R&D Head Club
Clinical Trial Performance Survey in 2023

Excerpt

May 2024 [ver.1]

- This report is an excerpt from a distributed report to a R&D Head Club member company for a research discussion.
- Expenses for this report were borne by member companies of R&D Head Club.
- For the secondary use of this document, see p.45.

Data Center & Working Group Members

The 2023 survey questionnaire was designed, conducted, and analyzed, and this report authored, by a working group made up of representatives from the following 5 companies who were appointed by the R&D Head Club.
In addition, since the questionnaire included questions about the intellectual property of the participating companies, a third-party vendor was assigned, and all study sponsor names and study center names were masked so that the identities of the responding companies would not be known. The masked data were used for data totalization and analysis of the questionnaire.

Performance Working Group members　(abc order)

• Astellas Pharma Inc.	CMO Office, Strategic Operations	Yoshihito Komoriya
• Eli Lilly Japan K.K	Clinical Development	Hiroyuki Sato
• Janssen Pharmaceutical K.K.	Global Clinical Operations Japan	Dai Kawaratani
• Takeda Pharmaceutical Co., Ltd.	Development Operations Excellence	Yuuji Minami
• Pfizer R&D Japan G.K.	Portfolio & Project Management,	Kei Yamashita

Contents

I. Participating Companies

The survey has been conducted since 2004. The following 21 member companies of the R&D Head Club participated in 2023 survey.

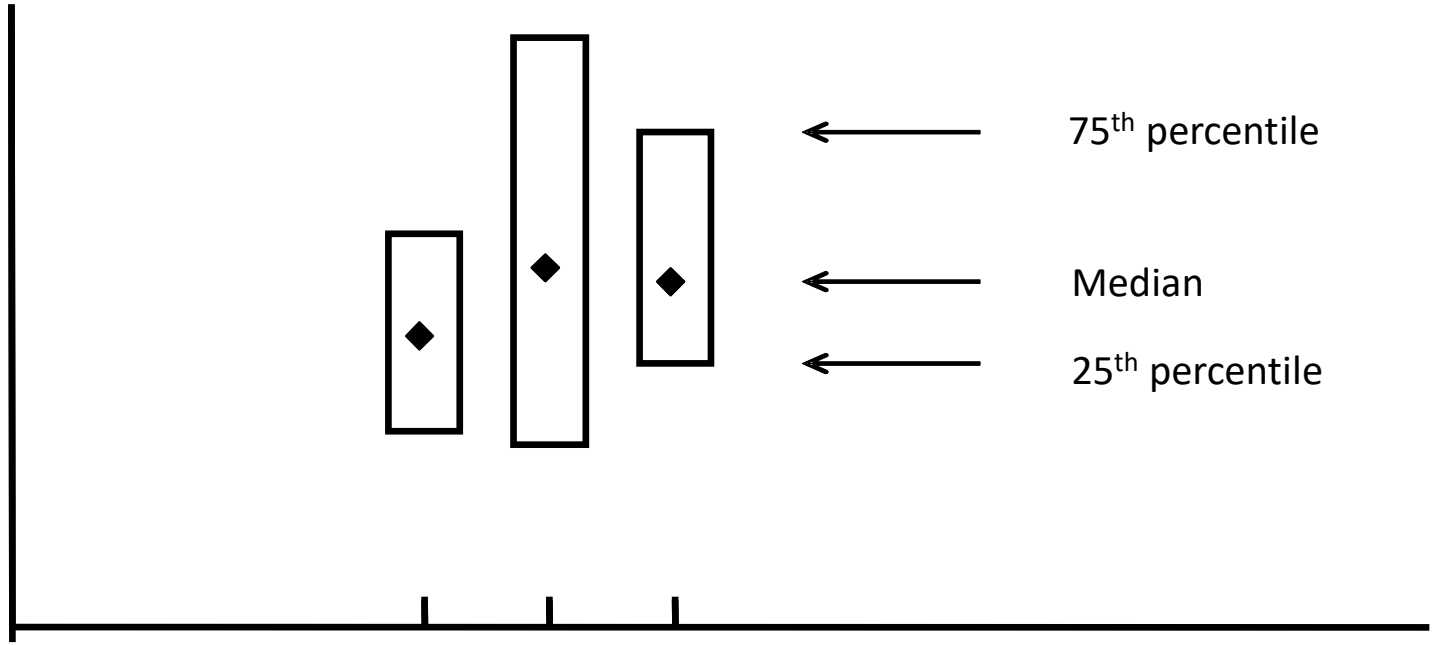
- **AbbVie GK**
- **Amgen K.K.**
- **Astellas Pharma Inc.**
- **AstraZeneca K.K.**
- **Bayer Yakuhin, Ltd**
- **Bristol-Myers Squibb K.K.**
- **Chugai Pharmaceutical Co., Ltd.**
- **Daiichi Sankyo Co., Ltd..**
- **Eisai Co., Ltd.**
- **Eli Lilly Japan K.K.**
- **GlaxoSmithKline K.K.**
- **Janssen Pharmaceutical K.K.**
- **JAPAN TOBACCO INC**
- **MSD K.K.**
- **Nippon Boehringer Ingelheim Co., Ltd.**
- **Novartis Pharma K.K.**
- **Otsuka Pharmaceutical Co., Ltd.**
- **Pfizer R&D Japan G.K.**
- **Sanofi K.K.**
- **Shionogi & Co., Ltd.**
- **Takeda Pharmaceutical Co., Ltd.**

II. Trials Targeted and Survey Items

- The survey has been conducted since 2004, and data is currently accumulated every 2 years

- Trials targeted by 2023 survey
  - Studies completed between April 1, 2021 and March 31, 2023. (For 2 years)
  - Completed studies were regarded as completed with submission of the final report at the final study site in principle. Therefore, it should be noted that the results of the present data totalization do not include data of studies that required a long period of time to complete the study (studies that have not been completed at the time of the survey in fiscal year 2023).
  - Studies to be included were all clinical trials (including 'Oncology Phase I' and the vaccine study for healthy adults), except for the Phase4 and the healthy volunteer Phase1.
  - Data collected were comparatively investigated by dividing the period based on the starting year of each study into three segments "2013 to 2015," "2016 to 2018," and "2019 to 2022."
  - The data of the overseas sites in the global studies are used only for comparison between the global studies and the domestic studies and tabulation of the global studies in Background.

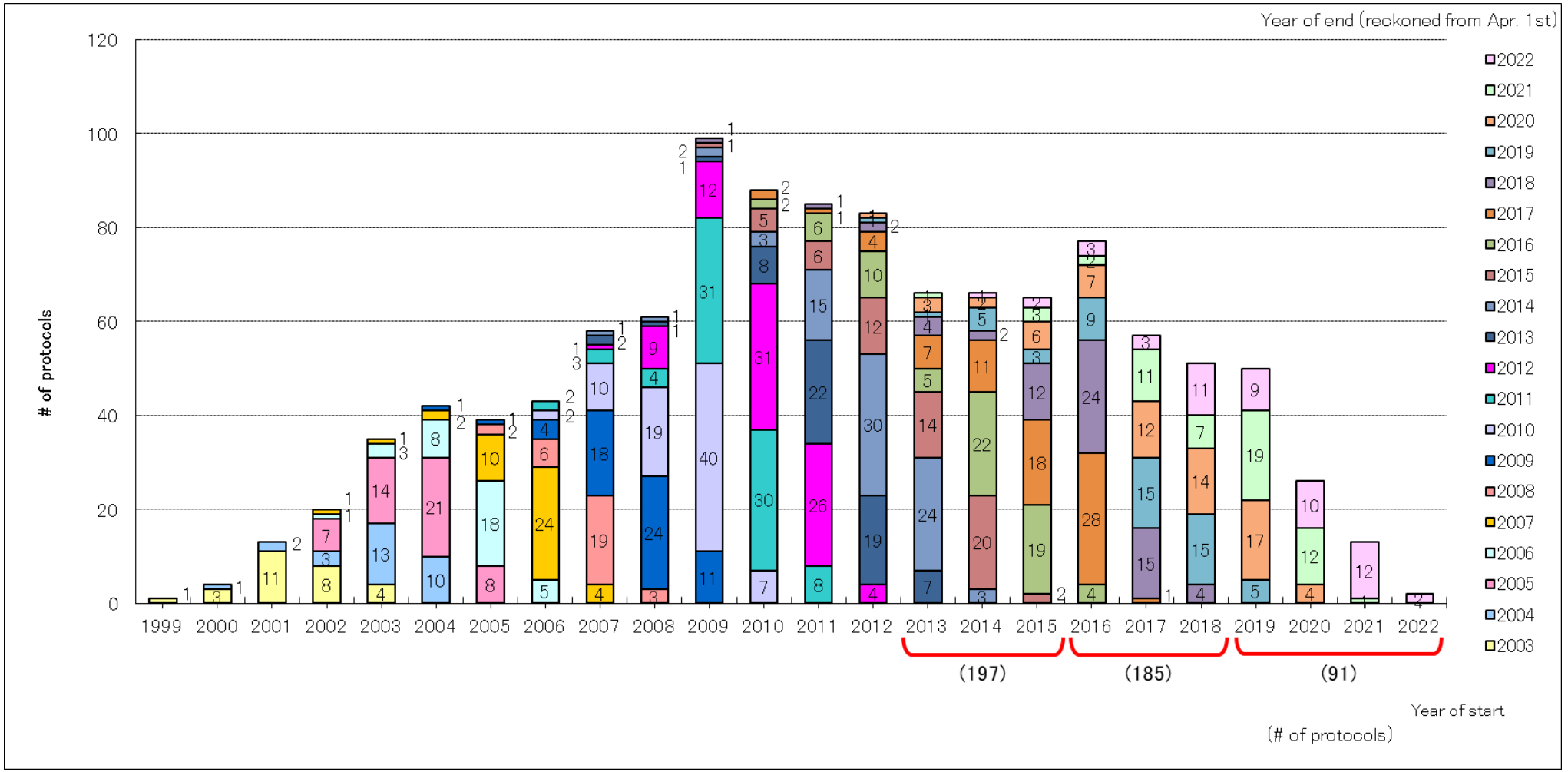
Explanation of a Figure and Box Plot



The lower and upper end of the box in the plot represent respectively 25% point and 75% point of the sample, and the diamond in the center represents 50% point (median).

III-1 Background

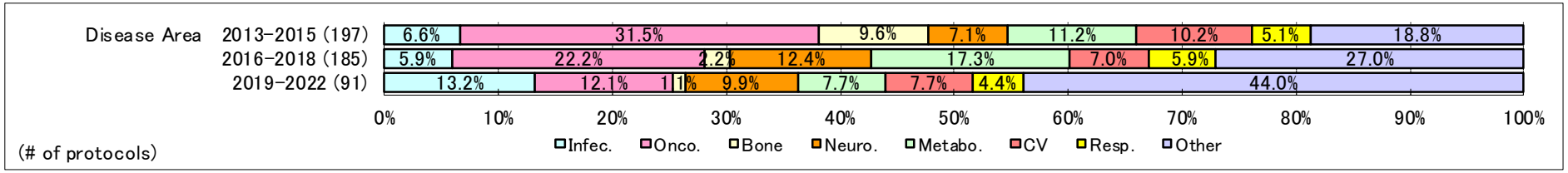
III-1-1 Number of Protocols by Starting Year and Ending Year

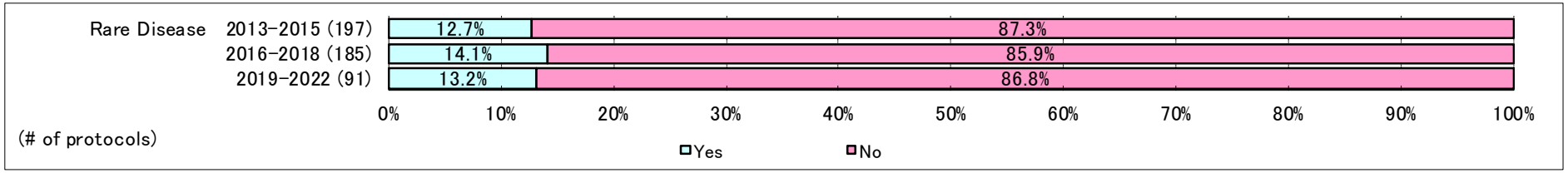


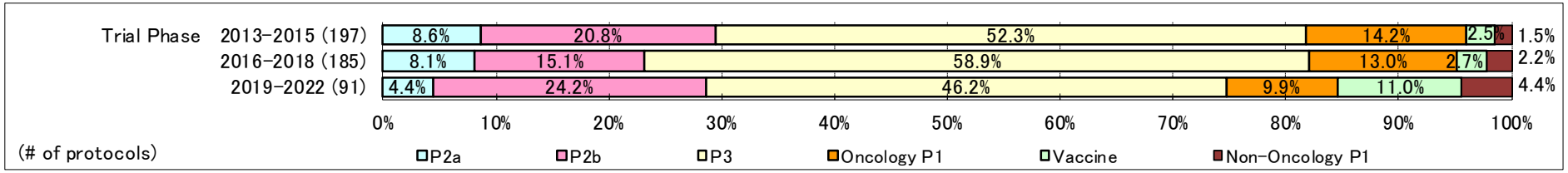
Horizontal axis: study starting year, vertical axis: number of studies by study starting year, legend label (right): study ending year

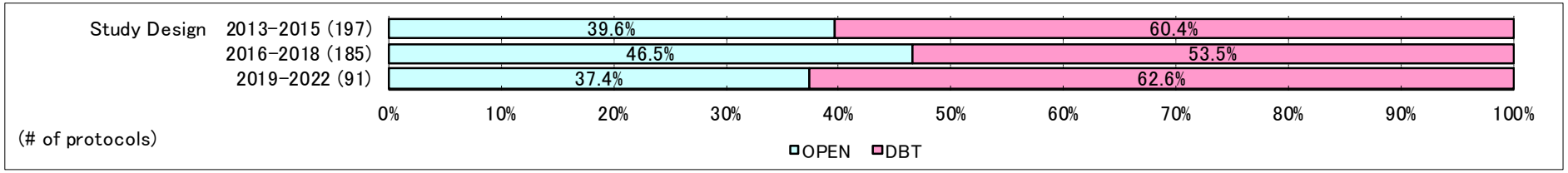
Since this survey is performed on the basis of completed studies, special attention should be paid to non-inclusion of data of studies that takes a long time to complete (i.e., studies not completed at the time of the 2023 survey) particularly in years "2019-2022." （Applicable to all tables and figures follows）

