

Initiative on Rare and Undiagnosed Diseases (IRUD) Rare Disease Consortium Japan (RDCJ) Japan Pharmaceutical Manufacturers Association (JPMA)







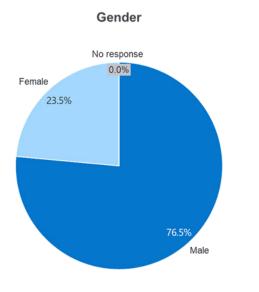
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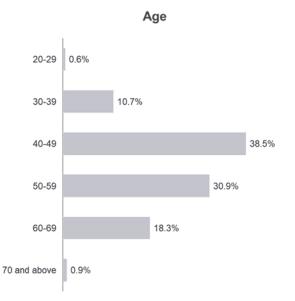
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Data section (quantitative and qualitative survey results)

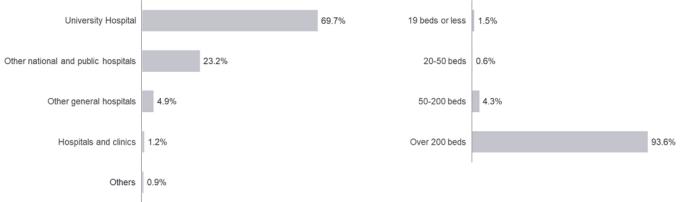
3. Survey methodology overview: Respondent demographics



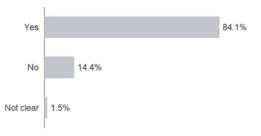


Type of facility

Number of hospital beds at affiliated facilities

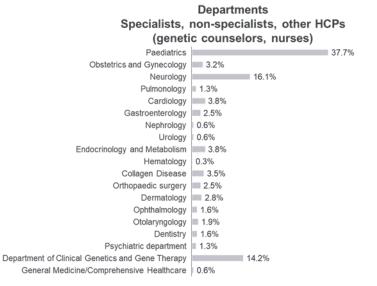


Availability of specialized staff at affiliated facilities



Years of experience in rare disease treatment for support specialists, non-specialists, and other HCPs (genetic counselors and nurses)





Region/area of affiliated facility

9.2%

11.6%

11.9%

12.2%

12.8%

22.9%

19.3%

Hokkaido and Tohoku

Chubu/Hokuriku

Chugoku and Shikoku

Kansai

Kyushu

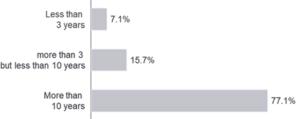
Northern Kanto and Koshinetsu

Tokyo Metropolitan Area/South Kanto

Disease area (Clinical researcher - basic and applied, clinical researcher development)

	development)	
Paediatric disease		30.0%
Gynecologic disease	2.9%	Less
Neuromuscular disease		27.1%
Respiratory disease	0.0%	
Circulatory disease	8.6%	more th but less than 10
Digestive system disease	1.4%	but less than To
Kidney disease	2.9%	
Urologic disease	0.0%	More 10
Endocrine and metabolic disease	4.3%	10
Hematologic disease	0.0%	
Allergy and rheumatic disease	4.3%	
Immunodeficiency disease	5.7%	
Skin disease	2.9%	
Ophthalmological disease	1.4%	
Otorhinolaryngological disease	0.0%	
Dental disease	1.4%	
Mental disease	0.0%	
All other hereditary disease	7.1%	

Years of experience in rare disease R&D (Clinical researcher - basic and applied, clinical researcher - development)





Major rare diseases involved in the past year (disease name and number of respondents) *These

results are based on the names of diseases reported by healthcare professionals

	Number of			Number of respondents		
# Disease name	[people]	#	Disease name	[people]	#	Disease name
1 Amyotrophic lateral sclero 2 Spinocerebellar degenera			Aarskog-Scott syndrome Aicardi-Goutiéres syndrome			CALJA Dysbacteriosis CASK
2 Spinocerebellar degenera	1011 22	102	Alcaldi-Goulieles syndrome		202	Dysbacteriosis CASK
3 Noonan syndrome	18		ATRX Syndrome			CHDED
4 Muscular dystrophies 5 Marfan's syndrome	18 15	104 105	CLIFFORD syndrome (NALCN) Fanconi syndrome			CMT1A Craniolenticulosutural dysplasia
					200	
 Spinal muscular atrophy Fabry's disease 	15 14		HBOC HNRNP disease			DM1 FG syndrome
B Duchenne muscular dystro			IgG4-related disease			FLNA-associated periventricular nodular heterotopia
mitochondrial disease	13	109	Marinesco-Sjogren syndrome (SIL1)	2 2	209	Floating Harbor syndrome
 achondroplastic dwarfism Hypophosphatasia 	<u>13</u> 13		MEN1 MSA			Good syndrome Gorlin syndrome
1 Hypophosphatasia 2 Sotos syndrome	13		Schaaf-Yang syndrome			GPI anchor deficiency
3 Ehlers-Danlos syndrome	12	113	Systemic scleroderma	2 2	213	GRIN1 Gene-Related Disorders
4 Kabuki Syndrome	12 12		Weaver syndrome			GSDIa GSDIb
5 Rett syndrome 6 Parkinson's disease	11		X-linked hypophosphatemic rickets Usher syndrome			Hb hammersmith
7 Familial Mediterranean Fe	ver 11		Imprinting Diseases	2 2	217	HDLS
8 Neurofibromatosis	11	118	Galactosalidosis			HLRCC HNRNPK disorder
9 Osler disease 0 Coffin-Siris syndrome	10 9	119	Klippel-Trenonnay-Weber syndrome Crohn's disease			HTLV-1 associated myelopathy
1 Tuberous sclerosis	9	121	Cockayne syndrome	2 2	221	HTRA1-associated cerebral small vessel disease
2 Osteogenesis imperfecta	9	122				hypomyelinating leukodystrophy-24 (HLD24)
3 Mucopolysaccharidosis ty 4 Short limbs	pe 2 9 9	123 124	Joubert syndrome Sturge-Weber syndrome			IgA vasuculitis Intellectual disability-facial dysmorphism syndrome
5 CHARGE syndrome	8	125	Valde-Biedl's syndrome	2 2	225	Jubert syndrome
6 Williams Syndrome	8	126	Brugada syndrome			KID syndrome
7 Myasthenia gravis	7 7	127	Beckwith-Wiedemann syndrome			KMS
 8 Hypertrophic cardiomyop 9 22q11.2 deletion syndrom 	athy 7 e 6	128 129	Porphyria Myopathy		228 229	L1 syndrome LRBA deficiency
0 Prader-Willi syndrome	6	130	Mitochondrial encephalomyopathy	2 2	230	LZTR1-related disorder
1 Huntington's disease	6	131				Malan syndrome MAPK8IP3-related neurodevelopmental disorders
2 Mucopolysaccharidoses 3 Multiple system atrophy	6		Lipoid adrenal hyperplasia Label's hereditary optic neuropathy			MAPK8IP3-related neurodevelopmental disorders MBD5 gene duplication
4 Dravet syndrome	5	134	Loeys-Dietz syndrome	2 2	234	MCAD deficiency
5 MELAS	5	135		2 2	235	MCT8 Disorders
6 Alport's syndrome 7 Citrin deficiency	5	136 137	Hereditary neuropathy Hereditary deafness			MECOM-related diseases MED13L
8 Epileptic encephalopathy	5		Familial hemophagocytic syndrome			Megalencephaly-Polydactyly syndrome
9 Spinal and bulbar muscula	r atrophy 5	120	Oculocutaneous albinism	2 2	239	Microcephaly, seizures, and developmental delay(PNKI
 Spinal and bulbar muscula Xeroderma pigmentosum 	r atropny 5	139	Facioscapulohumeral muscular dystrophy			gene) MODY (Familial Onset Diabetes of the Young)
1 Multiple sclerosis	5	141	Pseudoparathyroidism	2 2	241	MOG antibody-associated neuropathy
2 Pulmonary arterial hyperte	nsion 5		Ankylosing spondylitis			Myhre syndrome
 Epidermolysis bullosa Fukuyama type congenita 	5 muscular dystrophy 5	143 144				NBIA(BPAN) NCL
5 Von Hippel-Lindau diseas	9 5	145	Restrictive cardiomyopathy	2 2	245	NF1
6 cardio-facio-cutaneous sy	ndrome 4	146	Left ventricular densification disorder	2 2		NLRC4 Defects
7 Hereditary transthyretin (A 8 MEN	TTRv) amyloidosis 4 4	147 148				NMDAR encephalitis OZEMA (Oocyte-zygote-embryo maturation arrest)
9 OTC deficiency	4	140	Fatty acid metabolism disorders	2 2	249	PALLISTER-KILLIAN SYNDROME
0 Rubinstein-Taybi syndron	e4	150	Neuromyelitis optica spectrum disorder	2 2	250	Phelan-McDermid syndrome
1 Wilson's disease 2 XLH	4 4	151 152	Autoimmune hepatitis Severe combined immunodeficiency			PIC3CA Pitt-Hopkins syndrome
 Angelman Syndrome Cryopyrin-associated per 	dic syndrome 4		Palmoplantar keratoderma			PKU
4 Cryopyrin-associated per 5 Epilepsy	bdic syndrome 4	154 155	Cardiac amyloidosis Progressive familial intrahepatic bile stagnation			PLCG2 Disorders MCSZ due to PNKP gene mutation
6 Nephronophthisis	4	156	Nephrogenic diabetes insipidus	2 2	256	Potocki-Lupski syndrome
7 Paraganglioma	4		Neuropsychiatric retardation			PROD3 Genetic Disorders
8 Rett's syndrome 9 Dilated cardiomyopathy	4 4		acromegaly Congenital diaphragmatic hernia			PSP Long QT syndrome
0 Primary immunodeficienc	disease 4	160	Congenital hypopituitarism	2 2	260	Rasopathy
 Progressive supranuclear 	palsy 4		Congenital ichthyosis	2 2	261	RhoBTB2-associated neurodevelopmental disorders
 sex differentiation disorde Congenital malformation 	r 4 yndrome 4	162 163	Congenital myasthenia Congenital hyperinsulinemia	2 2	262	Ritscher-Schinzel syndrome ROHHAD SYNDROME
4 Congenital disorder of gly	cosylation 4	163	Congenital adrenal hypoplasia			RORAT deficiency
5 Congenital myopathy	4	165	Anterior segment ocular dysgenesis			Russell-Silver syndrome (maternal UPD7)
6 Corticobasal degeneratio 7 Glucogon storage disease		166	Frontotemporal dementia			SAVI
7 Glycogen storage disease 8 Inclusion body myositis	4	167 168	Idiopathic interstitial pneumonia Spina bifida			SCA6 SCA8
 Baraitser-Winter syndrom FGF23-related hypophosy 		169 170	Adrenocortical carcinoma Chronic inflammatory demyelinating polyneuropath			SCN8A-Related Developmental and Epileptic Encephal SENDA/BPAN
1 MECP2 Duplication Synd	ome 3	171	Chronic granulomatosis	2 2	271	SETD5 Gene Disorders
2 Pompe's disease 3 VEXAS syndrome	3		Anhidrotic ectodermal dysplasia Retinal pigment degeneration			SHOX Disorders Shwartz Jampel Syndrome
3 VEXAS syndrome 4 WDR1 Deficiency	3	173	Disorders of organic acid metabolism			small vessel deisease with or without ocular anomalies
5 Down Syndrome	3	175	Gliform droplet corneal dystrophy	2 2	275	SPG80
6 Phenylketonuria	3	176	Trisomy 13 syndrome Chromosome 15 tetrasomy		276	Shprintzen-Goldberg syndrome Stickler syndrome
7 Prion disease 8 Bloom Syndrome	3	177 178	Chromosome 15 tetrasomy Chromosome 15 marker gene			Stickler syndrome TAFRO Castleman disease
9 Propionic acidemia	3	179	17q12 demented syndrome	1 2	279	TAFRO SYNDROME
) Moyamoya disease	3	180				Takenouchi-Kosaki syndrome
1 Lysosomal storage disea			22Q11.3 Deficit Dementia Syndrome		281	Temple syndrome
 Rosmund-Thomson synd Hereditary amyloid polyne 			2q17 Minimal Deficiency Syndrome Type 2 collagen disorder			VCTERL Union Ververi-Brady syndrome
4 Hereditary dystonia	3	184	3Q21 Microdeletion Syndrome	1 3	284	Vici syndrome
5 Primary sclerosing cholar	gitis 3	185	3q29 is demented syndrome	1 2	285	Walfram syndrome
 Autoinflammatory syndron Hereditary diffuse leukoer 		186	4p deletion syndrome	1 :	286	WDR45 Abnormality (BPAN)
7 spheroid	3		Partial deletion of chromosome 4 long arm			Wiedemann-Steiner syndrome
8 Vertebral amorphosis	3	188	5P-Syndrome			Xia Gibbs syndrome
 Congenital under-loss of 0 Nephrotic syndrome 	SPI 3 3	189 190	Trisomy mosaic 9 A20 Haploinsufficiency			X-linked syndromic neurodevelopmental disorders X-linked severe complex immunodeficiency
1 Chromosomal abnormalit			ADNP-related disorders (ADNP gene abnormalities			ZTTK syndrome
 Congenital cerebral hypor Craniofacial dysostosis 	nyelination 3 3		ADTKD Alagille syndrome			Amino acid metabolism disorders Argininosuccinic aciduria
4 cystic fibrosis	3		AMeDS			West Syndrome
5 Pneumocyliosis	3	195	ARID1B Related Disorders	1 3	295	Werner syndrome
6 Adrenoleukodystrophy	deficiency 2		ATR-X Bainbridge Report sundrome	1 2	296	Ulrich-type congenital muscular dystrophy
7 common variable immuno 8 Aniridia	deficiency 3 3	197 198				AIDS-related complex Albright's syndrome
 Systemic lupus erythemat 	osus 3	199	BPAN	1 3	299	Occipital Horn Syndrome
0 Trisomy 18 syndrome	2		CACNA1A related disorder			Ornithine transcarbamylase deficiency disease

#	Disease name [people]
301	Carney complex 1
302	CADASIL 1
	catecholamine-induced polymorphic ventricular
303	tachycardia 1
304	Galactosemia type IV 1 Carbamyl phosphate synthase 1 deficiency 1
305	Carbamyl phosphate synthase 1 deficiency 1
306	Kallmann syndrome 1
307	Galloway-Mowat syndrome 1
308	Cushing's disease 1
309	Kriefstra syndrome 1 Klippel-Feil syndrome 1
311	Glucose transporter type 1 deficiency 1
312	
313	Cretinism 1
314 315	Creutzfeldt-Jakob disease 1
316	Gaucher's disease 1 Gorin syndrome 1
317	Costello's syndrome 1
318	sarcoidosis 1
319	Sialidosis 1
320 321	Sjogren's syndrome 1 Cystine storage disease 1
322	Cystinuria 1
323	Dystonia 1
324	Dystrophinopathy 1
205	Citure Durandi aundre en
325	Silver Russell syndrome 1
326	sudanophilic leukodystrophy 1
327	Stevens-Johnson syndrome 1
328	Swyer syndrome 1
329	Other autosomal abnormalities 1
330 331	Turner's syndrome 1 Thanatoholic osteodysplasia 1
332	Treacher Collins syndrome 1
333	Niemann-Pick disease type C 1
334	Nemaline myopathy 1
335	Barth's syndrome 1 Birt-Hogg-Dube syndrome 1
336 337	Birt-Hogg-Dube syndrome 1 Byrne syndrome 1
338	Hutchinson-Gilford syndrome 1
339	Paramyotonia 1
340 341	Hyaline fibroma syndrome 1 Pitt-Hopkins syndrome 1
	Hirschsprung's disease related diseases 1
	Fanconi's anemia 1
	Blount's disease 1
	Freeman-Sheldon syndrome 1
	Prolactinoma 1 Behcet's disease 1
	Bethlem myopathy 1
349	Becker muscular dystrophy 1
350	Homocystinuria 1
351	Myotubular myopathy 1
352	Menkes' disease 1 Mendelian genotype Mycobacterium susceptible to
353	infection 1
354	Molybdenum coenzyme deficiency 1
355	Mowat Wilson Syndrome 1
356 357	Ewing's sarcoma 1 Lasopathy 1
357	Libman-Sacks endocarditis 1
359	Lifraumeny syndrome 1
360	Lynch syndrome 1
361	Lymphoproliferative disorder 1
362 363	Lymphangioleiomyomatosis 1 Lennox-Gastaut syndrome 1
364	Subacute necrotizing encephalomyelopathy 1
365	Ectopic ACTH-producing thymic carcinoids 1
366	Hereditary phosphorus metabolism disorders 1
367	Hereditary spherocytosis 1 Hereditary coagulation factor deficiency 1
500	Terestiany or againteen radior dentificing 1
369	Hereditary angioedema 1
370	Hereditary thrombocytopenia 1
371 372	Hereditary thrombotic tendency 1 Hereditary autoinflammatory diseases 1
372	Hereditary autoinflammatory diseases 1 Hereditary periodic paralysis 1
374	Hereditary neuromuscular diseases 1
375	Hereditary spinocerebellar degeneration 1
376	Hereditary hematopoietic disorders 1
	Hereditary multiple exostosis 1 Hereditary intellectual disability 1
510	The second second and second s
379	Hereditary dementia 1
	Relentless smooth tendon swelling syndrome of renal
	cells 1 Rhabdomyosarcoma 1
	Rhabdomyosarcoma 1 ossification of ligamentum flavum 1
383	Macular dystrophy 1
384	Familial amyloid neuropathy 1
385	Familial hypercholesterolemia 1
386	Ectodermai hypopiasia 1
387	Various chromosomal microdeletion (or duplicate) syndromes 1
388	
389	Eyes, teeth, and digital dysplasia 1
390	Basal cell nevus syndrome 1
204	Magalocophoku
	Megalocephaly 1 Macromaly-trichotomy syndrome 1
	Pontine cerebellar hypoplasia 1
394	Fulminant hepatitis 1
395	Polyarteritis nodosum 1
	hemophilia 1 Drimony biliony cholongitia
	Primary biliary cholangitis 1 Primary eruption insufficiency 1
	Cancer of unknown primary 1
	Isolated lens luxation 1

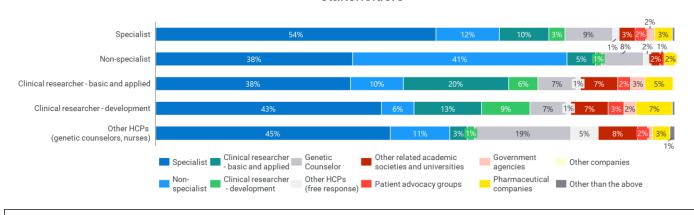
	Disease name	respondents [people]
	Good acid globule granulogranulotrus multiplea	
401	vasculitis	1
402	Eosinophilic sinusitis	1
403	Neutropenia	1
404	Anti-MuSK antibody positive myasthenia gravis	1
405	Antiphospholipid antibody syndrome	1
406	Antineutrophil cytoplasmic antibody-associated	1
408	vasculitis Thyroid ophthalmopathy	1
408	Hyperinsulin-hyperammonemia	1
409	Hypercitrullinemia	1
410	Osteomalacia	1
411 412	hypoplastic left heart syndrome Reticulodysplasia	1
413	trifunctional protein deficiency	1
414	Limb girdle muscular dystrophy	1
415	Lipoatrophy	1
416 417	Neuromyelitis optica Autoinflammatory disease-associated enteritis	1
418	Juvenile Alzheimer's disease	1
	Juvenile Parkinson's disease	1
420	Juvenile-onset bilateral sensorineural hearing loss	1
421 422	Periodic fever	1
422	Severe congenital neutropenia Severe drug eruption	1
424	Childhood hereditary disorders	1
	Alternating hemiplegia of childhood (ATP1A3	
425	abnormality)	1
426	Autosomal episomal (superior) polymorphic anchocytic kidneys	1
420	Autosomal latent (inferior) polycytic nepholis	1
428	Autosomal latent trichosis/attrichopathy	1
429	Autosomal latent polycystic kidney disease	1
430 431	Autosomal predominantly interductal renal disease Cardiac sarcoidosis	1
431	Cardiac sarcoloosis Cardiac Fabry disease	1
433	Cardiomyopathy, bradyarrhythmia	1
434	Neonatal diabetes mellitus	1
435 436	Neuroblastoma Intranuclear-inclusion body disease	1
436	Neuroendocrine tumor	1
438	Neurodevelopmental disorders	1
439	Progressive supranuclear palsy	1
440 441	Progressive myoclonic epilepsy fibrodysplasia ossificans progressiva	1
441	Progressive leukoencephalopathy	1
443	Bullous pemphigoid	1
444	Meningeal amyloidosis	1
445 446	Segawa disease Growth Disorder Disease	1
440	Congenital long QT syndrome	1
448	Congenital QT shortening syndrome	1
449	Congenital thrombomodulin disorder	1
450 451	Congenital hepatic fibrosis	1
451	Congenital tracheal stenosis Congenital bone marrow failure syndrome	1
	3	
453	Congenital heart disease	1
454 455	Congenital epidermal vesicular disease Congenital corticosteroid enzyme deficiency	1
455	Congenital contcosteroid enzyme denciency	1
457	Congenital immunodyspathy	1
458	Congenital immunodeficiency-associated enteritis	1
459	Frontotemporal degeneration	1
460 461	Early repolarization syndrome Total excretion empty remnants	1
462	Multisystem proteinosis	1
463	idiopathic multicentric Castleman's disease	1
464	Multicentric hand root bone foot root osteolysis	1
465	multiple abnormality	1
466	multiple lentigines syndrome Multiple endocrine neoplasia type 1	1
468		. 1
469	Basal ganglia degeneration	1
	Cerebral leukodegeneration single ventricle	1
472	Central diabetes insipidus	1
473	Nakajo-Nishimura syndrome	1
	Ulcerative colitis	1
475 476	Hyposodicemia and osteosodicoidosis Hyaprotic ectodermal hypoplasia	1
	Pemphigus	1
478	chondrodysplasia punctata	1
	Idiosyncratic/relegacious pulmonary arterial	
479	pulmonary hyperhememia	1
480	idiopathic basal ganglia calcification	1
481	Idiopathic small bowel ulcer	1
482	Idiopathic cardiomyopathy	1
483 484	heterotaxy syndrome Refractory brain formation disorder	1
484 485	Refractory brain formation disorder Infantile epileptic spasm syndrome	1
485	Infantile liver failure syndrome type 1	1
	urea cycle disorder	1
	Disorders of brain formation	1
	Cerebral small vessel disease cerebrotendinous xanthomatosis	1
. 50		•
	Pustular psoriasis	1
492	Seeded epidermic actinic pokeratosis	1
493 ⊿04	Pulmonary Langerhans histiocytosis Panhypopituitarism	1 1
494	Dermatosis leukoplasma	1
496	Hypertrophic duritis	1
497	pachydermoperiostosis	1
498	Atypical hemolytic uremic syndrome	1
499 500	Microchromosomal structural abnormalities Arrhythmogenic right ventricular cardiomyopathy	1
	,	•

#

#	Disease name	Number of respondents [people]
501	Complicated congenital heart disease	1
502	hemimegalencephaly	1
503	Chronic thromboembolic pulmonary hypertension	1
504	asplenia syndrome	1
505	Immune thrombocytopenia	1
506	immunodeficiency disease	1
507	Ataxia telangiectasia	1
508	Hair-hepatic-bowel syndrome	1
509	Spastic paraplegia	1
510	Spastic paraplegia	1



Figure 3-1: Percentage of people with experience of collaboration with other professionals and stakeholders



■Survey: Web survey

■Question: Regarding your activities related to rare diseases in the past year, have you collaborated with others? Please answer with an integer between 0 and 10 so that the total for the people you collaborated with is 100%.

