

UNIVERSITÀ CATTOLICA del Sacro Cuore



ALTEMS

ALTA SCUOLA DI ECONOMIA
E MANAGEMENT DEI SISTEMI SANITARI



Laboratorio sul Management delle Sperimentazioni Cliniche

RAPPORTO 2023

P R E S E N T A Z I O N E

altems.unicatt.it

5 dicembre 2023



Attività del Laboratorio MSC

La pandemia COVID-19, ha avuto tra i suoi effetti quello di portare alla ribalta il tema ed il settore delle sperimentazioni cliniche.

È diventato improvvisamente chiaro come **un ecosistema di ricerca clinica efficace**, ben organizzato e di alto valore scientifico diventi addirittura **un fattore cruciale per la sopravvivenza della nazione, come società e come sistema economico**.

Si è verificata una importante presa di coscienza da parte di istituzioni e pubblica opinione, portando **un riposizionamento positivo della ricerca clinica da elemento di costo ad asset di alto valore**.

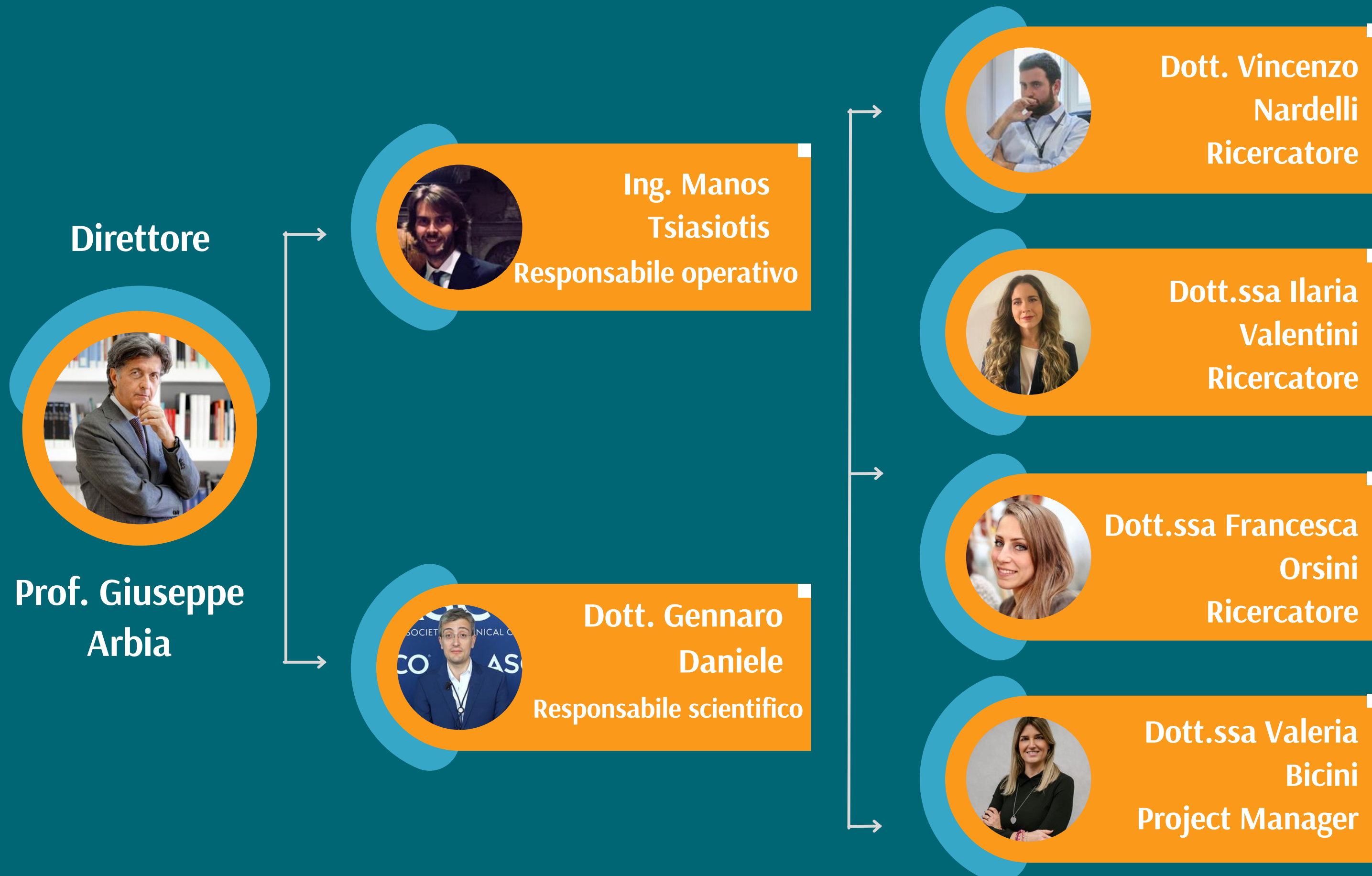
Progetti anni precedenti

- Averted costs 2020 e 2021
- Valore delle Sperimentazioni Cliniche 2021
- Indicatore sullo Stato del Settore Ricerca Clinica 2022

Sponsor Laboratorio MSC 2023



Organigramma Laboratorio MSC



Indicatore di Qualità Clinical Trial Sites (CTS)



Perché un indicatore di qualità?