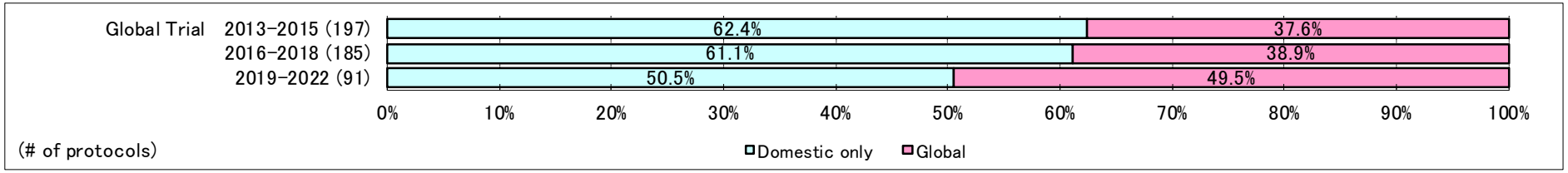
III-1-5 Background of Protocols 1



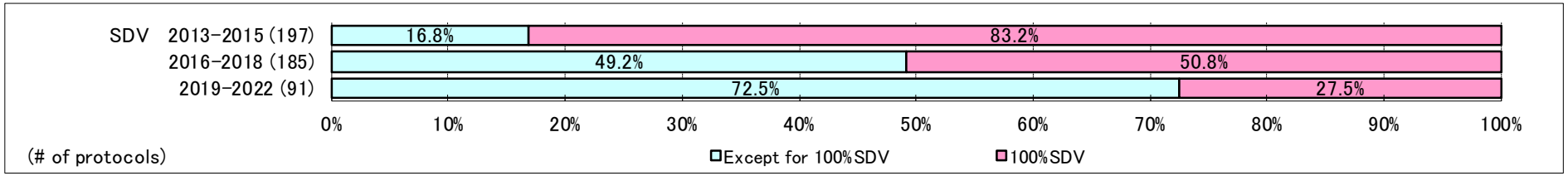


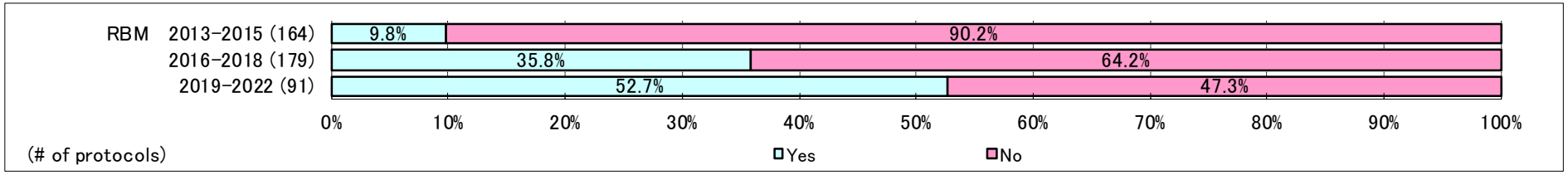




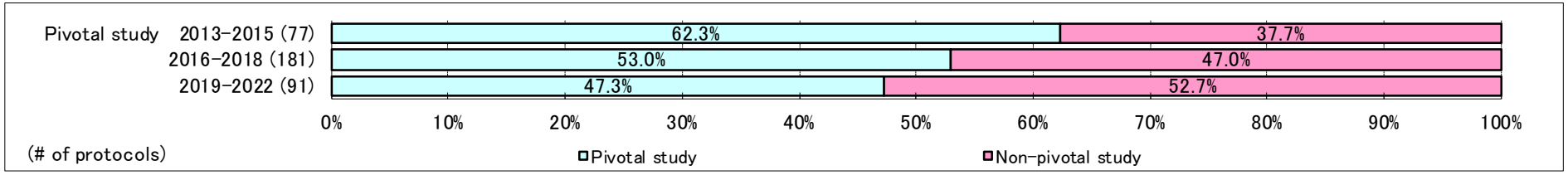


III-1-5 Background of Protocols 2

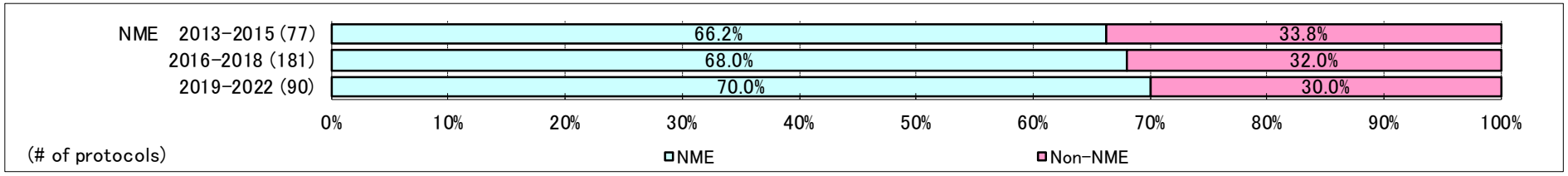




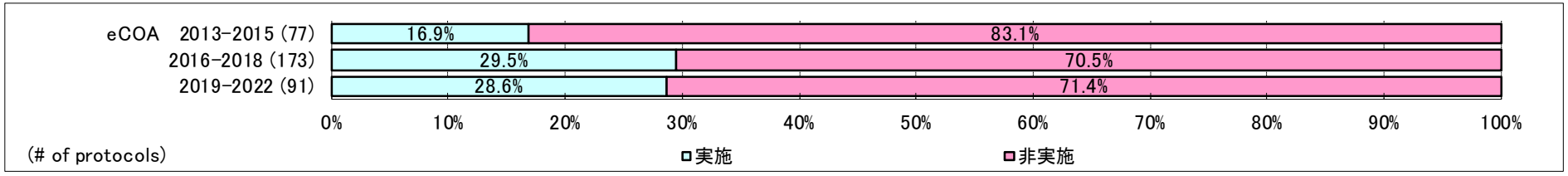
(Survey started in 2017)



(Survey started in 2019)

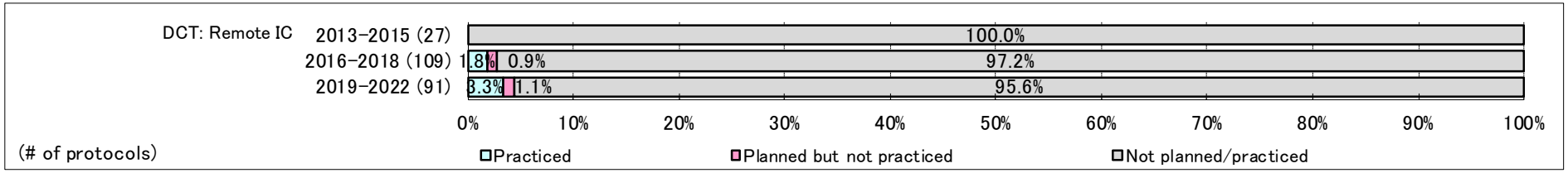


(Survey started in 2019)

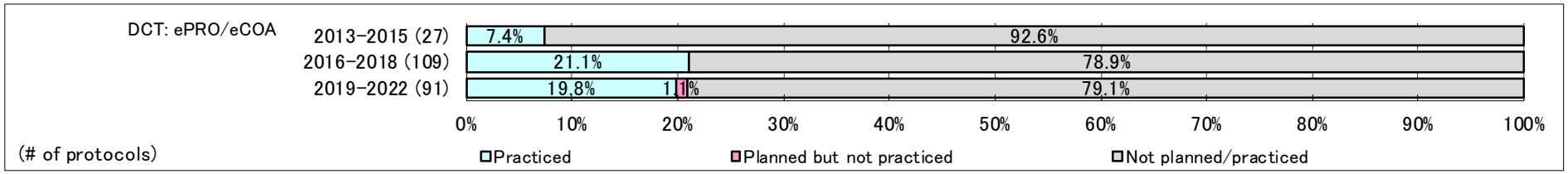


(Survey started in 2019)

III-1-5 Background of Protocols 3



(Survey started in 2021)



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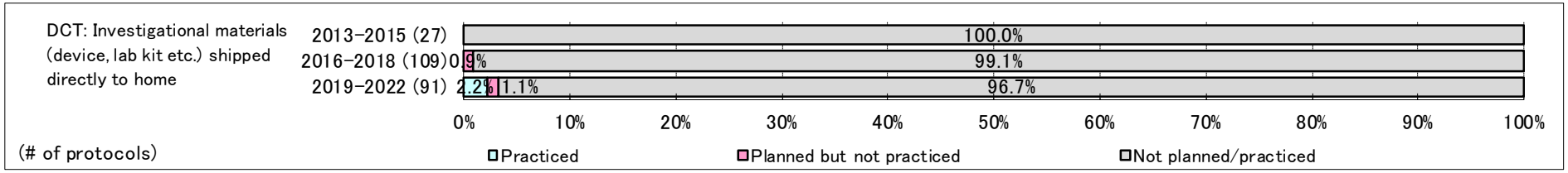
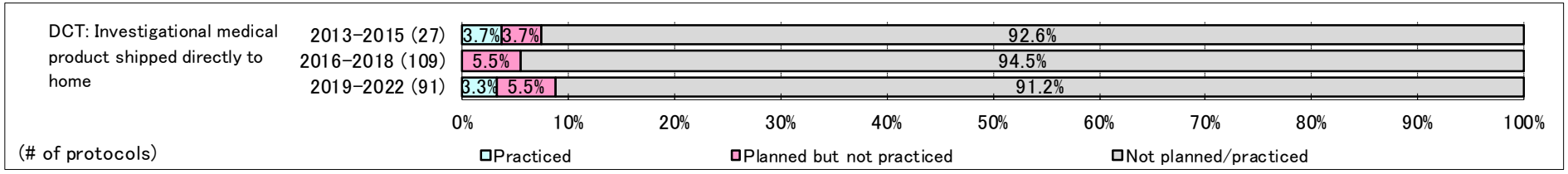


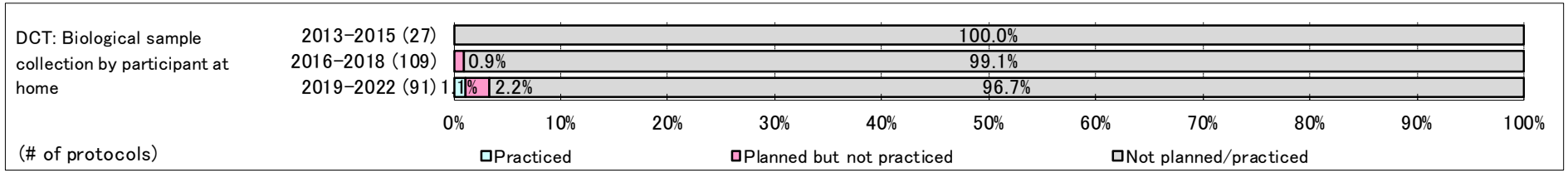
(Survey started in 2021)



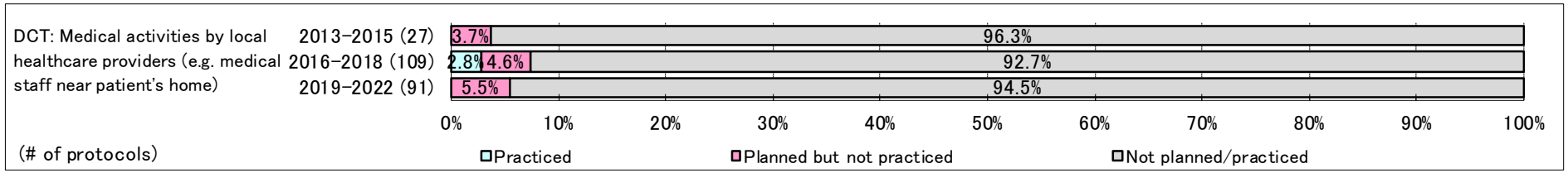
(Survey started in 2021)

Practiced: Was planned as a study and practiced in at least 1 subject.
Planned but not practiced: Was planned as a study, but not practiced.
Not planned/practiced: Not planned as a study.

III-1-5 Background of Protocols 4



(Survey started in 2021)



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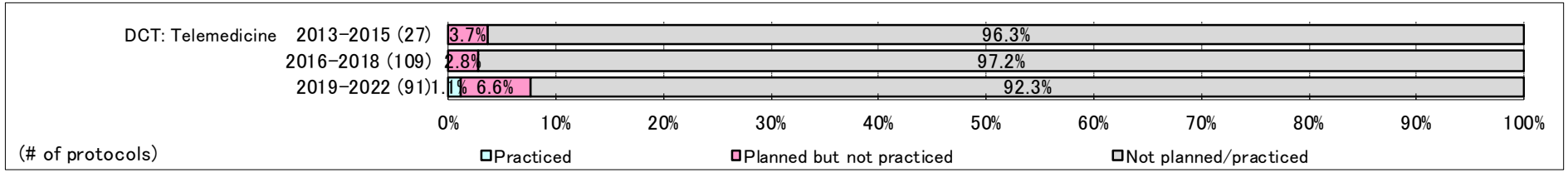

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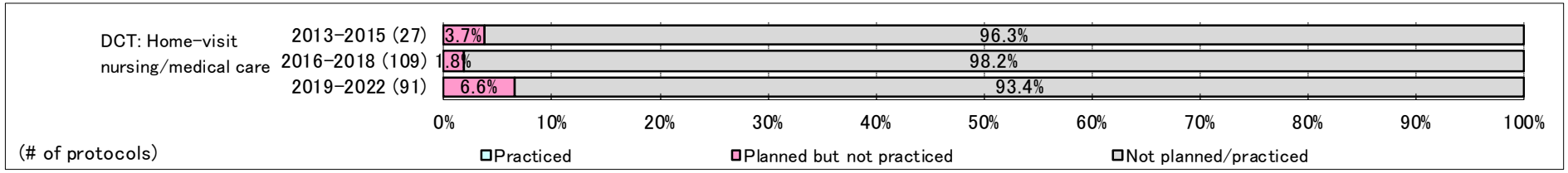
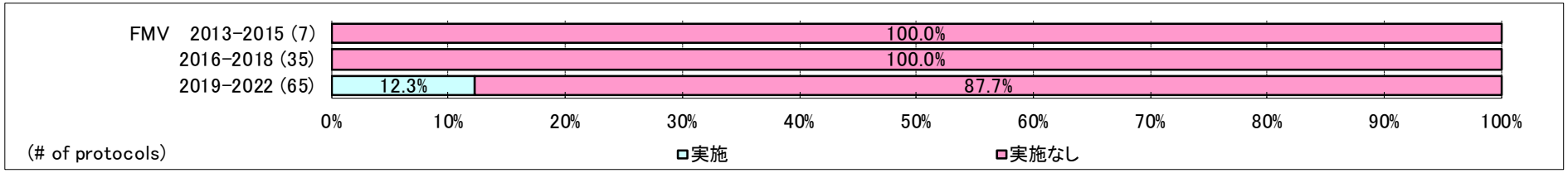


(Survey started in 2021)

Practiced: Was planned as a study and practiced in at least 1 subject.
Planned but not practiced: Was planned as a study, but not practiced.
Not planned/practiced: Not planned as a study.

III-1-5 Background of Protocols 5

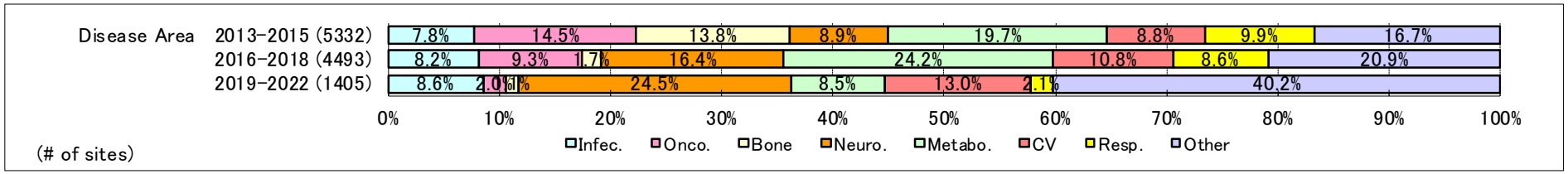


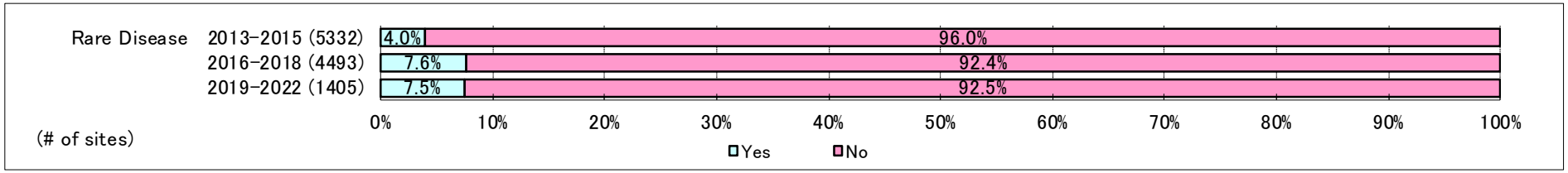
(Survey started in 2021)

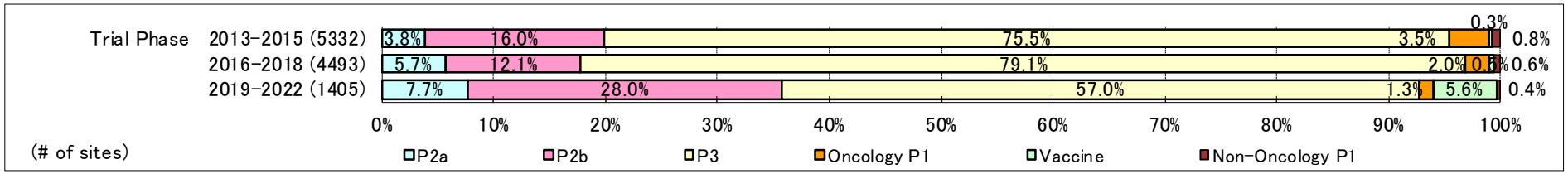
Conducted FMV, Not Conducted of FMV

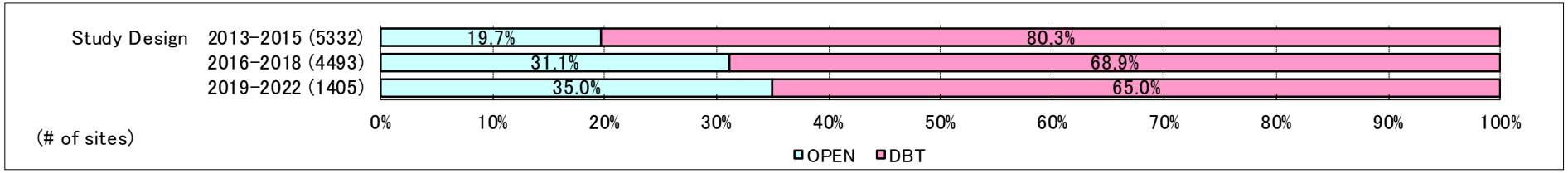
FMV：Study cost calculations based on Fair Market Value (market-based pricing).