■ Subjects: 327 specialists, non-specialists, clinical researchers (basic and applied), clinical researchers (development), and other HCPs (genetic counselors and nurses)

Figure 3-2: Attitude and motivation towards activities related to rare diseases - Top selection result



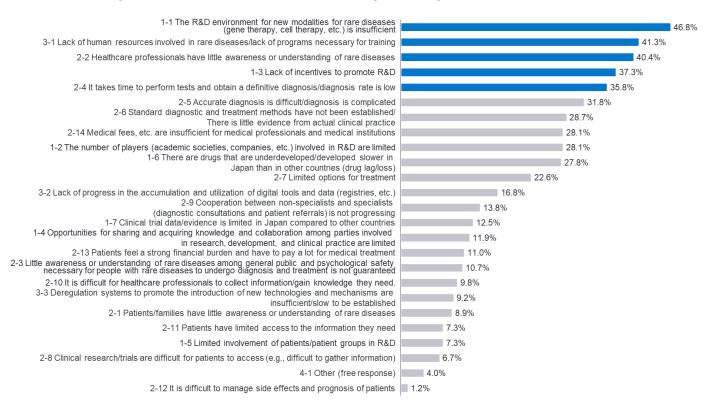
■Survey: Web survey

■Question: Please choose the top three that apply to you regarding your attitude and motivation for participating in activities related to rare diseases (ranking format)

■ Subjects: 327 specialists, non-specialists, clinical researchers (basic and applied), clinical researchers (development) and other HCPs (genetic counselors and nurses)

4.1.1 Overall landscape of challenges in rare diseases in Japan

Figure 4.1.1-1: Overview of the challenges facing rare diseases in Japan



Survey: Web survey

■Question: What are the most pressing challenges regarding rare diseases in Japan? (Select 5)

■ Subjects: 327 specialists, non-specialists, clinical researchers (basic and applied), clinical researchers (development) and other HCPs (genetic counselors and nurses)

Figure 4.1.1-2: Overall landscape of the challenges facing rare diseases • A by occupation • B by medical department • C by disease research area • D by region • E by professional staff availability

Α	Specialist (n=270)		Clinical researchers C (basic and applied) (n=61)	(dovelopment)	Other HCPs (genetic ounselors, nurses) (n=23)
1-1 The R&D environment for new modalities for rare diseases (gene therapy, cell therapy, etc.) is insufficient	47.0%	37.7%	55.7%	60.5%	60.9%
1-2 The number of players (academic societies, companies, etc.) involved in R&D are few/limited	31.1%	20.8%	32.8%	30.2%	13.0%
1-3 Lack of incentives to promote research and development	39.6%	22.6%	63.9%	58.1%	13.0%
1-4 Opportunities for sharing and acquiring knowledge and collaboration among parties involved in research, development and clinical practice are limited	11.5%	11.3%	18.0%	14.0%	13.0%
1-5 Limited involvement of patients/patient advocacy groups in R&D	6.7%	5.7%	11.5%	7.0%	8.7%
1-6 There are drugs that are underdeveloped/developed slower in Japan than in other countries (drug lag/loss)	30.4%	24.5%	29.5%	34.9%	21.7%
1-7 Clinical trial data/evidence is limited in Japan compared to other countries	13.7%	1.9%	6.6%	11.6%	21.7%
2-1 Patients/families have little awareness or understanding of rare diseases	8.9%	7.5%	3.3%	4.7%	4.3%
2-2 Healthcare professionals have little awareness or understanding of rare diseases	38.9%	52.8%	31.1%	34.9%	39.1%
2-3 There is little awareness of rare diseases among general public and psychological safety required for people with rare diseases to undergo diagnosis and treatment is not guaranteed	10.4%	22.6%	3.3%	4.7%	8.7%
2-4 It takes time to perform tests and obtain a definitive diagnosis/diagnosis rate is low	35.6%	52.8%	27.9%	30.2%	30.4%
2-5 Accurate diagnosis is difficult/diagnosis is complicated	31.5%	37.7%	29.5%	30.2%	30.4%
2-6 Standard diagnostic and treatment methods have not been established/There is little evidence from actual clinical practice	28.5%	30.2%	13.1%	14.0%	39.1%
2-7 Limited options for treatment	23.7%	18.9%	16.4%	18.6%	17.4%
	5.9%	7.5%	6.6%	4.7%	13.0%
2-9 Cooperation between non-specialists and specialists (diagnostic consultations and patient referrals) is not progressing	12.6%	22.6%	11.5%	14.0%	17.4%
2-10 It is difficult for healthcare professionals to collect the information/gain knowledge they need	7.4%	20.8%	4.9%	9.3%	13.0%
2-11 Patients have limited access to the information they need	7.0%	0.0%	8.2%	2.3%	13.0%
2-12 It is difficult to manage side effects and prognosis of patients	1.5%	1.9%	0.0%	0.0%	4.3%
2-13 Patients feel a strong financial burden and have to pay a lot for medical treatment	11.9%	7.5%	13.1%	9.3%	4.3%
2-14 Medical fees, etc. are insufficient for healthcare professionals and medical institutions	27.8%	30.2%	29.5%	20.9%	26.1%
3-1 Lack of human resources involved in rare diseases/lack of programs necessary for training	40.0%	39.6%	37.7%	46.5%	56.5%
3-2 Lack of progress in the accumulation and utilization of digital tools and data (registries, etc.)	16.3%	17.0%	14.8%	18.6%	21.7%
3-3 Deregulation systems to promote the introduction of new technologies and mechanisms are insufficient/slow to be established	8.1%	3.8%	19.7%	14.0%	8.7%
4-1 Other (free response)	4.1%	1.9%	11.5%	7.0%	0.0%

■Survey: Web survey

■Question: Please answer the most important issue you feel is related to rare diseases in Japan (choose 5, multiple choice)

■Subjects: 327 specialists, non-specialists, clinical researchers (basic and applied), clinical researchers (development) and other HCPs (genetic counselors and nurses)

В		Pediatrics (n=119)	Neurology (n=51)	Department of Clinical Genetics/Gene Therapy (n=45)	Other medical departments Total (n=101)
	1-1 The R&D environment for new modalities for rare diseases	51.3%	49.0%	44.4%	39.6%
	(gene therapy, cell therapy, etc.) is insufficient 1-2 The number of players (academic societies, companies, etc.) involved in R&D are fewilimited	27.7%	35.3%	15.6%	32.7%
	1-3 Lack of incentives to promote research and development	36.1%	43.1%	28.9%	36.6%
	1-4 Opportunities for sharing and acquiring knowledge and collaboration among parties involved in research, development and clinical practice are limited	9.2%	11.8%	15.6%	12.9%
	1-5 Limited involvement of patients/patient advocacy groups in R&D	4.2%	11.8%	6.7%	6.9%
	1-6 There are drugs that are underdeveloped/developed slower in Japan than in other countries (drug lag/loss)	30.3%	27.5%	26.7%	27.7%
	1-7 Clinical trial data/evidence is limited in Japan compared to other countries	10.1%	7.8%	15.6%	15.8%
	2-1 Patients/families have little awareness or understanding of rare diseases	7.6%	5.9%	8.9%	11.9%
	2-2 Healthcare professionals have little awareness or understanding of rare diseases	45.4%	29.4%	48.9%	38.6%
	2-3 There is little awareness of rare diseases among general public and psychological safety required for people with rare diseases to undergo diagnosis and treatment is not guaranteed	10.1%	9.8%	8.9%	13.9%
	2-4 It takes time to perform tests and obtain a definitive diagnosis/diagnosis rate is low	45.4%	35.3%	26.7%	29.7%
	2-5 Accurate diagnosis is difficult/diagnosis is complicated	27.7%	33.3%	28.9%	37.6%
	2-6 Standard diagnostic and treatment methods have not been established/There is little evidence from actual clinical practice	29.4%	31.4%	26.7%	29.7%
	2-7 Limited options for treatment	16.0%	39.2%	8.9%	28.7%
	2-8 Clinical research/trials are difficult for patients to access (e.g., difficult to gather information)	5.9%	7.8%	8.9%	6.9%
	2-9 Cooperation between non-specialists and specialists (diagnostic consultations and patient referrals) is not progressing	14.3%	11.8%	8.9%	16.8%
	2-10 It is difficult for healthcare professionals to collect the information/gain knowledge they need	11.8%	2.0%	13.3%	9.9%
	2-11 Patients have limited access to the information they need	5.0%	5.9%	15.6%	5.9%
	2-12 It is difficult to manage side effects and prognosis of patients	0.0%	3.9%	0.0%	2.0%
	2-13 Patients feel a strong financial burden and have to pay a lot for medical treatment	16.8%	5.9%	4.4%	10.9%
	2-14 Medical fees, etc. are insufficient for healthcare professionals and medical institutions	30.3%	27.5%	37.8%	21.8%
	3-1 Lack of human resources involved in rare diseases/lack of programs necessary for training	36.1%	41.2%	60.0%	37.6%
	3-2 Lack of progress in the accumulation and utilization of digital tools and data (registries, etc.)	16.8%	15.7%	15.6%	17.8%
	3-3 Deregulation systems to promote the introduction of new technologies and mechanisms are insufficient/slow to be established	7.6%	5.9%	17.8%	5.9%
	4-1 Other (free response)	5.0%	2.0%	6.7%	2.0%

*Medical departments with 15 or more respondents selected





■Survey: Web survey

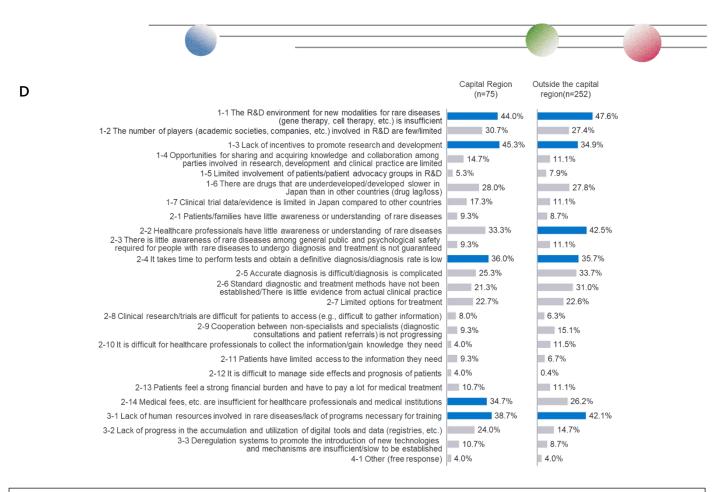
Question: Please answer the question about the most pressing challenges surrounding rare diseases in Japan (choose 5, multiple choice)
 Subjects: 316 specialists, non-specialists, and other HCPs (genetic counselors and nurses)

Pediatrics Neuromuscular Other disease areas С (n=21) disease (n=19) total (n=30) 1-1 The R&D environment for new modalities for rare diseases 61.9% 47.4% 50.0% (gene therapy, cell therapy, etc.) is insufficient 33.3% 36.8% 33.3% 1-2 The number of players (academic societies, companies, etc.) involved in R&D are few/limited 1-3 Lack of incentives to promote research and development 57.9% 56.7% 1-4 Opportunities for sharing and acquiring knowledge and collaboration among parties involved in research, development and clinical practice are limited 19.0% 21.1% 10.0% 1-5 Limited involvement of patients/patient advocacy groups in R&D 4 8% 15.8% 13 3% 1-6 There are drugs that are underdeveloped/developed slower in Japan than in other countries (drug lag/loss) 23.8% 36.8% 26.7% 6.7% 1-7 Clinical trial data/evidence is limited in Japan compared to other countries 4.8% 21.1% 2-1 Patients/families have little awareness or understanding of rare diseases 5.3% 0.0% 4.8% 2-2 Healthcare professionals have little awareness or understanding of rare diseases 38.1% 21.1% 36.7% 2-3 There is little averages of rare diseases among general public and psychological safety required for people with rare diseases to undergo diagnosis and treatment is not guaranteed 0.0% 3.3% 4.8% 28.6% 2-4 It takes time to perform tests and obtain a definitive diagnosis/diagnosis rate is low 26.3% 30.0% 2-5 Accurate diagnosis is difficult/diagnosis is complicated 21.1% 33.3% 30.0% 2-6 Standard diagnostic and treatment methods have not been established/There is little evidence from actual clinical practice 28.6% 5 3% 16.7% 2-7 Limited options for treatment 14.3% 15.8% 23.3% 2-8 Clinical research/trials are difficult for patients to access (e.g., difficult to gather information) 0.0% 10.5% 6.7% 2-9 Cooperation between non-specialists and specialists (diagnostic consultations and patient referrals) is not progressing 14.3% 15.8% 6.7% 2-10 It is difficult for healthcare professionals to collect the information/gain knowledge they need 4.8% 5.3% 6.7% 2-11 Patients have limited access to the information they need 9.5% 0.0% 10.0% 0.0% 0.0% 2-12 It is difficult to manage side effects and prognosis of patients 0.0% 2-13 Patients feel a strong financial burden and have to pay a lot for medical treatment 14.3% 5.3% 16.7% 2-14 Medical fees, etc. are insufficient for healthcare professionals and medical institutions 31.6% 20.0% 33.3% 3-1 Lack of human resources involved in rare diseases/lack of programs necessary for training 28.6% 52 6% 43.3% 3-2 Lack of progress in the accumulation and utilization of digital tools and data (registries, etc.) 21.1% 13.3% 3-3 Deregulation systems to promote the introduction of new technologies and mechanisms are insufficient/slow to be established 9.5% 15.8% 26.7% 4-1 Other (free response) 4.8% 10.5% 13.3%

*Research areas with 15 or more respondents were selected

Survey: Web survey

- ■Question: Please answer the question about the most pressing challenges surrounding rare diseases in Japan (choose 5, multiple choice)
- Subjects: 70 clinical researchers (basic and applied), clinical researchers (development)



■Survey: Web survey

Question: Please answer the most important issue you feel is related to rare diseases in Japan (choose 5, multiple choice)
 Subjects: 327 specialists, non-specialists, clinical researchers (basic and applied), clinical researchers (development) and other HCPs (genetic

counselors and nurses)

E	Professional staff available (n=275)	No specialized staff (n=47)
1-1 The R&D environment for new modalities for rare diseases (gene therapy, cell therapy, etc.) is insufficient 1-2 The number of players (academic societies, companies, etc.) involved in R&D are fewlimited	48.7%	25.5%
1-2 The humber of players (academic societies, conjentives, tec.) involved in read are terminined 1-3 Lack of incentives to promote research and development 1-4 Opportunities for sharing and acquiring knowledge and collaboration among parties involved in research, development and clinical practice are limited 1-5 Limited involvement of patients/patient advocacy groups in R&D 1-6 There are drugs that are underdeveloped/developed slower in Japan than in other countries (drug lag/loss) 1-7 Clinical trial data/evidence is limited in Japan compared to other countries 2-1 Patients/families have little awareness or understanding of rare diseases	25.7% 35.3% 12.4% 6.9% 28.4% 12.4% 7.6%	23.5 % 48.9% 8.5% 27.7% 14.9%
2-2 Healthcare professionals have little awareness or understanding of rare diseases 2-3 There is little awareness of rare diseases among general public and psychological safety required for people with rare diseases to undergo diagnosis and treatment is not guaranteed 2-4 It takes time to perform tests and obtain a definitive diagnosis/diagnosis rate is low 2-5 Accurate diagnosis is difficult/diagnosis is complicated 2-6 Standard diagnostic and treatment methods have not been established/There is little evidence from actual clinical practice 2-7 Limited options for treatment	41.1% 10.2% 37.1% 31.6% 29.8% 20.4%	36.2% 14.9% 25.5% 31.9% 23.4% 34.0%
2-8 Clinical research/trials are difficult for patients to access (e.g., difficult to gather information) 2-9 Cooperation between non-specialists and specialists (diagnostic consultations and patient referrals) is not progressing 2-10 It is difficult for healthcare professionals to collect the information/gain knowledge they need	6.9% 13.8% 9.1%	6.4% 10.6% 10.6%
2-11 Patients have limited access to the information they need	7.6%	4.3% 0.0%
2-12 It is difficult to manage side effects and prognosis of patients 2-13 Patients feel a strong financial burden and have to pay a lot for medical treatment	12.0%	6.4%
2-14 Medical fees, etc. are insufficient for healthcare professionals and medical institutions	29.8%	19.1%
3-1 Lack of human resources involved in rare diseases/lack of programs necessary for training	41.1%	44.7%
 3-2 Lack of progress in the accumulation and utilization of digital tools and data (registries, etc.) 3-3 Deregulation systems to promote the introduction of new technologies and mechanisms are insufficient/slow to be established 4-1 Other (free response) 	16.4% 7.3% 4.0%	21.3% 19.1% 4.3%



- Survey: Web survey
- Question: Please answer the question about the most pressing challenges surrounding rare diseases in Japan (choose 5, multiple choice)
- Subjects: 327 specialists, non-specialists, clinical researchers (basic and applied), clinical researchers (development) and other HCPs (genetic

counselors and nurses)

Figure 4.1.1-3: The big picture of the challenges facing rare diseases



Survey: Web survey

■Question: Please answer the question about the most pressing challenges surrounding rare diseases in Japan (choose 5, multiple choice)

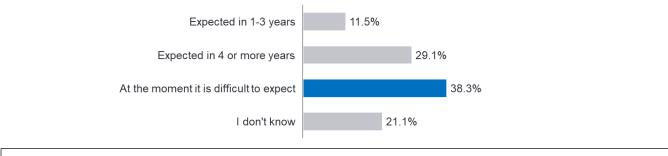
Subjects: 327 specialists, non-specialists, clinical researchers (basic and applied), clinical researchers (development) and other HCPs (genetic counselors and nurses)

Figure 4.1.1-4: Challenges related to rare diseases and expectations of stakeholders (keywords from qualitative interviews)



4.1.2 Challenges in research and development

Figure 4.1.2-1: Expectations for progress in R&D leading to fundamental treatment of rare diseases



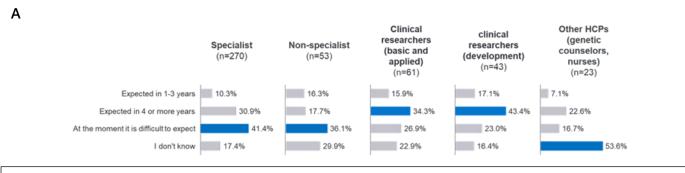
Survey: Web survey

■Question: Please answer the question about the rare disease you answered in Q13 (Please answer the main rare disease names among your activities related to rare diseases in the past year (up to 5 names allowed)). Do you expect progress in research and development that will lead to a fundamental treatment for the rare disease?

■ Subjects: 327 specialists, non-specialists, clinical researchers (basic and applied), clinical researchers (development) and other HCPs (genetic counselors and nurses)

Figure 4.1.2-2: Expectations for progress in R&D leading to fundamental treatment of rare diseases

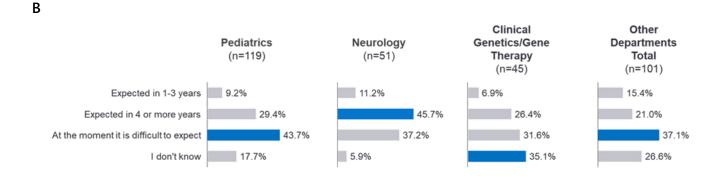
- A by occupation / B by medical department



Survey: Web survey

■Question: Please answer the question about the rare disease you answered in Q13. Do you expect progress in R&D leading to a fundamental treatment for the rare disease? (Q13: Please answer the name of the main rare disease among your activities related to rare diseases in the past year (up to 5 answers possible)

■Subjects: 327 specialists, non-specialists, clinical researchers (basic and applied), clinical researchers (development) and other HCPs (genetic counselors and nurses)



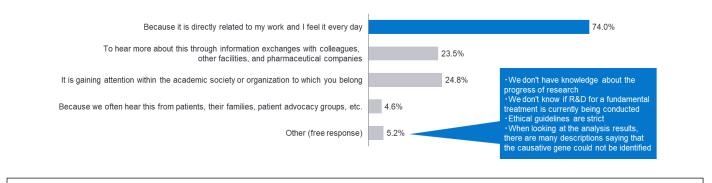


■Survey: Web survey

■Question: Please answer the question about the rare disease you answered in Q13. Do you expect progress in R&D leading to a fundamental treatment for the rare disease? (Q13: Please answer the name of the main rare disease among your activities related to rare diseases in the past year (up to 5 answers possible)

■Subjects: 316 specialists, non-specialists, and other HCPs (genetic counselors and nurses)

Figure 4.1.2-3: Reasons for expecting progress in R&D leading to fundamental treatments of rare diseases



Survey: Web survey

■Question: Please answer the reason (multiple choices possible)

■Subjects: 327 specialists, non-specialists, clinical researchers (basic and applied), clinical researchers (development) and other HCPs (genetic counselors and nurses)

Figure 4.1.2-4: Reasons for expectation of progress in R&D leading to fundamental treatment of rare

diseases - by occupation

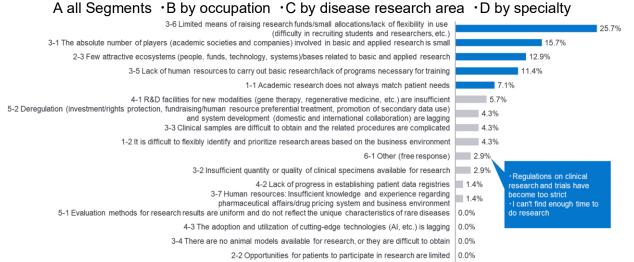
	Specialist (n=270)	Non-specialist (n=53)	Clinical researcher (basic and applied) (n=61)	Clinical researcher (development) (n=43)	Other HCPs (genetic counselors, nurses) (n=23)
Because it is directly related to my work and I feel it every day To hear more about this through information exchanges with colleagues, other facilities, and pharmaceutical companies It is gaining attention within the academic society or organization to which you belong	77.8% 23.7% 25.6%	60.4% 30.2% 24.5%	78.7% 29.5% 24.6%	93.0% 25.6% 27.9%	60.9% 13.0% 26.1%
Because we often hear this from patients, their families, patient advocacy groups, etc.	5.6%	3.8%	3.3%	7.0%	8.7%
Other (free response)	3.3%	5.7%	8.2%	0.0%	13.0%

■Survey: Web survey

■Question: Please answer the reason (multiple choices possible)

■Subjects: 327 specialists, non-specialists, clinical researchers (basic and applied), clinical researchers (development) and other HCPs (genetic counselors and nurses)

Figure 4.1.2-5: Challenges in basic and applied research – Top selection results :



2-1 Few opportunities for sharing knowledge and collaboration between companies, academic societies, and patient advocacy groups 0.0%

