to the rising public profile of these conditions following diverse efforts by governmental health authorities, patient awareness and advocacy groups, affected individuals and their caregivers, and clinicians. Patients have started to benefit from greater recognition of rare diseases and the challenges faced by under-resourced health systems.

Policy developments reflect this increased profile on the Asia-Pacific public health agenda. Some prominent developments include:

- The Australian government launched the country’s first National Strategic Action Plan for Rare Diseases in February 2020;
- Japan has rare disease policies going back to the 1970s, but in 2014, new legislation was passed to assist those with such conditions. In 2015 it ramped up the search for causes and treatments when the newly-founded Agency for Medical Research and Development (AMED) made rare and intractable diseases one of its nine priority areas;
- Also in 2015, South Korea’s Parliament passed the *Rare Disease Management Act*, requiring the Ministry of Health and Welfare to develop plans for the prevention, diagnosis, treatment and research into rare diseases;
- Taiwan has fewer recent initiatives due to its highly-regarded, long-standing efforts. These began in earnest when it passed the world’s fifth rare disease and orphan drug act in 2000. That said, Taiwan has continued to improve provision, most recently in late 2017 with its publication of the Rare Diseases and Rare Genetic Disorders Care and Services Plan.

Emerging market countries are also taking important steps. Yi'ou Wang—secretary-general of the Illness Challenge Foundation, a Chinese rare disease patient group—notes that “China has made rapid progress on policy in this area in recent years”. Although no formal rare disease legislation exists, China’s National Health Commission created an Expert Committee of Rare Disease Treatment and Support in 2016 and published its first national list of rare diseases two years later. Meanwhile, adds Ms Wang, an increasing number of orphan drugs are receiving approval and, since October 2019, large Chinese medical insurance schemes appear to be looking at ways to improve coverage.

At the international level, APEC has had a Life Sciences Innovation Forum Rare Disease Network since 2016. In late 2018, it launched APEC’s Rare Disease Action Plan, the goal of which is to provide member economies with a policy framework for dealing with these conditions.¹

Measuring up: The size of the rare disease challenge

What is the nature and extent of the health burden that has prompted these national and international responses? Any answer must begin with an important caveat: in the words of Mr Vijayendran, this field suffers from “a distinct lack of data”. This is particularly notable in Asia-Pacific where estimates, rather than hard numbers, are common. A clear example comes from China. Its Centre for Disease Control supposes—quite reasonably given the size of the country’s population—that China has the world’s

largest number of people with rare diseases (16.8m in 2014).² National figures on incidence and prevalence exist for only 14 of the 121 rare diseases on China’s recently-issued national list. A recent study found that available Chinese data “are limited and typically lack accuracy, uniformity, and timeliness”.³

Aside from the prevalence of insufficient or inaccurate data, definitions of rare disease—including even the numbers affected before a condition ceases to be rare—vary widely between countries, making comparison and aggregation even more problematic.

Amid the statistical uncertainty, the vast number of rare diseases and their marked collective impact on health systems is nonetheless clear. Orphanet, an influential 37-nation consortium maintains the world’s leading database of rare diseases. Using the EU’s broad definition of conditions with a prevalence of less than one per 2,000 population, Orphanet’s so-called epidemiological file contained 6,172 known, unique rare disorders in October 2018.⁴ Since new conditions continue to be discovered, the common estimate of 6,000 to 7,000 may be roughly accurate, but the breadth of this approximation also reflects our current lack of comprehensive knowledge.

Data are only available for around half of the diseases on the Orphanet list. In some cases, information is lacking as no relevant studies exist. For other conditions, such as rare cancers, infections, and poisonings—which together make up a little over 1,000 of the epidemiological file’s entries—incidence is a better measure of burden than prevalence.

¹ APEC, *Action Plan on Rare Diseases*, 2018.

² Peipei Song *et al.*, “Innovative measures to combat rare diseases in China,” *Intractable & Rare Diseases Research*, 2017.

³ Jiangjiang He *et al.*, “Incidence and prevalence of 121 rare diseases in China: Current status and challenges,” *Intractable & Rare Diseases Research*, 2019.

⁴ Stéphanie Wakap, “Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database,” *European Journal of Human Genetics*, 2019.

Where prevalence figures are available, most rare diseases affect only a small number of people worldwide at any one time. According to Orphanet data, 85% of rare disorders with known prevalence have less than one existing case per million people. Nevertheless, the sheer number of diseases (along with the higher prevalence of more common but still rare conditions) has a noticeable collective impact. Overall, between 3.5% and 5.9% of the world's population have at least one of the Orphanet conditions.⁵ The inclusion of unidentified rare diseases, rare cancers, infectious diseases and poisonings would push this number toward the frequently cited figure of about one in 15 people having a rare disease worldwide.

A study based on medical records in Western Australia found that 2% of the total population were admitted to hospital with a rare disease in 2010. The study notes that the true burden of such conditions is likely higher because data were available for only 467 diseases. In addition, an unknown number of people may not have been hospital in-patients in 2010, instead using outpatient, primary care, or no medical services at all.⁶

Overall, an estimate of around 6% of the Asia-Pacific population affected by a rare disease in any given year, is reasonable.

To put the burden in context, Elizabeth Elliott—professor of Paediatrics and Child Health at the University of Sydney and director of the Australian Paediatric Surveillance Unit (APSU)—estimates that because there are so many rare diseases the overall burden in Australia is similar to that of diabetes or asthma.

The financial cost to health systems, meanwhile, is even higher than the preceding figures suggest. The 2% of Western Australia's population with such conditions in 2010 accounted for 10% of all hospital discharges and 11% of hospital costs.⁷

Spending on rare conditions is rising substantially, in part because of greater health system coverage. In Taiwan, Min-Chieh Tseng—co-founder of the Taiwan Foundation for Rare Diseases—reports that National Health Insurance spending on medical and drug expenses for rare diseases grew from US\$17m in 2005 to US\$196m in 2018.

⁵ Ibid. Pg. 8.

⁶ Caroline Walker *et al.*, "The collective impact of rare diseases in Western Australia," *Genetics in Medicine*, 2017.

⁷ Ibid.

Section II. Overarching challenges in managing rare diseases

Our research indicates that rare disease policies in Asia-Pacific face both general, overarching challenges and a number of large but more specific issues. First, general challenges take the form of workable definitions, quality of care delivery and knowledge among healthcare professionals.

United in diversity: To what extent do rare diseases constitute a coherent category?

Existing rare disease policies implicitly assume that it makes sense to address this group of conditions collectively, but the sheer diversity of these disorders should not be underestimated. As Sonoko Misawa—associate professor at Chiba University’s Graduate School of Medicine—puts it, almost all of these diseases present “completely different symptoms, treatment options and degrees of disability”.

Many are genetic—comprising 72% of the Orphanet database—but other causes exist as well. Cancers make up 11% of the Orphanet disorders, while the condition that helped launch Japanese public health interest in rare diseases in the 1960s, subacute myelo-optic neuropathy (SMON), was traced to overuse of a then over-the-counter diarrhoea medicine. Most conditions (70%) are paediatric onset, but the study from Western Australia found mean and median ages of hospitalisation to be in the 50s for those with rare diseases. While some rare diseases are chronic conditions which can last decades, many others mean infants are unlikely to live beyond the first week of life, or as Richard Vines—chair of the patient group Rare Cancers Australia—comments, “just long enough for their parents’ hearts to break”.