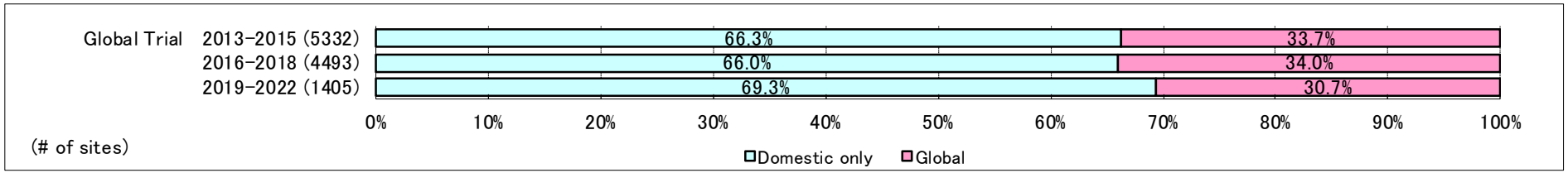
III-1-7-1 Background of Sites 1



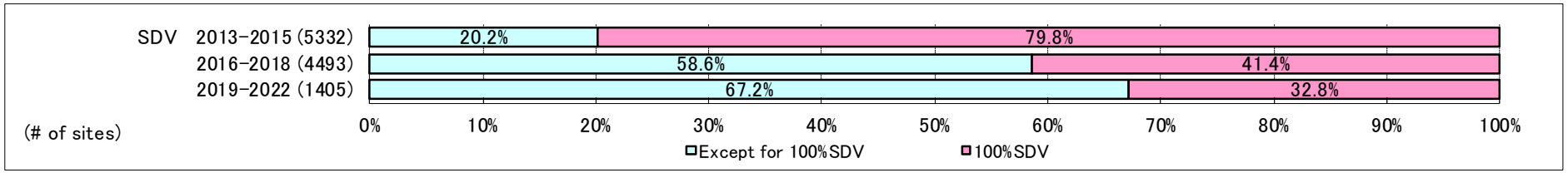


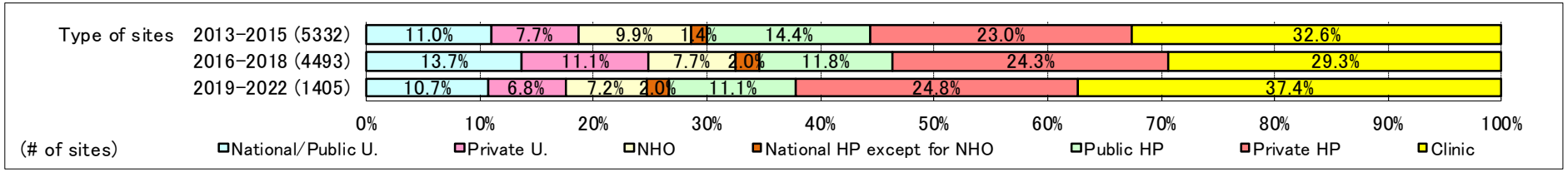


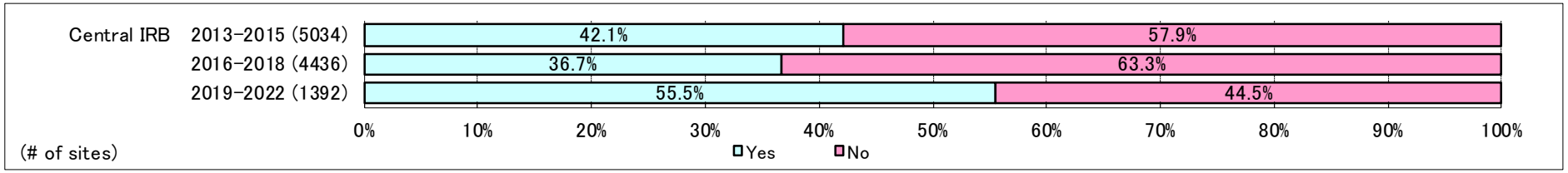


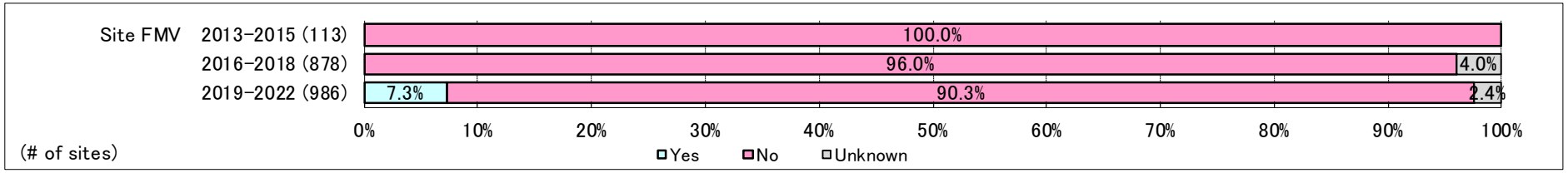


III-1-7-2 Background of Sites 2



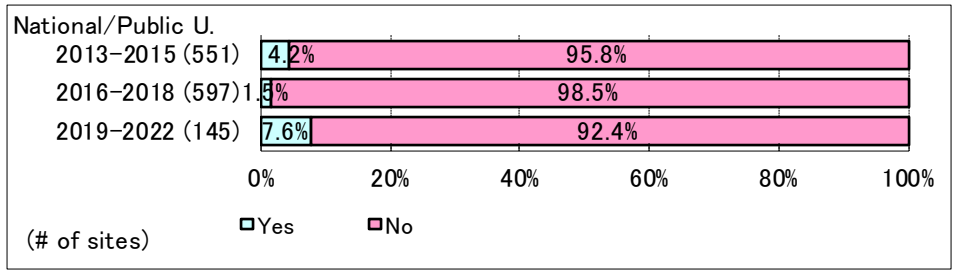


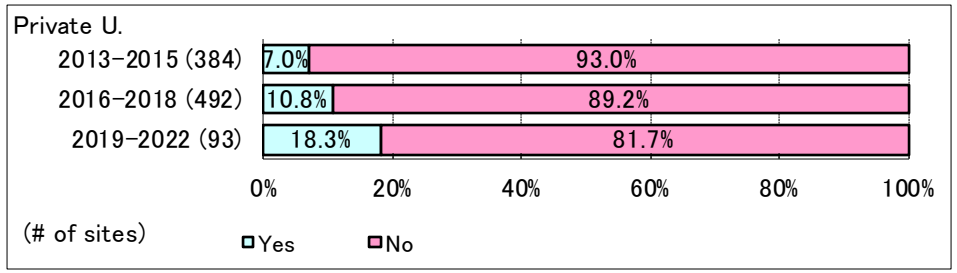


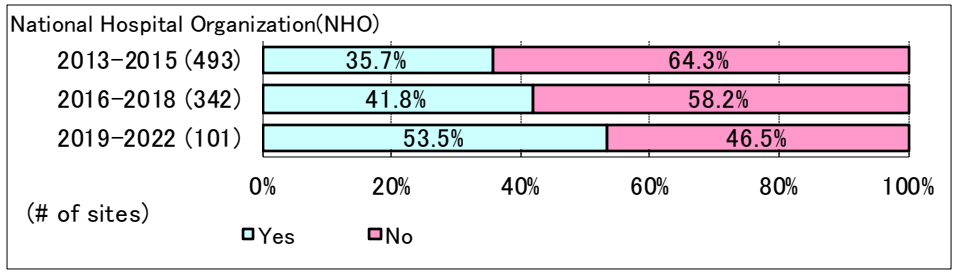


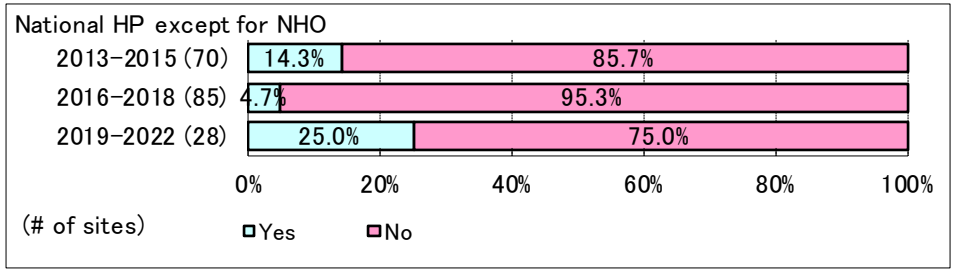
(Survey started in 2021)

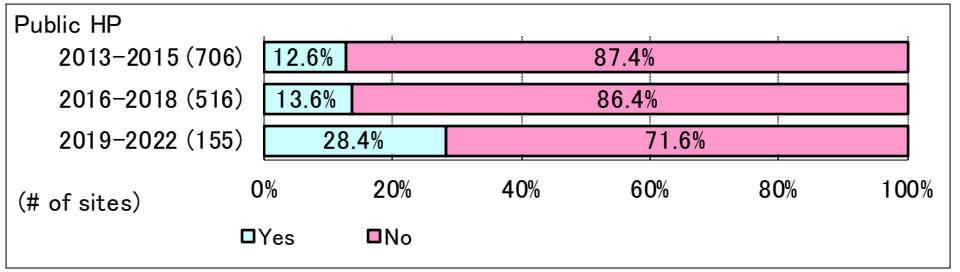
III-1-7-3 Central IRB [Sub analysis]