Α

В

	Clinical researcher (basic and applied) (n=61)	Clinical researcher (development) (n=43)
1-1 Academic research does not always match patient needs	8.2%	9.3%
1-2 It is difficult to flexibly identify and prioritize research areas based on the business environment 2-1 Few opportunities for sharing knowledge and collaboration between companies, academic societies, and patient advocacy groups 2-2 Opportunities for patients to participate in research are limited	4.9% 0.0% 0.0%	2.3% 0.0% 0.0%
2-3 Few attractive ecosystems (people, funds, technology, systems)/bases related to basic and applied research	13.1%	16.3%
3-1 The absolute number of players (academic societies and companies) involved in basic and applied research is small	13.1%	16.3%
3-2 Insufficient quantity or quality of clinical specimens available for research	3.3%	2.3%
3-3 Clinical samples are difficult to obtain and the related procedures are complicated	4.9%	2.3%
3-4 There are no animal models available for research, or they are difficult to obtain	0.0%	0.0%
 3-5 Lack of human resources to carry out basic research/lack of programs necessary for training 3-6 Limited means of raising research funds/small allocations/lack of flexibility in use (difficulty in recruiting students and researchers, etc.) 3-7 Human resources: Insufficient knowledge and experience regarding pharmaceutical affairs/drug pricing system and business environment 4-1 R&D facilities for new modalities (gene therapy, regenerative medicine, etc.) are insufficient 4-2 Lack of progress in establishing patient data registries 4-3 The adoption and utilization of cutting-edge technologies (AI, etc.) is lagging 5-1 Evaluation methods for research results are uniform and do not reflect the unique characteristics of rare diseases 5-2 Deregulation (investment/rights protection, fundraising/human resource preferential treatment, promotion of secondary data use) and system development (domestic and international collaboration) are lagging 	13.1% 24.6% 1.6% 4.9% 0.0% 0.0% 0.0% 4.9%	11.6% 16.3% 2.3% 7.0% 2.3% 0.0% 0.0% 7.0%
6-1 Other (free response)	3.3%	4.7%

c					
	Pediatric disease (n=21)		Neurom dise (n=	ase	Other disease areas total (n=30)
1-1 Academic research does not always match patient needs	4.8%		5.3%		10.0%
1-2 It is difficult to flexibly identify and prioritize research areas based on the business environment 2-1 Few opportunities for sharing knowledge and collaboration between companies, academic societies, and patient advocacy groups	4.8% 0.0%		0.0% 0.0%		6.7% 0.0%
2-2 Opportunities for patients to participate in research are limited	0.0%		0.0%		0.0%
2-3 Few attractive ecosystems (people, funds, technology, systems)/bases related to basic and applied research	9.5%		10.5%	6	16.7%
3-1 The absolute number of players (academic societies and companies) involved in basic and applied research is small	23.8%		15	.8%	10.0%
3-2 Insufficient quantity or quality of clinical specimens available for research	4.8%		0.0%		3.3%
3-3 Clinical samples are difficult to obtain and the related procedures are complicated	0.0%		0.0%		10.0%
3-4 There are no animal models available for research, or they are difficult to obtain	0.0%		0.0%		0.0%
3-5 Lack of human resources to carry out basic research/lack of programs necessary for training	4.8%			21.1%	10.0%
3-6 Limited means of raising research funds/small allocations/lack of flexibility in use (difficulty in recruiting students and researchers, etc.) 3-7 Human resources: Insufficient knowledge and experience regarding pharmaceutical	3:	3.3%		21.1%	23.3%
3-7 Human resources: Insufficient knowledge and experience regarding pharmaceutical affairs/drug pricing system and business environment	4.8%		0.0%		0.0%
4-1 R&D facilities for new modalities (gene therapy, regenerative medicine, etc.) are insufficient	4.8%		10.5%	6	3.3%
4-2 Lack of progress in establishing patient data registries	0.0%		0.0%		3.3%
4-3 The adoption and utilization of cutting-edge technologies (AI, etc.) is lagging	0.0%		0.0%		0.0%
5-1 Evaluation methods for research results are uniform and do not reflect the unique characteristics of rare diseases	0.0%		0.0%		0.0%
5-2 Deregulation (investment/rights protection, fundraising/human resource preferential treatment, promotion of secondary data use) and system development (domestic and international collaboration) are lagging	0.0%		10.5%	6	3.3%
6-1 Other (free response)	4.8%		5.3%		0.0%
			plied	Clinical	. Translational
D	Basic Research (n=53)	non-	rch and clinical (n=25)	research and trials (n=44)	Research (n=25)
1-1 Academic research does not always match patient needs	7.5%	·	12.0%	4.5%	8.0%
1-2 It is difficult to flexibly identify and prioritize research areas based on the business environment	5.7%	8.0	%	0.0%	4.0%
2-1 Few opportunities for sharing knowledge and collaboration between companies, academic societies, and patient advocacy groups	0.0%	0.0%		0.0%	0.0%
2-2 Opportunities for patients to participate in research are limited	01070	0.0%		0.0%	0.0%
2-3 Few attractive ecosystems (people, funds, technology, systems)/bases related to basic and applied research	10.270		16.0%	15.9%	20.0%
3-1 The absolute number of players (academic societies and companies) involved in basic and applied research is smal	10.270	4.0%		18.2%	
3-2 Insufficient quantity or quality of clinical specimens available for research	3.8%	4.0%		4.5%	4.0%

3-1 The absolute number of players (academic societies and companies) involved in basic and applied research is small	13.2%	4.0%	18.2%	12.0%
3-2 Insufficient quantity or quality of clinical specimens available for research	3.8%	4.0%	4.5%	4.0%
3-3 Clinical samples are difficult to obtain and the related procedures are complicated	5.7%	0.0%	2.3%	4.0%
3-4 There are no animal models available for research, or they are difficult to obtain	0.0%	0.0%	0.0%	0.0%
3-5 Lack of human resources to carry out basic research/lack of programs necessary for training	11.3%	8.0%	13.6%	8.0%
3-6 Limited means of raising research funds/small allocations/lack of flexibility in use (difficulty in recruiting students and researchers, etc.)	24.5%	20.0%	22.7%	12.0%
3-7 Human resources: Insufficient Knowledge and experience regarding harmaceutical affairs/drug pricing system and business environment	1.9%	4.0%	0.0%	4.0%
4-1 R&D facilities for new modalities (gene therapy, regenerative medicine, etc.) are insufficient	5.7%	8.0%	6.8%	4.0%
4-2 Lack of progress in establishing patient data registries	0.0%	0.0%	2.3%	0.0%
4-3 The adoption and utilization of cutting-edge technologies (AI, etc.) is lagging	0.0%	0.0%	0.0%	0.0%
5-1 Evaluation methods for research results are uniform and do not reflect the unique characteristics of rare diseases	0.0%	0.0%	0.0%	0.0%
5-2 Deregulation (investment/rights protection, fundraising/human resource preferential treatment, promotion of secondary data use) and system development (domestic and international collaboration) are lagging	5.7%	12.0%	4.5%	12.0%
6-1 Other (free response)	1.9%	4.0%	4.5%	8.0%

■Survey: Web survey

■Question: Please select the top 5 challenges that you feel are most important in basic and applied research (ranking format)

■Subjects: 70 clinical researchers (basic and applied) and clinical researchers (development)

Figure 4.1.2-6: Challenges in basic and applied research – Top 5 Selection Results : A all segments ·B by occupation ·C by disease research area ·D by specialty

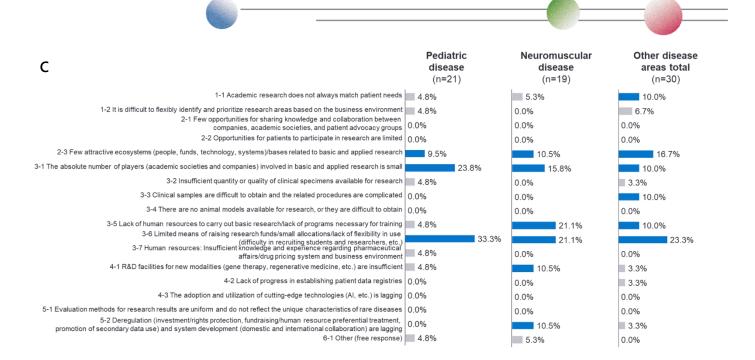
3-6 Limited means of raising research funds/small allocations/lack of flexibility in use (difficulty in recruiting students and researchers, etc.)	70.0%
3-5 Lack of human resources to carry out basic research/lack of programs necessary for training	52.9%
3-1 The absolute number of players (academic societies and companies) involved in basic and applied research is small	47.1%
3-3 Clinical samples are difficult to obtain and the related procedures are complicated	35.7%
2-3 Few attractive ecosystems (people, funds, technology, systems)/bases related to basic and applied research	35.7%
4-1 R&D facilities for new modalities (gene therapy, regenerative medicine, etc.) are insufficient	34.3%
1-2 It is difficult to flexibly identify and prioritize research areas based on the business environment	32.9%
1-1 Academic research does not always match patient needs	30.0%
5-1 Evaluation methods for research results are uniform and do not reflect the unique characteristics of rare diseases	28.6%
5-2 Deregulation (investment/rights protection, fundraising/human resource preferential treatment, promotion of secondary data use) and system development (domestic and international collaboration) are lagging	25.7%
4-2 Lack of progress in establishing patient data registries	22.9%
3-2 Insufficient quantity or quality of clinical specimens available for research	20.0%
4-3 The adoption and utilization of cutting-edge technologies (AI, etc.) is lagging	14.3%
3-4 There are no animal models available for research, or they are difficult to obtain	14.3%
3-7 Human resources: Insufficient knowledge and experience regarding pharmaceutical affairs/drug pricing system and business environment	11.4%
2-2 Opportunities for patients to participate in research are limited	11.4%
2-1 Few opportunities for sharing knowledge and collaboration between companies, academic societies, and patient advocacy groups	10.0%

6-1 Other (free response) 2.9%

Clinical Clinical researcher researcher (basic and (development) (n=43) applied) (n=61) 8.2% 9.3% 1-1 Academic research does not always match patient needs 1-2 It is difficult to flexibly identify and prioritize research areas based on the business environment 4.9% 2.3% 2-1 Few opportunities for sharing knowledge and collaboration between companies, academic societies, and patient advocacy groups 0.0% 0.0% 2-2 Opportunities for patients to participate in research are limited 0.0% 0.0% 2-3 Few attractive ecosystems (people, funds, technology, systems)/bases related to basic and applied research 13.1% 16.3% 13.1% 16.3% 3-1 The absolute number of players (academic societies and companies) involved in basic and applied research is small 2.3% 3-2 Insufficient quantity or quality of clinical specimens available for research 3.3% 3-3 Clinical samples are difficult to obtain and the related procedures are complicated 4.9% 2.3% 3-4 There are no animal models available for research, or they are difficult to obtain 0.0% 0.0% 3-5 Lack of human resources to carry out basic research/lack of programs necessary for training 13.1% 11.6% 3-6 Limited means of raising research funds/small allocations/lack of flexibility in use (difficulty in recruiting students and researchers, etc.) 3-7 Human resources: Insufficient Knowledge and experience regarding pharmaceutical 24.6% 16.3% 2.3% 1.6% affairs/drug pricing system and business environment 4-1 R&D facilities for new modalities (gene therapy, regenerative medicine, etc.) are insufficient 4.9% 7.0% 2.3% 4-2 Lack of progress in establishing patient data registries 0.0% 4-3 The adoption and utilization of cutting-edge technologies (AI, etc.) is lagging 0.0% 0.0% 5-1 Evaluation methods for research results are uniform and do not reflect the unique characteristics of rare diseases 0.0% 0.0% 5-2 Deregulation (investment/rights protection, fundraising/human resource preferential treatment, promotion of secondary data use) and system development (domestic and international collaboration) are lagging 7.0% 4.9% 6-1 Other (free response) 3.3% 4.7%



В



D	Basic Research (n=53)	Applied research and non-clinical trials (n=25)	Clinical Research and Trials (n=44)	Translational Research (n=25)
1-1 Academic research does not always match patient needs	32.1%	40.0%	25.0%	32.0%
1-2 It is difficult to flexibly identify and prioritize research areas based on the business environment 2-1 Few opportunities for sharing knowledge and collaboration between companies, academic societies, and patient advoccy groups	0.070	36.0%	31.8% 11.4%	24.0%
2-2 Opportunities for patients to participate in research are limited	11.3%	8.0%	4.5%	12.0%
2-3 Few attractive ecosystems (people, funds, technology, systems)/bases related to basic and applied research	37.7%	44.0%	36.4%	36.0%
3-1 The absolute number of players (academic societies and companies) involved in basic and applied research is small	41.5%	32.0%	50.0%	44.0%
3-2 Insufficient quantity or quality of clinical specimens available for research	18.9%	16.0%	20.5%	16.0%
3-3 Clinical samples are difficult to obtain and the related procedures are complicated	39.6%	32.0%	36.4%	36.0%
3-4 There are no animal models available for research, or they are difficult to obtain	15.1%	20.0%	15.9%	12.0%
3-5 Lack of human resources to carry out basic research/lack of programs necessary for training 3-6 Limited means of raising research funds/small allocations/lack of flexibility in use (difficulty in recruiting students and researchers, etc.) 3-7 Human resources: Insufficient knowledge and experience regarding phamaceutical affairs/drug pricing system and business environment	67.9%	44.0% 72.0%	54.5% 68.2%	60.0% 64.0% 12.0%
4-1 R&D facilities for new modalities (gene therapy, regenerative medicine, etc.) are insufficient	00.270	44.0%	36.4%	40.0%
4-2 Lack of progress in establishing patient data registries	22.6%	20.0%	27.3%	28.0%
4-3 The adoption and utilization of cutting-edge technologies (AI, etc.) is lagging	15.1%	16.0%	15.9%	20.0%
5-1 Evaluation methods for research results are uniform and do not reflect the unique characteristics of rare diseases	26.4%	12.0%	25.0%	20.0%
5-2 Deregulation (investment/rights protection, fundraising/human resource preferential treatment, promotion of secondary data use) and system development (domestic and international collaboration) are lagging	24.5%	40.0%	25.0%	32.0%
6-1 Other (free response)	1.9%	4.0%	4.5%	8.0%

Survey: Web survey

5

■Question: Please answer by selecting the top 5 challenges that you feel are most important in basic and applied research (ranking format) ■Subjects: 70 clinical researchers (basic and applied) and clinical researchers (development)

Figure 4.1.2-7: Challenges in development and clinical trials – Top selection result : A all segments **•**B by occupation **•**C by disease research area **•**D by specialty

Α	
3-4 Limited means of raising funds for development and clinical trials	27.1%
3-3 Lack of human resources to handle development and clinical trials/Lack of programs necessary for training	14.3%
4-1 The development and clinical trial environment for new modalities (gene therapy, regenerative medicine, etc.) is insufficient	12.9%
1-1 Product development is lagging or not being developed compared to overseas (drug/device lag/loss)	11.4%
3-2 The number of patients is small, making it difficult to recruit patients for clinical trials	7.1%
2-3 Few attractive ecosystems (people, funds, technology, systems)/bases related to development and clinical trials	7.1%
5-1 Deregulation (investment protection/fundraising/preferential treatment for human resources, promotion of secondary use of data) and system development are lagging	5.7%
3-1 The absolute number of players (academic societies and companies) involved in development and clinical trials is small	5.7%
2-1 Few opportunities for sharing knowledge and collaboration between companies, academic societies, and patient advocacy groups	2.9%
6-1 Other (free response)	1.4%
4-5 Lack of cooperation from clinicians and patients in obtaining clinical data	1.4%
4-4 Insufficient quantity or quality of clinical data available for development	1.4%
4-2 Difficulty in manufacturing new modalities for development and clinical trials (gene therapy, regenerative medicine, etc.)	1.4%
4-6 Compared to other countries, Japan is lagging behind in adopting and utilizing cutting-edge development methods	0.0%
4-3 Difficulty in searching for clinical trial information	0.0%

2-2 Opportunities for patients to participate in clinical trials are limited 0.0%

В

1-1 Product development is lagging or not being developed compared to overseas (drug/device lag)9.8%16.3%2-1 There are few opportunities for sharing knowledge and collaboration between companies, academic societies, and patient advocacy groups 2-2 Opportunities for patients to participate in clinical trials are limited 3-3 Attractive ecosystem for development and clinical trials (people, funds, technology, systems) / Few bases 3-2 The number of players (academic societies and companies) involved in development and clinical trials is small 3-2 The number of patients is small, making it difficult to recruit patients for clinical trials 3-3 Lack of human resources for development and clinical trials/lack of training programs 3-4 There are limited means of raising funds for development and clinical trial 3-4 There are limited means of raising funds for development and clinical trial 4-1 The development and clinical trial environment for new modalities (gene therapy, regenerative medicine, etc.) is insufficient 4-3 Difficulty in searching for clinical trial information 4-3 Difficulty in searching for clinical trial information 4-5 Lack of cooperation from clinicians and patients in obtaining clinical data 4-6 Compared to other countries, Japan is lagging in adopting and utilizing cutting-edge development method 6-1 Deregulation (investment protection/fundraising/human resource preferential treatment promotion of secondary data walable of there ensponse 6-1 Other (free response)9.8%4.7%0.0%0.0%0.0%0.0%1.6.%2.3%1.6.%0.0%2.3 w0.0%1.6.%0.0%1.6.%0.0%1.6.%0.0%1.6.%0.0%1.6.%0.0%1.6.%0.0%1.6.% <th></th> <th>Clinical researchers (basic and applied) (n=61)</th> <th>Clinical researchers (development) (n=43)</th>		Clinical researchers (basic and applied) (n=61)	Clinical researchers (development) (n=43)
2-2 Opportunities for patients to participate in clinical trials are limited 0.0% 0.0% 2-3 Attractive ecosystem for development and clinical trials (people, funds, technology, systems) / Few bases 0.0% 6.6% 11.6% 3-1 The absolute number of players (academic societies and companies) involved in development and clinical trials is small 3.3% 7.0% 3-2 The number of patients is small, making it difficult to recruit patients for clinical trials 3.3% 14.0% 3-3 Lack of human resources for development and clinical trials/lack of training programs 3.4 There are limited means of raising funds for development and clinical trials 27.9% 20.9% 4-1 The development and clinical trial environment for new modalities (gene therapy, regenerative medicine, etc.) is insufficient 11.6% 9.3% 4-2 Difficulty in manufacturing new modalities for development and clinical trials (gene therapy, regenerative medicine, etc.) 1.6% 0.0% 4-4 Insufficient quantity or quality of clinical data available for development 0.0% 0.0% 0.0% 4-5 Lack of cooperation from clinicians and patients in obtaining clinical data 1.6% 0.0% 0.0% 1.6% 0.0% 0.0% 0.0% 0.0% 0.0% 0.0% 0.0% 0.0% 0.0% 0.0% 0.0% 0.0% 0.0%	1-1 Product development is lagging or not being developed compared to overseas (drug/device lag)	9.8%	16.3%
2-3 Attractive ecosystem for development and clinical trials (people, funds, technology, systems) / Few bases 6.6% 11.6% 3-1 The absolute number of players (academic societies and companies) involved in development and clinical trials is small 3.3% 7.0% 3-2 The number of players (academic societies and companies) involved in development and clinical trials is small 3.3% 7.0% 3-2 The number of patients is small, making it difficult to recruit patients for clinical trials 8.2% 4.7% 3-3 Lack of human resources for development and clinical trials/lack of training programs 16.4% 14.0% 3-4 There are limited means of raising funds for development and clinical trials 27.9% 20.9% 4-1 The development and clinical trial environment for new modalities (gene therapy, regenerative medicine, etc.) is insufficient 11.6% 2.3% 4-2 Difficulty in manufacturing new modalities for development and clinical trials (gene therapy, regenerative medicine, etc.) 1.6% 0.0% 4-3 Difficulty in searching for clinical data available for development 0.0% 0.0% 0.0% 4-4 Insufficient quantity or quality of clinical ata available for development 1.6% 0.0% 0.0% 4-5 Lack of cooperation from clinicians and patients in obtaining clinical data 1.6% 0.0% 0.0% 0.0% 0.0% 0.0%	2-1 There are few opportunities for sharing knowledge and collaboration between companies, academic societies, and patient advocacy groups	3.3%	4.7%
3-1 The absolute number of players (academic societies and companies) involved in development and clinical trials is small 3.3% 7.0% 3-2 The number of patients is small, making it difficult to recruit patients for clinical trials 8.2% 4.7% 3-3 Lack of human resources for development and clinical trials/lack of training programs 16.4% 14.0% 3-4 There are limited means of raising funds for development and clinical trials 27.9% 20.9% 4-1 The development and clinical trial environment for new modalities (gene therapy, regenerative medicine, etc.) is insufficient 11.5% 9.3% 4-2 Difficulty in manufacturing new modalities for development and clinical trials (gene therapy, regenerative medicine, etc.) 1.6% 0.0% 4-4 Insufficient quantity or quality of clinical data available for development 1.6% 0.0% 4-5 Lack of cooperation from clinician and patients in obtaining clinical data 1.6% 0.0% 4-6 Compared to other countries, Japan is lagging in adopting and utilizing cutting-edge development methods, 5-1 Deregulation (investment protection/fundraising/human resource preferential treatment, promotion of secondary data use) and system development are lagging 0.0% 0.0% 6.6% 7.0%	2-2 Opportunities for patients to participate in clinical trials are limited	0.0%	0.0%
3-2 The number of patients is small, making it difficult to recruit patients for clinical trials 8.2% 4.7% 3-3 Lack of human resources for development and clinical trials/lack of training programs 16.4% 14.0% 3-4 There are limited means of raising funds for development and clinical trials 27.9% 20.9% 4-1 The development and clinical trial environment for new modalities (gene therapy, regenerative medicine, etc.) is insufficient 1.6% 9.3% 4-2 Difficulty in manufacturing new modalities for development and clinical trials (gene therapy, regenerative medicine, etc.) 1.6% 0.0% 4-3 Difficulty in searching for clinical data available for development 1.6% 0.0% 4-4 Insufficient quantity or quality of clinical data available for development 1.6% 0.0% 4-5 Lack of cooperation from clinicians and patients in obtaining clinical data 1.6% 0.0% 4-6 Compared to other countries, Japan is lagging in adopting and utilizing cutting-edge development methods 0.0% 0.0% 5-1 Deregulation (investment protection/fundraising/human resource preferential treatment, promotion of secondary data use) and system development are lagging 6.6% 7.0%	2-3 Attractive ecosystem for development and clinical trials (people, funds, technology, systems) / Few bases	6.6%	11.6%
3-3 Lack of human resources for development and clinical trials/lack of training programs 16.4% 3-4 There are limited means of raising funds for development and clinical trials 27.9% 4-1 The development and clinical trial environment for new modalities (gene therapy, regenerative medicine, etc.) is insufficient 11.5% 9.3% 4-2 Difficulty in manufacturing new modalities for development and clinical trials (gene therapy, regenerative medicine, etc.) 1.6% 2.3% 4-2 Difficulty in manufacturing new modalities for development and clinical trials (gene therapy, regenerative medicine, etc.) 1.6% 0.0% 4-3 Difficulty in searching for clinical trial information 0.0% 0.0% 0.0% 4-4 Insufficient quantity or quality of clinical data available for development 1.6% 0.0% 4-5 Lack of cooperation from clinicians and patients in obtaining clinical data 1.6% 0.0% 4-6 Compared to other countries, Japan is lagging in adopting and utilizing cutting-edge development methods 0.0% 0.0% 5-1 Deregulation (investment protection/fundraising/human resource preferential treatment, promotion of secondary data use) and system development are lagging 6.6% 7.0%	3-1 The absolute number of players (academic societies and companies) involved in development and clinical trials is small	3.3%	7.0%
3-4 There are limited means of raising funds for development and clinical trials 27.9% 20.9% 4-1 The development and clinical trial environment for new modalities (gene therapy, regenerative medicine, etc.) is insufficient 11.5% 9.3% 4-2 Difficulty in manufacturing new modalities for development and clinical trials (gene therapy, regenerative medicine, etc.) 1.6% 2.3% 4-2 Difficulty in manufacturing new modalities for development and clinical trials (gene therapy, regenerative medicine, etc.) 1.6% 0.0% 4-3 Difficulty in searching for clinical trial information 0.0% 0.0% 0.0% 4-4 Insufficient quantity or quality of clinical data available for development 1.6% 0.0% 4-5 Lack of cooperation from clinicians and patients in obtaining clinical data 1.6% 0.0% 4-6 Compared to other countries, Japan is lagging in adopting and utilizing cutting-edge development methods 0.0% 0.0% 5-1 Deregulation (investment protection/fundraising/human resource preferential treatment, promotion of secondary data use) and system development are lagging 6.6% 7.0%	3-2 The number of patients is small, making it difficult to recruit patients for clinical trials	8.2%	4.7%
4-1 The development and clinical trial environment for new modalities (gene therapy, regenerative medicine, etc.) is insufficient 11.5% 9.3% 4-2 Difficulty in manufacturing new modalities for development and clinical trials (gene therapy, regenerative medicine, etc.) 1.6% 2.3% 4-3 Difficulty in searching for clinical trial information 0.0% 0.0% 0.0% 4-4 Insufficient quantity or quality of clinical data available for development 1.6% 0.0% 0.0% 4-5 Lack of cooperation from clinician and patients in obtaining clinical data 1.6% 0.0% 0.0% 4-6 Compared to other countries, Japan is lagging in adopting and utilizing cutting-edge development methods 0.0% 0.0% 0.0% 5-1 Deregulation (investment protection/fundraising/human resource preferential treatment, promotion of secondary data use) and system development are lagging 6.6% 7.0%	3-3 Lack of human resources for development and clinical trials/lack of training programs	16.4%	14.0%
4-2 Difficulty in manufacturing new modalities for development and clinical trials (gene therapy, regenerative medicine, etc.) 1.6% 2.3% 4-3 Difficulty in searching for clinical trial information 0.0% 0.0% 4-4 Insufficient quantity or quality of clinical data available for development 1.6% 0.0% 4-5 Lack of cooperation from clinicians and patients in obtaining clinical data 1.6% 0.0% 4-6 Compared to other countries, Japan is lagging in adopting and utilizing cutting-edge development methods 0.0% 0.0% 5-1 Deregulation (investment protection/fundraising/human resource preferential treatment, promotion of secondary data use) and system development are lagging 6.6% 7.0%	3-4 There are limited means of raising funds for development and clinical trials	27.9%	20.9%
4-3 Difficulty in searching for clinical trial information 0.0% 0.0% 4-4 Insufficient quantity or quality of clinical data available for development 1.6% 0.0% 4-5 Lack of cooperation from clinicians and patients in obtaining clinical data 1.6% 0.0% 4-6 Compared to other countries, Japan is lagging in adopting and utilizing cutting-edge development methods 0.0% 0.0% 5-1 Deregulation (investment protection/fundraising/human resource preferential treatment, promotion of secondary data use) and system development are lagging 0.0% 7.0%	4-1 The development and clinical trial environment for new modalities (gene therapy, regenerative medicine, etc.) is insufficient	11.5%	9.3%
4-4 Insufficient quantity or quality of clinical data available for development 1.6% 0.0% 4-5 Lack of cooperation from clinicians and patients in obtaining clinical data 1.6% 0.0% 4-6 Compared to other countries, Japan is lagging in adopting and utilizing cutting-edge development methods 0.0% 0.0% 5-1 Deregulation (investment protection/fundraising/human resource preferential treatment, promotion of secondary data use) and system development are lagging 0.6% 7.0%	4-2 Difficulty in manufacturing new modalities for development and clinical trials (gene therapy, regenerative medicine, etc.)	1.6%	2.3%
4-5 Lack of cooperation from clinicians and patients in obtaining clinical data 1.6% 0.0% 4-6 Compared to other countries, Japan is lagging in adopting and utilizing cutting-edge development methods 0.0% 0.0% 5-1 Deregulation (investment protection/fundraising/human resource preferential treatment, promotion of secondary data use) and system development are lagging 0.6% 7.0%	4-3 Difficulty in searching for clinical trial information	0.0%	0.0%
4-6 Compared to other countries, Japan is lagging in adopting and utilizing cutting-edge development methods 0.0% 0.0% 5-1 Deregulation (investment protection/fundraising/human resource preferential treatment, promotion of secondary data use) and system development are lagging 0.0% 0.0%	4-4 Insufficient quantity or quality of clinical data available for development	1.6%	0.0%
5-1 Deregulation (investment protection/fundraising/human resource preferential treatment, promotion of secondary data use) and system development are lagging 6.6% 7.0%	4-5 Lack of cooperation from clinicians and patients in obtaining clinical data	1.6%	0.0%
promotion of secondary data use) and system development are lagging 0.0% 7.0%		0.0%	0.0%
		6.6%	7.0%
		1.6%	2.3%