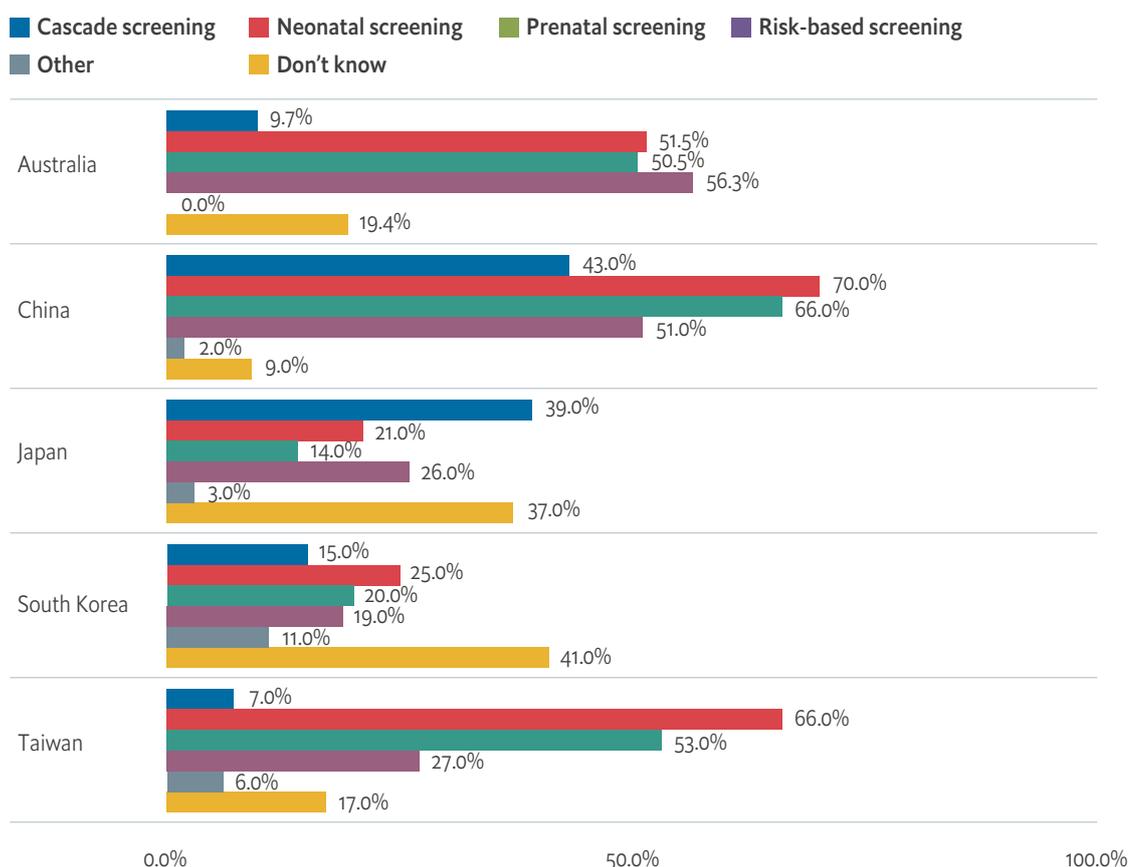
Amid this diversity there are important shared issues faced by those with rare diseases and their loved ones. Dr Elliott explains that “all of these patients and families have common problems: delays in diagnosis; clinicians who may not understand the symptoms; difficulty in accessing treatment; the cost of multi-disciplinary care; the fact that these conditions are chronic and complex; and that they have a huge impact on patients and families financially, socially, and psychologically”. Ritu Jain—president of the Asia-Pacific Alliance of Rare Disease Organisations (APARDO) and a faculty member at the Nanyang Technological University’s School of Humanities—notes that the feeling of being affected by an unusual, poorly-understood disorder can also bring a sense of isolation.

As noted above, rare disease policies are proliferating but no standard template exists. Each country’s efforts have a distinct history, which can affect how officials approach this challenge. Taiwan’s efforts, for example, arose in large part from patient advocacy. Accordingly they support a broader range of patient social and medical needs than many. The flip side seems to be a more restrictive definition of which diseases qualify for support.

According to a survey of clinicians conducted for this study, various forms of genetic testing for rare diseases are used frequently in several Asia-Pacific countries. Japan, however, has lower levels of neonatal screening and a greater tendency to focus on testing the relatives of those diagnosed with such conditions. The latter is called cascade screening. Takeya Adachi of the Japanese Agency for Medical Research and Development (AMED) suggests that this may reflect how SMON was a predominantly adult condition, while in other countries paediatric genetic disorders were a bigger early focus of the rare disease field [see Figure 1].

Figure 1

Survey responses for frequency of rare disease screening techniques used in five Asia-Pacific markets.



The apparent simplicity of the term “rare disease” has proved deceptive and interpretations vary widely. Any plausible definition must grapple with what is rare enough to fall into this group. Our survey respondents agree. When asked which elements should be included in a rare disease policy, 94% thought some indication of prevalence helped define the category—though no consensus existed on the actual prevalence figure. Health policy-makers in our study markets diverge further in setting

numerical boundaries between the common and the rare:

- For Australia, the only national figure comes from its orphan drug regulations which adopted the EU definition of five cases per 10,000 population in 2017. Previously, the regulations set the boundary at fewer than 2,000 total cases across the country—about one-fifth of the permitted prevalence in the EU guidelines.⁸

⁸ Australian Department of Health, *Orphan drug designation eligibility criteria*, 2018; Government of Australia, *Therapeutic Goods Regulations 1990* (updated 1 January 2017), 2017.

- China has no formal definition, although local medical experts generally accept a cut-off of one per 10,000 population for neonatal diseases, and one in 500,000 for others. Any numerical boundary enshrined in policy would be largely moot, since epidemiological data are sparse.⁹
- Since 2015 Japan has had two definitions under its rare and intractable disease policy. Any condition affecting fewer than 50,000 people in the country (roughly 3.9 per 10,000 population) falls into this category. Also included are disorders deemed to be intractable or difficult which affect up to 180,000 people (14.2 per 10,000).¹⁰
- South Korea's Rare Disease Management Act defines these conditions as any affecting fewer than 20,000 people in the country (approximately 3.9 cases per 10,000). As a concession to the pronounced data challenges in this field, it also includes conditions "whose number of carriers is unknown because diagnosis [...] is difficult".¹¹
- Taiwan does not have a number set in regulation or law but authorises its Review Committee for Rare Diseases and Orphan Drugs to set and regularly review the target prevalence for its policies. Since 2000, says Dr Chao-Chun Wu—deputy director-general of the Health Promotion Administration—any disease affecting less than one person per 10,000 population is deemed rare.