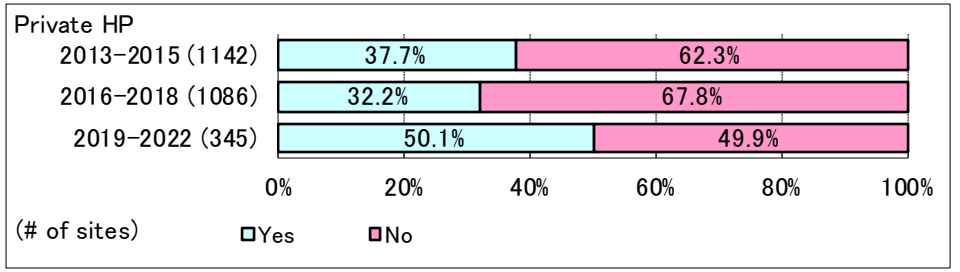


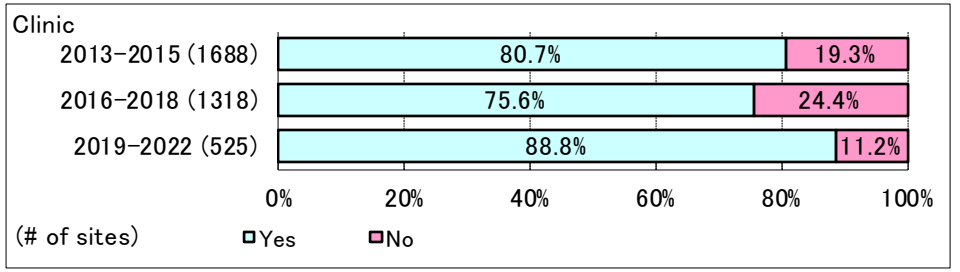






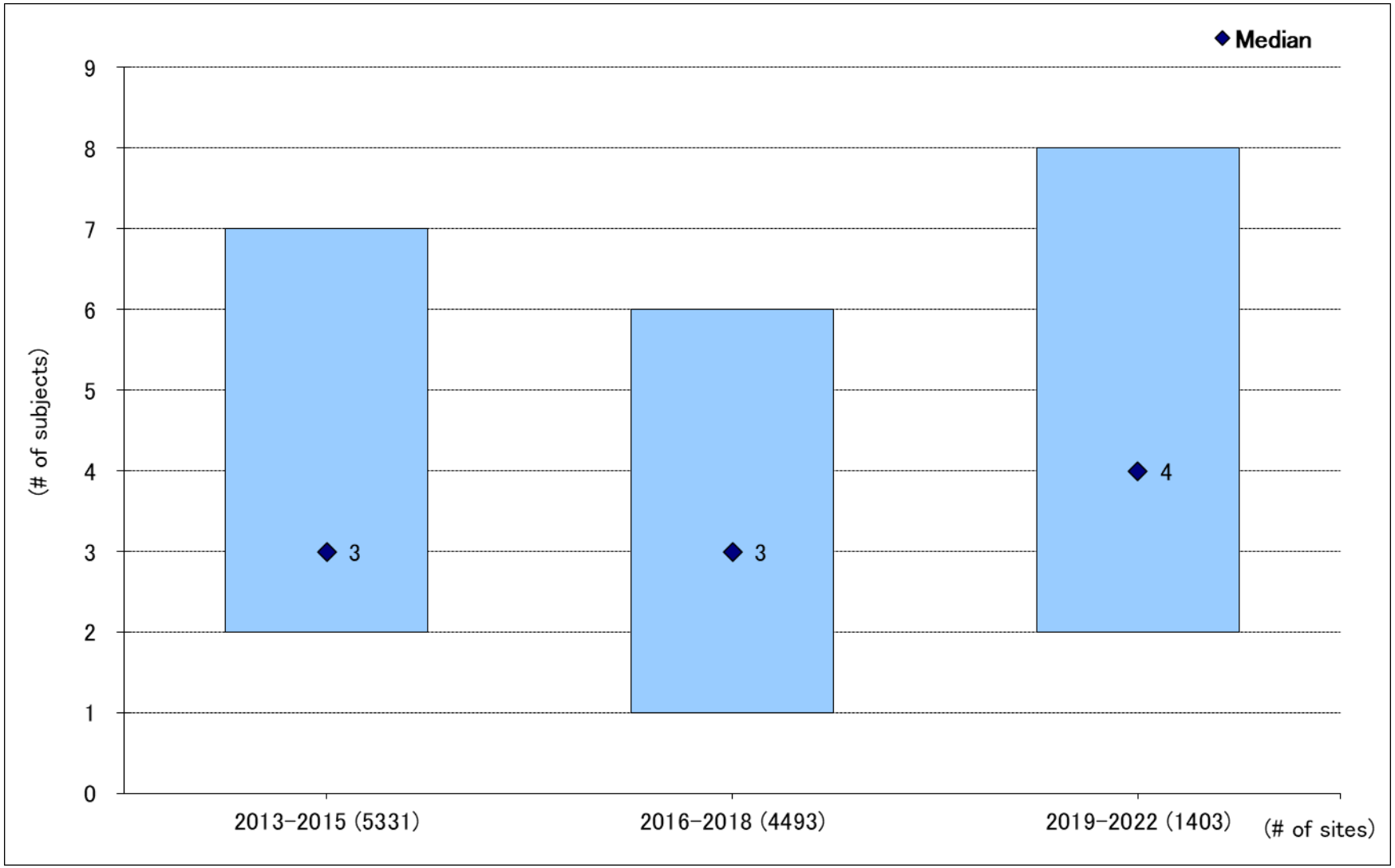




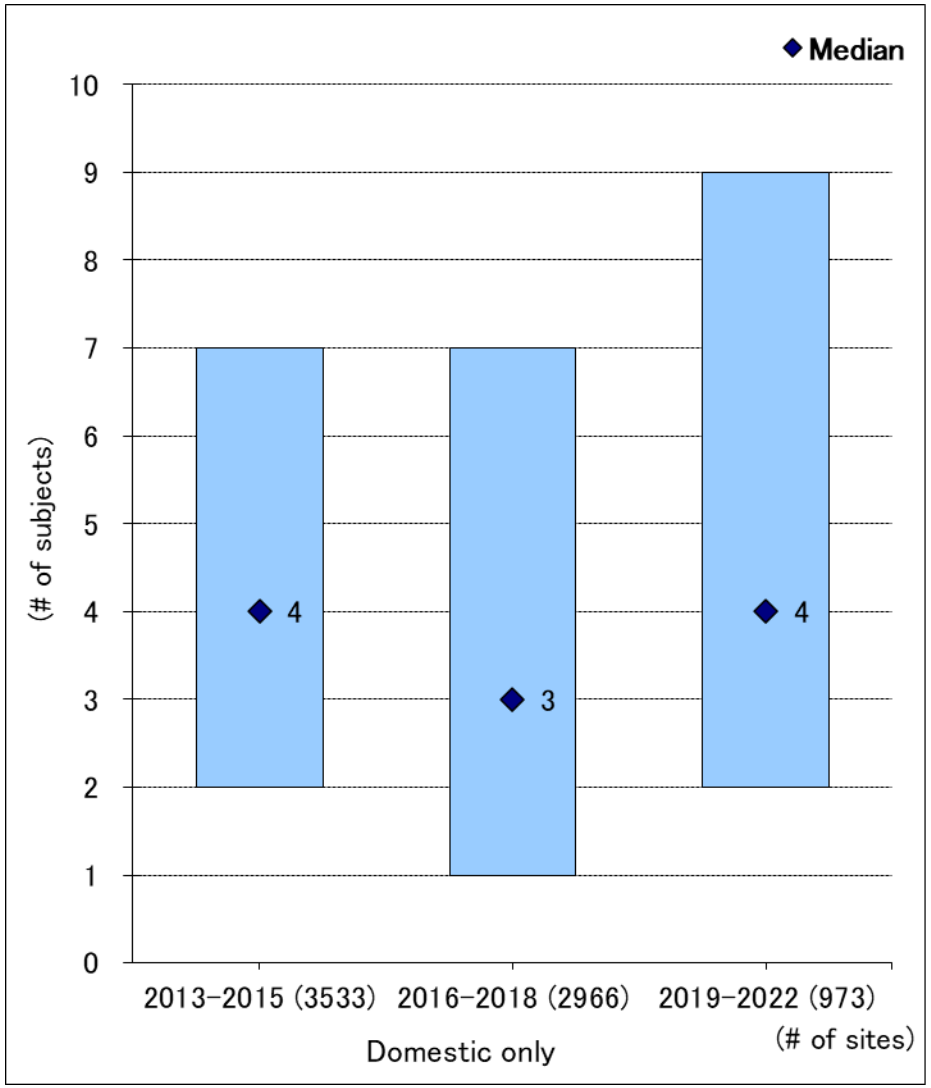


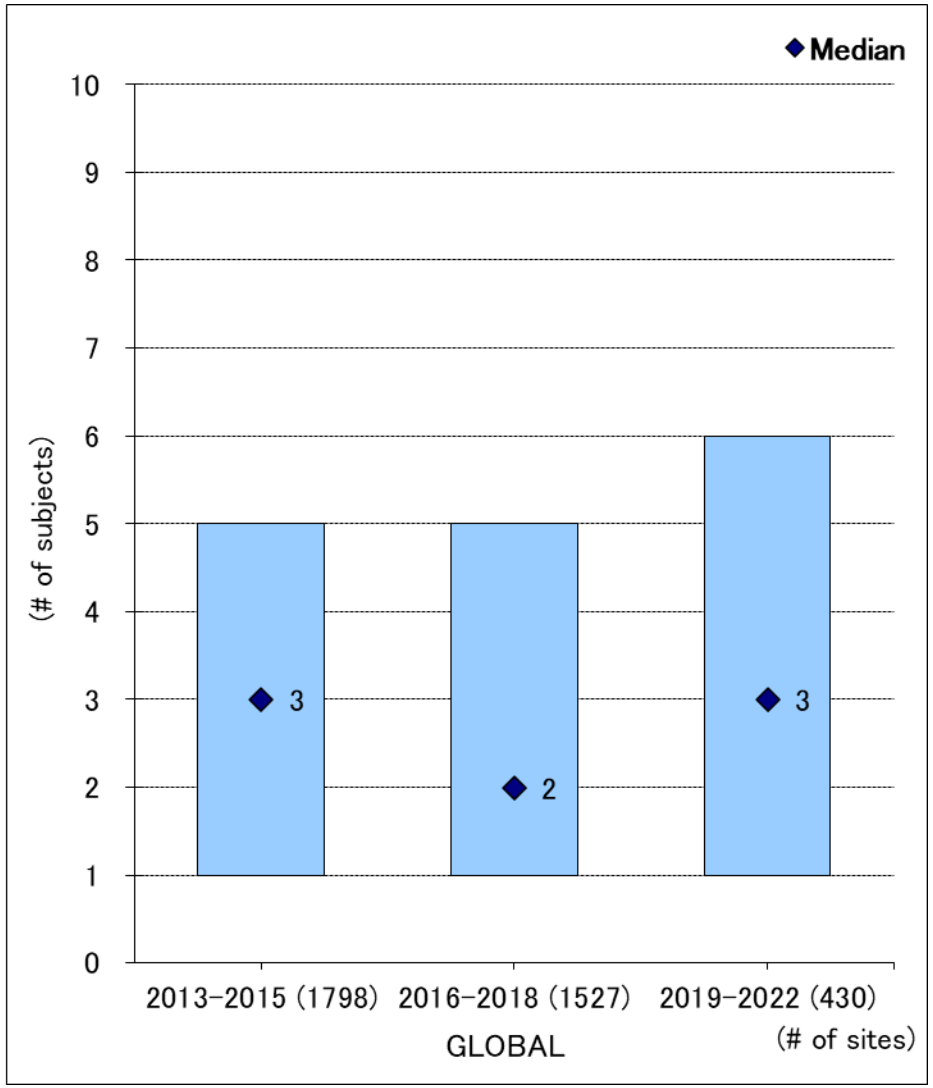
III-2 Enrollment

III-2-1 Number of Enrolled Subjects per Site

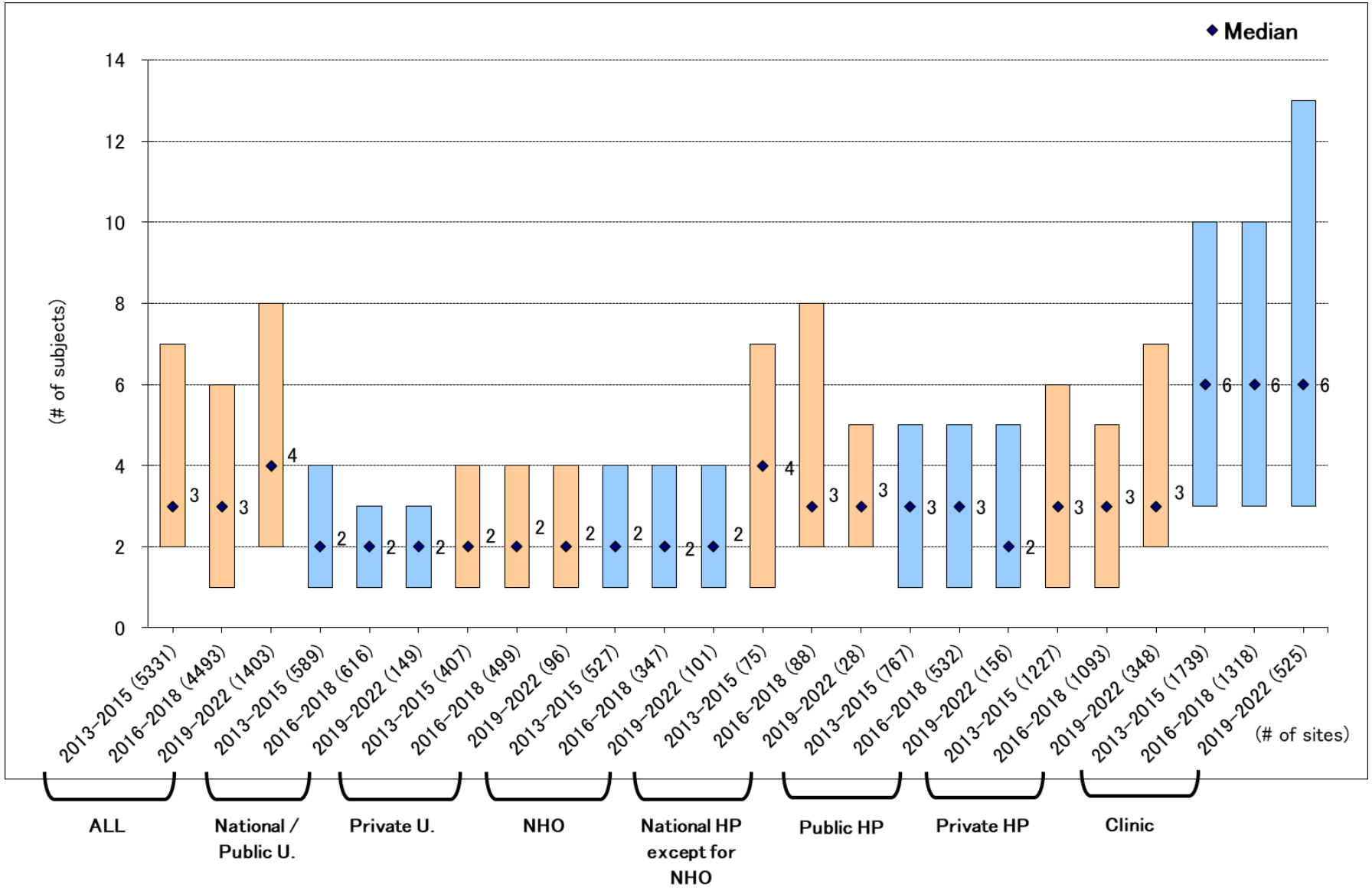


III-2-1-1 Number of Enrolled Subjects per Site for each Domestic or Global Trial

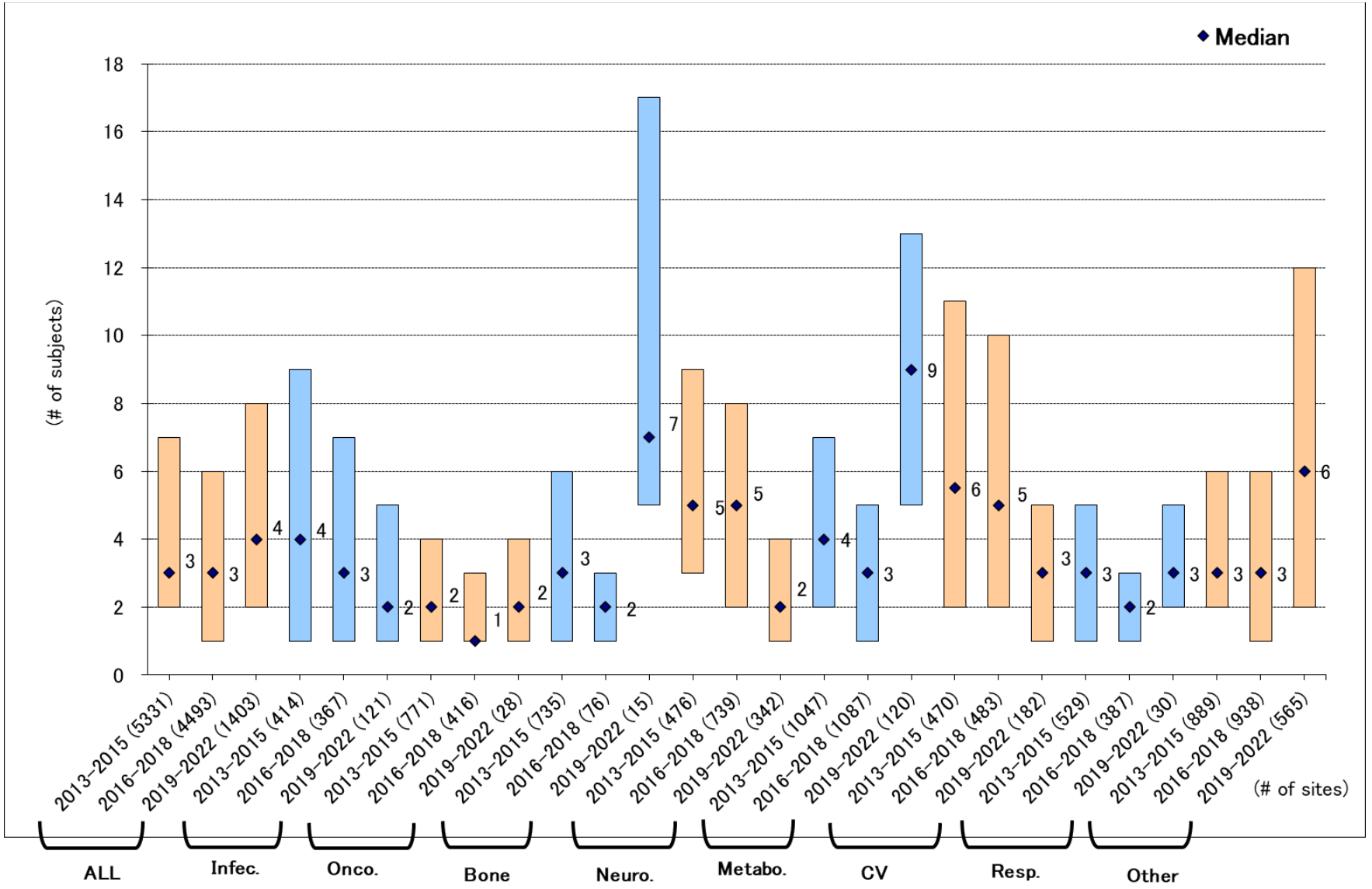




III-2-2 Number of Enrolled Subjects per Site by Type of Site

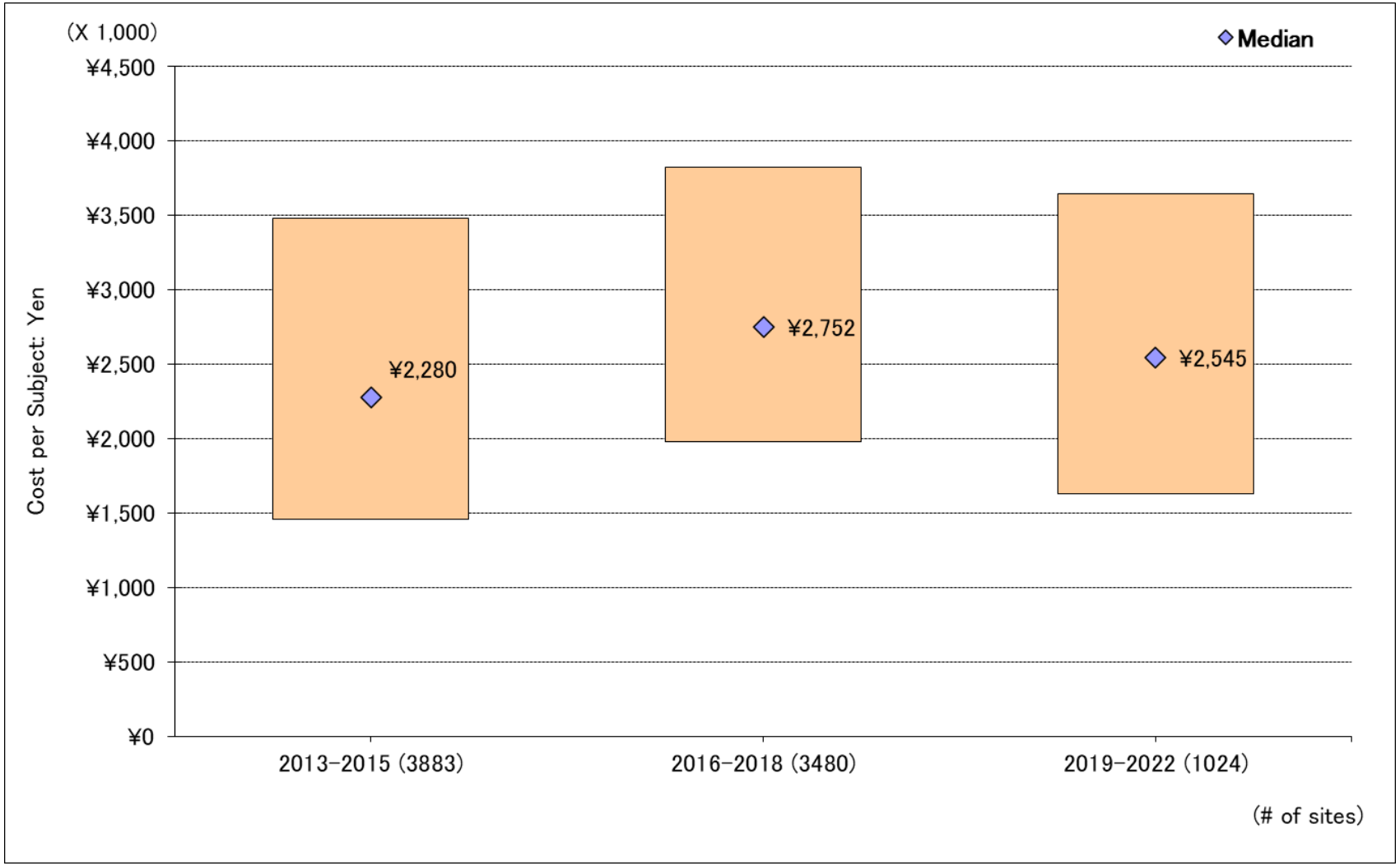


III-2-3 Number of Enrolled Subjects per Site by Disease Area



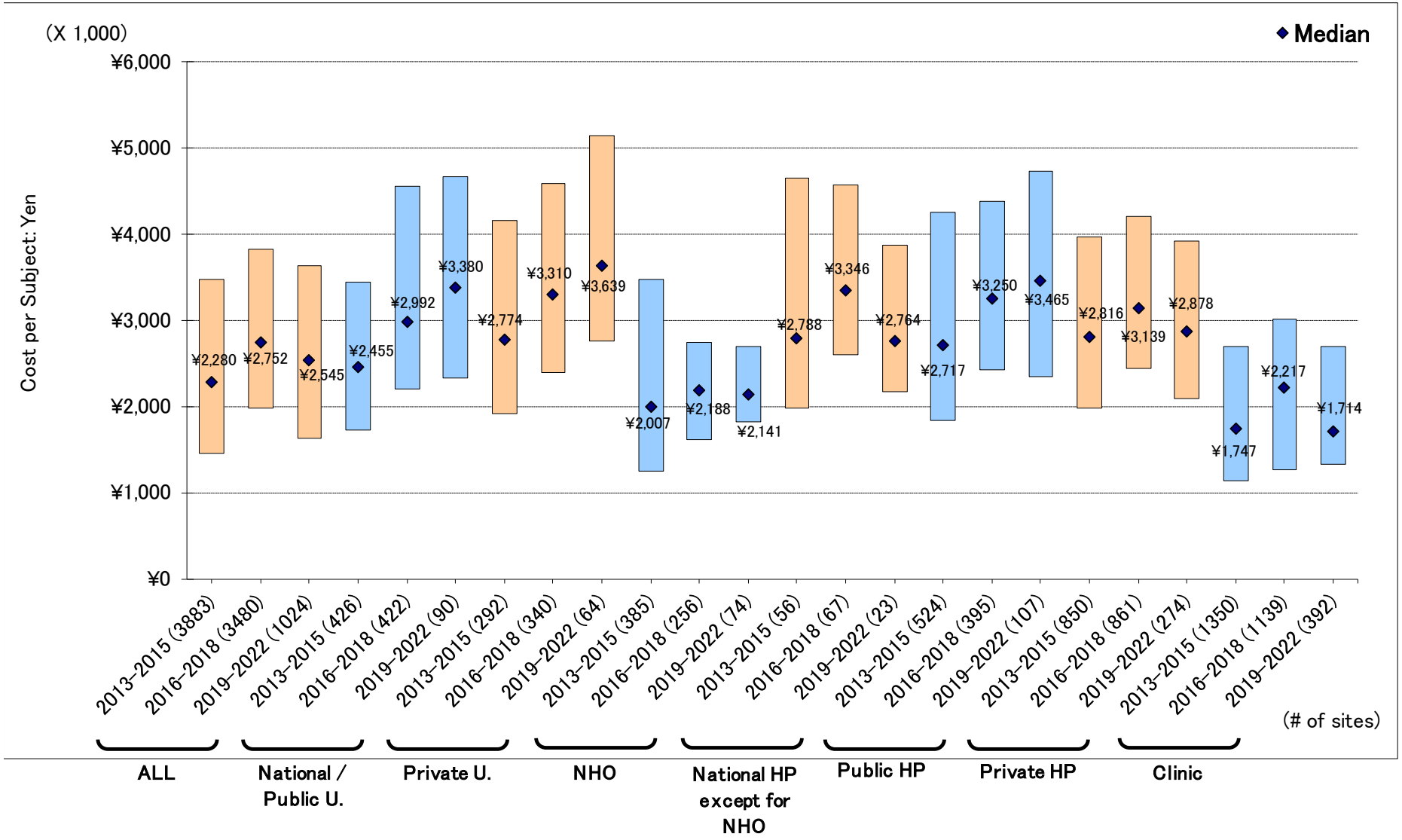
III-3 Cost

III-3-1 Cost per Enrolled Subject