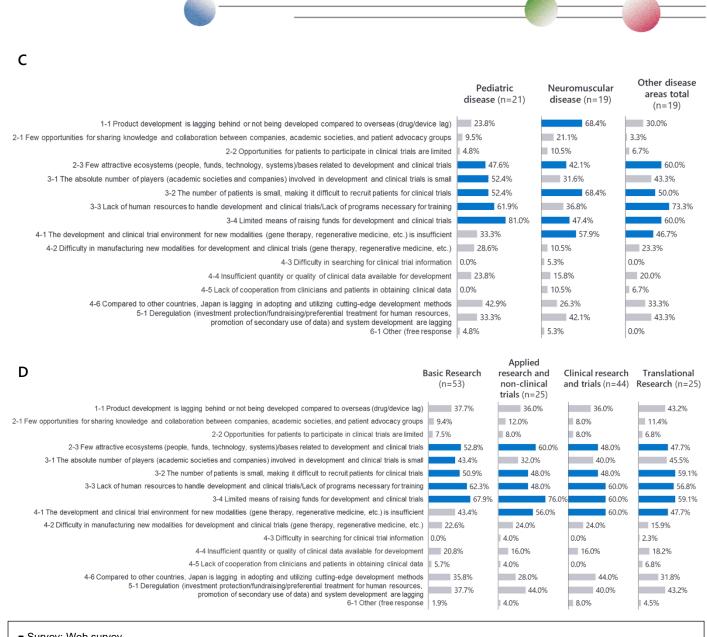
C	Paediatric diseases (n=21)	Neuromuscular diseases (n=19)	Other disease areas total (n=19)
1-1 Product development is lagging or not being developed compared to overseas (drug/device lag)	0.0%	26.3%	10.0%
2-1 There are few opportunities for sharing knowledge and collaboration between companies, academic societies, and patient advocacy groups	9.5%	0.0%	0.0%
2-2 Opportunities for patients to participate in clinical trials are limited	0.0%	0.0%	0.0%
2-3 Attractive ecosystem for development and clinical trials (people, funds, technology, systems) / Few bases	0.0%	5.3%	13.3%
3-1 The absolute number of players (academic societies and companies) involved in development and clinical trials is small	4.8%	5.3%	6.7%
3-2 The number of patients is small, making it difficult to recruit patients for clinical trials	4.8%	15.8%	3.3%
3-3 Lack of human resources for development and clinical trials/lack of training programs	23.8%	10.5%	10.0%
3-4 There are limited means of raising funds for development and clinical trials	42.9%	15.8%	23.3%
4-1 The development and clinical trial environment for new modalities (gene therapy, regenerative medicine, etc.) is insufficient	9.5%	10.5%	16.7%
4-2 Difficulty in manufacturing new modalities for development and clinical trials (gene therapy, regenerative medicine, etc.)	0.0%	0.0%	3.3%
4-3 Difficulty in searching for clinical trial information	0.0%	0.0%	0.0%
4-4 Insufficient quantity or quality of clinical data available for development	0.0%	0.0%	3.3%
4-5 Lack of cooperation from clinicians and patients in obtaining clinical data	0.0%	0.0%	3.3%
	0.0%	0.0%	0.0%
5-1 Deregulation (investment protection/fundraising/human resource preferential treatment, promotion of secondary data use) and system development are lagging	4.8%	5.3%	6.7%
	0.0%	5.3%	0.0%

D	Basic Research (n=53)	Applied research and non-clinical trials (n=25)	Clinical research and trials (n=44)	Translational Research (n=25)
1-1 Product development is lagging or not being developed compared to overseas (drug/device la	ag) 📕 7.5%	8.0%	15.9%	4.0%
2-1 There are few opportunities for sharing knowledge and collaboration between companies, academic societies, and patient advocacy group	ps 1.9%	4.0%	2.3%	0.0%
2-2 Opportunities for patients to participate in clinical trials are limit	ed 0.0%	0.0%	0.0%	0.0%
2-3 Attractive ecosystem for development and clinical trials (people, funds, technology, systems) / Few bas	es 🗾 7.5%	8.0%	11.4%	16.0%
3-1 The absolute number of players (academic societies and companies) involved in development and clinical trials is sn	nall 5.7%	0.0%	4.5%	4.0%
3-2 The number of patients is small, making it difficult to recruit patients for clinical tri-	als 9.4%	4.0%	6.8%	4.0%
3-3 Lack of human resources for development and clinical trials/lack of training progra	ms 15.1%	12.0%	15.9%	16.0%
3-4 There are limited means of raising funds for development and clinical tri	als 30.2%	6 32.09	6 22.7%	24.0%
4-1 The development and clinical trial environment for new modalities (gene therapy, regenerative medicine, etc.) is insufficient	ent 🗾 11.3%	16.0%	11.4%	16.0%
4-2 Difficulty in manufacturing new modalities for development and clinical trials (gene therapy, regenerative medicine, et	c.) 1.9%	4.0%	0.0%	0.0%
4-3 Difficulty in searching for clinical trial informat	on 0.0%	0.0%	0.0%	0.0%
4-4 Insufficient quantity or quality of clinical data available for development	ent 1.9%	0.0%	2.3%	0.0%
4-5 Lack of cooperation from clinicians and patients in obtaining clinical da	ata 1.9%	0.0%	0.0%	0.0%
4-6 Compared to other countries, Japan is lagging in adopting and utilizing cutting-edge development metho		0.0%	0.0%	0.0%
5-1 Deregulation (investment protection/fundraising/human resource preferential treatmen promotion of secondary data use) and system development are lagg		8.0%	4.5%	12.0%
6-1 Other (free response		4.0%	2.3%	4.0%

- Survey: Web survey
- Question: Please select the top 5 challenges you feel are most challenging regarding development and clinical trials (ranked)
- 70 clinical researchers (basic and applied) and clinical researchers (development)

Figure 4.1.2-8: Challenges in development and clinical trials – Top 5 Selection Results : A all segments ·B by occupation ·C by disease research area ·D by specialty





Survey: Web survey

Question: Please select the top 5 challenges you feel are most challenging regarding development and clinical trials (ranked)

■ 70 clinical researchers (basic and applied) and clinical researchers (development)

In Japan, when it comes to R&D and the social implementation of new technologies/systems, social consensus tends to take precedence, and there is a tendency for insufficient discussion on 'what should be prioritized for the patient in front of us.' Japanese society is one in which risk and challenge cannot be tolerated and there is strong pressure to conform, but if patients and their families can tolerate the risks, there should be a system in place that allows them to receive treatment and other assistance on an exceptional basis. This culture of placing too much emphasis on the ethical values of society in general over the will of the patient is an obstacle to R&D and clinical trials in Japan. (Clinical researcher (basic and applied) / Other hereditary disease)

The construction of patient data registries has not progressed due to high hurdles in academic cliques and research ethics. For example, registries for disorders of sex development already exist in about 20 countries in the EU, but Japan does not yet have one.

(Clinical researcher (basic and applied) / Pediatrics)

⁶⁶ There is a **shortage of human resources and training programs** to carry out basic and applied research and working at a university inevitably means a large amount of administrative and clerical work unrelated to rare diseases, so the limited number of people who are hubs in the field of rare diseases need to have the time and financial flexibility to take on this challenge.

(Clinical researcher (basic and applied) / Pediatrics)

•• Obtaining clinical samples is difficult and the related procedures are complicated. When obtaining clinical samples from other facilities, they must go through the IRB, which has strict document submission requirements and even when discussing with overseas researchers and companies, the strictness of the document submission requirements can become an obstacle and cause negotiations to stall.

In addition, there is a lack of information exchange between different industries regarding what seeds (basic research results and technologies that lead to the development of new treatments and medical technologies) are desired, **making** *it difficult to flexibly identify and prioritize research areas based on the business environment*. There should be more opportunities for exchange with healthcare professionals as the hub.

(Clinical researcher (development) / Endocrinology and Metabolic Disease)

⁶⁶ The biggest challenge in the world of basic and applied research is always how to obtain research funds and gather colleagues to work with.

I feel that the lack of understanding of rare diseases among young people is leading to a shortage of human resources, so I feel that it is necessary to convey the need for development of diagnosis and treatment for rare diseases through lectures and speeches, but as a prerequisite for doing this, I would like the government to actively provide research funding for rare diseases. On the other hand, national research institutes have no university affiliations, so it is difficult to sustain a sustainable supply of young researchers, and even institutes with abundant budgets that are in urban areas have difficulty securing human resources.

(Clinical researcher (basic and applied) / neuromuscular disease)

⁵⁵ The insufficient environment for new modalities makes it difficult to secure materials, which is an impediment to the development of new modalities.

Specifically, while there seem to be few facilities in Japan that manufacture cells for cell therapy, in Europe and the United States, GMP manufacturing facilities/CPCs are attached to the medical schools of leading universities. (Clinical researcher (basic and applied) / neuromuscular disease)

As Japan's domestic economy and population shrinks and the number of domestic bases for foreign companies decreases, it is becoming unclear to foreign companies who can concretely discuss domestic development, and this situation is **accelerating drug loss**.

(Clinical researcher (basic and applied) / neuromuscular disease)

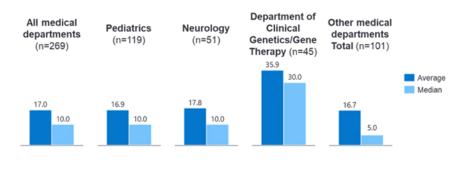
Compared to cancer, the national budget and personnel for research, development, and clinical practice are small, and there is **a lack of human resources, educators, and programs** in particular, which means there is no system or foundation for systematically allocating and training human resources, resulting in a lack of speed compared to Europe and the United States. In addition to educating specialists, we believe that we need to fundamentally reconsider not only the way in which diversity and genetics education is provided in primary education. (Clinical researcher (development) / All other hereditary disease) **Information on the progress of development should be systematically organized and made more accessible to patients and healthcare professionals.** This could encourage patients to seek medical treatment and motivate them to go to the hospital, which could ultimately lead to an improvement in the diagnosis rate. (Other HCPs (Genetic counselors and nurses) / Department of Clinical Genetics and Gene Therapy)

I am involved in a clinical trial for achondroplasia, but it is **extremely difficult to recruit subjects who meet the conditions**. One of the reasons is that the subjects are not fully informed. If there was a system where clinical trial information was centrally collected and it was possible to narrow down clinical trial information and subject information that meets the conditions, it would be convenient for both healthcare professionals and subjects. Also, since it is often difficult to recruit subjects even if a drug that has already been approved in the US or EU is approved in Japan later, it is desirable to accelerate participation in international joint clinical trials. (Specialist / Pediatrics)

Because rare diseases affect only a small number of patients, there is little economic incentive for pharmaceutical companies, and the low motivation of industry is a clear barrier. (Clinical researchers (basic and applied) / Endocrinology and Metabolic Disease)

4.1.4 Challenges in diagnosis

Figure 4.1.4-1: Number of patients with suspected rare diseases referred to specialists/year



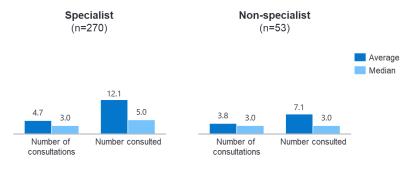
*Analysis results excluding responses of 200 or more as outliers

Survey: Web survey

■Question: Q6 If you answered '1. Responsible for making diagnostic and treatment decisions as a clinical doctor (specialist/quasi-specialist)' to the question about your occupation, please tell us how many patients with suspected rare diseases you are referred to each year (numeric answer)

■Subjects: 269 specialists

Figure 4.1.4-2: Number of consultations related to diagnosis/year



*Analysis results excluding responses of 100 or more as outliers

Survey: Web survey

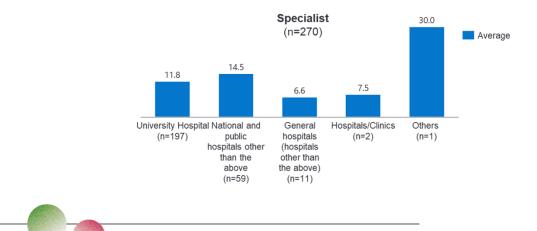
Α

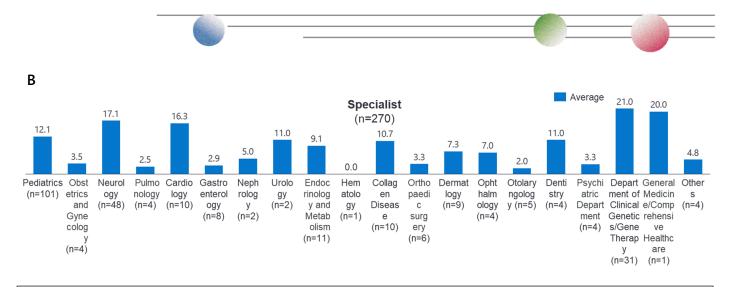
■Question: Regarding consultations related to rare disease diagnoses, how many times per year do you consult with others? (Answer with a number)

■Subjects: 302 specialists and non-specialists

Figure 4.1.4-3: Number of rare disease diagnoses consulted by specialists/year

- A by affiliated institution \cdot B by medical department





■Survey: Web survey

■Question: Regarding consultations related to the diagnosis of rare diseases, please answer how many times per year you receive consultations (numeric answer)

■Subjects: 270 specialists

Figure 4.1.4-4: Duration and Number of Facilities Involved in Reaching a Definitive Diagnosis

- A: Overall, B: by medical department

Α

	Less than	Less than	More than	More than	
	6 months	1 year	1 year	3 years	Total
1 facility	19.6%	4.5%	5.5%	1.5%	31.2%
2 facilities	13.6%	15.6%	11.1%	3.5%	43.7%
3 facilities	0.5%	3.5%	6.5%	4.0%	14.6%
4 facilities	2.0%	1.5%	2.0%	5.0%	10.6%
Total	35.7%	25.1%	25.1%	14.1%	100.0%

В

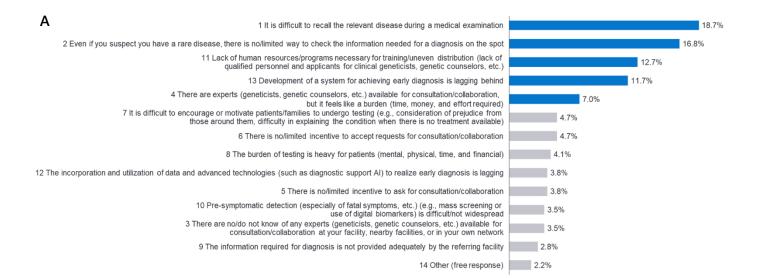
		Pediat (n=11						Neurol (n=5				
	Less than	Less than	More than	More than			Less than	Less than	More than	More than		
	6 months	1 year	1 year	3 years	Total		6 months	1 year	1 year	3 years	Total	
1 facility	25.6%	2.4%	8.5%	2.4%	39.0%	1 facility	2.9%	0.0%	0.0%	0.0%		2.9%
2 facilities	14.6%	12.2%	12.2%	2.4%	41.5%	2 facilities	8.8%	23.5%	11.8%	2.9%		47.1%
3 facilities	0.0%	1.2%	7.3%	4.9%	13.4%	3 facilities	0.0%	5.9%	14.7%	2.9%		23.5%
4 facilities and above	1.2%	1.2%	0.0%	3.7%	6.1%	4 facilities and above	2.9%	2.9%	11.8%	8.8%		26.5%
Total	41.5%	17.1%	28.0%	13.4%	100.0%	Total	14.7%	32.4%	38.2%	14.7%	1	00.0%
		Departm Clinic						Other me				
		Genetics, Therapy ((n=45)					departm Total (n=	=101)			
		Therapy (Less than	(n=45) More than	More than			Less than	Total (n=	= 101) More than	More than		
	6 months	Therapy (Less than 1 year	(n=45) More than 1 year	3 years	Total		6 months	Total (n= Less than 1 year	=101) More than 1 year	3 years	Total	
1 facility	6 months 17.4%	Therapy (Less than 1 year 4.3%	(n=45) More than 1 year 8.7%	3 years 4.3%	34.8%	1 facility	6 months 21.7%	Total (n= Less than 1 year 10.0%	= 101) More than 1 year 3.3%	3 years 0.0%		35.0%
1 facility 2 facilities	6 months 17.4% 13.0%	Therapy (Less than 1 year 4.3% 8.7%	(n=45) More than 1 year 8.7% 8.7%	3 years 4.3% 4.3%	34.8% 34.8%	1 facility 2 facilities	6 months 21.7% 15.0%	Total (n= Less than 1 year 10.0% 18.3%	= 101) More than 1 year 3.3% 10.0%	3 years 0.0% 5.0%		48.3%
1 facility 2 facilities 3 facilities	6 months 17.4% 13.0% 0.0%	Therapy (Less than 1 year 4.3% 8.7% 8.7%	(n=45) More than 1 year 8.7% 8.7% 0.0%	3 years 4.3% 4.3% 4.3%	34.8% 34.8% 13.0%	1 facility 2 facilities 3 facilities	6 months 21.7% 15.0% 1.7%	Total (n= Less than 1 year 10.0% 18.3% 3.3%	= 101) More than 1 year 3.3% 10.0% 3.3%	3 years 0.0% 5.0% 3.3%		48.3% 11.7%
1 facility 2 facilities	6 months 17.4% 13.0%	Therapy (Less than 1 year 4.3% 8.7%	(n=45) More than 1 year 8.7% 8.7% 0.0% 0.0%	3 years 4.3% 4.3% 4.3% 8.7%	34.8% 34.8%	1 facility 2 facilities	6 months 21.7% 15.0%	Total (n= Less than 1 year 10.0% 18.3% 3.3% 0.0%	=101) More than 1 year 3.3% 10.0% 3.3% 0.0%	3 years 0.0% 5.0% 3.3% 3.3%		48.3%

■Survey: Web survey

■Question: Please tell us how long it took for the most recent rare disease patient to be diagnosed after their first visit, and to which medical institution they were referred after their first visit (select one)

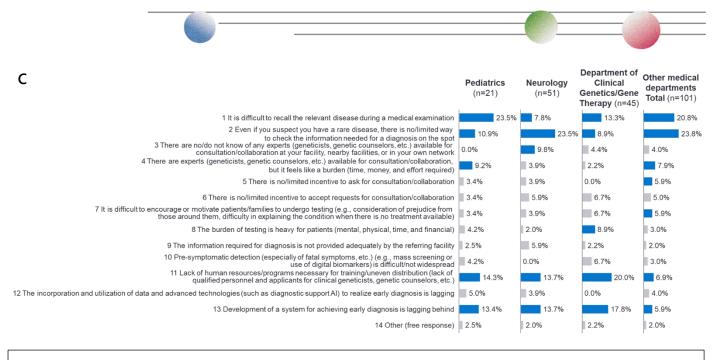
■Subjects: 270 specialists

Figure 4.1.4-5: Problems in diagnosis – Top selection result : A all segments •B by occupation •C by medical department



	Specialist (n=270)	Non-specialist (n=53)	Other HCPs (genetic counselors, nurses) (n=23)
1 It is difficult to recall the relevant disease during a medical examination	17.8%	26.4%	17.4%
2 Even if you suspect you have a rare disease, there is no/limited way	16.7%	28.3%	13.0%
to check the information needed for a diagnosis on the spot 3 There are no/do not know of any experts (geneticists, genetic counselors, etc.) available for consultation/collaboration at your facility, nearby facilities, or in your own network	3.3%	1.9%	4.3%
4 There are experts (geneticists, genetic counselors, etc.) available for consultation/collaboration, but it feels like a burden (time, money, and effort required)	7.4%	5.7%	0.0%
5 There is no/limited incentive to ask for consultation/collaboration	3.7%	3.8%	4.3%
6 There is no/limited incentive to accept requests for consultation/collaboration	5.6%	0.0%	0.0%
7 It is difficult to encourage or motivate patients/families to undergo testing (e.g., consideration of prejudice from those around them, difficulty in explaining the condition when there is no treatment available)	4.4%	1.9%	8.7%
8 The burden of testing is heavy for patients (mental, physical, time, and financial)	3.7%	5.7%	8.7%
9 The information required for diagnosis is not provided adequately by the referring facility	2.6%	3.8%	4.3%
10 Pre-symptomatic detection (especially of fatal symptoms, etc.) (e.g., mass screening or use of digital biomarkers) is difficult/not widespread	2.6%	3.8%	8.7%
11 Lack of human resources/programs necessary for training/uneven distribution (lack of qualified personnel and applicants for clinical geneticists, genetic counselors, etc.)	12.6%	11.3%	26.1%
2 The incorporation and utilization of data and advanced technologies (such as diagnostic support AI) to realize early diagnosis is lagging	4.4%	0.0%	0.0%
13 Development of a system for achieving early diagnosis is lagging behind	13.0%	7.5%	0.0%
14 Other (free response)	2.2%	2.2%	4.3%

В

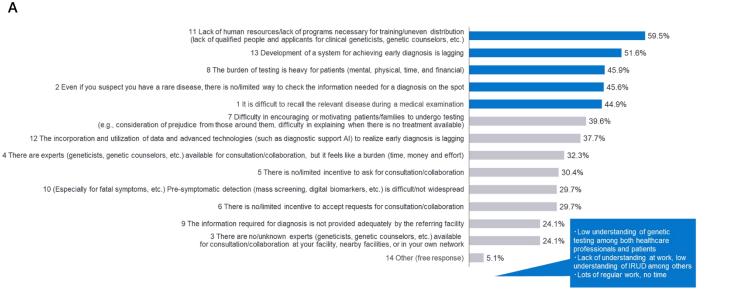


Survey: Web survey

Α

- ■Question: Please answer by selecting the top 5 most pressing challenges related to the diagnosis (ranking format)
- ■Subjects: 316 specialists, non-specialists, and other HCPs (genetic counselors and nurses)

Figure 4.1.4-6: Problems in diagnosis - Top 5 Selection Results : A all segments ·B by occupation ·C by medical department





Survey: Web survey

■Question: Please select the top 5 most pressing challenges you feel are related to diagnosis (ranking format)

■Subjects: 316 specialists, non-specialists, and other HCPs (genetic counselors and nurses)

There is still room for improvement in diagnosis in the field of pediatric medicine, and ideally, diagnosis would be made more accurately and quickly than it is now. Since diseases can have irreversible adverse effects on the growth of pediatric patients and on the formation of their personalities through life with their families, **early intervention by medical institutions and support for creating an environment where parents can feel at ease when dealing with pediatric patients should be provided**.