The national variations do not reflect disagreements over how to define some objective medical attribute of "rarity". The world's disease burden is more of a continuum than a series of easily-discernible, measurable categories. At one end are a high number of low-prevalence conditions. As prevalence rises, the number of diseases decreases markedly. Even within the rare disease category, the 4.2% most common conditions account for roughly 80% of all patients. The next most common 7% of the remaining disorders account for over 90% of those affected.¹² As Japan's loosening of its prevalence restrictions in 2015 shows, even diseases with a greater number of cases may share the difficulties associated with less common ones.

Prevalence is often an inappropriate measure of burden. Dr Elliott explains that "not all rare diseases have a genetic origin. We are interested in rare accidents, infections, adverse drug reactions as well. The whole concept needs to be extended". Mr Vines, comments that his organisation tends to use figures based on incidence because of the high fatality rate of rare cancers.

Instead, prevalence definitions reflect the necessities of policy administration. Decision-makers must know where and when to apply their resources. As a result, policy goals and resources greatly shape which diseases count as "rare". Mr Tseng, believes this explains Taiwan's more restrictive prevalence limit than Australia's.

⁹ Jiangjiang He *et al.*, "China has officially released its first national list of rare diseases," *Intractable and Rare Diseases Research*, 2018.

¹⁰ Pacific Bridge Medical, "Japan Orphan Drug Update 2017," 2017; Economist Intelligence Unit calculations.

¹¹ Korea Legislation Research Institute. Available at: http://elaw.klri.re.kr/eng_service/lawView.do?hseq=43655&lang=ENG

¹² Stéphanie Wakap, "Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database," *European Journal of Human Genetics*, 2019; Economist Intelligence Unit calculations.

The latter comes from orphan drug regulation, representing relatively little cost for a government. In Taiwan's case, the number is used to help shape how many people will receive assistance, and this "correlates with the budget," Mr Tseng explains.

This link to policy also explains some of the additional factors which go into rare disease definitions. In Taiwan, for example, they need to be severe and difficult to diagnose conditions, presumably because those affected by easy-to-treat illnesses with little impact on quality of life are unlikely to need substantial state assistance. Similarly, Japan's rare disease policy has long included an emphasis on supporting patients and families. Under its rules, *Nan-Byo* conditions (a Japanese portmanteau for rare and intractable disease) not only need to be rare but also long-term and of indeterminable cause.¹³ In China, meanwhile, policymakers look more narrowly at the possible population benefits from existing medical interventions. Its list of rare diseases therefore focuses on relatively common ones for which some treatment is available.¹⁴

The Chinese example shows that prevalence and other criteria are more often guidelines for officials than formal rules. In China, Japan, South Korea, and Taiwan, patients' conditions must be recognised as "rare" by the state if they are to benefit from relevant health and welfare policies. In that sense, whether a condition is "rare" ultimately depends on whether officials say that it is.

The number of disorders recognised as "rare" by governments is much smaller than Orphanet's 6,172: in China it is 121,⁴ Japan 333,⁵ South Korea 927,⁶ and Taiwan 223 or 339.¹⁷ The higher number in South Korea may be attributable to the fact that, unlike Taiwan and Japan, it does not offer extensive social support to patients and has a 10% co-pay for treatment costs.

This does not mean that different national definitions, especially among clinicians and researchers, could not benefit from convergence. Takeya Adachi of Japan's Agency for Medical Research and Development notes that the International Rare Diseases Research Consortium is trying to bring this about.

However, this is a complex undertaking and a broader consensus that covers all fields is unlikely to come about soon. As Mr Tseng explains, "the definition depends on with whom we are communicating, such as reporters, scientists, health system staff, industry, or government officials. Each have different concepts regarding rare disease."

¹³ Mitsuko Ushikubo, "Palliative Care in Japan for Individuals with Amyotrophic Lateral Sclerosis," in Marco Cascella, ed., *Highlights on Several Underestimated Topics in Palliative Care*, 2017.

¹⁴ Jiangjiang He *et al.*, "China has officially released its first national list of rare diseases," *Intractable and Rare Diseases Research*, 2018.

¹⁵ Japan Intractable Diseases Information Centre, web page accessed 15 January 2020.

¹⁶ "Government to subsidize treatment of 100 rare diseases," *The Korea Herald*, 4 December 2018.

¹⁷ For an explanation of the Taiwanese number, see Box 3.

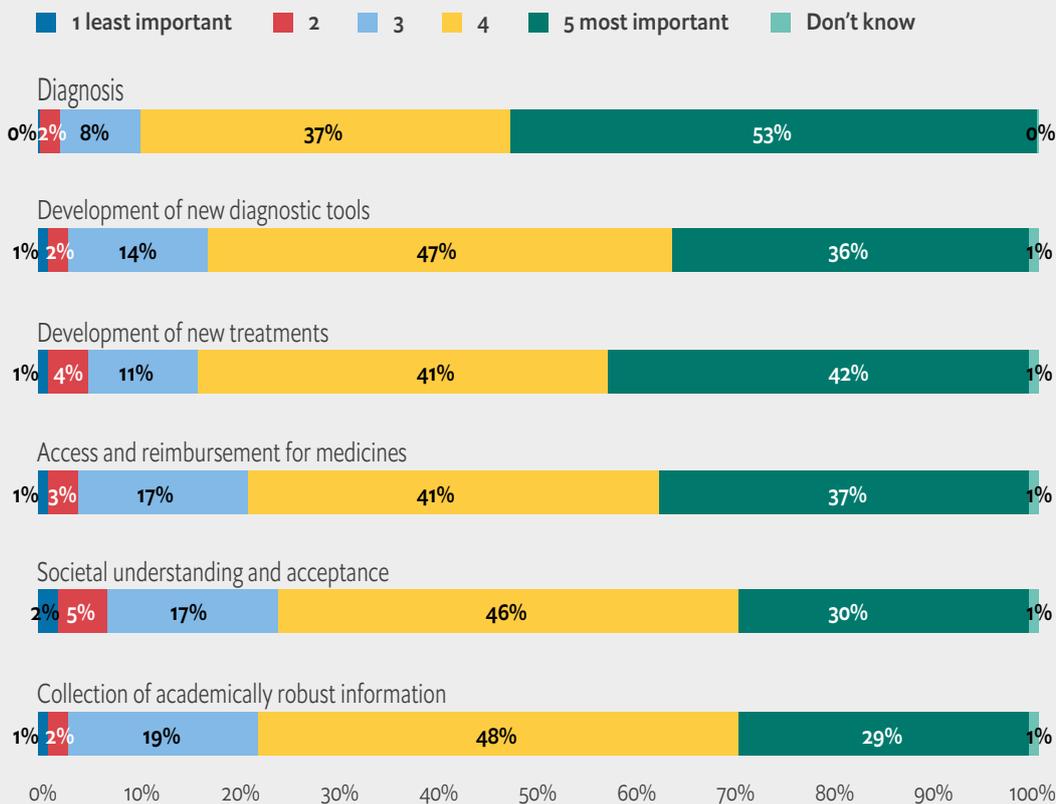
Box 1: Which diseases count?