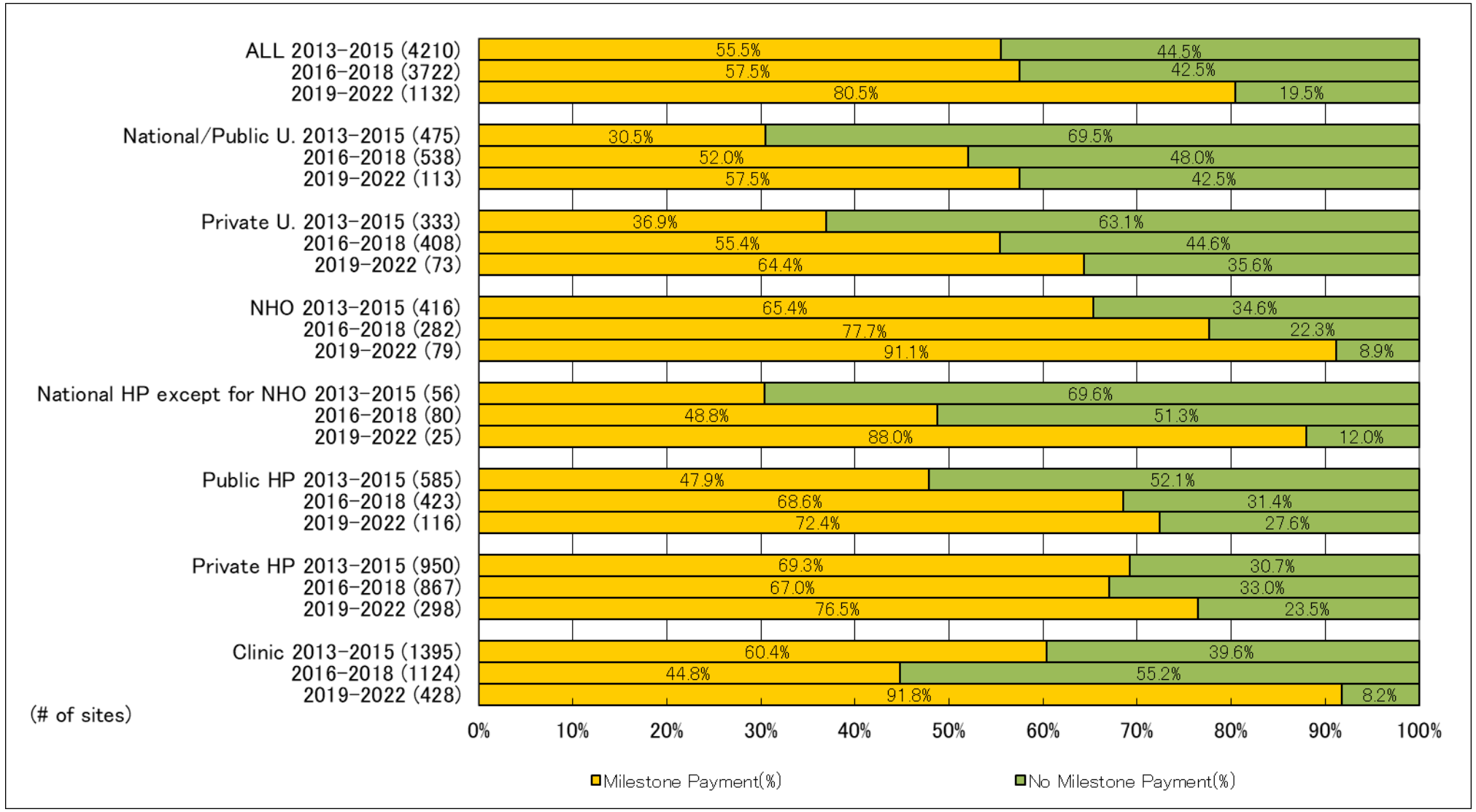
Vertical axis：Costs per subject (total payment to study sites and SMO)

III-3-2 Cost per Enrolled Subject by Type of Site

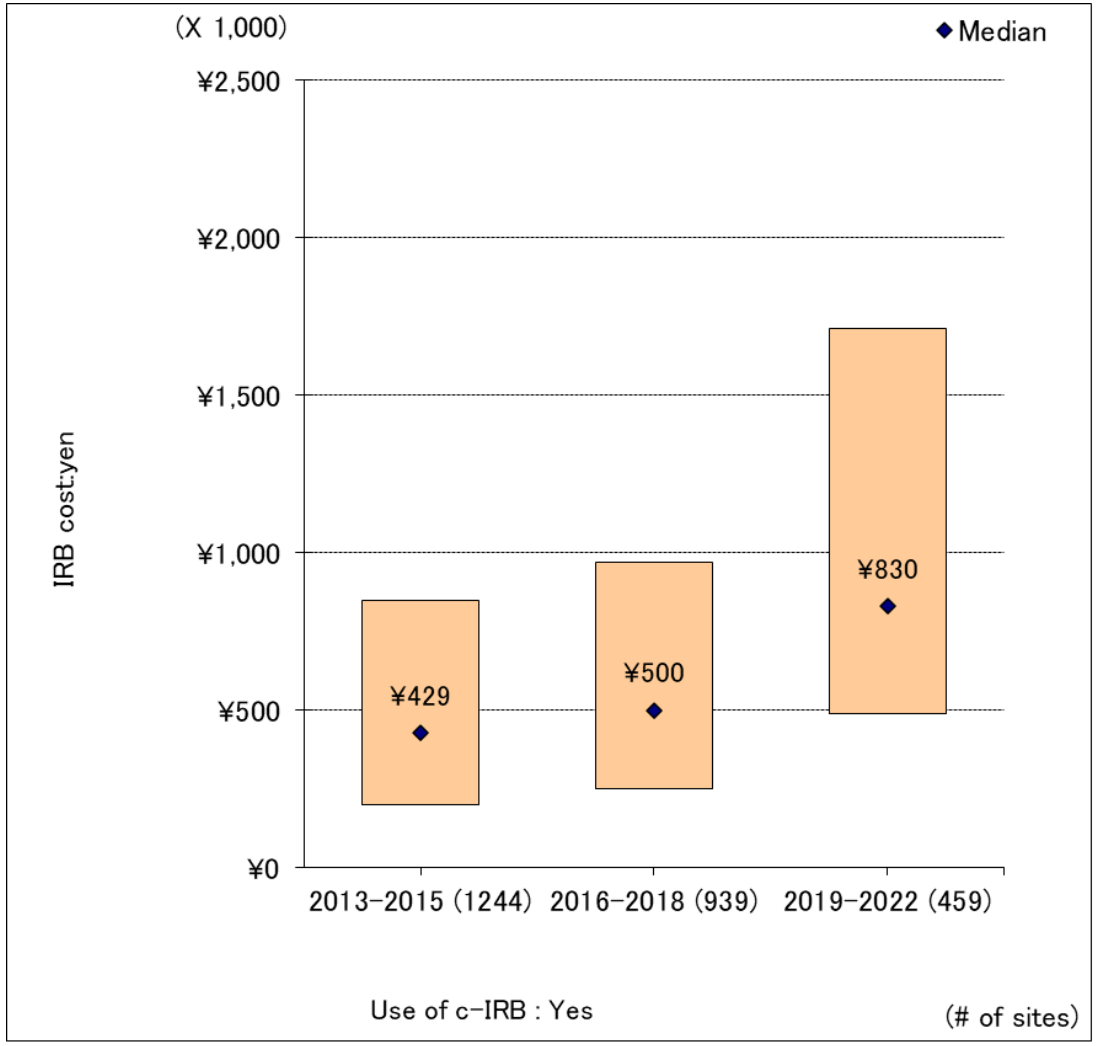


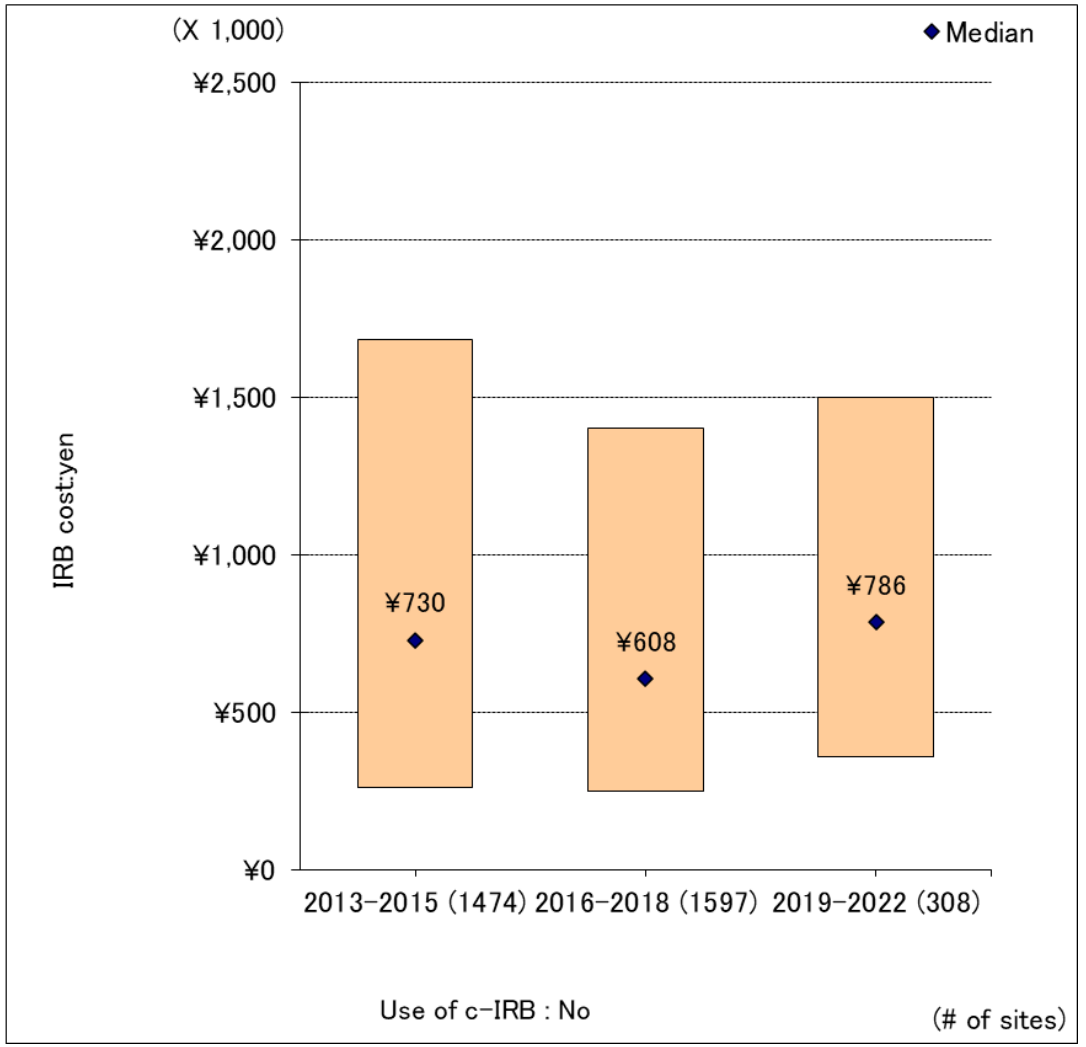
Vertical axis：Costs per subject (total payment to study sites and SMO)

III-3-4 Implementation of Milestone Payment in Site by Type of Site



III-3-11-1 IRB Cost: [Sub analysis] Utilization of c-IRB



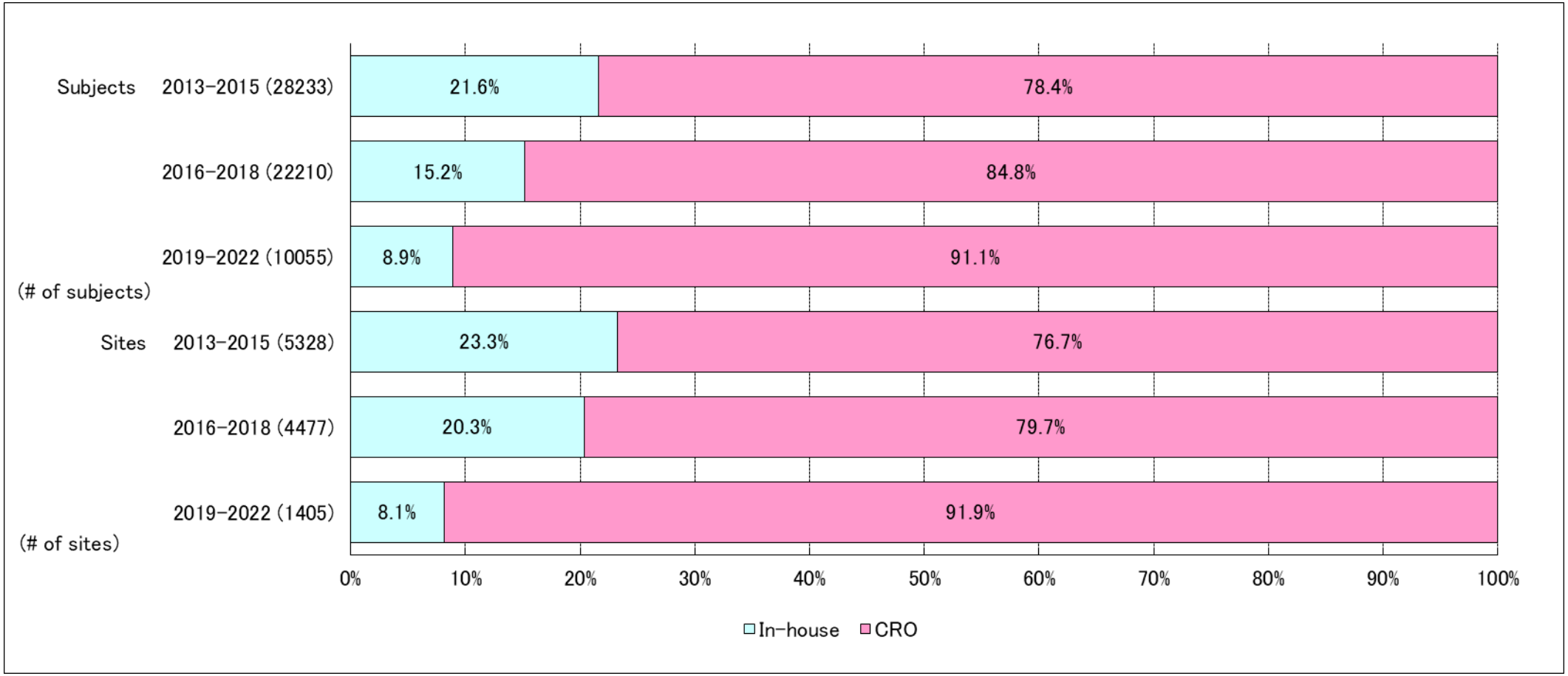


Vertical axis: Total IRB cost paid to study sites and SMO

Due to the inappropriate error label on IRB costs in the previous (prior2017) survey form entry check, some of the IRB cost data may not have been properly collected in the before 2017 survey.