(Specialist / Pediatrics)

To reduce the number of facilities and the time it takes to reach a definitive diagnosis, it is necessary to make it easy for cases to accumulate and to provide good access for patients. It is unrealistic to make a definitive diagnosis at

the first visit, but it is desirable to reach a specialized hospital such as a university hospital once and have the diagnosis confirmed there. To reduce the burden on patients, it is important to avoid repeated transfers to hospitals over a wide area, and the aim should be to complete the diagnosis at a specialized facility. In addition, **to lower the psychological hurdle for referring doctors, it is essential to clearly indicate where facilities and specialists specializing in rare disease medicine are located, as well as the referral criteria**.

(Specialist / Collagen Disease)

I feel that the high hurdles in terms of knowledge, technology, and cost (cost/effort) for both doctors and patients when it comes to genetic testing are an issue. I think it is important to have patients understand the advantages and disadvantages of genetic testing before referring them to a hospital that can perform the test, but especially in urban areas where hospital performance is less clear than in rural areas, there is no guarantee that the hospital has a doctor with sufficient knowledge and experience in genetic testing, so it is not possible to refer patients easily or irresponsibly. Furthermore, it is rare to receive feedback on the patient's test results from the hospital, and even if an appropriate diagnosis is not made, it is difficult to grasp the situation and it is not possible to get the diagnosis back on track. Therefore, I feel that there is a need to visualize information on doctors/facilities with sufficient knowledge of genetic testing and genetic diseases that can be tested at each hospital, and a platform to share test results between specialists and non-specialists.

(Non-specialist / Neurology)

There is no/limited access to the information necessary for diagnosis at the time of consultation, and patients must rely on information provided by websites, papers, and pharmaceutical companies that they find by trial and error. I feel that the lack of evidence at the time of diagnosis is an issue. (Non-specialist / Pediatrics)

Patients feel burdened by the tests, and it is difficult to motivate them to undergo the tests. In fact, when patients undergo the tests, they must pay for the treatment themselves, which places a heavy financial and mental burden on them.

(Other HCPs (genetic counselors and nurses) / Department of Clinical Genetics and Gene Therapy)

Even if you consult with IRUD, it takes a year for the test results to come out, so as a genetic counselor, I have seen the distress that patients are experiencing. The testing company and others are dealing with the situation carefully, but from the patient's perspective, more timely action is needed. (Other HCPs (genetic counselors, nurses) / Department of Clinical Genetics and Gene Therapy)

For doctors who have just started working with rare diseases, **not only ideals and motivation are important**, **but also incentives related to remuneration, time and workload**. What young doctors today are looking for is to work efficiently and fairly as specialists, and degrees and titles themselves are not very motivating.

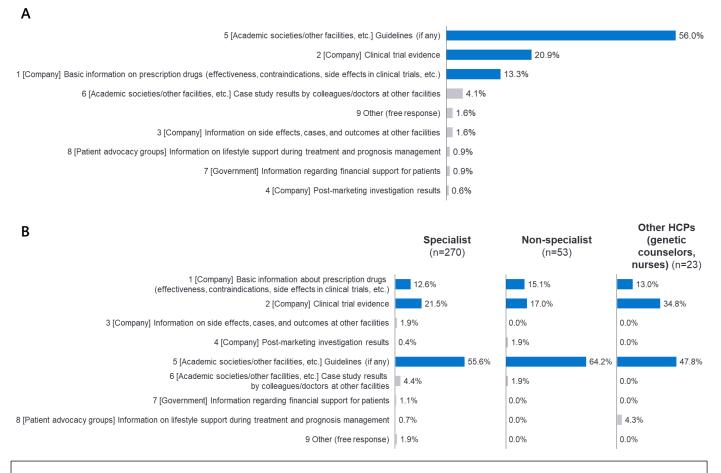
(Clinical researcher (development) / neuromuscular disease)

4.1.5 Challenges in treatment and prognosis management

Figure 4.1.5-1: Types of information collected and used in treatment and prognosis management –

Top selection result :

A all segments ·B by occupation



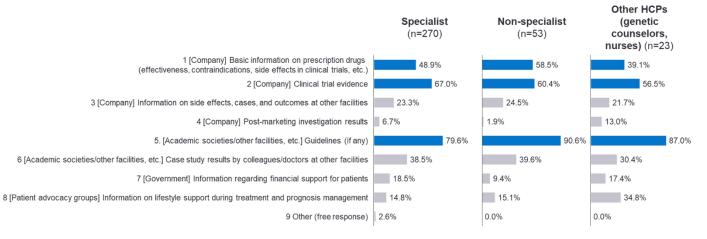
Survey: Web survey

■Question: Please answer up to the top three types of information that you consider important to collect and use in treatment and prognosis management (ranking format)

Figure 4.1.5-2: Types of information collected and used in treatment and prognosis management – Top 3 Selection Results : A all segments ·B by occupation





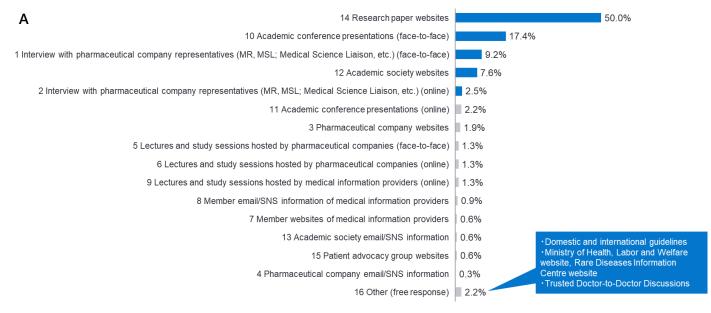


■Survey: Web survey

■Question: Please answer the top three types of information that you consider important to collect and use in treatment and prognosis management (ranking format)

Figure 4.1.5-3: Sources of information collected and utilized in treatment and prognosis management – Top selection results :

A all segments ·B by occupation



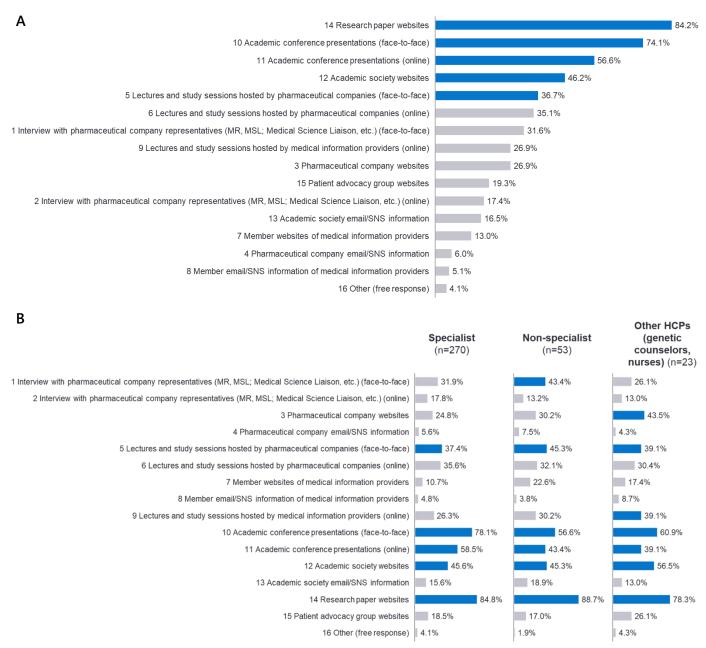
Other HCPs (genetic Specialist Non-specialist (n=270) (n=53) counselors. nurses) (n=23) 1 Interview with pharmaceutical company representatives (MR, MSL; Medical Science Liaison, etc.) (face-to-face) 📕 8.9% 17.0% 17.4% 2 Interview with pharmaceutical company representatives (MR, MSL; Medical Science Liaison, etc.) (online) 2.2% 3.8% 0.0% 0.0% 3 Pharmaceutical company websites 1.9% 1.9% 4 Pharmaceutical company email/SNS information 0.4% 0.0% 0.0% 5 Lectures and study sessions hosted by pharmaceutical companies (face-to-face) 1.5% 0.0% 0.0% 0.0% 6 Lectures and study sessions hosted by pharmaceutical companies (online) 0.7% 3.8% 7 Member websites of medical information providers 0.4% 1.9% 0.0% 8 Member email/SNS information of medical information providers 0.0% 1.1% 0.0% 9 Lectures and study sessions hosted by medical information providers (online) 1.5% 3.8% 4.3% 10 Academic conference presentations (face-to-face) 18.1% 11.3% 17.4% 11 Academic conference presentations (online) 2.6% 0.0% 0.0% 13.2% 12 Academic society websites 6.3% 8.7% 13 Academic society email/SNS information 0.7% 0.0% 0.0% 14 Research paper websites 51.1% 43.4% 43.5% 15 Patient advocacy group websites 0.4% 0.0% 4.3% 16 Other (free response) 2.2% 0.0% 4.3%

■Survey: Web survey

В

■Question: Please select your top 5 preferred sources (media/channels) of information to be collected and utilized in treatment and prognosis management (ranked)

Figure 4.1.5-4: Sources of information collected and utilized in treatment and prognosis management – Top 3 selection results : A all segments ·B by occupation

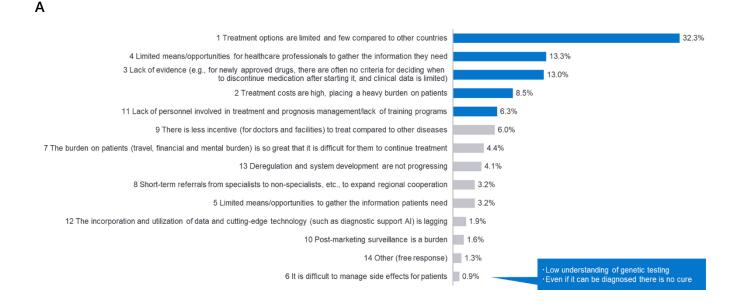


Survey: Web survey

■Question: Please select your top 5 preferred sources (channels) of information to be collected and utilized in treatment and prognosis management (ranked)

Figure 4.1.5-5: Challenges in treatment and prognosis management – Top selection results:

A all segments ·B by occupation



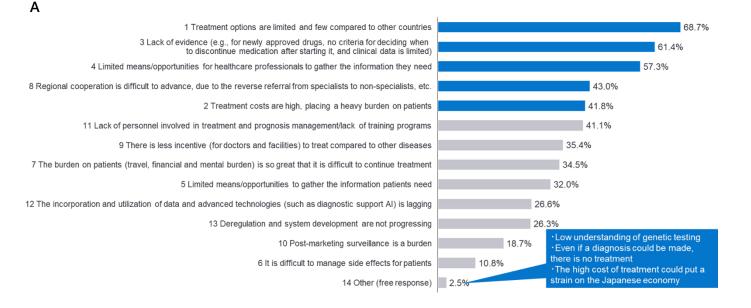
В	Specialist (n=270)	Non-specialist (n=53)	Other HCPs (genetic counselors, nurses) (n=23)
1 Treatment options are limited and few compared to other countries	32.6%	24.5%	43.5%
2 Treatment costs are high, placing a heavy burden on patients	8.9%	11.3%	4.3%
3 Lack of evidence (e.g., for newly approved drugs, no criteria for deciding when to discontinue medication after starting it, and clinical data is limited)	14.4%	5.7%	17.4%
4 Limited means/opportunities for healthcare professionals to gather the information they need	11.5%	22.6%	13.0%
5 Limited means/opportunities to gather the information patients need	3.0%	1.9%	4.3%
6 It is difficult to manage side effects for patients	1.1%	1.9%	0.0%
7 The burden on patients (travel, financial and mental burden) is so great that it is difficult to continue treatment	4.4%	1.9%	4.3%
8 Regional cooperation is difficult to advance, due to the reverse referral from specialists to non-specialists, etc.	3.0%	9.4%	0.0%
9 There is less incentive (for doctors and facilities) to treat compared to other diseases	6.3%	3.8%	0.0%
10 Post-marketing surveillance is a burden	1.9%	1.9%	0.0%
11 Lack of personnel involved in treatment and prognosis management/lack of training programs	4.8%	13.2%	4.3%
12 The incorporation and utilization of data and advanced technologies (such as diagnostic support AI) is lagging	2.2%	0.0%	0.0%
13 Deregulation and system development are not progressing	4.8%	1.9%	4.3%
14 Other (free response)	1.1%	0.0%	4.3%

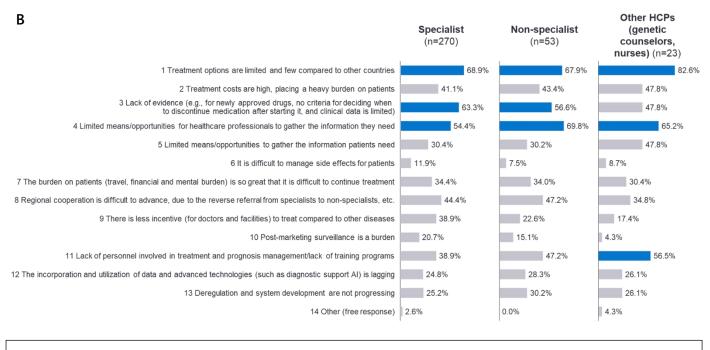
■Survey: Web survey

■Question: Please select the top 5 challenges you feel are most important in terms of treatment and prognosis management (ranking format) ■Subjects: 316 specialists, non-specialists, and other HCPs (genetic counselors and nurses)



A all segments ·B by occupation





Survey: Web survey

Question: Please select the top 5 challenges you feel are most challenging regarding treatment and prognosis management (ranking format)
 Subjects: 316 specialists, non-specialists, and other HCPs (genetic counselors and nurses)

General Because patient test data is personal information, it is not shared between facilities, and accessible actual clinical data is limited. A process and infrastructure are needed to determine diagnostic and treatment plans for specific patients based on shared evidence.

(Clinical researcher (development) / Endocrinology and Metabolic Disease)

I feel that there are many areas where disease-specific guidelines have not yet been established.
(Clinical researcher (development) / Immunodeficiency disease)

When a specialist refers a patient to a non-specialist, the **non-specialist may not accept the patient if the disease is highly specialized**. Pediatric diseases tend to be highly specialized, so many people find it difficult to deal with such referrals.

(Non-specialist / Pediatrics)

C There is a lack of knowledge about rare diseases even among healthcare professionals, which means that they are unable to provide guidance and advice to patients in a timely manner. As a result, cases are referred to the genetics department, which can place a heavy burden on certain individuals, so it is necessary to raise the level of knowledge among healthcare professionals, including doctors. At our hospital, a limited number of genetic counselors oversee all inquiries, but it seems that many of the inquiries are ones that doctors could have answered. (Other HCPs (genetic counselors, nurses) / Clinical genetics, genetics department)

Che high cost of rare disease treatment is an issue. If the disease is designated as intractable, the government provides subsidies, but it seems like a difficult topic when considering medical economics. I also feel that commuting to distant university hospitals is a burden on patients. Even if patients are examined at large hospitals, they return to their hometowns, so we need to strengthen cooperation systems, such as sharing information with local medical institutions that can provide treatment.

(Other HCPs (genetic counselors and nurses) / Department of Clinical Genetics and Gene Therapy)

When gathering information for treatment, most literature is in English, so the language barrier is a hurdle, making it **difficult to gather information and gain knowledge**, and ultimately increasing the workload of healthcare professionals.

(Specialist / Pediatrics)

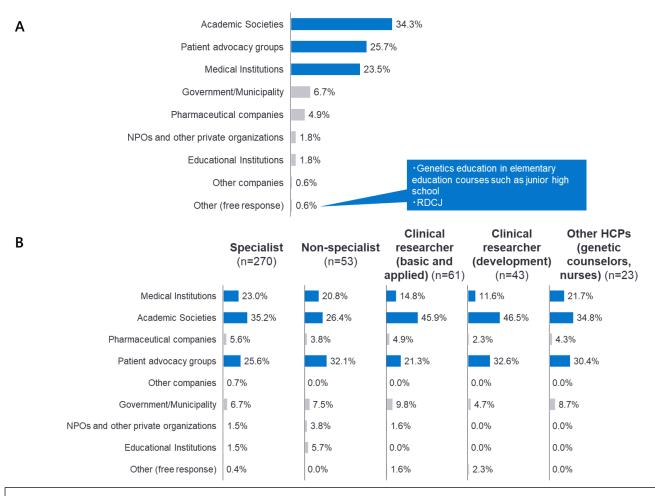
I feel that efforts regarding diagnostic and therapeutic drugs are lagging other countries. When I was having trouble dealing with a patient, I had the opportunity to contact a doctor in the United States directly, and in the United States, I was able to obtain new medicines and treat the patient quickly. In Japan, too, in research and development and clinical practice, I feel that a scheme is needed to smoothly incorporate new technologies and treatments once a certain period has been completed, based on the premise that rare diseases have a different criticality than other diseases.

(Specialist / Pediatrics)

4.1.6 Challenges in disease awareness activities

Figure 4.1.6-1: Effective organization for disease awareness activities (for patients and their families)

- Top selection results : A all segments ·B by occupation



Survey: Web survey

■Question: Please answer three options that you feel are effective in raising awareness about rare diseases (for patients and their families) (ranking format)

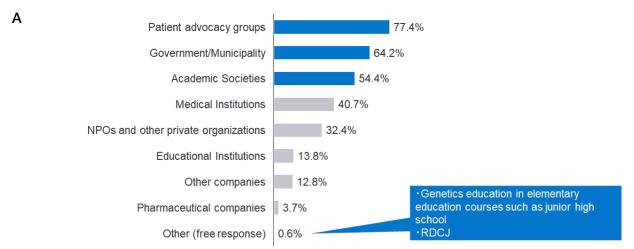
■Subjects: 327 specialists, non-specialists, clinical researchers (basic and applied), clinical researchers (development) and other HCPs (genetic counselors and nurses)

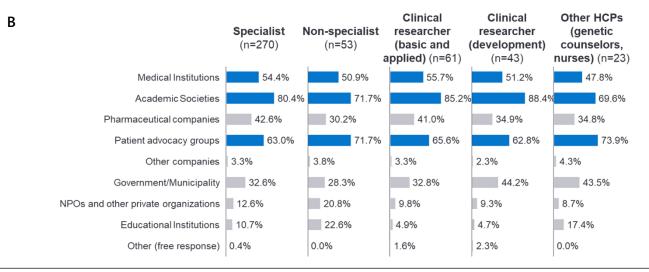
37



families) - Top 3 selection results :

A all segments ·B by occupation





Survey: Web survey

■Question: Please select three options that you feel are effective in raising awareness about rare diseases (for patients and their families) (ranking format)

■Subjects: 327 specialists, non-specialists, clinical researchers (basic and applied), clinical researchers (development) and other HCPs (genetic counselors and nurses)

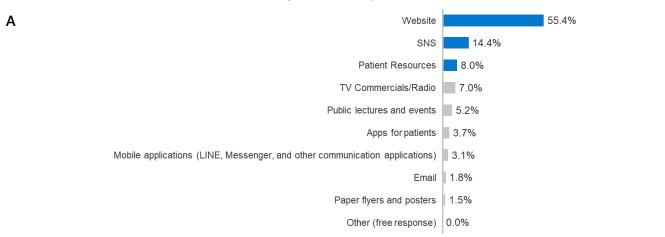
38



Figure 4.1.6-3: Effective media/channels for disease awareness activities (for patients and their

families) - Top selection results :

A all segments ·B by occupation



В	Specialist I (n=270)	Non-specialist (n=53)	Clinical researcher (basic and pplied) (n=61)	Clinical researcher (development) (n=43)	Other HCPs (genetic counselors, nurses) (n=23)
Website	56.3%		54.1%	48.8%	39.1%
Email	2.2%	0.0%	4.9%	7.0%	0.0%
Apps for patients	3.7%	3.8%	3.3%	2.3%	4.3%
Mobile apps (LINE, Messenger, and other communication apps used on mobile phones)	3.3%	3.8%	4.9%	4.7%	0.0%
SNS	12.2%	22.6%	13.1%	14.0%	21.7%
Paper flyers and posters	1.9%	0.0%	3.3%	4.7%	4.3%
Patient Resources	8.5%	5.7%	1.6%	9.3%	17.4%
TV Commercials/Radio	7.0%	15.1%	6.6%	2.3%	13.0%
Public lectures and events	4.8%	3.8%	8.2%	7.0%	0.0%
Other (free response)	0.0%	0.0%	0.0%	0.0%	0.0%

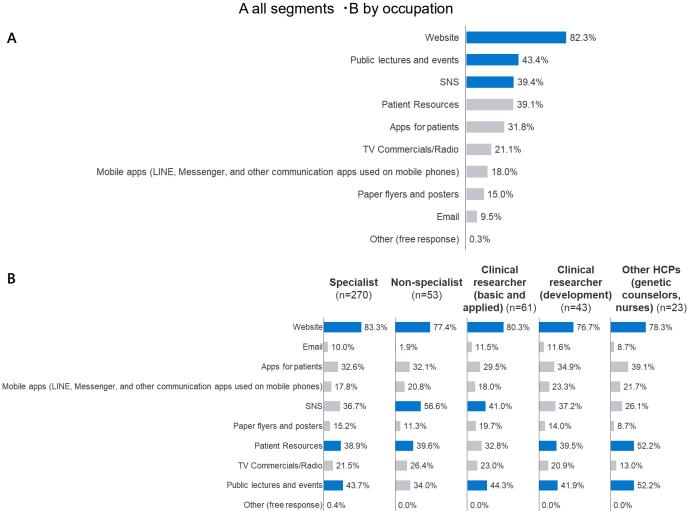
■Survey: Web survey

■Question: Please choose the three most effective media/channels for raising awareness about rare diseases (for patients and their families) (ranked)



Figure 4.1.6-4: Effective media/channels for disease awareness activities (for patients and their

families) – Top 3 selection results :



Survey: Web survey

■Question: Please choose the three most effective media/channels for raising awareness about rare diseases (for patients and their families) (ranked)

Figure 4.1.6-5: Effective organization for disease awareness activities (for healthcare professionals)

– Top selection results :

A all segments $\cdot B$ by occupation

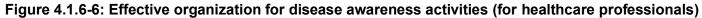
A Academic Societies	71.9%
Medical Institutions	15.6%
Pharmaceutical companies	5.2%
Patient advocacy groups	4.0%
Government/Municipality	2.1%
NPOs and other private organizations	0.6%
Educational Institutions	0.3%
Other companies	0.3%
Other (free response)	0.0%

В

SpecialistNon-specialist(n=270)(n=53)	researcher (basic and applied) (n=61)	researcher (development) (n=43)	(genetic counselors, nurses) (n=23)
Medical Institutions 14.4%	14.8%	11.6%	17.4%
Academic Societies 72.6% 67.9%	75.4%	76.7%	73.9%
Pharmaceutical companies 5.2% 5.7%	3.3%	4.7%	8.7%
Patient advocacy groups 3.7%	4.9%	7.0%	0.0%
Other companies 0.4% 0.0%	0.0%	0.0%	0.0%
Government/Municipality 2.6% 0.0%	1.6%	0.0%	0.0%
NPOs and other private organizations 0.7% 0.0%	0.0%	0.0%	0.0%
Educational Institutions 0.4% 0.0%	0.0%	0.0%	0.0%
Other (free response) 0.0% 0.0%	0.0%	0.0%	0.0%