Common definitions allow for coherent discussion. According to our survey respondents, they also have a vital role in addressing various issues related to rare diseases. On average, those surveyed

consider a unified definition of rare disease as somewhere between “very” and “most” important to facilitate diagnosis, treatment, and data gathering, and even societal understanding of these disorders [Figure 2].

Figure 2

Survey respondents ranking of importance for elements of rare disease definitions



Inconsistent care quality

The most striking finding from our survey is how often care for those with a rare disease falls short. Respondents estimate that on average only around a third (33%) of their patients receive the best evidence-based care. Various factors make such treatment unlikely to be available [Figure 3].

Similarly, on a scale of 1 to 5, respondents ranked how effective their health systems are in addressing different aspects of rare disease diagnosis and management. The average results for speed of diagnosis, initiation of treatment and overall quality of care fell between 3.4 and 3.7. In other words, health care providers are more likely to say that those with rare diseases are receiving adequate, but not excellent, care [Figure 4].

In some cases, even these survey results may present an overoptimistic picture. On average, respondents from China give their health system the highest grades for speed and quality of any in the survey. However, Dong Dong—research assistant professor at the Chinese University of Hong Kong—reports that her own detailed surveys of clinicians in the country suggest that “Chinese doctors’ knowledge about rare diseases is not as good as they think. They are very confident, but there is misunderstanding and incorrect treatment”.

Figure 3

Survey responses reporting average proportion of patients managed with the optimal to sub-optimal care in five Asia-Pacific markets.

- Managed with the best evidence-based care
- Not managed with the best evidence-based care due to lack of clinical practice guidelines
- Not managed with the best evidence-based care due to lack of regulatory approval of medicine
- Not managed with the best evidence-based care due to lack of funding for testing/treatment
- Not managed with the best evidence-based care for other reasons

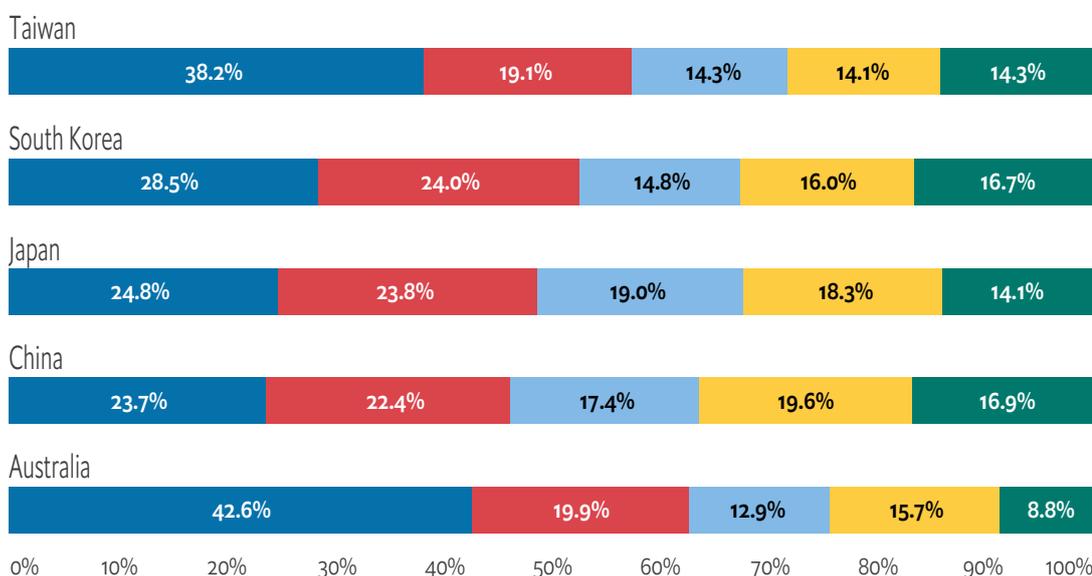


Figure 4

Survey responses showing healthcare practitioners rating of their healthcare system’s efficiency in managing rare diseases.



Only around a third of survey respondents’ patients received the best evidence-based care

Generalisations can obscure as much as they reveal. In Japan, for example, Dr Adachi sees a marked difference between the more common rare diseases and those which are relatively scarce. Patients living with the former tend to benefit from rare disease policies and programmes. They often obtain very good treatment. Those whose conditions are not recognised *Nan-Byo* diseases are more likely to receive only adequate care. Similarly, paediatrician Dr Elliott says that in Australia “some children get excellent care, others get adequate care, and some fall between the cracks. It is partly dependent on where you live. Children in rural and remote settings have

poor access to services and are more likely to present late”.

It also depends on the extent to which health systems are able to address the frequently multi-faceted needs of rare disease patients. “The largest problem is fragmentation of care,” says Mr Vijayendran. “We are all looking at different parts of the equation. Why don’t we approach this from a multi-disciplinary perspective?” Dr Bellgard agrees. He notes that that clinical centres of excellence with multiple experts can provide very good care. He cites as exemplars those dedicated to treating Fabry disease and Motor Neurone disease in Australia. Conversely, if the condition is unrecognised, individual clinicians isolated in general health systems will not do as well.

Limited knowledge and experience

“There is just not enough clinical knowledge of rare disease,” says Dr Bellgard. “That is the root challenge.”

Our survey results bear this out. When asked to rank their colleagues’ knowledge of rare disease on a scale from 1 (very poor) to 5 (very good), respondents expressed only middling confidence. On average, they gave peers a score of just 3.1. Taking out the perhaps over-confident Chinese answers, the average drops to slightly closer to “poor” than to “good” (2.9). Even among specialists, only 28% think that their fellow experts have “good” or “very good” knowledge of this field (4 or 5).



Only 28% of specialist respondents think their fellow experts have sufficient knowledge of rare diseases

Results from other survey queries indicate that this assessment may be well-deserved. For example, 34% of respondents are unaware of whether a unified definition of “rare disease” exists in their health system. Similarly, 35% do not know if a rare disease policy exists, which would presumably affect their understanding of what the health system could offer patients.

Despite the importance of patient groups in helping to support those with a rare disease, 44% of respondents are unaware whether such organisations exist in their jurisdiction. A further 12% incorrectly believe that they do not.



44% of survey respondents are not aware of patient organisations and 12% incorrectly report they don’t exist in their jurisdiction

Failure to know about these groups can have a direct impact on quality of patient care. Dr Gareth Baynam, a clinical geneticist and director of the Undiagnosed Diseases Program in the Genetic Services of Western Australia, notes that “the patient voice, advocacy groups, and those representing the rare disease community are the most effective determinant of change” within health systems.

These survey responses are consistent with our interviewees’ experience. As Dr Jiaan-Der Wang—director of the Centre for Rare Diseases and Haemophilia at Taichung Veterans General Hospital—explains: “Low levels of knowledge about rare disease among medical personnel are common worldwide, not only in the Asia-Pacific region.”

A 2017 survey of Australian paediatricians showed that less than half believed that rare diseases were adequately covered during medical training and 28% felt unprepared to treat such patients.¹⁸ “The bottom line,” says Dr Elliott, whose APSU conducted the research, “is that doctors feel inadequately skilled and want more knowledge and resources”.