III-4 Monitoring Performance

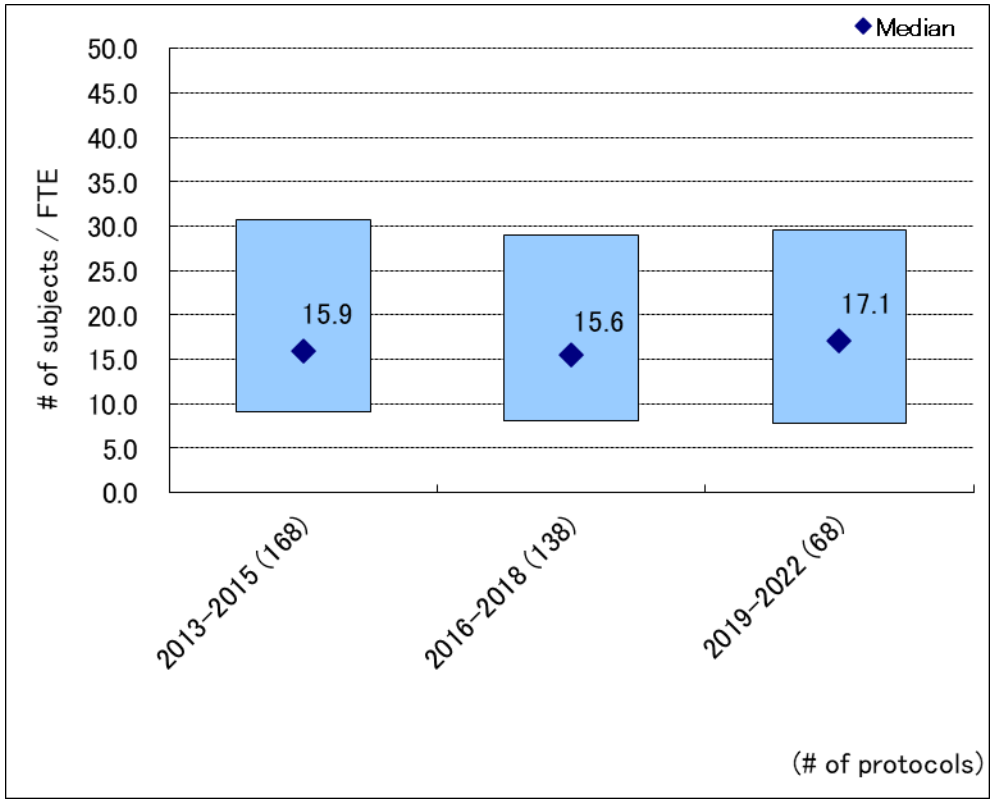
III-4-1 Proportion the Number of Enrolled Subjects and Sites by Affiliation



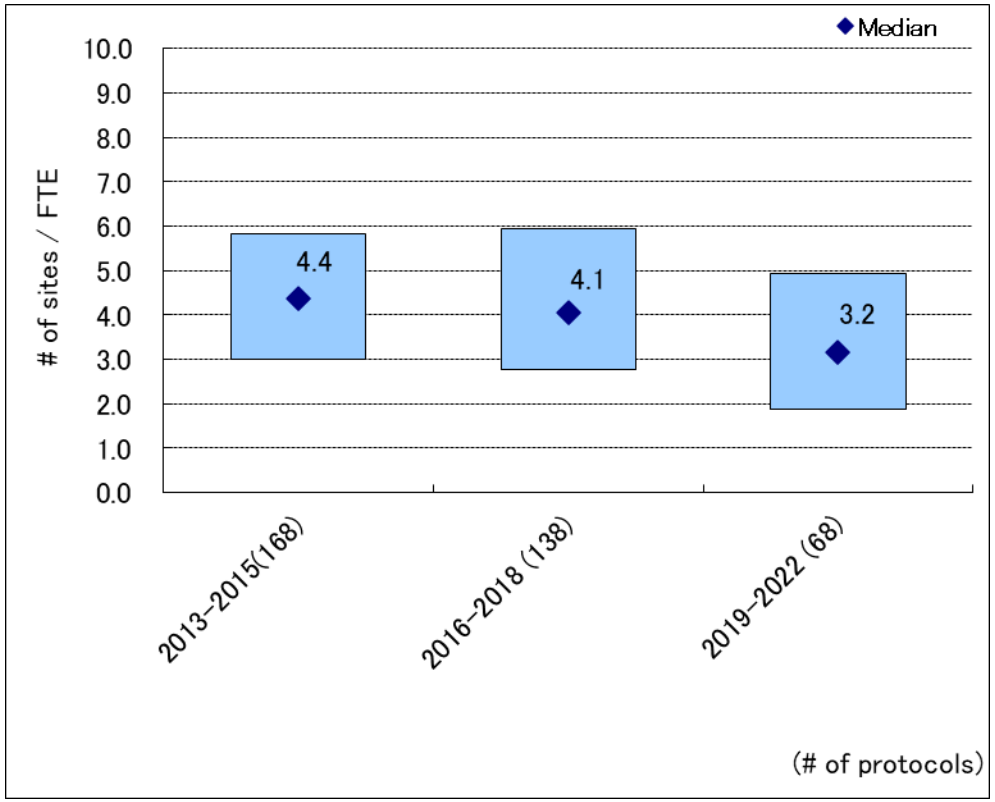
Vertical axis：Proportions of enrolled subjects and study sites were compared by affiliation of monitors (in-house or CRO).

III-4-2/3 Number of Sites/Enrolled Subjects per Monitoring (FTE) by Affiliation

III-4-2 Number of Enrolled Subjects per Monitoring (FTE) by Affiliation



III-4-3 Number of Sites per Monitoring (FTE) by Affiliation



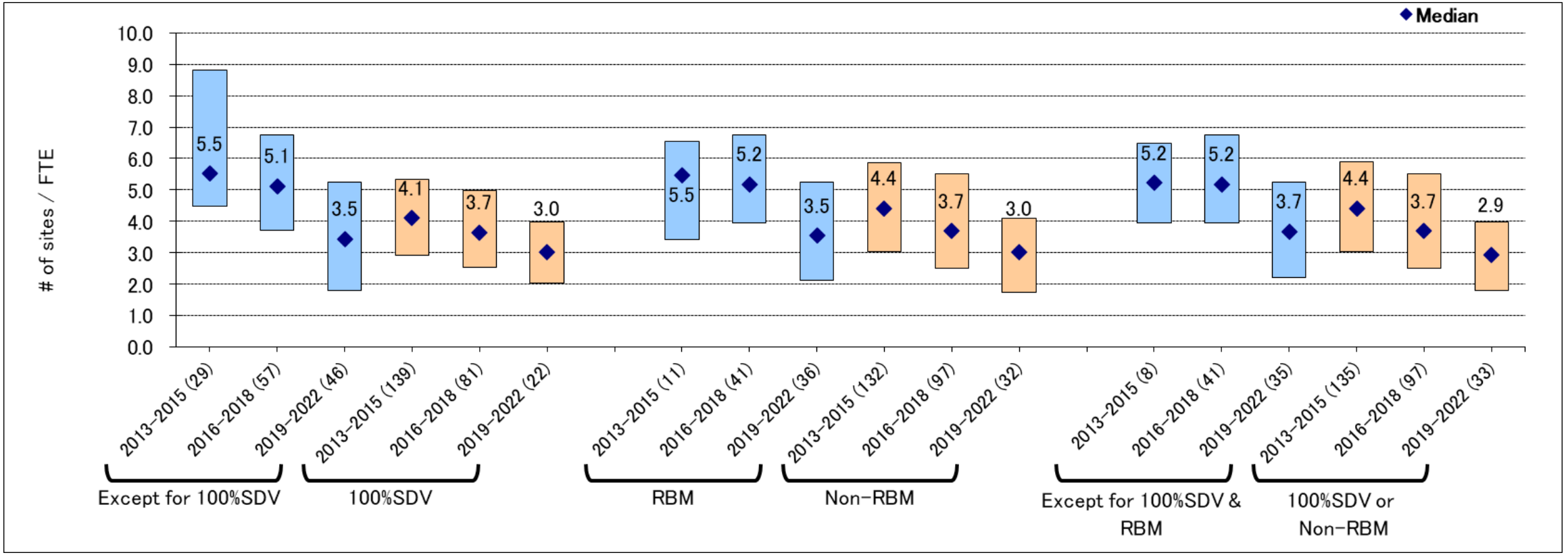
1 FTE (Full Time Equivalent) =One person works for 100% of standard labor time a year.

III-4-3-2/3/4 Number of Sites per Monitoring (FTE) by Affiliation and SDV

III-4-3-2 Sub-analysis with or without 100%SDV

III-4-3-3 Sub analysis with or without RBM

III-4-3-4 Sub analysis with or without 100%SDV & RBM



- **Except for 100% SDV:** The number of sites per monitor 1FTE in the protocol with the answer that non-100% SDV, such as sampling and RBM, was performed
- **100% SDV:** The number of sites per monitor 1FTE in the protocol with the answer that 100% SDV was performed

- **RBM:** The number of sites per monitor 1FTE in the protocol with the answer that RBM was performed
- **Non-RBM:** The number of sites per monitor 1FTE in the protocol with the answer that RBM was not performed

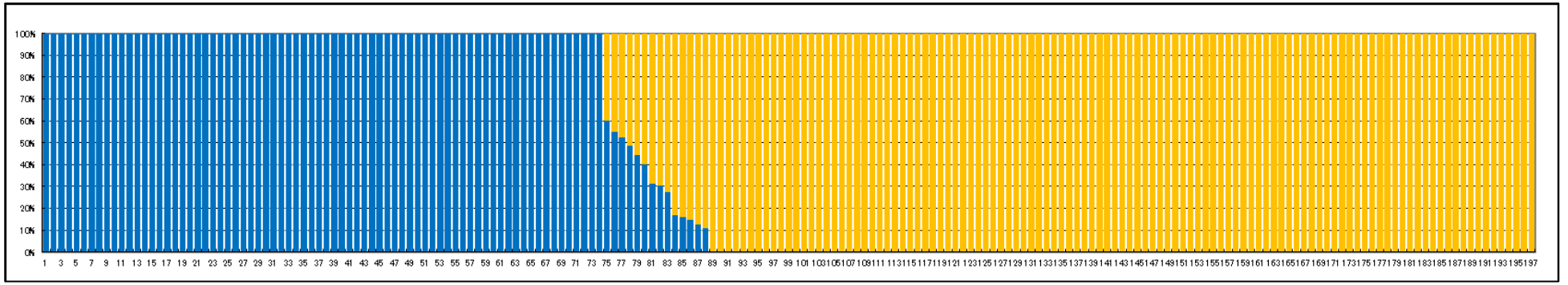
- RBM (Risk Based Monitoring)

- **Except for 100% SDV & RBM:** The number of sites per monitor 1FTE in the protocol with the answer that non-100% SDV, such as sampling and RBM, was performed and RBM was performed.
- **100% SDV or Non-RBM:** The number of sites per monitor 1FTE in the protocol with the answer that full SDV was performed or RBM was not performed

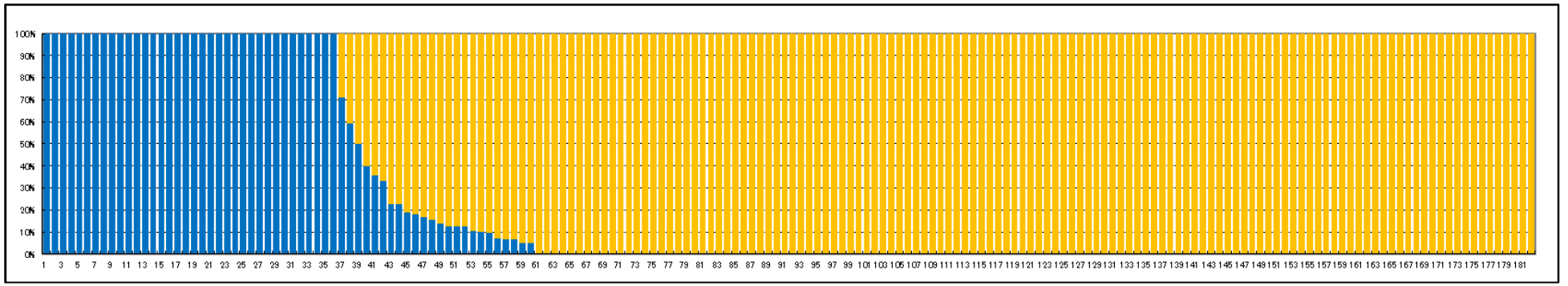
(# of protocols)

III-4-6-2 Proportion of CRA Outsourcing in Total Sites

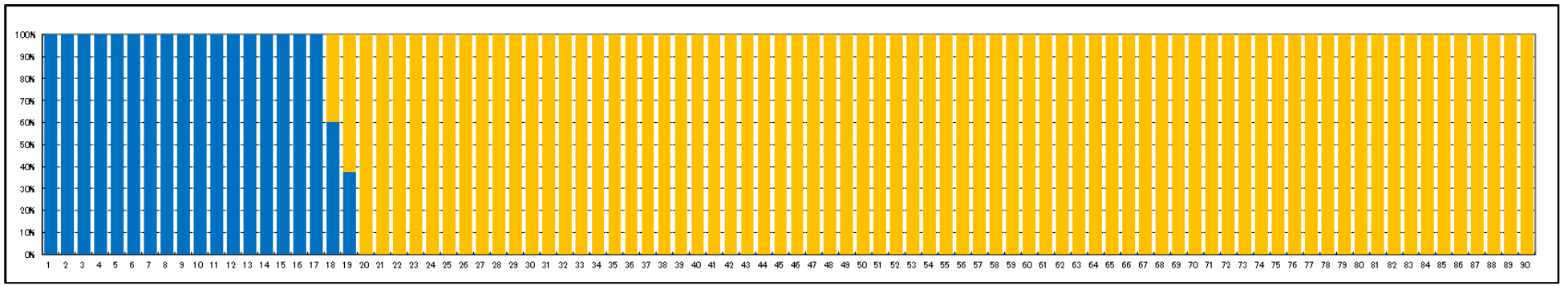
2013-2015



2016-2018



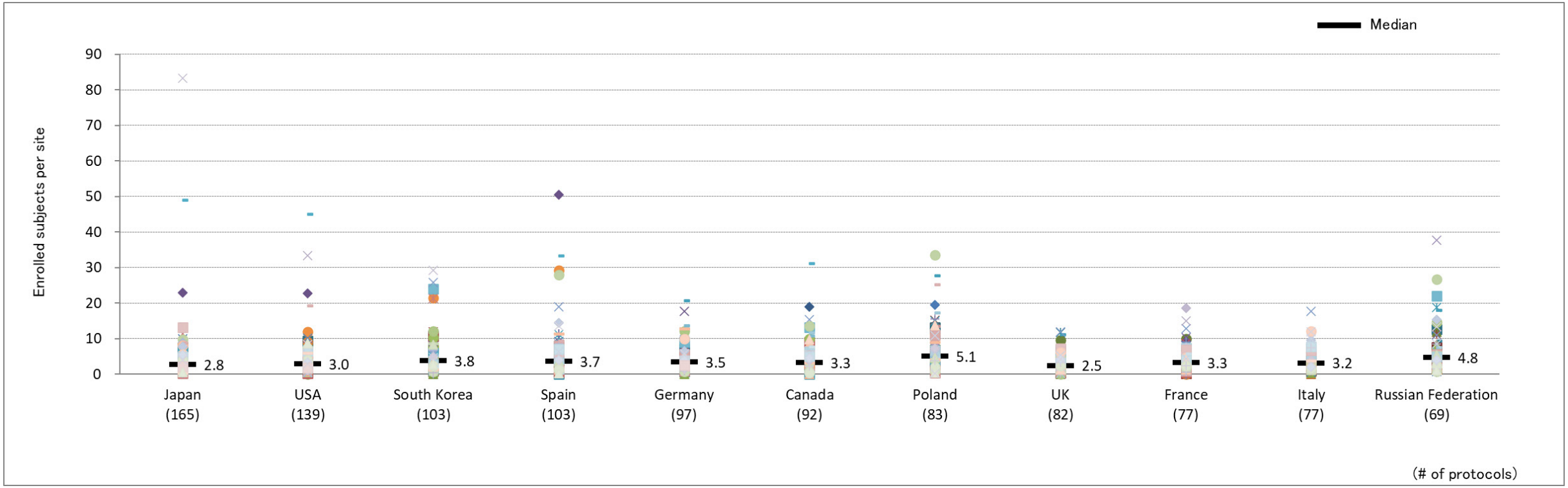
2019-2022



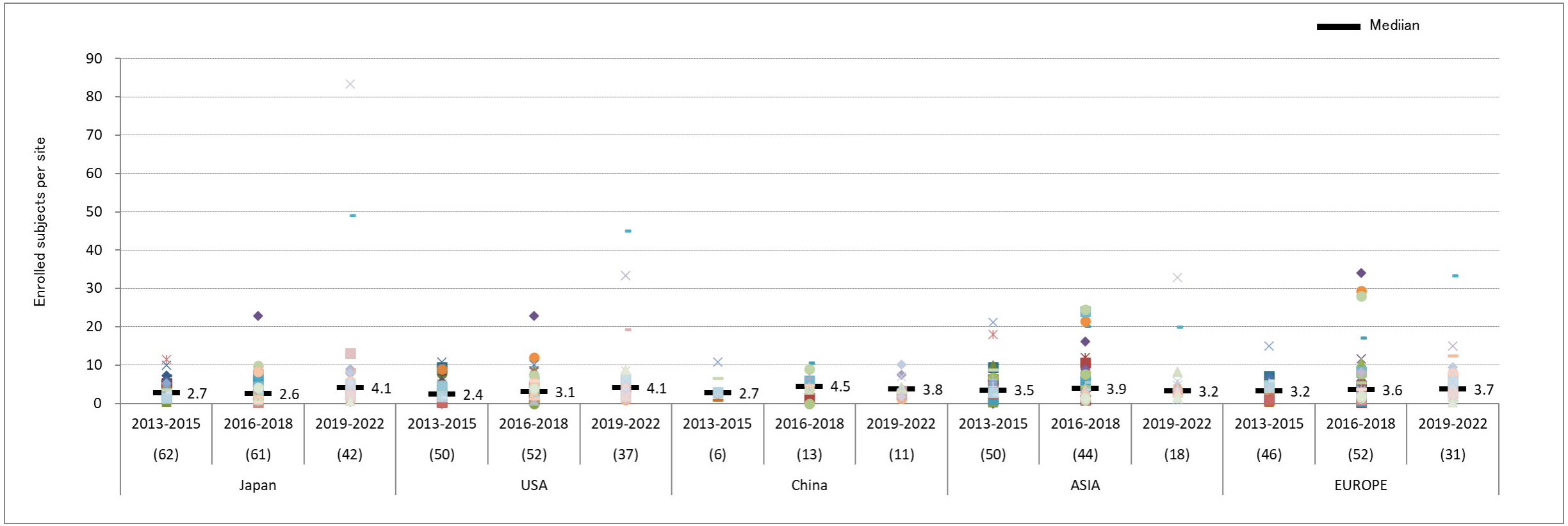
Vertical axis: Protocol (posted for each protocol)　　Affiliation of monitor ■：In-house)、■：CRO

III-5 Global

III-5-3-1 Number of Enrolled Subjects per Site by Most Frequent Top 10 Countries in Global Studies Scatter Plot (2013-2022)



III-5-3-1-3-1 Number of Enrolled Subjects per Site by Region Classification in Global Studies Scatter Plot