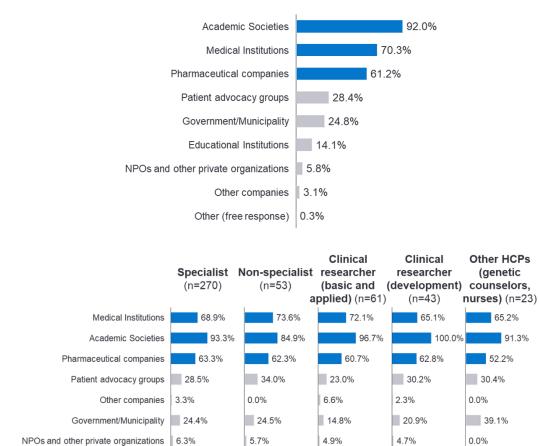
■Survey: Web survey

■Question: Please select three options that you feel are effective in raising awareness of rare diseases (for healthcare professionals) (ranking format)



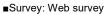
– Top 3 selection results :





В

Α



Educational Institutions

Other (free response) 0.4%

11.5%

■Question: Please select three options that you feel are effective in raising awareness of rare diseases (for healthcare professionals) (ranking format)

19.7%

1.6%

14.0%

0.0%

21.7%

0.0%

15.1%

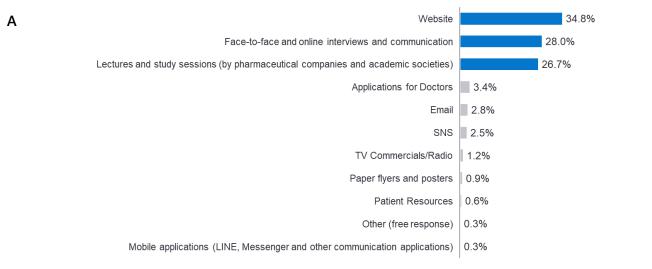
0.0%



Figure 4.1.6-7: Effective media/channels for disease awareness activities (for healthcare

professionals) – Top selection results :

A all segments ·B by occupation



	Specialist (n=270)	Non-specialist (n=53)	Clinical researcher (basic and applied) (n=61)	Clinical researcher (development) (n=43)	Other HCPs (genetic counselors, nurses) (n=23)
Face-to-face and online interviews and communication	30.9%	24.5%	20.0%	30.2%	27.3%
Website	35.1%	32.1%	33.3%	32.6%	40.9%
Email	2.7%	1.9%	8.3%	7.0%	0.0%
Apps for Doctors	2.3%	9.4%	5.0%	2.3%	4.5%
Mobile apps (LINE, Messenger, and other communication apps used on mobile phones)	0.0%	0.0%	0.0%	0.0%	0.0%
SNS	0.0%	1.9%	0.0%	2.3%	4.5%
Lectures and study sessions (by pharmaceutical companies and academic societies)	27.0%	30.2%	33.3%	25.6%	22.7%
Paper flyers and posters	1.2%	0.0%	0.0%	0.0%	0.0%
Patient Resources	0.8%	0.0%	0.0%	0.0%	0.0%
TV Commercials/Radio	1.2%	0.0%	0.0%	0.0%	4.5%
Other (free response)	0.4%	0.0%	1.7%	0.0%	0.0%

■Survey: Web survey

В

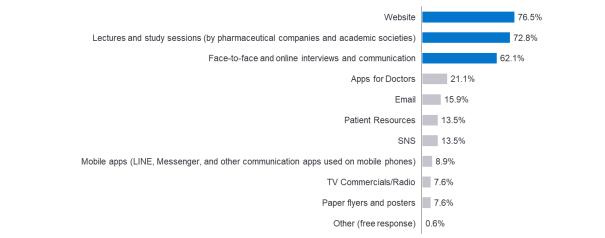
Question: Please choose the three most effective media/channels for raising awareness of rare diseases (for healthcare professionals) (ranked)

■Subjects: 327 specialists, non-specialists, clinical researchers (basic and applied), clinical researchers (development) and other HCPs (genetic counselors and nurses)

43

Figure 4.1.6-8: Effective media/channels for disease awareness activities (for healthcare professionals) – Top 3 selection results :

A all segments •B by occupation



Clinical Clinical Other HCPs Specialist Non-specialist researcher researcher (genetic (n=270) (development) (n=53) (basic and counselors, applied) (n=61) (n=43) nurses) (n=23) 57.4% 43.5% Face-to-face and online interviews and communication 64.6% 60.4% 58.1% 73.9% Website 79.5% 69.8% 77.0% 72.1% 16.7% 7.5% 21.3% 23.3% 8.7% Email 20.5% 26.4% 16.4% 18.6% 21.7% Apps for Doctors 13.0% Mobile apps (LINE, Messenger, and other communication apps used on mobile phones) 8.7% 7.5% 6.6% 11.6% SNS 10.6% 15.1% 11.5% 11.6% 17.4% Lectures and study sessions (by pharmaceutical companies and academic societies) 69.8% 78.3% 74.5% 81.1% Paper flyers and posters 7.6% 7.5% 9.8% 9.3% 8.7% Patient Resources 14.4% 13.2% 11.5% 14.0% 21.7% 13.0% 11.6% 11.3% TV Commercials/Radio 7.2% 8.2% Other (free response) 0.8% 0.0% 1.6% 0.0% 0.0%

■Survey: Web survey

Α

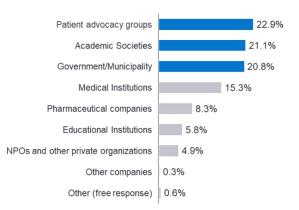
В

■Question: Please choose the three most effective media/channels for raising awareness of rare diseases (for healthcare professionals) (ranked)

Figure 4.1.6-9: Effective organization for disease awareness activities (for the public) - Top selection

results:

A all segments ·B by occupation



Clinical Clinical **Other HCPs** Specialist Non-specialist researcher researcher (genetic (basic and (development) counselors, (n=270) (n=53) applied) (n=61) (n=43) nurses) (n=23) Medical Institutions 15.2% 7.5% 13.1% 14.0% 21.7% Academic Societies 22.2% 15.1% 26.2% 23.3% 13.0% 5.7% 9.3% Pharmaceutical companies 8.9% 13.1% 8.7% 30.2% 23.0% 30.2% Patient advocacy groups 22.6% 13.0% 1.9% 0.0% 0.0% 0.0% Other companies 0.0% 21.9% 18.9% 18.0% 20.9% 30.4% Government/Municipality NPOs and other private organizations 4.8% 5.7% 1.6% 0.0% 0.0% 13.0% Educational Institutions 4.1% 13.2% 4.9% 0.0% Other (free response) 0.4% 1.9% 0.0% 2.3% 0.0%

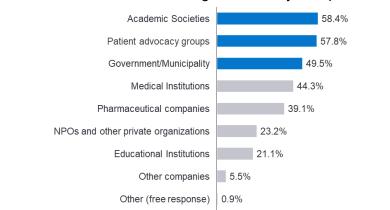
■Survey: Web survey

Α

В

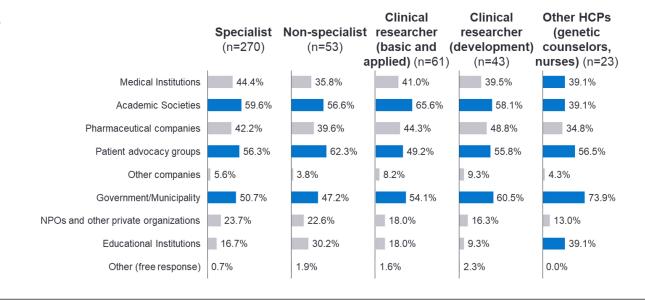
■Question: Please select three options that you feel are effective in raising awareness of rare diseases (for the general public) (ranking format)

Figure 4.1.6-10: Effective organization for disease awareness activities (for the public) – Top 3 selection results : A all segments •B by occupation



В

Α



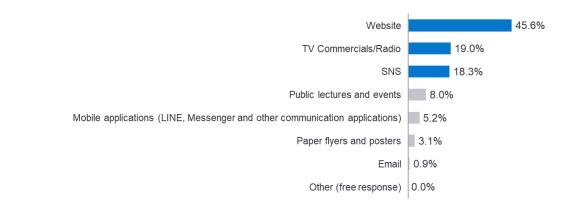
■Survey: Web survey

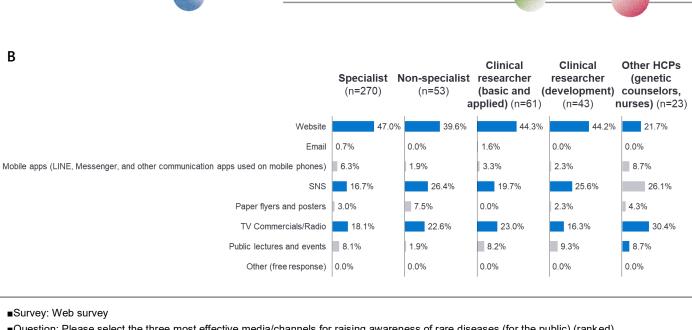
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■Question: Please select three options that you feel are effective in raising awareness of rare diseases (for the public) (ranking format)

■Subjects: 327 specialists, non-specialists, clinical researchers (basic and applied), clinical researchers (development) and other HCPs (genetic counselors and nurses)

Figure 4.1.6-11: Effective media/channels for disease awareness activities (for the public) – Top selection result : A all segments ·B by occupation





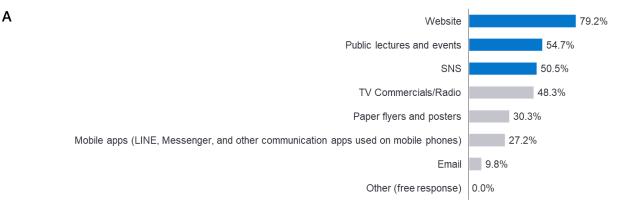
■Question: Please select the three most effective media/channels for raising awareness of rare diseases (for the public) (ranked)

■Subjects: 327 specialists, non-specialists, clinical researchers (basic and applied), clinical researchers (development) and other HCPs (genetic counselors and nurses)

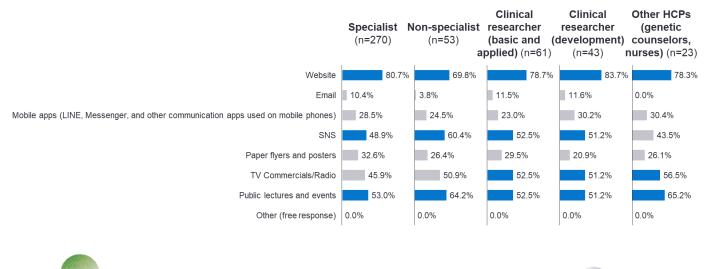
Figure 4.1.6-12: Effective media/channels for disease awareness activities (for the public) - Top 3

selection results :

A all segments ·B by occupation



В



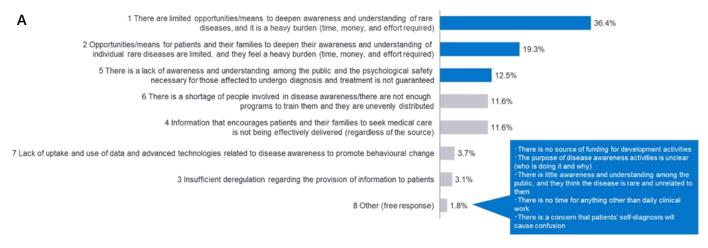


■Survey: Web survey

■Question: Please select the three media/channels that you think are effective for in-depth awareness activities (for the general public) on rare diseases (ranked)

Subjects: 327 specialists, non-specialists, clinical researchers (basic and applied), clinical researchers (development) and other HCPs (genetic counselors and nurses)

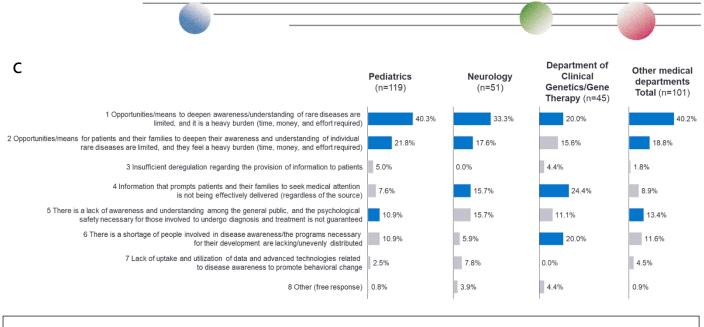
Figure 4.1.6-13: Challenges in disease awareness activities – Top selection results : A all segments ·B by occupation ·C by medical department ·D by disease research area



В	Specialist (n=270)	Non-specialist (n=53)	Clinical researcher (basic and applied) (n=61)	Clinical researcher (development) (n=43)	Other HCPs (genetic counselors, nurses) (n=23)
1 Opportunities/means to deepen awareness/understanding of rare diseases are limited, and it is a heavy burden (time, money, and effort required)	38.1%	41.5%	21.3%	25.6%	17.4%
2 Opportunities/means for patients and their families to deepen awareness and understanding of individual rare diseases are limited and they feel a heavy burden (time, money, and effort required)	18.1%	15.1%	24.6%	16.3%	34.8%
3 Insufficient deregulation regarding the provision of information to patients	2.2%	3.8%	0.0%	0.0%	8.7%
4 Information that would encourage patients and their families to seek medical care is not being effectively delivered (regardless of the source)	11.1%	20.8%	13.1%	20.9%	26.1%
5 There is a lack of awareness and understanding among the public, and psychological safety necessary for those involved to undergo diagnosis and treatment is not guaranteed	12.2%	9.4%	11.5%	11.6%	4.3%
6 There is a shortage of people involved in disease awareness/the programs necessary for their development are lacking and unevenly distributed	11.5%	7.5%	16.4%	11.6%	4.3%
7 Lack of uptake and utilization of data and advanced technologies related to disease awareness to promote behavioural change	4.4%	0.0%	6.6%	7.0%	0.0%
8 Other (free response)	2.2%	1.9%	6.6%	7.0%	4.3%

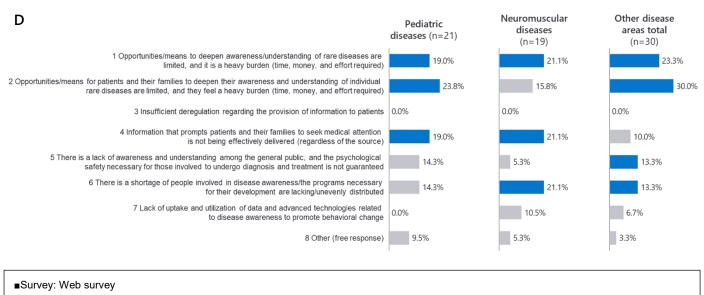
Survey: Web survey

Question: Please select the three most important challenges in relation to disease awareness activities (ranked)



- ■Survey: Web survey
- ■Question: Please select the three most important challenges in relation to disease awareness activities (ranked)

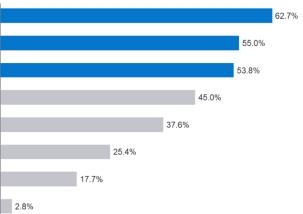
■Subjects: 316 specialists, non-specialists, and other HCPs (genetic counselors and nurses)



■Question: Please select the three most important challenges in relation to disease awareness activities (ranked)

■Subjects: 70 clinical researchers (basic and applied) and clinical researchers (development)

Figure 4.1.6-14: Challenges in disease awareness activities – Top 3 selection results : A all segments ·B by occupation ·C by medical department ·D by disease research area



2 Opportunities/means for patients and their families to deepen awareness and understanding of individual rare diseases are limited and they feel a heavy burden (time, money, and effort required)

 Opportunities/means to deepen awareness/understanding of rare diseases are limited, and it is a heavy burden (time, money, and effort required)
 There is a shortage of people involved in disease awareness/the programs necessary for their development are lacking and unevenly distributed
 Information that would encourage patients and their families to seek medical care is not being effectively delivered (regardless of the source)

5 There is a lack of awareness and understanding among the public, and psychological safety necessary for those involved to undergo diagnosis and treatment is not guaranteed

7 Lack of uptake and utilization of data and advanced technologies related to disease awareness to promote behavioural change

3 Insufficient deregulation regarding the provision of information to patients

8 Other (free response)

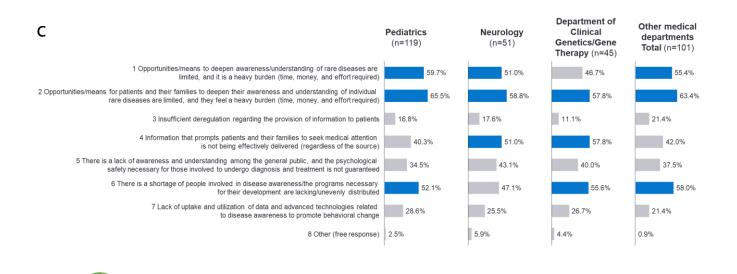
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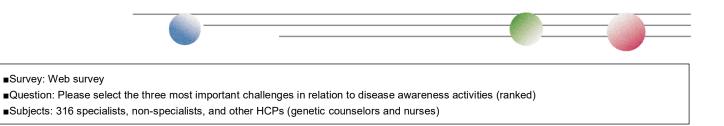
Α

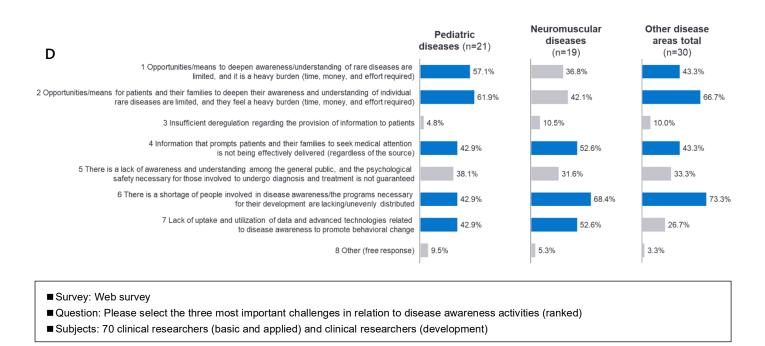
	Specialist (n=270)	Non-specialist (n=53)	Clinical researcher (basic and applied) (n=61)	Clinical researcher (development) (n=43)	Other HCPs (genetic counselors, nurses) (n=23)	
1 Opportunities/means to deepen awareness/understanding of rare diseases are limited, and it is a heavy burden (time, money, and effort required)	55.2%	66.0%	44.3%	48.8%	43.5%	
2 Opportunities/means for patients and their families to deepen their awareness and understanding of individual rare diseases are limited, and they feel a heavy burden (time, money, and effort required)	63.7%	54.7%	57.4%	55.8%	69.6%	
3 Insufficient deregulation regarding the provision of information to patients	18.5%	17.0%	9.8%	9.3%	13.0%	
4 Information that prompts patients and their families to seek medical attention is not being effectively delivered (regardless of the source)	45.2%	54.7%	42.6%	41.9%	69.6%	
5 There is a lack of awareness and understanding among the general public, and the psychological safety necessary for those involved to undergo diagnosis and treatment is not guaranteed	37.4%	35.8%	36.1%	30.2%	39.1%	
6 There is a shortage of people involved in disease awareness/the programs necessary for their development are lacking/unevenly distributed	53.0%	43.4%	63.9%	67.4%	43.5%	
7 Lack of uptake and utilization of data and advanced technologies related to disease awareness to promote behavioral change	23.7%	26.4%	39.3%	39.5%	17.4%	
8 Other (free response)	3.3%	1.9%	6.6%	7.0%	4.3%	

■Survey: Web survey

■Question: Please select the three most important challenges in relation to disease awareness activities (ranked)







⁶⁶ Due to the **uneven distribution of human resources** and bases involved in rare diseases, there are some regions where opportunities to learn about rare diseases are not provided, especially in the training curriculum for medical interns. In such cases, there are no rare disease role models during the career development stage, so young doctors lose the opportunity to become interested in/motivated by rare diseases. In such a situation, the result is that human resources involved in rare diseases are not developed.

It is also **difficult for patients to gather the information they need**. Because patients do not know the tools to use to gather information or the optimal way to search, the hurdle of gathering information is even higher than for healthcare professionals. Not being able to obtain or understand information causes anxiety in patients, so it is felt to be an issue. (Specialist / Pediatrics)

There is a lack of accurate and up-to-date information provided to patients and their families, and many patients do not visit the hospital in the first place because their parents are not aware that there are treatments available for their child's developmental delays. Many patients and families of pediatric patients do not recognize or understand the disease, testing methods, or benefits of diagnosis before the patient even seeks a diagnosis. (Non-specialist / Pediatrics)

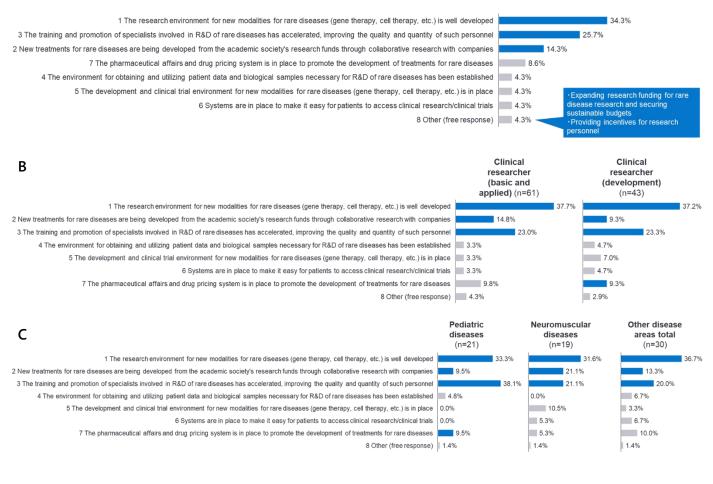
As discussed at the Genomic Medicine Promotion conference, in Japan, even within the family, there is prejudice in society where conflict exists, and people feel discriminatory attitudes even if they don't tell others about it. To solve these problems, it is necessary to foster awareness that 'everyone has genetic changes' through genetic education for children, and to create a system that makes it easy for anyone to go out into society. (Other HCPs (genetic counselors, nurses) / Department of Clinical Genetics and Gene Therapy) I feel that information regarding diagnosis made through genetic testing that directly leads to treatment has not yet been sufficiently constructed and disseminated to healthcare professionals. (Clinical researcher (development) / Endocrinology and Metabolic Disease)

It is difficult to convey correct information to patients, considering the differences in their positions and **levels of understanding.** Prior knowledge, expectations, and enthusiasm vary from person to person, and there is a risk that healthcare professionals will be misled if they communicate without sufficient knowledge. (Specialist / Pediatrics)

4.2.1 Ideal state in research, development and clinical practice

Figure 4.2.1-1: What research and development should be like – Top selection result : A all segments •B by occupation •C by disease research area• D by specialty