¹⁸ Yvonne Zurynski, *et al.*, “Rare disease: A national survey of paediatricians’ experiences and needs,” *BMJ Paediatrics Open*, 2017.

Similarly, in 2018 Ms Dong helped to conduct a survey of several hundred Chinese hospital doctors. These were originally sourced via rare disease patient groups and as a group had much greater medical education levels and years of experience than doctors in the country overall. Nevertheless, Ms Dong found that only 24% of these claimed to have a good knowledge of rare diseases". The patient experience in the country suggests that these findings are no fluke. Yi'ou Wang observes that "doctors who can accurately diagnose and treat rare diseases in China are themselves still relatively rare".

One obvious reason for this limited knowledge among clinicians is, in Dr Misawa's words, "the overwhelmingly few cases encountered in daily practice". Our survey reveals substantial variance in the frequency with which medical personnel see new presentations: 13% see more than one new rare disease case per month, but 14% (including 10% of specialists) report never having seen a rare disease patient in their entire career. Overall, the median rate is one new case per year.



14% of survey respondents—including 10% of specialists—report never having seen a rare disease patient in their entire career

Given the thousands of disorders falling into the rare disease group, a doctor or nurse who encounters the average one case per year may see only a handful with any clinical similarity across an entire career. Nor are these clinicians necessarily going to have experience with the same conditions as their peers.

When asked which rare diseases they had treated, our 503 respondents came up with 305 separate disorders. For 189 of these, just one clinician reported a case. The most often reported conditions among these rare diseases were those affecting the nervous systems (eg amyotrophic lateral sclerosis, multiple sclerosis), eyes or skin (eg albinism) and blood (eg haemophilia).

Finally, as one survey participant told us, knowledge of the disease in question is sometimes of limited relevance: "As a GP, most of my experience in this regard is seeing a patient who is under the care of an appropriate specialist for a rare disease, but for an unrelated reason." However infrequently an individual clinician sees a rare disease, they need to be better-informed if health systems are to more effectively address these conditions as a whole. Dr Baynam explains that "the biggest global barrier to better diagnosis and treatment is the lack of awareness of the possibility of rare disease" when a new case presents.

Making the necessary knowledge available at the right time

How can health systems give busy clinicians relevant information on a specific rare condition when needed? Improved basic education on the general issues around rare disease is a necessary start. Mr Tseng explains that the topic receives insufficient emphasis in formal medical education. Dr Baynam agrees that "the complete lack of a cohesive response in many medical curricula is striking". Several interviewees also mention the potential benefit of making training available within continuing clinical education programmes as a "shortcut"—Dr Misawa's word—to more widespread understanding among medical professionals.

Even so, education and training on rare diseases in general can go only so far. “You have to be realistic,” Dr Bellgard says. “You can’t be a specialist in everything, and it would be almost impossible for even one jurisdiction to have one expert for each of the 7,000 rare diseases.” He notes that the APEC Rare Disease Action Plan therefore encourages governments to audit existing clinical skills across the entire health system before developing referral schemes and other ways to plug knowledge gaps. The latter might well include co-operation with experts and specialist centres based in other jurisdictions.

Several experts also put hope in the potential of information technology to assist. For example, test results within electronic health records could flag up when a given rare disease might be an issue for the patient. Dr Baynam explains that this is “a key opportunity to provide on-the-go education to the clinician that is relevant to the patient at the time”. Similarly, Yukiko Nishimura—founder and president of NPO ASrid (the Advocacy Service for Rare and Intractable Diseases’ Multi-Stakeholders in Japan), a group which acts as an intermediary between patients and other actors in the area of rare disease—argues that “clinicians do not know every rare disease. For conditions where a definitive diagnosis can be derived from, say, image data, it is possible to make early detection and an early definitive diagnosis using information technology”.

Before such technology can be effective, health systems will need to address “the lack of patient data to meaningfully incise

into in order to determine evidence-based approaches,” comments Mr Vijayendran. As a result, on average our respondents rank the gathering of epidemiological data as a “very important” element of any rare disease policy (score of 4 on a scale of 1=least important to 5=most important).

The necessary work is just now beginning. Only within the last few years have specific codes for rare diseases been included within the International Classification of Disease framework, allowing general insurance and health systems to accurately record the basics of diagnosis and treatment for these conditions. Dr Baynam stresses the potential importance of this development. “The single most important thing for sustainable health system interventions is rare disease coding in health data sets. We need to make these patients visible in health systems.”

Ultimately, more widespread use of detailed disease registries—rather than analysis of general insurance and medical records—will need to undergird data-informed tools for clinicians. Work here is also underway: Rare Voices Australia is pushing for an integrated registration strategy;¹⁹ China health authorities are working on a National Rare Diseases Registry System which is projected to cover 50 conditions by 2020;²⁰ and AMED has begun the Rare Disease Data Registry of Japan (RADDAR-J) project which involves encouraging researchers to create individual disease registries (see Box 2)²¹

¹⁹ Paul Lacaze *et al.*, “Rare disease registries: a call to action,” *Internal Medicine Journal*, 2017.

²⁰ Peipei Song *et al.*, “Innovative measures to combat rare diseases in China,” *Intractable & Rare Diseases Research*, 2017.

²¹ Yoshihiko Furusawa *et al.*, “National platform for Rare Diseases Data Registry of Japan,” *Learning Health Systems*, 2019.

Even detailed national registries will often not be enough because of what Dr Adachi describes as the “n=1 problem”. Data analysis cannot say much when based on a single person—or at most a few people—with any given disorder. Greater aggregation of data is an essential next step.

Achieving this will require substantial effort. Dr Bellgard explains that, even setting aside the regulatory and privacy issues of international data sharing, information in health systems is typically generated for a single purpose rather than being amenable to multiple uses. The value of combining clinical notes, patient-reported outcomes, research results and medical insurance data—to name but a few—from any number of countries is huge, especially in a field where good

information is so sorely lacking. Accordingly, “we have to be in the business of building global registries,” Dr Bellgard says.

He and his colleagues recently published a conceptual framework for a rare disease registry and analytics platform which recognises the variety of potential information inputs and provides multiple kinds of analysis, from treatment research and development to clinical decision support.²² This will be a long-term goal. For now, APEC’s Rare Disease Action Plan encourages member economies to come to a consensus on the best way to manage and store patient data so that it can be multipurpose and to develop the technical and legal infrastructure needed to use and share it internationally.²³

Box 2: Efforts to improve diagnosis in South Korea and Japan

South Korea and Japan provide notable examples of undiagnosed disease programmes. Rather than creating traditional, single-location one-stop shops, information technology is used to connect a wide network of expert clinicians and share cutting-edge data tools.

In 2017, the South Korea Ministry of Health and Welfare released a 2017–2021 road map for the diagnosis, treatment and management of rare diseases. This comprises four strategies around building an evidence base, establishing a basis for diagnosis and treatment, expanding diagnosis and treatment support, and strengthening R&D. As a first step, the

Korean Undiagnosed Disease Programme (KUDP) began as a small pilot project with under 100 patients in 2017. An expert, multi-disciplinary consortium of paediatric and adult medical specialists (based at a total of six institutions) collectively considered each new case. Any patients for whom referees had provided insufficient information had to be dropped. The others were divided into three categories: those who were probably undiagnosed due to a lack of clinical awareness on the part of their original physicians; those who were diagnosed but unconfirmed because of genetic abnormalities; and those with an unknown condition. Overall, the consortium—collaborating with international experts—

²² Matthew Bellgard *et al.*, “RD-RAP: beyond rare disease patient registries, devising a comprehensive data and analytic framework,” *Orphanet Journal of Rare Diseases*, 2019.