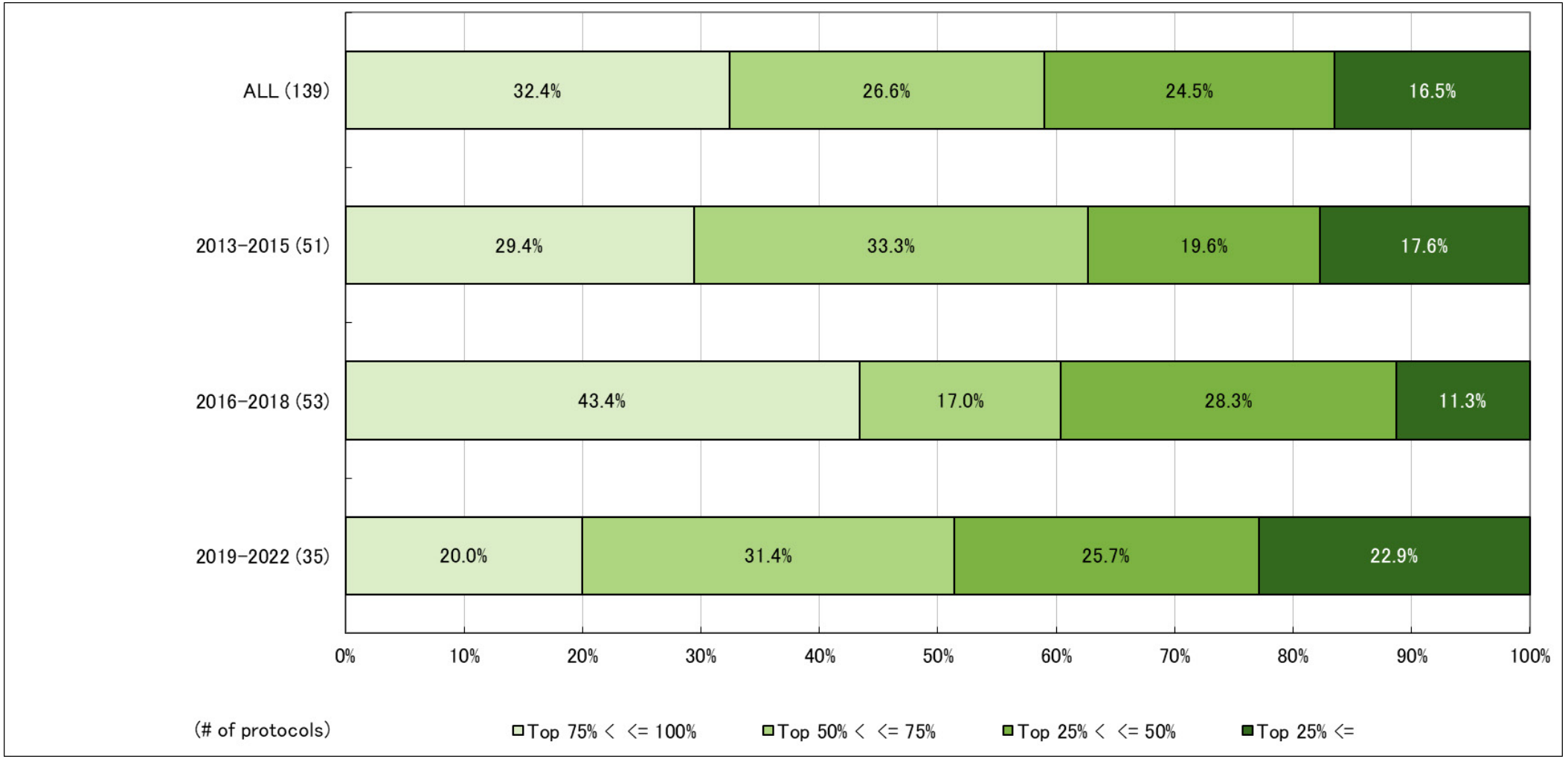


ASIA : Hong Kong, South Korea, Taiwan EUROPE : France, Germany, Italy, Spain, UK

(# of protocols)

Numbers of enrolled subjects per site in the global study in the three segments of study starting years were compared among Japan, the US, China, Asia, and Europe.

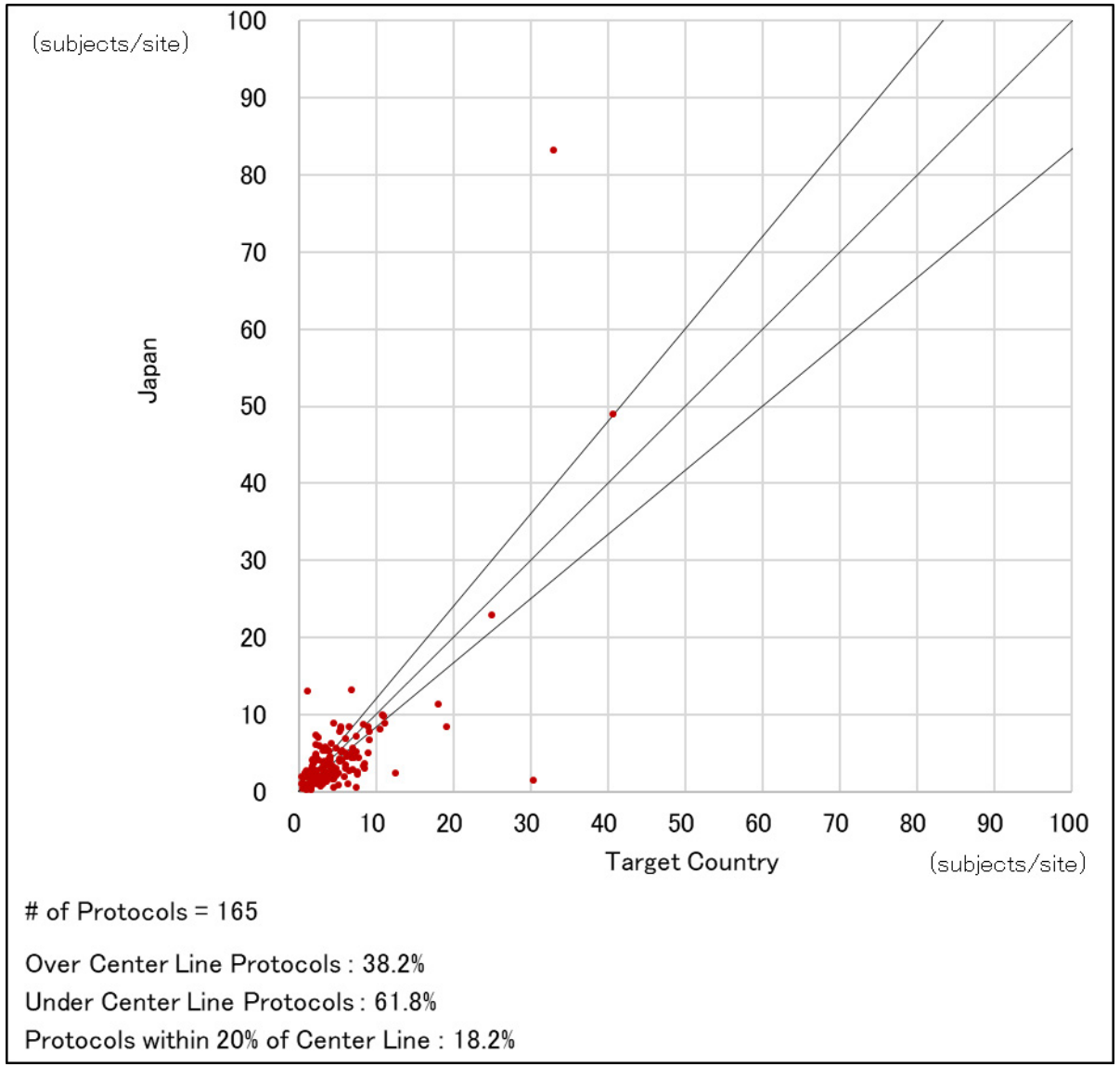
III-5-7-1-1 Classification of Number of Enrolled Subjects per Site in Japan in Global Studies



In the global studies, the proportion of the number of the protocols in each classification when the number of subjects treated with drug per site in each country is ranked in the same protocol for each country and when the order of Japan is divided into 4 categories (Within upper 25%, upper 25 to 50%, upper 50 to 75%, and 75 to 100%)

The protocols of the clinical trials conducted in 4 or more countries including Japan are included.

III-5-8-1-1 Number of Enrolled Subjects per Site in Global Studies (2013-2022) (Japan vs Target Country)



[Explanation of Figure]

- For the global studies, the number of subjects treated with drug per study site in Japan is plotted on the vertical axis and the number of subjects treated drug per study site in the overseas countries is plotted on the horizontal axis for each protocol.
- The lines in the figure show differences of 0% and ±20% in the number of subjects treated with drug per site between Japan and overseas.
- **Over Center Line (%):** Percentage of the protocols in which the number of subjects treated with drug per site in Japan are higher than the target (target countries)
- **Under Center Line (%):** Percentage of the protocols in which the number of subjects treated with drug per site in Japan are lower than the target (target countries)
- **Protocols within 20% of Center Line**: Percentage of the protocols when the difference between the number of subjects treated per site in Japan and the number of subjects within 20% is assumed to be equivalent

[Target Countries]
US, France, Germany, Italy, Spain, UK, Hong Kong, South Korea, Taiwan, and China

III-5-8-6-1 Number of Enrolled Subjects per Site in Global Studies (2013-2022)
< Heat map with focus on 'Over Center Line' >

inferior | < 20% | 21~30% | 31~40% | 41~50% | 51~60% | > 60% | superior

	Target Country *	USA	EUROPE	ASIA	CHINA
# of Protocols	165	139	129	112	30
Over Center Line ***	38.2%	54.7%	41.9%	39.3%	26.7%

Onco./Non-Onco.	Target Country *		USA		EUROPE		ASIA		CHINA	
	Onco.	Non-Onco.	Onco.	Non-Onco.	Onco.	Non-Onco.	Onco.	Non-Onco.	Onco.	Non-Onco.
# of Protocols	43	122	34	105	29	100	33	79	5	25
Over Center Line ***	32.6%	40.2%	55.9%	54.3%	41.4%	42.0%	33.3%	41.8%	20.0%	28.0%

Rare/Non-Rare	Target Country *		USA		EUROPE		ASIA		CHINA	
	Rare	Non-Rare	Rare	Non-Rare	Rare	Non-Rare	Rare	Non-Rare	Rare	Non-Rare
# of Protocols	21	144	20	119	16	113	11	101	5	25
Over Center Line ***	38.1%	38.2%	65.0%	52.9%	37.5%	42.5%	36.4%	39.6%	20.0%	28.0%

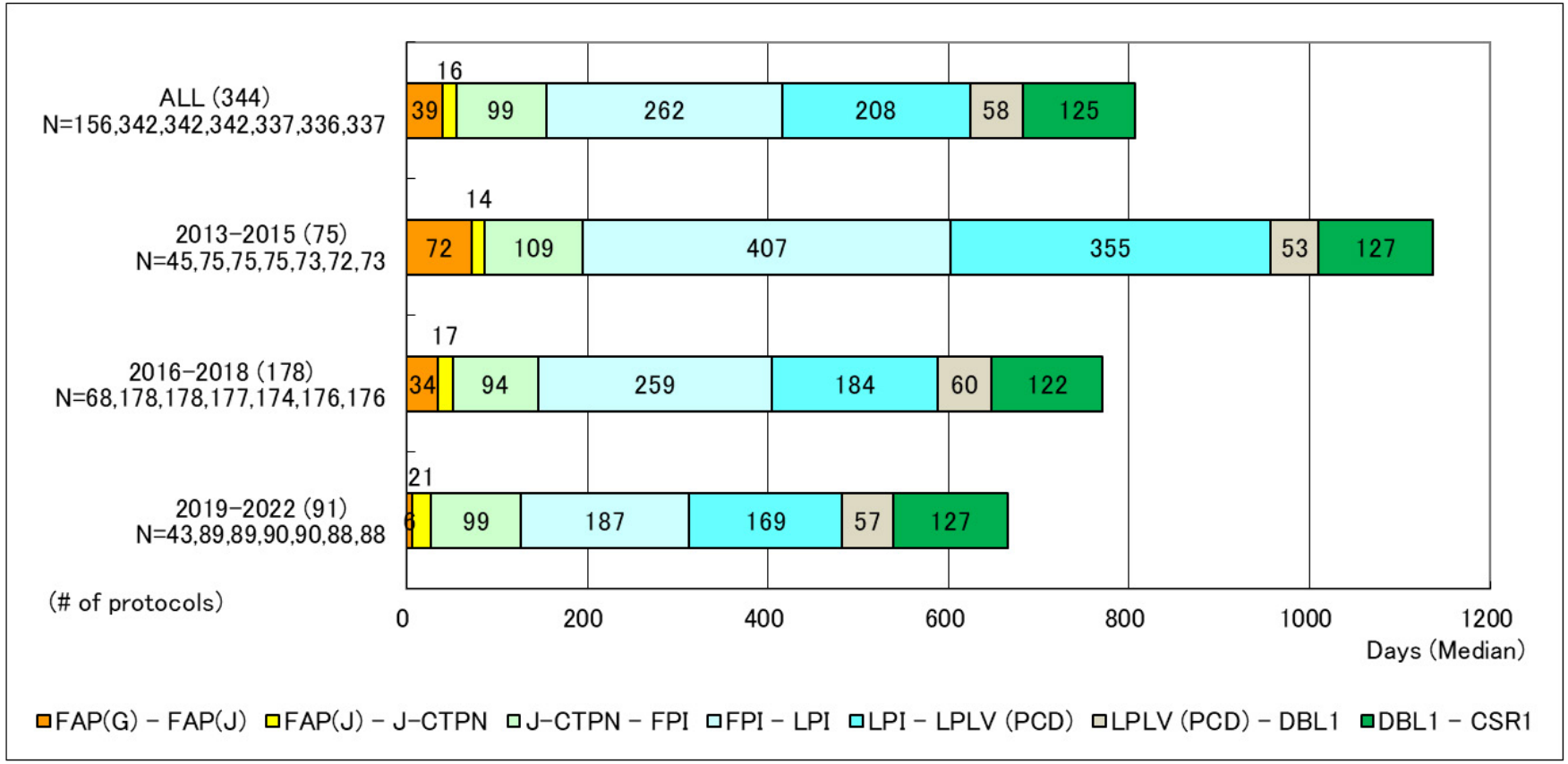
Trial Scale Small/Large **	Target Country *		USA		EUROPE		ASIA		CHINA	
	Small	Large	Small	Large	Small	Large	Small	Large	Small	Large
# of Protocols	69	96	56	83	46	83	35	77	9	21
Over Center Line ***	44.9%	33.3%	60.7%	50.6%	50.0%	37.3%	40.0%	39.0%	11.1%	33.3%

* Total of the following 10 countries --- USA, EUROPE (France, Germany, Italy, Spain, UK), ASIA (Hong Kong, South Korea, Taiwan) and China
** Trial Scale Small: Under 300 Objective Cases, Trial Scale Large: 300 or more Objective Cases
*** Over Center Line: Percentage (%) of the number of protocols that the number of subjects treated with drug at each site is higher (superior) in Japan than in the target countries (regions)

For other than 'Over Center Line', see p.46.

III-6 Cycle time

III-6-1-1-1 Cycle-time



（2019年調査開始）

N numbers are listed from left to right: FAP (G)-FAP (J), FAP (J)-J-CTPN, J-CTPN-FIP, FIP-LPI, LPI-LPLV (PCD), LPLV(PCD)-DBL 1, DBL 1-CSR 1.

FAP: Final Approved Protocol FAP (G)－FAP (J) shows a difference in the number of days in global studies between overseas and Japan.

CTPN: Submission date of clinical trial notification, **FIP:** First Patient In, **LPI:** Last Patient In, **LPLV**: Last Patient Last Visit,

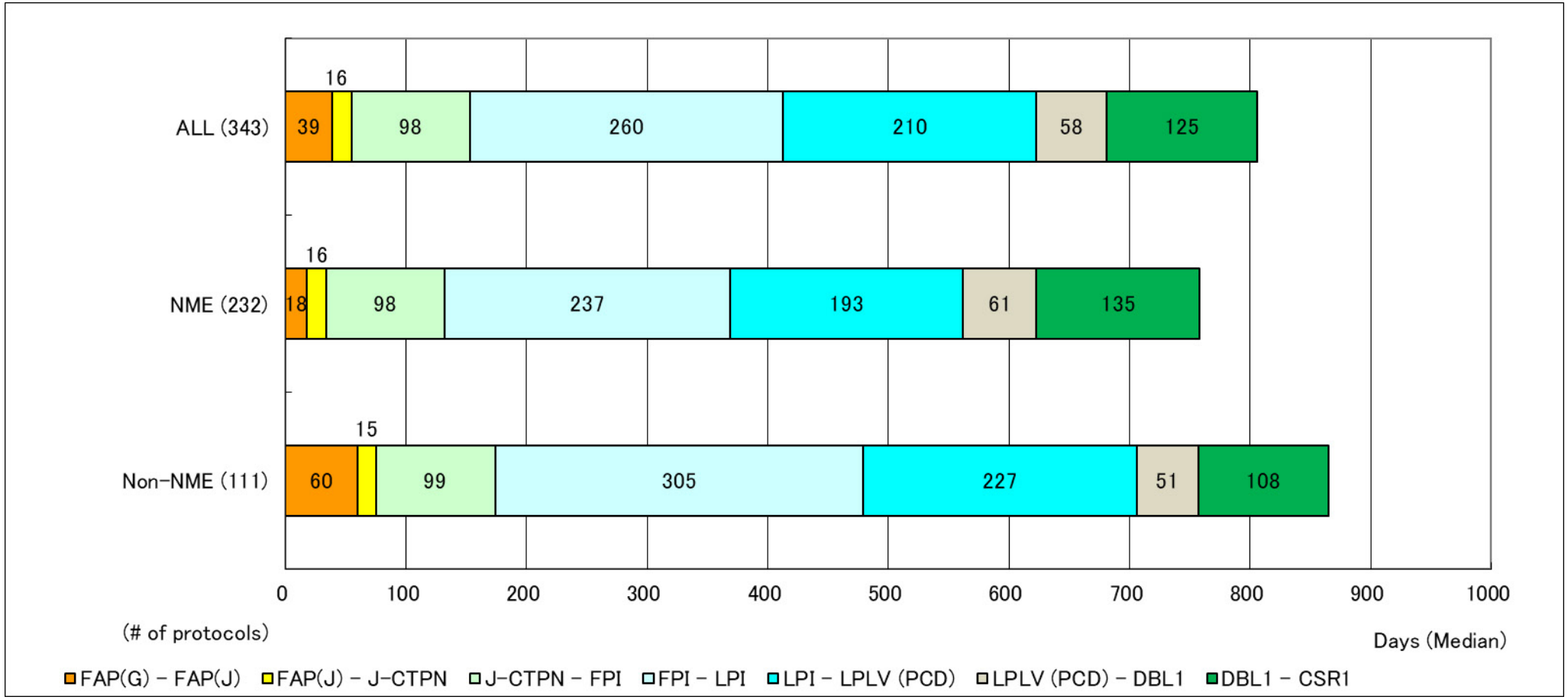
PCD: Primary Completion Date (When the study was still ongoing after filing an approval application, the date when the last subject was tested or intervened for the purpose of collecting final data on primary results in accordance with a pre-designated protocol)

DBL 1: Database Lock 1 (The date when the database for approval application is fixed), **CSR 1**: Clinical Study Report 1 (The date when the clinical study report for approval application is completed)

Please note that there are few protocols for the segment of years 2013-2015 due to the start of this survey item in 2019.