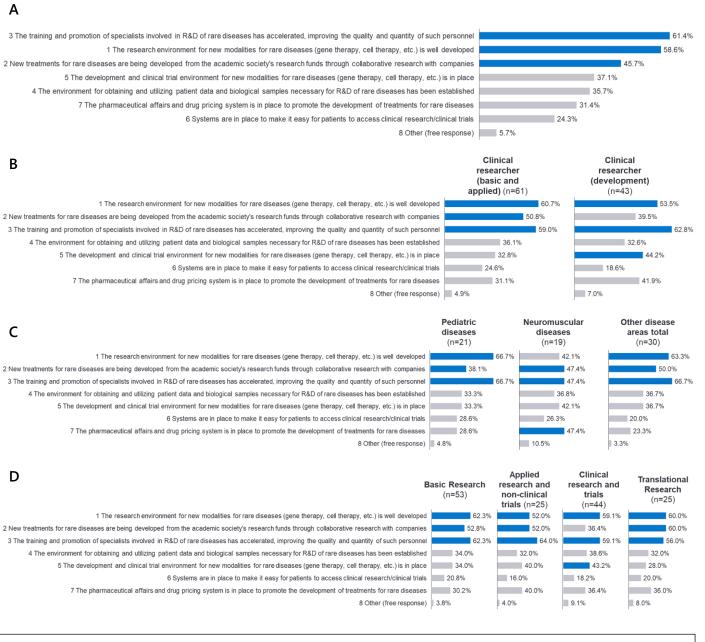
D	Basic Research (n=53)	Applied research and non-clinical trials (n=25)	Clinical research and trials (n=44)	Translational Research (n=25)
1 The research environment for new modalities for rare diseases (gene therapy, cell therapy, etc.) is well developed	39.6%	36.0%	36.4%	44.0%
2 New treatments for rare diseases are being developed from the academic society's research funds through collaborative research with companies	5 15.1%	12.0%	6.8%	16.0%
3 The training and promotion of specialists involved in R&D of rare diseases has accelerated, improving the quality and quantity of such personne	22.6%	20.0%	22.7%	12.0%
4 The environment for obtaining and utilizing patient data and biological samples necessary for R&D of rare diseases has been established	1 3.8%	4.0%	6.8%	4.0%
5 The development and clinical trial environment for new modalities for rare diseases (gene therapy, cell therapy, etc.) is in place	1.9%	8.0%	6.8%	0.0%
6 Systems are in place to make it easy for patients to access clinical research/clinical trials	3.8%	4.0%	4.5%	4.0%
7 The pharmaceutical affairs and drug pricing system is in place to promote the development of treatments for rare diseases	9.4%	12.0%	9.1%	12.0%
8 Other (free response)) 2.9%	1.4%	4.3%	2.9%

Survey: Web survey

■Question: Based on the research and development challenges you have answered so far, please choose the top three that you agree are the way things should be (ranked)

■Subjects: 70 clinical researchers (basic and applied) and clinical researchers (development)

Figure 4.2.1-2: What research and development should be like – Top 3 selection results : A all segments ·B by occupation ·C by disease research area · D by specialty



Survey: Web survey

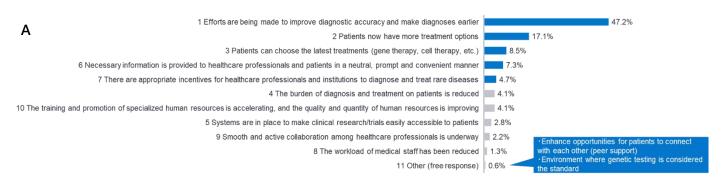
■Question: Based on the research and development challenges you have answered so far, please choose the top three that you agree are the way things should be (ranked)

■Subjects: 70 clinical researchers (basic and applied) and clinical researchers (development)

54

Figure 4.2.1-3: What should happen in clinical practice – Top selection result:

A all segments ·B by occupation ·C by medical department



В	Specialist Non- (n=270) (Other HCPs (genetic counselors, nurses) (n=23)
1 Efforts are being made to improve diagnostic accuracy and make diagnoses earlier	49.3%	39.6%	39.1%
2 Patients now have more treatment options	18.1%	15.1%	13.0%
3 Patients can choose the latest treatments (gene therapy, cell therapy, etc.)	6.7%	15.1%	17.4%
4 The burden of diagnosis and treatment on patients is reduced	4.1%	3.8%	4.3%
5 Systems are in place to make clinical research/trials easily accessible to patients	2.2%	5.7%	0.0%
6 Necessary information is provided to healthcare professionals and patients in a neutral, prompt and convenient manner	7.0%	7.5%	8.7%
7 There are appropriate incentives for healthcare professionals and institutions to diagnose and treat rare diseases	5.2%	1.9%	0.0%
8 The workload of medical staff has been reduced	1.5%	0.0%	0.0%
9 Smooth and active collaboration among healthcare professionals is underway	2.6%	1.9%	0.0%
10 The training and promotion of specialized human resources is accelerating, and the quality and quantity of human resources is improving	3.0%	9.4%	13.0%
11 Other (free response)	0.4%	0.0%	4.3%

C	Pediatrics (n=119)	Neurology (n=51)	Department of Clinical Genetics/Gene Therapy (n=45)	Other medical departments Total (n=101)
1 Efforts are being made to improve diagnostic accuracy and make diagnoses earlier	50.4%	33.3%	46.7%	50.5%
2 Patients now have more treatment options	10.9%	31.4%	11.1%	19.8%
3 Patients can choose the latest treatments (gene therapy, cell therapy, etc.)	9.2%	9.8%	11.1%	5.9%
4 The burden of diagnosis and treatment on patients is reduced	3.4%	3.9%	2.2%	5.9%
5 Systems are in place to make clinical research/trials easily accessible to patients	3.4%	2.0%	0.0%	4.0%
6 Necessary information is provided to healthcare professionals and patients in a neutral, prompt and convenient manner	7.6%	5.9%	13.3%	5.0%
7 There are appropriate incentives for healthcare professionals and institutions to diagnose and treat rare diseases	5.9%	3.9%	2.2%	5.0%
8 The workload of medical staff has been reduced	2.5%	2.0%	0.0%	0.0%
9 Smooth and active collaboration among healthcare professionals is underway	3.4%	2.0%	2.2%	1.0%
10 The training and promotion of specialized human resources is accelerating, and the quality and quantity of human resources is improving	3.4%	5.9%	8.9%	2.0%
11 Other (free response)	0.0%	0.0%	2.2%	1.0%

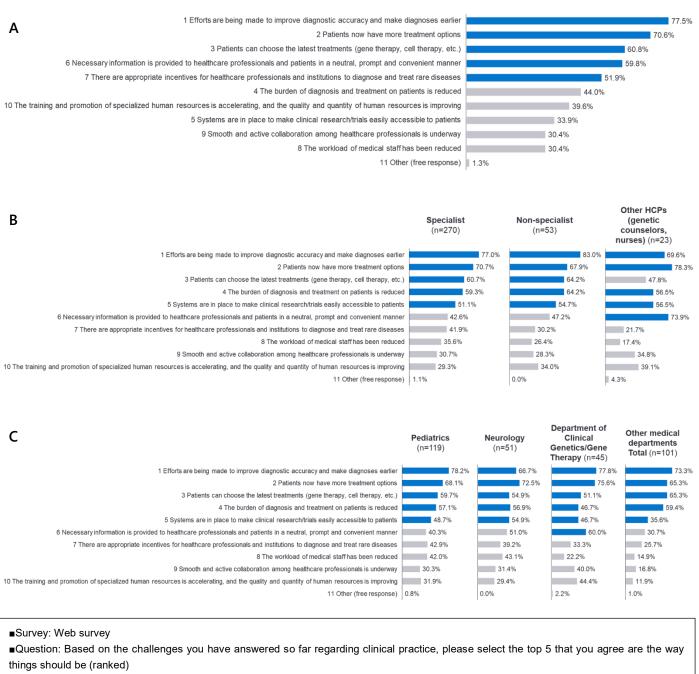
■Survey: Web survey

■Question: Based on the challenges you have answered so far regarding clinical practice, please select the top 5 that you agree are the way things should be (ranked)

■Subjects: 316 specialists, non-specialists, and other HCPs (genetic counselors and nurses)

Figure 4.2.1-4: What should happen in clinical practice – Top 3 selection results :

A all segments ·B by occupation ·C by medical department



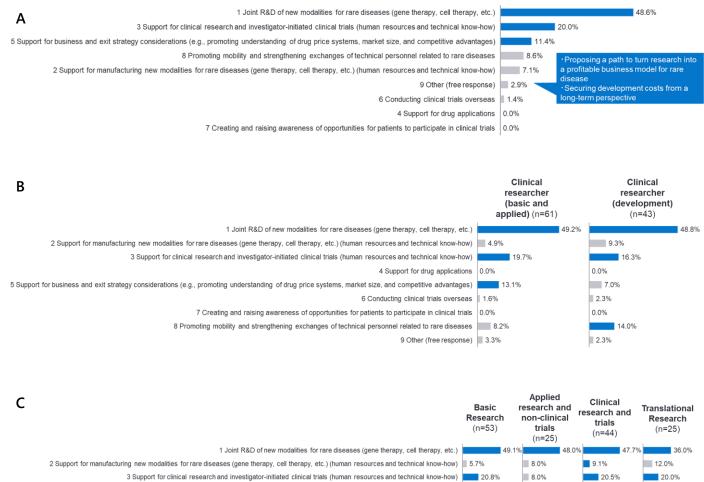
Subjects: 316 specialists, non-specialists, and other HCPs (genetic counselors and nurses)

56

4.2.2 Expectations for the pharmaceutical industry

Figure 4.2.2-1: Expectations for the pharmaceutical industry in research and development – Top

selection result : A all segments ·B by occupation ·C by specialty



4 Support for drug applications 0.0%

5 Support for business and exit strategy considerations (e.g., promoting understanding of drug price systems, market size, and competitive advantages) 15.1% 6 Conducting clinical trials overseas 0.0% 0.0% 7 Creating and raising awareness of opportunities for patients to participate in clinical trials 0.0% 0.0%

8 Promoting mobility and strengthening exchanges of technical personnel related to rare diseases 7.5% 6.6% 8.0%

9 Other (free response) 1.9%

0.0%

0.0%

9.1%

2.3%

0.0%

4.5%

0.0%

0.0%

0.0%

4.0%

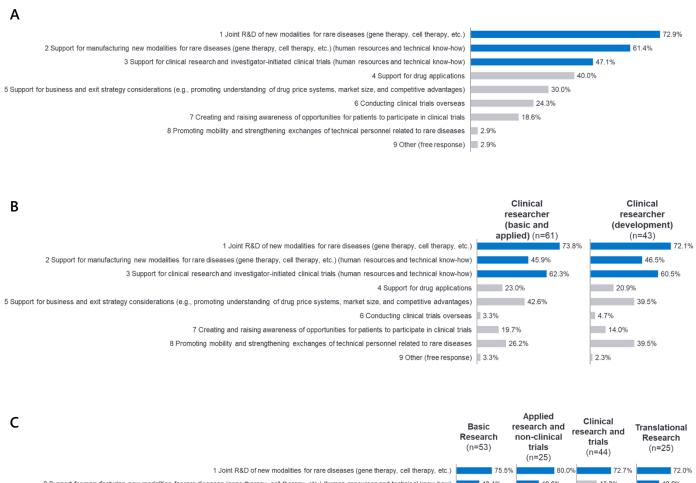
20.0%

■Survey: Web survey

■Question: Please list your top three expectations for the pharmaceutical industry to achieve the ideal state (ranked)

■Subjects: 70 clinical researchers (basic and applied) and clinical researchers (development)

Figure 4.2.2-2: Expectations for the pharmaceutical industry in research and development – Top 3 selection results : A all segments ·B by occupation ·C by specialty



2 Support for manufacturing new modalities for rare diseases (gene therapy, cell therapy, etc.) (human resources and technical know-how)	49.1%	48.0%	43.2%	48.0%
3 Support for clinical research and investigator-initiated clinical trials (human resources and technical know-how)	62.3%	52.0%	59.1%	60.0%
4 Support for drug applications	26.4%	16.0%	22.7%	16.0%
5 Support for business and exit strategy considerations (e.g., promoting understanding of drug price systems, market size, and competitive advantages)	39.6%	44.0%	45.5%	44.0%
6 Conducting clinical trials overseas	1.9%	4.0%	4.5%	0.0%
7 Creating and raising awareness of opportunities for patients to participate in clinical trials	17.0%	12.0%	15.9%	16.0%
8 Promoting mobility and strengthening exchanges of technical personnel related to rare diseases	26.4%	40.0%	31.8%	40.0%
9 Other (free response)	1.9%	4.0%	4.5%	4.0%

■Survey: Web survey

■Question: Please list your top three expectations for the pharmaceutical industry to achieve the ideal state (ranked)

■Subjects: 70 clinical researchers (basic and applied) and clinical researchers (development)

Figure 4.2.2-3: Expectations for the pharmaceutical industry in clinical practice - Top selection

result : A all segments ·B by occupation

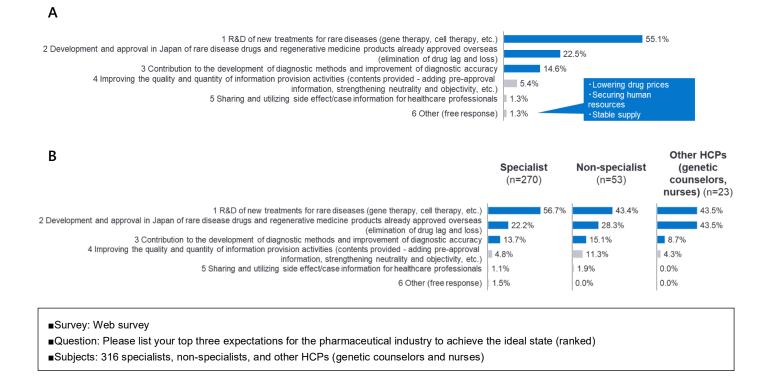
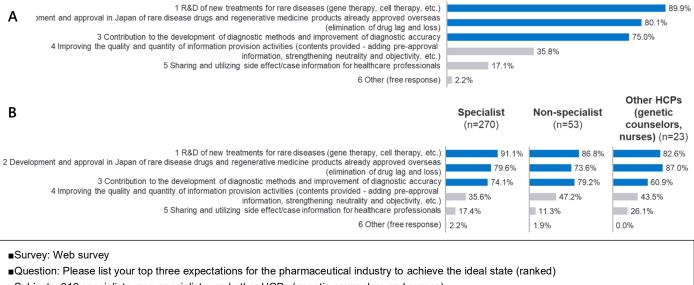


Figure 4.2.2-4: Expectations for the pharmaceutical industry in clinical practice - Top 3 selection

result : A all segments ·B by occupation



We hope to be able to communicate clinical trial information to patients and healthcare professionals in an easy-tounderstand manner, and to **develop new drugs**.

(Specialist / Pediatrics)

In the past, when I recommended testing for a patient who may have a genetic disease, the patient told me, 'I don't want to get tested if there is no treatment,' so I have high hopes for pharmaceutical companies to **develop treatments** and reduce drug waste. I think that knowing that treatments exist will encourage patients to go to the hospital and face their disease.

(Non-specialist / Neurology)

There are university institutions that conduct research like that conducted by companies, so I think it would be good if there were more opportunities for joint research between academia and pharmaceutical companies. Also, when academia tries to contact pharmaceutical companies, they don't know the companies' areas of focus or expertise, so they don't know who to contact, and the procedures are complicated, so I would like companies to disclose information about themselves to academia and clarify who to contact. (Non-specialist / Pediatrics)

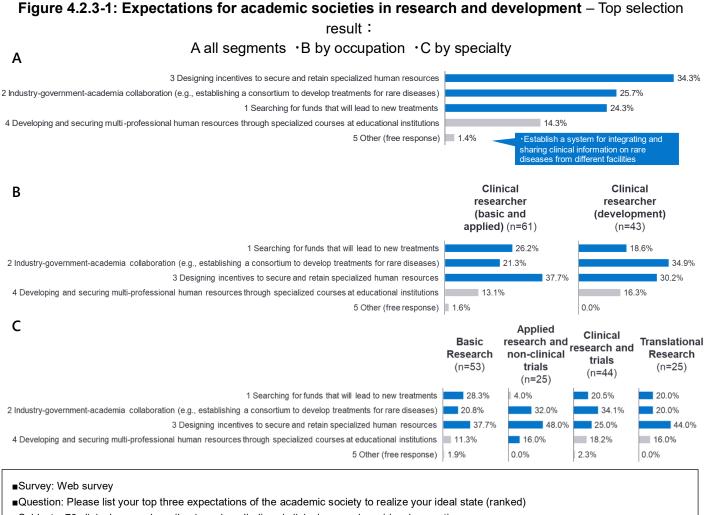
I hope to create collaborative opportunities with academia and build closer ties. I believe that an environment in which academia, pharmaceutical companies, and patient groups can naturally interact daily, such as by **sending researchers from pharmaceutical companies to academia or creating joint research spaces**, will become a very important ecosystem for the development of new drugs.

(Clinical researcher (basic and applied) / neuromuscular disease)

I would like to see more efforts put into **drug discovery and testing/diagnosis accuracy improvement for rare diseases**. Specifically, I would like to see the progress of rare disease research made visible, with continued updates and improved accessibility, a system built for the accumulation of genetic analysis data in Japan, and the development of domestically produced drugs.

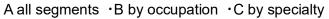
(Clinical researcher (basic and applied) / neuromuscular disease)

4.2.3 Expectations for academic societies



■Subjects: 70 clinical researchers (basic and applied) and clinical researchers (development)

Figure 4.2.3-2: Expectations for academic societies in research and development – Top 3 selection result :





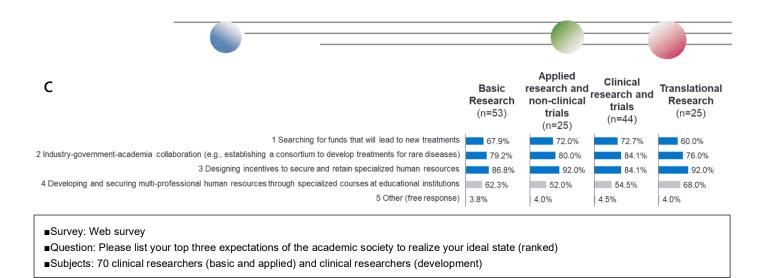


Figure 4.2.3-3: Expectations for academic societies in clinical practice - Top selection result :

A all segments ·B by occupation

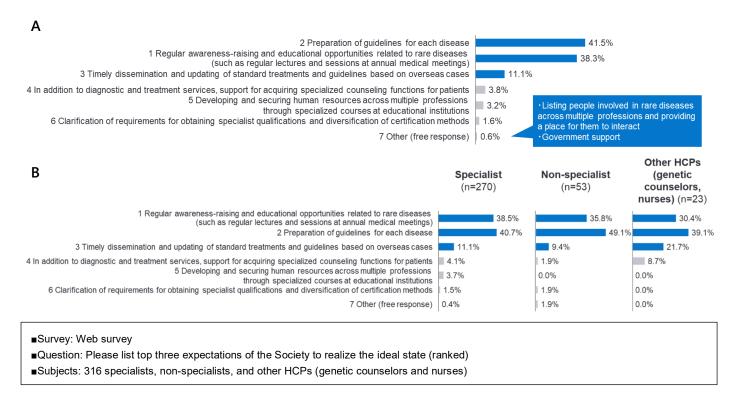
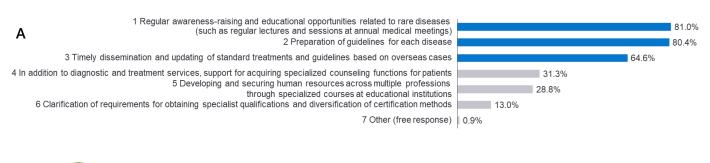
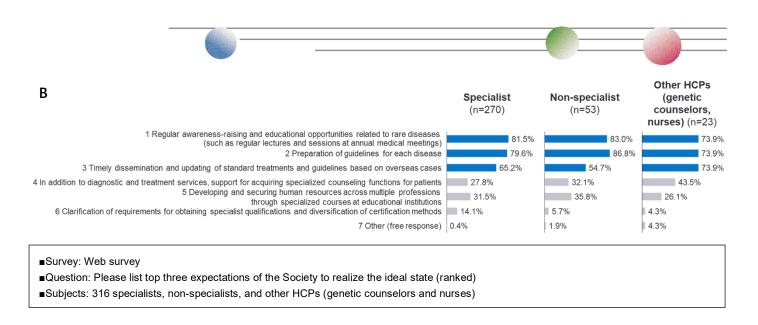


Figure 4.2.3-4: Expectations for academic societies in clinical practice - Top 3 selection result :



A all segments ·B by occupation



⁶⁶Many of the patients who come to our hospital are referred from other hospitals, but some doctors at other hospitals are unsure of which patients they can refer to their hospital, so we feel it is necessary to strengthen awareness of the referral criteria to each facility. We should **clarify which facilities have what kind of expertise and the referral criteria to specialized facilities for each disease and accelerate cooperation between medical institutions**. (Specialist / Pediatrics)

It is hoped that the academic society will strengthen its presence in rare disease awareness activities for patients and healthcare professionals. In addition, as the number of cases of people moving from universities to pharmaceutical companies is increasing, to **create a workplace where specialized human resources can do what they really want and where treatment is guaranteed**, it is necessary to operate a financially independent organization, such as covering research expenses from investment fund profits. (Specialist / Collagen Disease)

To create an environment where referral sources can refer patients with peace of mind in a timely manner, we hope to see **coordination regarding the mechanism for referrals from non-specialists to specialists**. (Non-specialist / Neurology)

I would like them to collect and disseminate accurate information regarding treatment and diagnostic needs. (Non-specialist / Pediatrics)

Solution I want the government to convey voices that individual patients cannot convey as a unified academic opinion backed by academia. I believe that academic societies can complement the correctness and volume of individual patients' voices. The Internet has improved access to information, but it has also led to the spread of incorrect information and different interpretations. Therefore, I want academic societies to clearly communicate what information is correct and what is incorrect.

(Clinical researcher (development) / All other hereditary disease)

From the perspective of human resource development, it can take four to five years to obtain specialist certification within an academic society, and since young people who are interested in rare diseases are particularly valuable, a more flexible system design, such as a grading system, may be necessary to broaden the base of expertise.