²³ APEC, Action Plan on Rare Diseases, 2018.

determined definitive diagnoses for 39% of all tested individuals. The pilot team even discovered one new disorder.²⁴

The government is expanding the programme as part of a wider improvement in rare disease care. The number of centres treating these conditions was to increase from the four in 2018 to 12 by March 2020. Younjhin Ahn of the Division of Rare Diseases at the Korean National Institute of Health Centre for Biomedical Sciences, reports that the KUDP will seek out referrals of difficult cases from these centres.

They will also continue “creating and promoting programmes that support diagnosis, so that patients do not get missed in the healthcare system”. The goal is to be able to diagnose any known disease within one year.

The Japanese Initiative on Rare and Undiagnosed Diseases (IRUD), established in 2015, has reached a broader scale. Patients at primary care clinics who go undiagnosed for six months, and whose conditions seem to be genetic, are referred to one of more than 400 IRUD partner hospitals. There, multi-disciplinary IRUD diagnosis committees review each case.

Any successful diagnosis is then communicated back to the referring primary care clinic where, ideally, the patient receives genetic counselling and, if available, treatment.²⁵ As of mid-2018, IRUD has helped confirm more than 1,000 diagnoses, with a success rate of 37%. It has also identified 18 new diseases.²⁵

Although a higher frequency of diagnosis is clearly desirable, the estimated number of undiagnosed cases of rare disease in Japan is just over 37,000.²⁶ Thus, even this incomplete progress as the programme finds its feet has made a small dent in the overall problem.

The next phase of the project, IRUD Beyond, aims to improve the diagnosis rate, increase international data sharing on rare disease and use the genetic insights from the diagnosis of particular conditions to inform research on treatments. So far, nine candidates have been identified for further study.

Dr Adachi, who has been closely involved with IRUD, notes two particular lessons from the initiative. One is the need to find a way to “promote and incentivise collaboration,” in particular data sharing by patients and small hospitals. As a first step, IRUD has introduced what it calls “micro-attribution”, and has created the IRUD Exchange database which makes visible where data on its systems has come from.

The other is that, while acknowledging the individuals behind data sources, these kinds of programmes show how important it is to think big. “Global data sharing is essential to improved diagnosis,” Dr Adachi explains. Both IRUD and KUDP work with researchers overseas when encountering low-frequency or unrecognised disorders.

Progress is simply impossible unless information from every case can be aggregated and examined together.

²⁴ Soo Yeon Kim *et al.*, “The Korean undiagnosed diseases program: lessons from a one-year pilot project,” *Orphanet Journal of Rare Diseases*, 2019

²⁵ “Meeting to fast track progress on rare disease research,” *Nanbyo Research from Japan* (web site), 15 March 2019.

²⁶ Takeya Adachi *et al.*, “Survey on patients with undiagnosed diseases in Japan,” *Orphanet Journal of Rare Diseases*, 2018.

Section III. Prioritising the response in Asia-Pacific

The difficulties in providing those living with rare diseases the care and services they need are numerous. In our study, medical professionals were asked about how frequently 18 different issues posed problems in this field. The scale used was from 1 (meaning “never a difficulty”) to 5 (“always a challenge”). For every issue covered, the average response was well over 3, indicating that they created difficulties more often than not [Figure 5].



Survey respondents found all 18 elements of care covered in our survey to be difficulties more often than not, and the biggest problem was diagnosis.

Our survey responses and further research indicate that three main challenges must be prioritised.

Difficulties in diagnosis

Among the 18 issues covered in our survey, respondents highlighted something fundamental as the greatest challenge: obtaining a correct diagnosis. The problem is not just identifying the right condition, but doing so with reasonable speed. Respondents also believe this issue requires immediate attention: they ranked diagnosis of conditions, combined with their management, as the top priorities for national rare disease policies to address.

The concerns in this area should come as no surprise. Data from the US put the average time between the onset of symptoms and accurate diagnosis of a rare disease at 4.8 years.²⁷ The situation in Asia-Pacific is no better. In Australia, data from a survey of adults with rare diseases published in 2016 indicate that their average time to diagnosis was 4.7 years, with an average of five different doctors consulted during that time. Just as important as these averages is the variety of experience. Nearly half of patients had a diagnosis within a year, but for 10% it took more than 20 years.²⁸ Ms Dong reports a similar range from her surveys of Chinese rare disease patients.

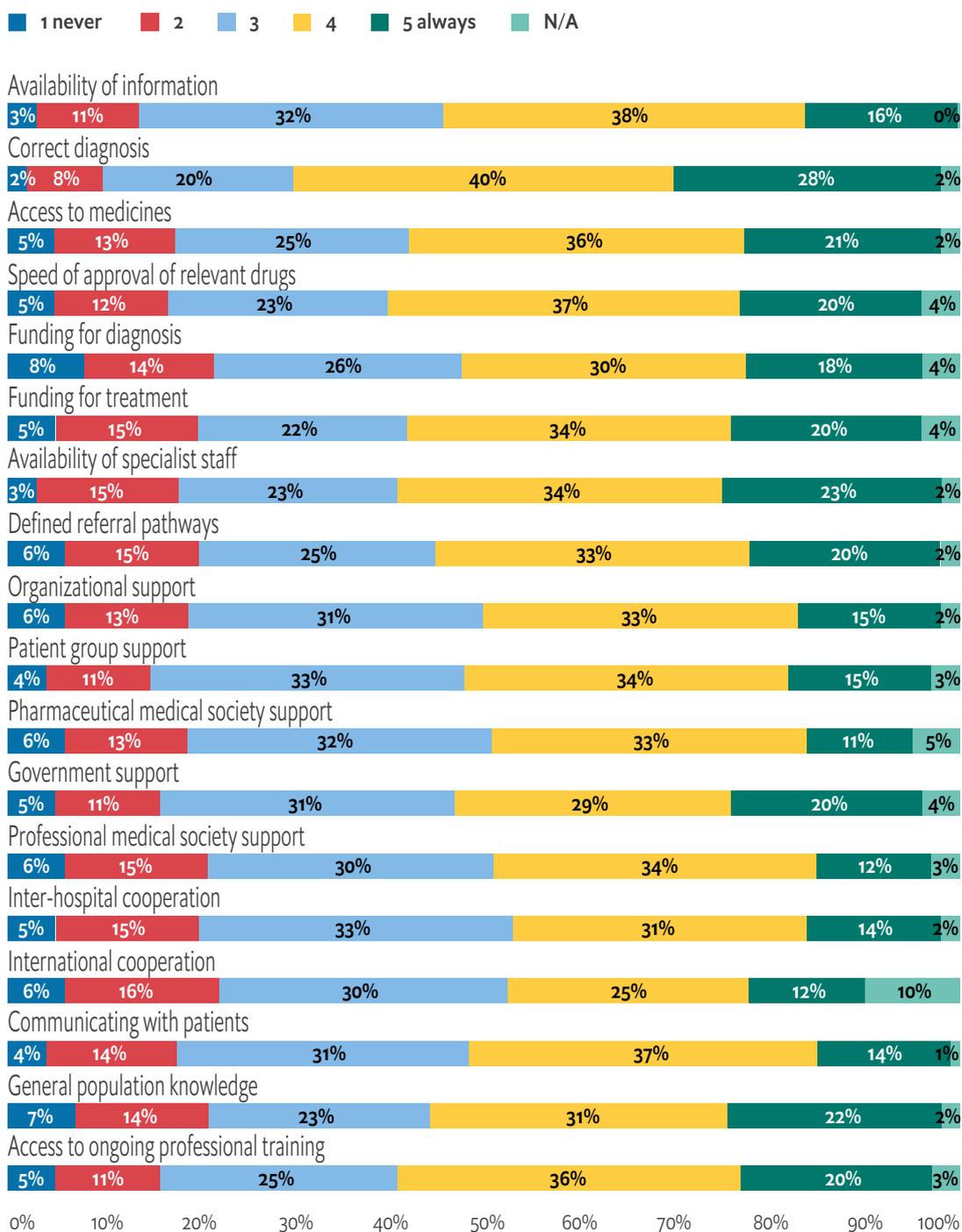
The delays have clear disease management implications, notes Dr Baynam. “Diagnosis is the portal to the best medical care and where we currently have the greatest opportunity to transform patients’ lives at scale.” The damage arising from delay and error often goes beyond the purely medical. Mr Vijayendran says that, in many cases, for patients and families “the big questions are ‘what is happening and why?’ These are deeper, philosophical and psycho-social issues that are deeply personal for each patient and their family members. It can be difficult to begin coping, adjusting and moving forward until a proper diagnosis allows people to stop asking ‘why’ in this way.”