III-6-1-5-1 Cycle-time by Type of NME (2013-2022)

（2019年調査開始）



FAP: Final Approved Protocol FAP (G)－FAP (J) shows a difference in the number of days in global studies between overseas and Japan.

CTPN: Submission date of clinical trial notification, **FIP:** First Patient In, **LPI:** Last Patient In, **LPLV**: Last Patient Last Visit,

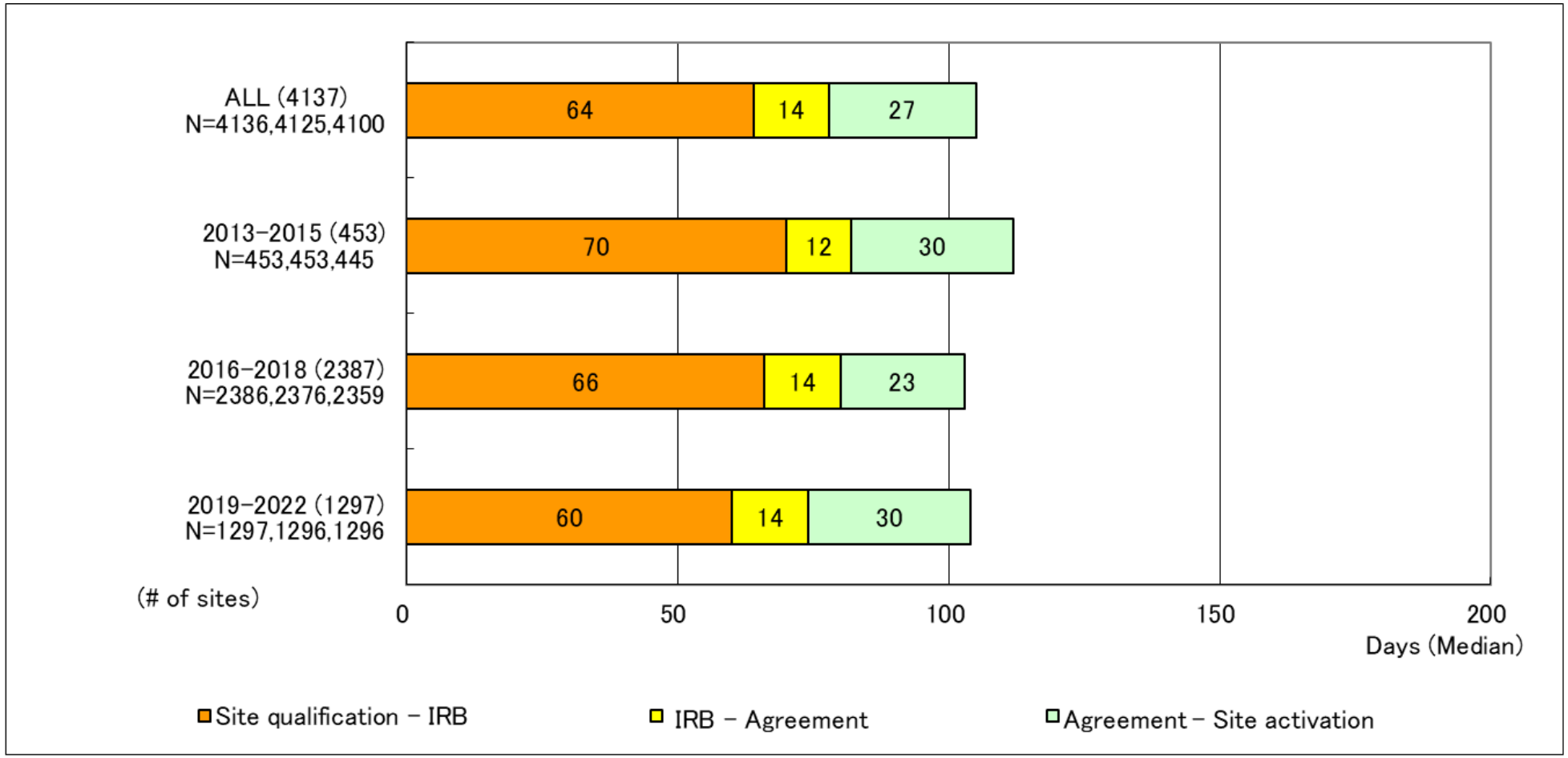
PCD: Primary Completion Date (When the study was still ongoing after filing an approval application, the date when the last subject was tested or intervened for the purpose of collecting final data on primary results in accordance with a pre-designated protocol)

DBL 1: Database Lock 1 (The date when the database for approval application is fixed), **CSR 1**: Clinical Study Report 1 (The date when the clinical study report for approval application is completed)

NME（New Molecular Entity）
Non-NME（Non-New Molecular Entity）

Please note that there are few protocols for the segment of years 2013-2015 due to the start of this survey item in 2019.

III-6-2-1-1 Days to Site qualification – IRB – Agreement – Site activation



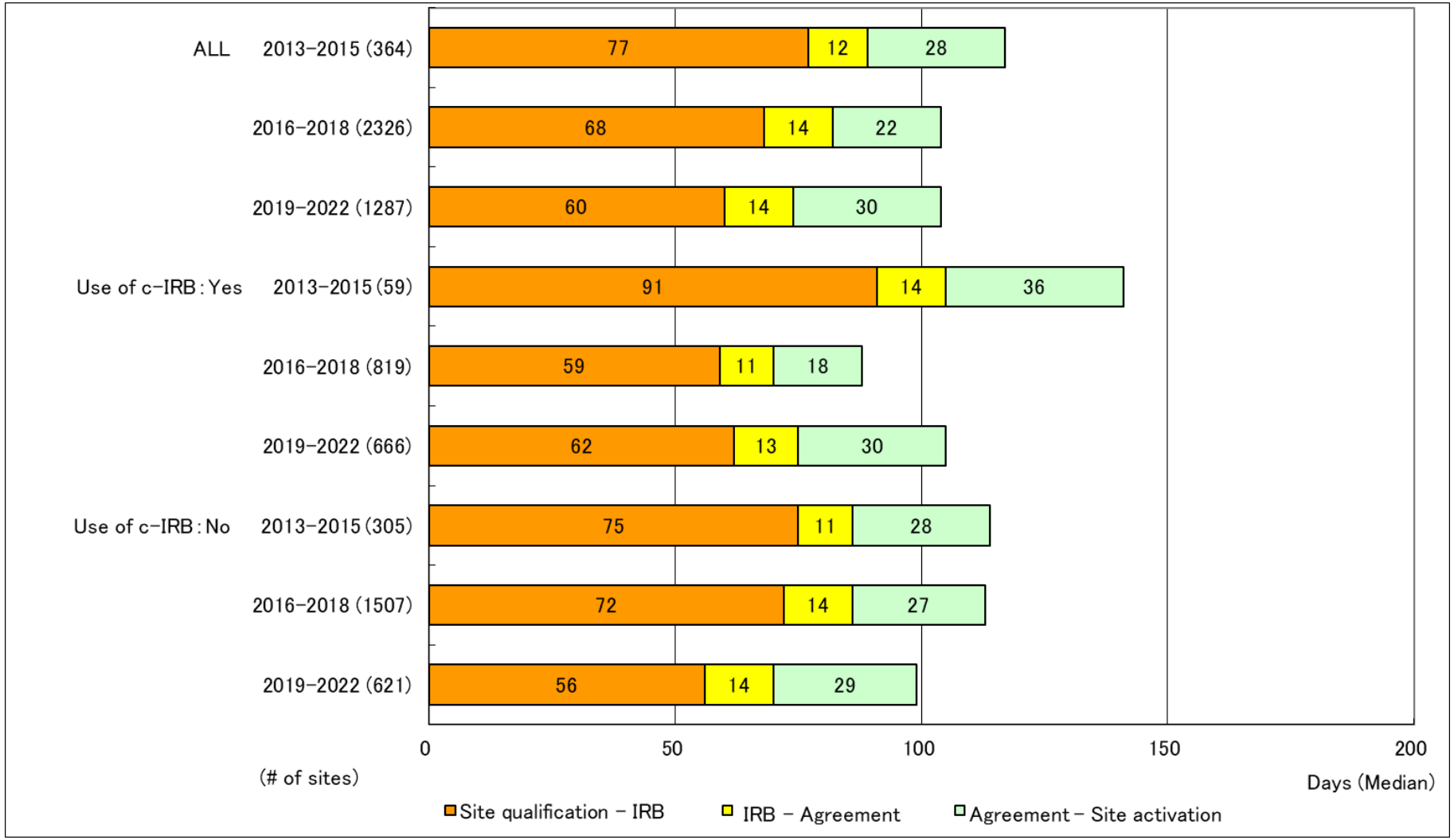
（2019年調査開始）

N numbers are listed from left to right: Site qualification-IRB, IRB-Agreement, and Agreement-Site activation.

Year : Year of Site qualification

Please note that there are few protocols for the segment of years 2013-2015 due to the start of this survey item in 2019.

III-6-2-3-1 Days to Site qualification – IRB – Agreement – Site activation by Central IRB



（2019年調査開始）

Year : Year of Site qualification

Please note that there are few protocols for the segment of years 2013-2015 due to the start of this survey item in 2019.

Ⅳ-1 Summary

- **III-1 Background**
  - ✓ Disease Area: The oncology area showed a decrease over time, while the percentage of the other area (including vaccines) increased. [Figure III-1-5]
  - ✓ Monitoring method: 'Methods other than 100% SDV (e.g. sampling)' and 'RBM' has increased significantly. [Figure III-1-5]
  - ✓ eCOA: Increased [Figure III-1-5]
  - ✓ DCT: Introduction of ePRO/eCOA takes a lead. Direct shipment of investigational medical product to homes, medical activities at local healthcare providers' institutions, telemedicine, and home visit nursing/medical care are being further implemented.[Figure III-1-5]
  - ✓ Introduction of FMV: Increased (Implementation confirmed in the latest classification (2019 to 2022)) [Figure III-1-5]
  - ✓ Central IRB: There are large differences in the use status depending the management classification of medical institutions [Figure III-1-7-3] [Continuing issue]
- **III-2 Enrollment**
  - ✓ The number of subjects treated with drug per institution (median) is 3 to 4 subjects: No change over time [Figure III-2-1, III-2-1-1] [Continuing issue]
- **III-3 Cost**
  - ✓ Milestone payment implementation rate: Increased [increased to about 81% in the latest classification (2019 to 2022)] [Figure III-3-4]
  - ✓ IRB Cost: In the classifications of 2013 to 2015 and 2016 to 2018, c-IRB was low, while it was high in the latest classification (2019 to 2022). [The reason has not been identified at present (April 2024).] [Figure III-11-1]
- **III-4 Monitoring Performance**
  - ✓ The number of subjects per monitor 1FTE: 17 subjects in the latest classification (2019 to 2022) with no change over time [Figure III-4-2] [Continuing issue]
  - ✓ The number of sites per monitor 1FTE: 3.2 sites in the latest classification (2019 to 2022) with no change over time [Figure III-4-3] [Continuing issue]
  - ✓ Percentages of "Numbers of in-house monitors" and "Number of CRO monitors": The percentage of CRO monitors increased [Figures III-4-1 and III-4-6-2]

Ⅳ-2 Summary

- **III-5 Global**
  - ✓ The number of subjects treated with drug per study site (median) in the global studies is comparable to that in countries/regions worldwide (US, China, Europe, and Asia). [Figure III-5-3-1-3-1]
  - ✓ The number of subjects treated with drug per site in the same study is smaller than that in China, Asia, and Europe [Figures III-5-8-6, III-5-8-6-1] [Continuing issue]
  - ✓ When the number of subjects treated with drug per site in each country is ranked in the same study in a multinational study, the number of the studies in which Japan was within the top 50% was 41%. (It increased to 48.6% in the latest classification (2019 to 22)) [Figure III-5-7-1-1] [Continuing issue]
- **III-6 Cycle time**
  - ✓ Cycle time of NME is shorter than that of non-NME [Figure III-6-1-5-1].
  - ✓ In the latest classification (2019 to 2022), the duration "from the date of site selection [Site qualification] to the date when the study can be conducted [Site activation] " is approximately 3.5 months (from the date of site selection [Site qualification] to the date of IRB meeting: approximately 2 months; from the date of IRB meeting to the date of contract: approximately 0.5 months; and from the date of contract to the date when the study can be conducted [Site activation] : approximately 1 month) [Figure III-6-2-1-1]

Secondary use of this result

This report has been prepared by R&D Head Club member companies by bringing together data in order to understand current clinical trial environment in Japan. Please note the following instruction when you use this material for the secondary use.

Preliminary actions for secondary use

- Please let the R&D Head Club secretariat know below contents by contact form in the R&D Head Club home page（https://rdhead-club.com/contact/）
  - User (name, affiliation, opportunity to use)
  - Where used (applicable pages and purpose of use*）

Ex.）
Name：Ichiro Suzuki
Affiliation ：ABC Pharma K.K.
Purpose for ues：Oral presentation in OOO annual meeting, MMM/DD/YYYY
Data of use： Slide #18
Introduction on current clinical cost in Japan

How to describe Source Data

- Source：R&D Head Club Clinical Trial Performance Survey 2023 https://rdhead-club.com/

*：It is to confirm that there is no discrepancy with the perception of R&D Head Club, and does not restrict secondary use.

III-5-8-6 Number of Enrolled Subjects per Site in Global Studies (2013-2022)

	Target Country *	USA	EUROPE	ASIA	CHINA
# of Protocols	165	139	129	112	30
Over Center Line	38.2%	54.7%	41.9%	39.3%	26.7%
Under Center Line	61.8%	43.9%	58.1%	59.8%	73.3%
Within 20% of Center Line	18.2%	21.6%	19.4%	20.5%	20.0%

Stratified by country/region

Stratified by Categories

Onco./Non-Onco.	Target Country *		USA		EUROPE		ASIA		CHINA	
	Onco.	Non-Onco.	Onco.	Non-Onco.	Onco.	Non-Onco.	Onco.	Non-Onco.	Onco.	Non-Onco.
# of Protocols	43	122	34	105	29	100	33	79	5	25
Over Center Line	32.6%	40.2%	55.9%	54.3%	41.4%	42.0%	33.3%	41.8%	20.0%	28.0%
Under Center Line	67.4%	59.8%	41.2%	44.8%	58.6%	58.0%	66.7%	57.0%	80.0%	72.0%
Within 20% of Center Line	20.9%	17.2%	20.6%	21.9%	13.8%	21.0%	12.1%	24.1%	20.0%	20.0%

Stratified by country/region

Rare/Non-Rare	Target Country *		USA		EUROPE		ASIA		CHINA	
	Rare	Non-Rare	Rare	Non-Rare	Rare	Non-Rare	Rare	Non-Rare	Rare	Non-Rare
# of Protocols	21	144	20	119	16	113	11	101	5	25
Over Center Line	38.1%	38.2%	65.0%	52.9%	37.5%	42.5%	36.4%	39.6%	20.0%	28.0%
Under Center Line	61.9%	61.8%	35.0%	45.4%	62.5%	57.5%	63.6%	59.4%	80.0%	72.0%
Within 20% of Center Line	9.5%	19.4%	15.0%	22.7%	31.3%	17.7%	0.0%	22.8%	0.0%	24.0%

Stratified by country/region

Trial Scale Small/Large **	Target Country *		USA		EUROPE		ASIA		CHINA	
	Small	Large	Small	Large	Small	Large	Small	Large	Small	Large
# of Protocols	69	96	56	83	46	83	35	77	9	21
Over Center Line	44.9%	33.3%	60.7%	50.6%	50.0%	37.3%	40.0%	39.0%	11.1%	33.3%
Under Center Line	55.1%	66.7%	37.5%	48.2%	50.0%	62.7%	57.1%	61.0%	88.9%	66.7%
Within 20% of Center Line	15.9%	19.8%	19.6%	22.9%	19.6%	19.3%	20.0%	20.8%	0.0%	28.6%

Stratified by country/region

* Total of the following 10 countries --- USA, EUROPE(France, Germany, Italy, Spain, UK), ASIA(Hong Kong, South Korea, Taiwan) and China
** Trial Scale Small: Under 300 Objective Cases, Trial Scale Large: 300 or more Objective Cases