(Clinical researcher (basic and applied) / Other hereditary disease)

4.2.4 Expectations for patient advocacy groups

Figure 4.2.4-1: Expectations for academic societies in clinical practice - Top selection result :

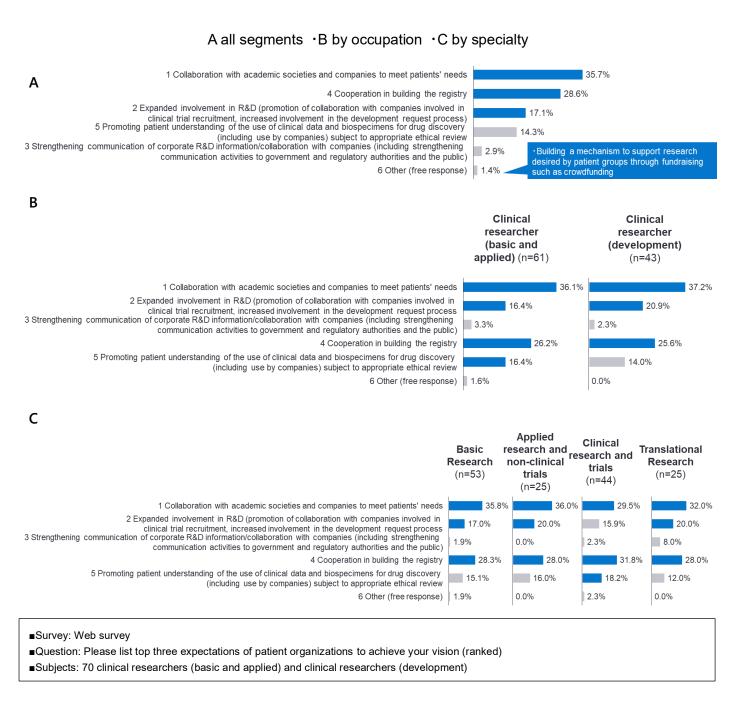
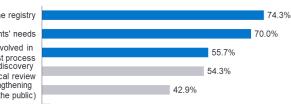




Figure 4.2.4-2: Expectations for academic societies in clinical practice - Top 3 selection result :

A all segments ·B by occupation ·C by specialty



4 Cooperation in building the registry

1 Collaboration with academic societies and companies to meet patients' needs

2 Expanded involvement in R&D (promotion of collaboration with companies involved in

clinical trial recruitment, increased involvement in the development request process 5 Promoting patient understanding of the use of clinical data and biospecimens for drug discovery

3 Strengthening communication of corporate R&D information/collaboration with companies (including use by companies) subject to appropriate ethical review communication activities to government and regulatory authorities and the public)

6 Other (free response) 2.9%

В

Α

	Clinical researcher (basic and applied) (n=61)	Clinical researcher (development) (n=43)
1 Collaboration with academic societies and companies to meet patients' needs	72.1%	69.8%
2 Expanded involvement in R&D (promotion of collaboration with companies involved in clinical trial recruitment, increased involvement in the development request process	55.7%	55.8%
3 Strengthening communication of corporate R&D information/collaboration with companies (including strengthening communication activities to government and regulatory authorities and the public)	44.3%	37.2%
4 Cooperation in building the registry	70.5%	79.1%
5 Promoting patient understanding of the use of clinical data and biospecimens for drug discovery (including use by companies) subject to appropriate ethical review	54.1%	55.8%
6 Other (free response)	3.3%	2.3%



		esearch and	earch and	anslational Research (n=25)
1 Collaboration with academic societies and companies to meet patients' needs	73.6%	84.0%	63.6%	80.0%
2 Expanded involvement in R&D (promotion of collaboration with companies involved in clinical trial recruitment, increased involvement in the development request process	56.6%	64.0%	54.5%	56.0%
3 Strengthening communication of corporate R&D information/collaboration with companies (including strengthening communication activities to government and regulatory authorities and the public)	47.2%	36.0%	29.5%	40.0%
4 Cooperation in building the registry	69.8%	68.0%	88.6%	68.0%
5 Promoting patient understanding of the use of clinical data and biospecimens for drug discovery (including use by companies) subject to appropriate ethical review	49.1%	44.0%	61.4%	56.0%
6 Other (free response)	3.8%	4.0%	2.3%	0.0%
	I	1	1	1

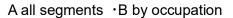
Survey: Web survey

■Question: Please list top three expectations of patient organizations to achieve your vision (ranked)

Subjects: 70 clinical researchers (basic and applied) and clinical researchers (development)



Figure 4.2.4-3: Expectations for patient groups in clinical practice - Top selection result :



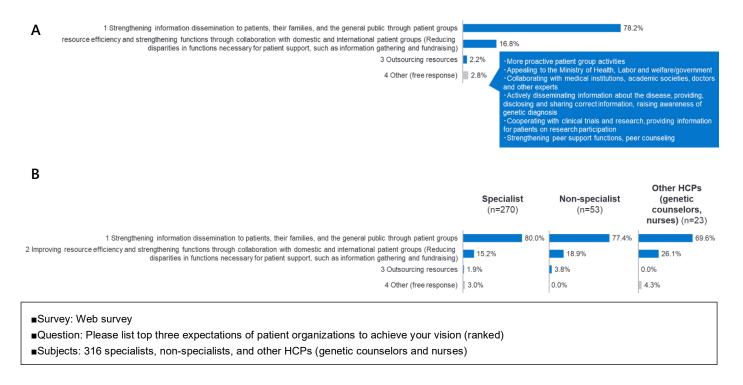
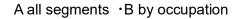
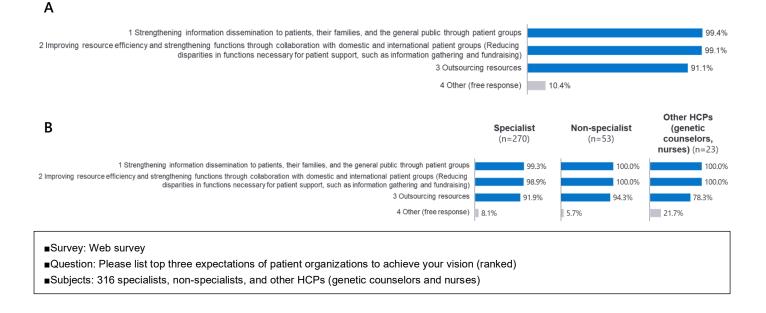


Figure 4.2.4-4: Expectations for patient groups in clinical practice - Top 3 selection result :





⁶⁶Currently, the activities of each patient group vary, but we would like patient groups to **improve peer support for patients and their families who cannot be supported by HCPs**, regardless of the disease. (Specialist / Pediatrics)

I would like them to collect and disseminate information about patients' needs regarding medical expenses, such as raising disease awareness and lowering drug prices.
(Specialist / Collagen Disease)

We believe that the existence/activities of patient groups have a major impact after a definitive diagnosis, so we hope that they will provide support to patients in how to **deal with the disease and in their daily lives**, mainly in prognosis management.

(Non-specialist / Neurology)

I want them to **improve their fundraising ability and medical literacy** to have a voice and initiative. Patient groups in Japan do not have the means to mobilize people, such as funds, so they inevitably have a weak voice. If **patient groups can provide funds for research and development**, they should be able to have a voice and initiative, just like patient groups in the West, where fundraising activities such as charities are active. (Basic and applied research doctor / neuromuscular disease)

⁶⁶ I would like them to **strengthen their activities to make themselves known**, such as media exposure, activities in the field of education, and crowdfunding. I think that by involving more stakeholders, creating contact points, and deepening mutual understanding, their activities will accelerate. (Clinical researcher (basic and applied) / Other hereditary disease)

As a patient advocacy group, I would like you to be **actively involved in research and development and clinical activities**. For example, I feel that the current registry registration is not in a state where it is easy for patients to register, and since there is no foundation for patient data, further development is not possible, so I would like patient advocacy groups to actively cooperate.

(Clinical researcher (development) / All other hereditary disease)

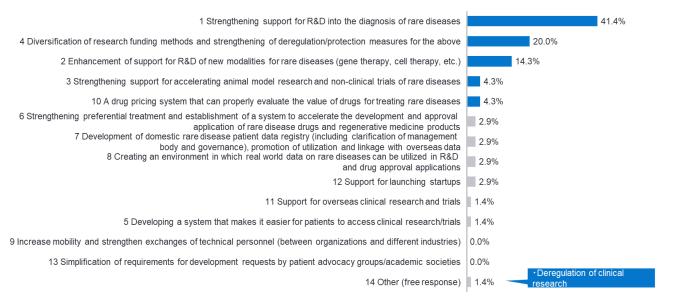
4.2.5 Expectations for government and regulatory authorities

Figure 4.2.5-1: Expectations for administrative and regulatory authorities in research and

development – Top selection result :

A all segments ·B by occupation ·C by specialty





D	Clinical researcher (basic and applied) (n=61)	Clinical researcher (development) (n=43)
1 Strengthening support for R&D into the diagnosis of rare diseases	36.1%	48.8%
2 Enhancement of support for R&D of new modalities for rare diseases (gene therapy, cell therapy, etc.)	14.8%	16.3%
3 Strengthening support for accelerating animal model research and non-clinical trials of rare diseases	4.9%	2.3%
4 Diversification of research funding methods and strengthening of deregulation/protection measures for the above	23.0%	16.3%
5 Developing a system that makes it easier for patients to access clinical research/trials	1.6%	2.3%
6 Strengthening preferential treatment and establishment of a system to accelerate the development and approval application of rare disease drugs and regenerative medicine products 7 Development of domestic rare disease patient data registry (including clarification of management body and governance), promotion of utilization and linkage with overseas data 8 Creating an environment in which real world data on rare diseases can be utilized in R&D and drug approval application	3.3% 3.3% 1.6%	2.3% 2.3% 2.3%
9 Increase mobility and strengthen exchanges of technical personnel (between organizations and different industries)	0.0%	0.0%
10 A drug pricing system that can properly evaluate the value of drugs for treating rare diseases	4.9%	2.3%
11 Support for overseas clinical research and trials	1.6%	0.0%
12 Support for launching startups	3.3%	2.3%
13 Simplification of requirements for development requests by patient advocacy groups/academic societies	0.0%	0.0%
14 Other (free response)	1.6%	2.3%

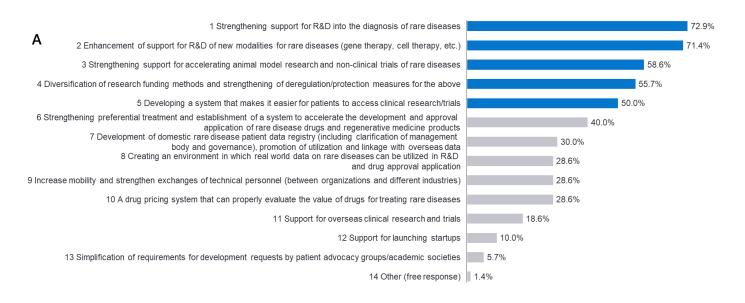
CApplied research and (n=2)Clinical research and (n=2)Clinical research and (n=2)Translational Research (n=2)1 Strengthening support for R&D into the diagnosis of rare diseases35.8032.0040.0038.0040.002 Enhancement of support for R&D of new modalities for rare diseases (gene therapy, cell therapy, cell 3 Strengthening support for accelerating animal model research and non-clinical trials of rare diseases38.0040.002.30040.003 Uversification of research funding methods and strengthening of deregulation/protection measures for the above S Developing a system that makes it easier for patients to accelerate the development and approval application of rare disease drugs and regenerative medicine product B Creating an environment in which real world data on rare diseases can be utilized in R&D4.0002.3000.0000.0009 Increase mobility and strengthen exchanges of technical personnel (between organizations and different industries and drug approval application and drug approval application4.2000.0000.0000.00010 A drug priorition system that can properly evaluate the undue of druge to trace increase data and drug approval application0.0000.0000.0000.00010 A drug priorition system that can properly evaluate the undue of druge to trace increase data and drug approval application0.0000.0000.0000.00010 A drug periorition system that can properly evaluate the undue of druge to trace increase and drug approval application0.0000.0000.0000.00010 A drug periorition system that can properly evaluate the undue of druge					
2 Enhancement of support for R&D of new modalities for rare diseases (gene therapy, cell therapy, cell therapy, etc.) 115.1% 20.0% 15.9% 8.0% 3 Strengthening support for accelerating animal model research and non-clinical trials of rare diseases 3.8% 0.0% 2.3% 8.0% 4 Diversification of research funding methods and strengthening of deregulation/protection measures for the above 24.5% 20.0% 22.7% 20.0% 5 Developing a system that makes it easier for patients to access clinical research/trials 1.9% 4.0% 0.0% 0.0% 7 Development of domestic rare disease patient data registry (including clarification of management body and governance), promotion of utilization and linkage with overseas datin two verseas dation and finding approval application of uses can be utilized in R&D and fund gapproval application 1.9% 0.0% 2.3% 0.0% 9 Increase mobility and strengthen exchanges of technical personnel (between organizations and different industries) 0.0% 0.0% 0.0% 0.0%	c	Research n	search and on-clinical trials	earch and Tr trials	Research
3 Strengthening support for accelerating animal model research and non-clinical trials of rare diseases 3.8% 0.0% 2.3% 8.0% 4 Diversification of research funding methods and strengthening of deregulation/protection measures for the above 24.5% 20.0% 22.7% 20.0% 5 Developing a system that makes it easier for patients to access clinical research/trials 1.9% 4.0% 2.3% 0.0% 6 Strengthening preferential treatment and establishment of a system to accelerate the development and approval application of rare disease drugs and regenerative medicine products 1.9% 4.0% 0.0% 0.0% 7 Development of domestic rare disease patient data registry (including clarification of management body and governance), promotion of utilization and linkage with overseas drug approval application 1.9% 4.0% 2.3% 4.0% 9 Increase mobility and strengthen exchanges of technical personnel (between organizations and different industries) 0.0% 0.0% 0.0% 0.0%	1 Strengthening support for R&D into the diagnosis of rare diseases	35.8%	32.0%	38.6%	44.0%
4 Diversification of research funding methods and strengthening of deregulation/protection measures for the above 24.5% 20.0% 22.7% 20.0% 5 Developing a system that makes it easier for patients to access clinical research/trials 1.9% 4.0% 2.3% 0.0% 6 Strengthening preferential treatment and establishment of a system to accelerate the development and approval application of rare disease drugs and regenerative medicine products 3.8% 4.0% 0.0% 0.0% 7 Development of domestic rare disease patient data registry (including clarification of management body and governance), promotion of utilization and linkage with overseas data 8 Creating an environment in which real world data on rare diseases can be utilized in R&D and drug approval application 1.9% 0.0% 2.3% 0.0% 9 Increase mobility and strengthen exchanges of technical personnel (between organizations and different industries) 0.0% 0.0% 0.0% 0.0%	2 Enhancement of support for R&D of new modalities for rare diseases (gene therapy, cell therapy, etc.)	15.1%	20.0%	15.9%	8.0%
5 Developing a system that makes it easier for patients to access clinical research/trials 1.9% 4.0% 2.3% 0.0% 6 Strengthening preferential treatment and establishment of a system to accelerate the development and approval application of rare disease drugs and regenerative medicine products 3.8% 4.0% 0.0% 0.0% 7 Development of domestic rare disease patient data registry (including clarification of management body and governance), promotion of utilization and linkage with overseas data 4.0% 2.3% 4.0% 9 Increase mobility and strengthen exchanges of technical personnel (between organizations and different industries) 0.0% 0.0% 0.0% 0.0%	3 Strengthening support for accelerating animal model research and non-clinical trials of rare diseases	3.8%	0.0%	2.3%	8.0%
6 Strengthening preferential treatment and establishment of a system to accelerate the development and approval application of rare disease drugs and regenerative medicine products. 3.8% 4.0% 0.0% 0.0% 7 Development of domestic rare disease patient data registry (including clarification of management body and governance), promotion of utilization and linkage with overseas data 4.0% 2.3% 4.0% 9 Increase mobility and strengthen exchanges of technical personnel (between organizations and different industries) 0.0% 0.0% 0.0% 0.0%	4 Diversification of research funding methods and strengthening of deregulation/protection measures for the above	24.5%	20.0%	22.7%	20.0%
application of rare disease drugs and regenerative medicine products 3.8% 4.0% 0.0% 0.0% 7 Development of domestic rare disease patient data registry (including clarification of management body and governance), promotion of utilization and linkage with overseas data 1.9% 4.0% 2.3% 4.0% 8 Creating an environment in which real world data on rare diseases can be utilized in R&D and drug approval application 0.0% 0.0% 0.0% 0.0% 9 Increase mobility and strengthen exchanges of technical personnel (between organizations and different industries) 0.0% 0.0% 0.0% 0.0%	5 Developing a system that makes it easier for patients to access clinical research/trials	1.9%	4.0%	2.3%	0.0%
7 Development of domestic rare disease patient data registry (including clarification of management body and governance), promotion of utilization and linkage with overseas data 8 Creating an environment in which real world data on rare diseases can be utilized in R&D and drug approval application 1.9% 4.0% 2.3% 4.0% 9 Increase mobility and strengthen exchanges of technical personnel (between organizations and different industries) 0.0% 0.0% 0.0% 0.0%			4.0%	0.0%	0.0%
8 Creating an environment in which real world data on rare diseases can be utilized in R&D and drug approval application 1.9% 0.0% 2.3% 0.0% 9 Increase mobility and strengthen exchanges of technical personnel (between organizations and different industries) 0.0% 0.0% 0.0% 0.0%	7 Development of domestic rare disease patient data registry (including clarification of management	1.9%	4.0%	2.3%	4.0%
	8 Creating an environment in which real world data on rare diseases can be utilized in R&D	1.9%	0.0%	2.3%	0.0%
10 A drug pricing system that can properly evaluate the value of drugs for treating rate diseases 5.7% 12.0% 13.0%	9 Increase mobility and strengthen exchanges of technical personnel (between organizations and different industries)	0.0%	0.0%	0.0%	0.0%
	10 A drug pricing system that can properly evaluate the value of drugs for treating rare diseases	5.7%	12.0%	4.5%	12.0%
11 Support for overseas clinical research and trials 1.9% 0.0% 2.3% 0.0%	11 Support for overseas clinical research and trials	1.9%	0.0%	2.3%	0.0%
12 Support for launching startups 3.8% 0.0% 4.5% 0.0%	12 Support for launching startups	3.8%	0.0%	4.5%	0.0%
13 Simplification of requirements for development requests by patient advocacy groups/academic societies 0.0% 0.0% 0.0%	13 Simplification of requirements for development requests by patient advocacy groups/academic societies	0.0%	0.0%	0.0%	0.0%
14 Other (free response) 0.0% 4.0% 2.3% 4.0%	14 Other (free response)	0.0%	4.0%	2.3%	4.0%

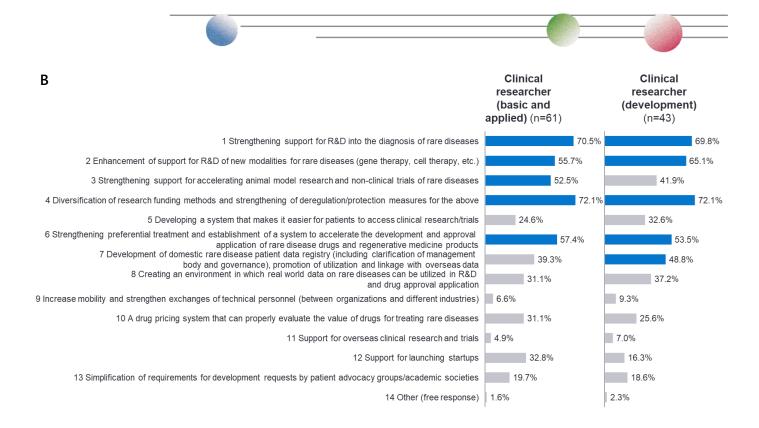
■Survey: Web survey

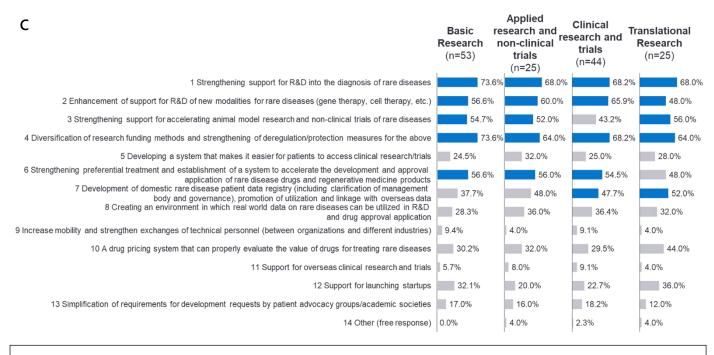
■Question: Please select top five expectations of government and regulatory authorities to achieve the ideal state (ranking format)

■Subjects: 70 clinical researchers (basic and applied) and clinical researchers (development)

Figure 4.2.5-2: Expectations for administrative and regulatory authorities in research and development – Top 3 selection result : A all segments ·B by occupation ·C by specialty





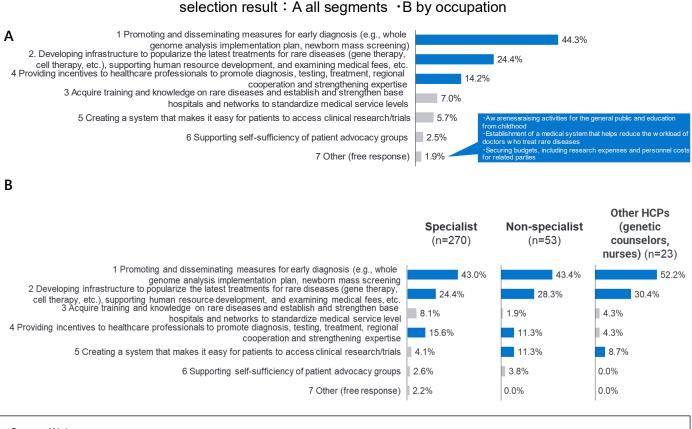


Survey: Web survey

■Question: Please select top five expectations of government and regulatory authorities to achieve the ideal state (ranking format)

■Subjects: 70 clinical researchers (basic and applied) and clinical researchers (development)

Figure 4.2.5-3: Expectations for government and regulatory authorities in clinical practice - Top



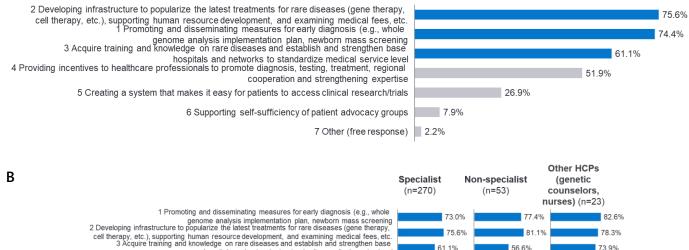
Survey: Web survey

Α

■Question: Please list top three expectations of government and regulatory authorities to achieve your ideal state (ranked)

■Subjects: 316 specialists, non-specialists, and other HCPs (genetic counselors and nurses)

Figure 4.2.5-4: Expectations for government and regulatory authorities in clinical practice – Top 3 selection result : A all segments ·B by occupation



 2 Developing infrastructure to popularize the latest treatments for fare diseases (gene therapy, cell therapy, etc.), supporting human resource development, and examining medical fees, etc. 3 Acquire training and knowledge on rare diseases and establish and strengthen base hospitals and networks to standardize medical service level 4 Providing incentives to healthcare professionals to promote diagnosis, testing, treatment, regional cooperation and strengthening expertise 53.7% 5 Creating a system that makes it easy for patients to access clinical research/trials 26.3% 30.2% 6 Supporting self-sufficiency of patient advocacy groups 7.8% 11.3%

> 7 Other (free response) 2.6%

43.4%

0.0%

26.1%

26.1%

13.0%

0.0%

■Survey: Web survey

- ■Question: Please list top three expectations of government and regulatory authorities to achieve your ideal state (ranked)
- ■Subjects: 316 specialists, non-specialists, and other HCPs (genetic counselors and nurses)

In clinical trials, information about clinical trials is not fully communicated to subjects, making it extremely difficult to recruit subjects who meet the conditions. If **clinical trial information were centrally collected** and there was a system that allowed users to narrow down clinical trial information and subject information that meets the conditions, it would be convenient for both healthcare professionals and subjects. (Specialist / Pediatrics)

••• I hope that income restrictions for patients who are eligible for subsidies (such as subsidies for families raising children with disabilities) will be lifted. Also, among the registered designated intractable diseases, there are diseases that qualify as designated intractable diseases based on the disease name alone, and diseases that are determined based on the disease name and severity, so in the latter case, there are patients who do not qualify as designated intractable diseases even though they need to go to the hospital regularly. I feel that there is currently a lack of support for such patients, so I would like to see **the number of designated intractable diseases eligible for subsidies expanded**.

(Specialist / Pediatrics)

To resolve the shortage of human resources at medical institutions, we need to see **incentives designed within academia** through personnel evaluation and rules on part-time work, such as securing the necessary budget for hiring and training full-time personnel and making it easier to startup ventures on campus. (Specialist / Collagen Disease)

⁶⁶ I would like to see deregulation of fundraising for each stakeholder involved in research and development, and the establishment of a **drug pricing system that makes it easier for companies to recoup their investments**. Rather than focusing on a set system, I would like to see ideas about how to achieve goals and how the government can be involved in helping to achieve those goals.

(Clinical researcher (basic and applied) / neuromuscular disease)

I hope that we can work to create a society in which 'patients can access the information and medicines they need' and 'patients and their families can live the same lives as healthy people' through a **significant increase in budgets and personnel, relaxation of the pharmaceutical industry's restrictions on the provision of information**, and a review of how genetic and diversity education is taught in primary education. (Clinical researcher (development) / All other hereditary disease)

⁶⁶I hope to see deregulation that will make it easier for industry-government-academia collaboration to proceed, genetic education for younger generations to help create a **society free of prejudice and friction**, and the establishment of mechanisms and systems that will allow people in rural areas to receive healthcare such as testing and examinations for rare diseases.

(Other HCPs (Genetic counselors and nurses) / Department of Clinical Genetics and Gene Therapy)

⁵⁶ Unless society increases its tolerance for failure, pharmaceutical companies will not be able to take on new



challenges. Since these are medicines for Japanese people, we need **deregulation to accelerate drug discovery** and encourage foreign capital restrictions and a return to Japan, so that domestic pharmaceutical companies can invest in medicines that accurately meet domestic needs.

(Clinical researcher (basic and applied) / All other hereditary disease)

Regarding use of this publication

- To maintain neutrality, this report uses survey data conducted by IRUD, RDCJ, and the Japan Pharmaceutical Manufacturers Association (JPMA) on behalf of a third-party organization (EY Strategy & Consulting Co., Ltd.)
- Although we strive to ensure the accuracy, validity, and timeliness of the information provided in this survey, we do not guarantee it
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