²⁷ Patti Engel *et al.*, “Physician and Patient Perceptions Regarding Physician Training in Rare Diseases,” *Journal of Rare Disorders*, 2013.

²⁸ Economist Intelligence Unit calculations based on Caron Molster *et al.*, “Survey of healthcare experiences of Australian adults living with rare diseases,” *Orphanet Journal of Rare Diseases*, 2016.

Figure 5

Survey responses reporting frequency of difficulty experienced in 18 areas of providing rare disease care.



An obvious barrier to effectiveness in this area is that no reliable test exists to identify many of the more than 6,000 known rare diseases in the world. That said, Dr Baynam estimates that existing tools could still allow the accurate diagnosis for about half of those living with such disorders in Western Australia, the region he knows best. “Improvements are certainly needed for the other half, but the biggest challenge today is getting those who are diagnosable tested. Currently, the road to doing so is a rocky one, or many times has not even yet been made.” Both South Korea and Japan have taken the first steps in that direction, in particular for the large number of rare genetic conditions. Their experience already shows that much can be achieved through such an approach [see Box 3].

The broader financial burden

The costs arising from living with a rare disease, or caring for someone who does, are substantial. Our survey respondents put funding of diagnosis and of treatment as the second and third most important elements of national rare disease policies. More striking, when we asked respondents to name the one action that would most improve the lives of those affected by rare diseases in their country or territory, 47% mentioned something related—either directly or indirectly—to financial support. That was by far the most common theme.



47% of survey respondents cited improving financial support as the single action that could most improve the lives of those living with rare diseases

The specific financial challenges often vary by country. Yi’ou Wang explains that, whatever the hopes that medical insurance may soon cover the health costs of rare disorders, currently “Chinese patients do have a heavy financial burden, with the vast majority of rare diseases not covered by medical insurance except by some local policies.” Ms Dong adds that medication and treatment are only part of the broader economic challenge for Chinese patients. They “often need to travel a long way to get diagnosis and treatment,” she explains, which some just cannot afford. She notes that several patients dropped out of a programme that promised to provide a new medicine for a specific rare disease at no charge. To stay in the programme, patients had to go to one of the seven designated hospitals in five cities in-person to pick up the drugs, three times a year, in addition to a mandatory annual examination. The cost of these trips alone put the scheme beyond the reach of some.

In more economically developed countries, health systems typically pay for effective medication—although not for every condition. South Korea, Taiwan, and Japan have programmes that cover these costs for a set list of rare diseases. Each has also been expanding the number of specific conditions covered, and Taiwan allows doctors to apply for new ones to be added. Nevertheless, it is possible to fall through the cracks. Dr Misawa explains that, although the Japanese list grew significantly in 2015, “due to limited budgets, patients with mild conditions have been excluded from the programme, subsidies for medical expenses have been reduced, and some of the responsibility for medical expenses has been transferred from the national government to local authorities. In addition, there is still a feeling of unfairness among patients whose diseases are not yet covered.”

Australia does not have a specific list of rare diseases for which it supports treatment but has a Life Saving Drugs Programme. This currently funds 16 expensive medicines that are demonstrated to improve survival for 10 very rare, life-threatening conditions, but are not subsidised through regular channels. Non-medical costs can also be substantial. Dr Elliott reports that the parents of all rare disease paediatric cases report huge out-of-pocket expenses. “Things like time lost from work caring for kids, appliances that children might need, some of which are covered by government but others not. Many patients require time in hospital and travel to different specialist clinics which are not co-ordinated, necessitating multiple trips.”

Dr Elliott adds that various initiatives exist which can help. A new Australian National Disability Insurance Scheme allows doctors to support applications for funding of various services, including respite care and special education. Similarly, the increasing use of tele-medicine should reduce the dislocation and cost of travel, especially for those living in rural and remote areas. Meanwhile, in partnership with the Korean Organisation for Rare Diseases, the Korean Ministry of Health and Welfare provides free accommodation to certain rare disease patients who need to travel to Seoul for expert medical care.

Making progress here is more than good patient support, believes Mr Tseng. It is a moral imperative. “Rare disease is a public, rather than an individual, issue. The occurrence of a rare disease is a random error which could have happened with each birth. Without government involvement or assistance, the large social and medical costs are unpredictable, and the supply-demand market model will be useless in meeting them.” Taiwan’s provision for those living with rare diseases provides an interesting example of efforts to meet this need [see Box 3].

Looking at the person beyond the disease

When asked about how well their territory does on different kinds of provision for those living with rare disease, on average respondents said that they did worst at supporting quality of life, autonomy and rights (3.4 on a scale of 1 to 5).



Supporting quality of life, autonomy and rights was the weakest aspect of care provision according to survey respondents

Quality-of-life related services, including social care, education and employment, are an integral part of the support that many living with rare disorders need. Indeed, 94% of rare conditions have no approved medical treatment.²⁹ Non-medical services are therefore of more immediate use than potential future treatments which may never exist.

Rare disease policies “can never be complete without a holistic acknowledgement of condition-related challenges,” Ms Jain explains. “Systems may be able to deliver healthcare, but unless patients are able to access services that facilitate mobility, education, employment, and social integration, those health policies will be incomplete. For example, if you give rare disease patients healthcare but no access to tailored transportation, those patients are still imprisoned.” Dr Baynam agrees on the magnitude of this issue. “If you think about health, education, disability, employment: any response needs to touch on those in a co-ordinated way.”

²⁹ APEC, *Action Plan on Rare Diseases*, 2018.

Where social assistance is lacking, the problems for those living with a rare disease can be extensive. They also have the potential to overlap with and further complicate the financial issues discussed above. In China, for example, a 2016 survey found that over 90% of those with a rare disease could not make enough money to cover their cost of living. They also had constrained lifestyles: more than 70% socialised with family or friends just a few times per year at most.³⁰ As Ms Dong says, “it is relatively easy to solve the medical burden, but disease-related non-medical expenses and barriers to education and employment have largely been ignored”.

Australia fares better than China but still falls short. In a recent survey, 82% of those with rare diseases reported having non-medical care needs arising from disability. Of these, 70% said that they did not have those

needs fully met under the country’s National Disability Insurance Scheme.³¹

In seeking to address the broader requirements of people living with rare conditions, Mr Vijayendran highlights “the absence of credible Asia-centric research and intelligence on the psychosocial needs of patients challenged by rare diseases, especially Asian data. A good starting point would be data aggregation anonymised patient registries with sufficient confidentiality and data privacy safeguards. We should not just stop there however, but go further into a deeper understanding of patient narratives.”

Even in the absence of extensive data, some positive steps are clearly possible, and these need not be isolated initiatives. Taiwan shows just how comprehensive they can be [see Box 3].

Box 3: Taiwan’s comprehensive approach

In the rare disease field, Gregory Vijayendran—chair of Rainbow Across Borders, an Asia-Pacific Rare disease patient umbrella group—observes that “Taiwan stands out; its orphan drug legislation is really quite gutsy”. The foundation of Taiwan’s approach to rare disease care is its *Rare Disease and Orphan Drugs Act*, passed in 2000, though this is not so much a comprehensive law in itself. Instead, says Chao-Chun Wu, deputy director-general of Taiwan’s Health Promotion Administration, it sets out the “legal protections to the basic healthcare

rights of rare disease patients”. Ten further laws amplify and put those protections into practice. Min-Chieh Tseng, co-founder of the Taiwan Foundation for Rare Diseases, adds that a particularly useful aspect of the act is its “focus on patients’ privileges rather than simply orphan drug development”.

Taiwan’s policies certainly do not ignore the medical side of the issue. To begin with, they seek to give health systems the tools to care for those living with rare diseases in multiple ways.

³⁰ Dong Dong and Yiu Wang, “Challenges of rare diseases in China,” *Lancet*, 2016.

³¹ The McKell Institute, *Disability & Rare Disease: Towards Person Centred Care for Australians with Rare Diseases*, 2019.

To cite a few examples: relevant medical school courses, seek to include the topic, as do ongoing professional education programmes; the government has approved 13 genetic and rare disease genetic testing facilities and 14 genetic consultation centres; and regulations have streamlined the approval and importation of orphan drugs, including by exempting the need for further testing of medications approved by any of the top ten pharmaceutical markets.

Under Taiwan's universal National Health Insurance (NHI), recognised rare diseases are collectively categorised as catastrophic conditions. This means that co-payments are not needed for treatments normally covered by the NHI. Certain interventions not usually paid for by NHI—such as domestic diagnostic testing, home medical equipment rental, and emergency medication—are fully covered for low- and middle-income individuals. Those with higher incomes have only a 20% co-pay.

Tests which need to occur in foreign countries have the same kind of coverage if approved by the Rare Diseases Board, says Dr Wu.

Finally, meeting the social needs of those living with rare diseases has long been a Taiwanese policy goal. Mr Tseng reports that, those with such disorders have been eligible to be registered as disabled since 2001. This status opens up access to certain subsidy and pension benefits, and employment rights.

Recently, the government decided that generic disability status was insufficient for the diverse needs of those living with rare conditions. In December 2017, it introduced the Rare Diseases and Rare Genetic Disorders Care and Services Plan, and Long-Term Care Plan to provide individualised psycho-social support and assistance for education.

But no system is perfect. Mr Tseng, for example, reports that multi-disciplinary care is impeded by the spread of relevant experts across hospital departments. While doctors who find a patient with an unregistered rare disease are able to apply for its inclusion, this is not straightforward. Dr Jian-Der Wang, Director of the Centre for Rare Diseases and Haemophilia at Taichung Veterans General Hospital, reports that “the application process is complicated and time-consuming. Most physicians give up unless they receive outside support”.

A final issue is that Taiwan's range of benefits apply only to those living with an officially recognised rare disease. The government's list currently has just 223 conditions. Dr Wu points out that because conditions are recognised by symptoms rather than genetic markers, various list entries include several conditions treated as distinct by Orphanet. In total, Taiwanese policy covers 339 separate ICD-10 codes. For those not on the list, in Dr Wang's opinion, the system still seems unfair despite government consultation with relevant stakeholders, including patients, on how to allocate the limited funds.

Conclusions: Raising the profile of rare diseases in Asia-Pacific

Rare diseases are increasingly recognised as a substantial challenge facing Asia-Pacific health systems. Governments across the region are initiating or strengthening policy initiatives and expanding what these policies cover. In doing so, they are addressing an often overwhelming challenge—sometimes a largely unified problem, sometimes one with anywhere from 6,000 to 7,000 individual faces. A comprehensive response to this disease burden is complex and multi-faceted, yet essential.

Our survey and research found a range of rare disease issues for health systems in Asia-Pacific:

- Although examples of high-quality, integrated, patient-centred practice exist, too often care is adequate rather than excellent.
- The necessary knowledge to treat rare diseases effectively is frequently lacking.
- Problems arise at almost every step of the medical side of rare disease care, with diagnosis presenting particular difficulties.
- The integrated social and financial care generally needed by those affected by rare disorders remains more aspiration than reality.

These difficulties are real but should not obscure the potential impact of continued effort in this field, Dr Baynam notes. “As well

as challenges there are huge opportunities. The scale of these for sustainable, high value care of rare diseases remains untapped.”

Important progress is already being made:

- Different countries are starting to gather the data for the information systems and registries that can support both the development of treatment and clinical decision support.
- APEC is looking for ways to ensure this is used to the greatest effect. Programmes for undiagnosed rare diseases in Korea and Japan are currently able to help a third of patients who were previously likely to wait for years before receiving a diagnosis.
- Taiwan sets a precedent by demonstrating what a coherent policy that integrates the medical, financial, and social needs of rare disease patients can look like.

Building on these initiatives is a necessity rather than a choice. As Dr Ahn says of Korea, policy changes and research advances mean that “patients have increased their interest and the voice of social demands is growing”. They will expect the same kind of patient-centred, integrated care that has become the goal for non-communicable diseases of all kinds. Achieving this will provide invaluable lessons for all care across the board. As Dr Bellgard explains, “if we can address rare disease patient needs, we will have a better health system”.

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