- Mancanza di standard qualità dei CTS
- Difficoltà di identificazione degli standard
- Eterogeneità organizzativa dei CTS
- Innovatività in rapida e continua evoluzione
- Competitività derivante dal nuovo contesto normativo Europeo (regolamento 536/14)
- Rischio di perdita di attrattività del sistema Italiano



Qualità: da dove partire?

Good Clinical Practice

- Standard internazionale di qualità etica e scientifica per la progettazione
- Standard minimi per lo svolgimento di ricerca clinica
- Cattura solamente gli aspetti clinici

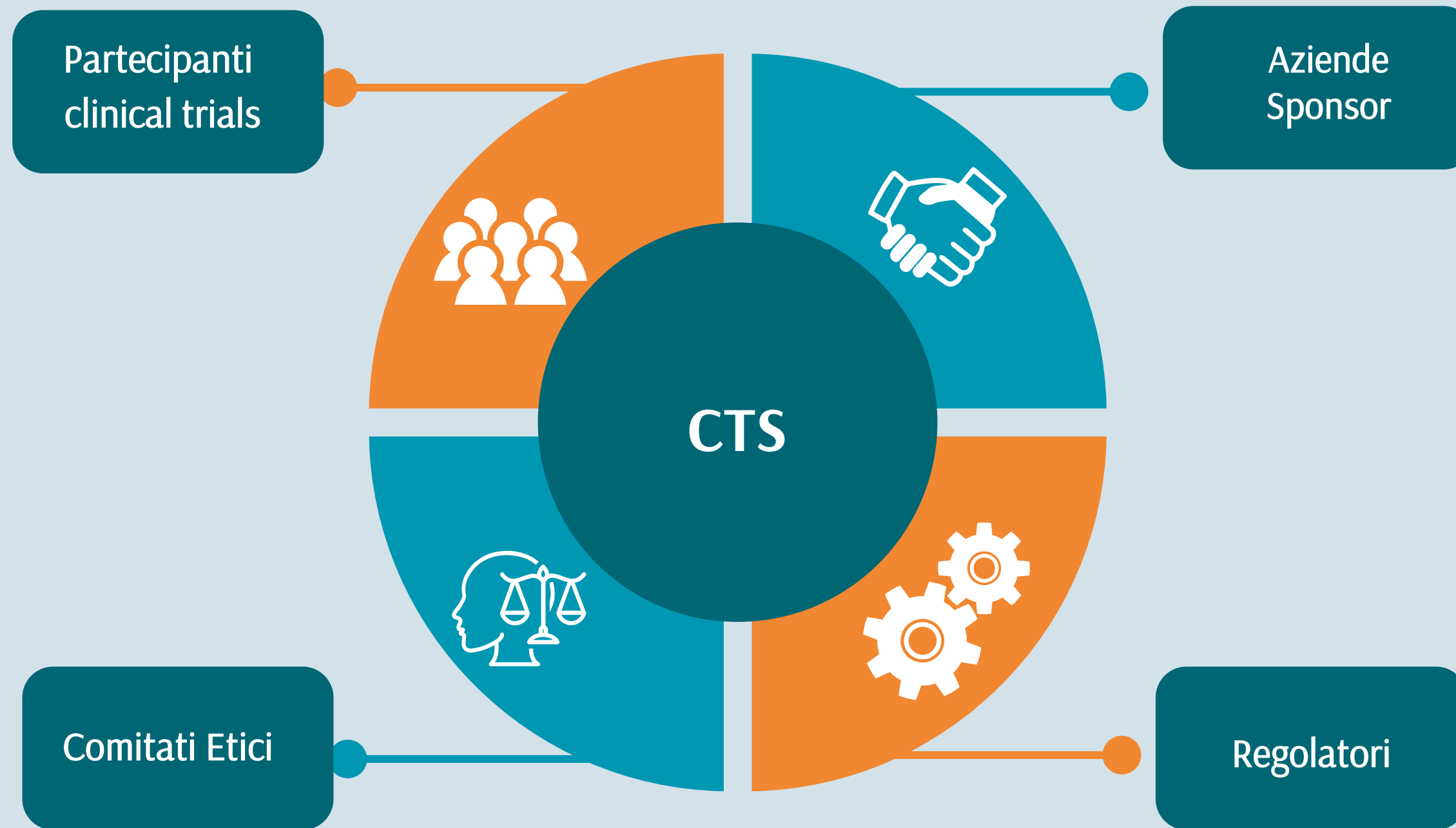
Cosa manca?

- Standards che catturino gli aspetti di qualità correlati all'intero sistema della ricerca clinica
- Standards che derivano dai CTS

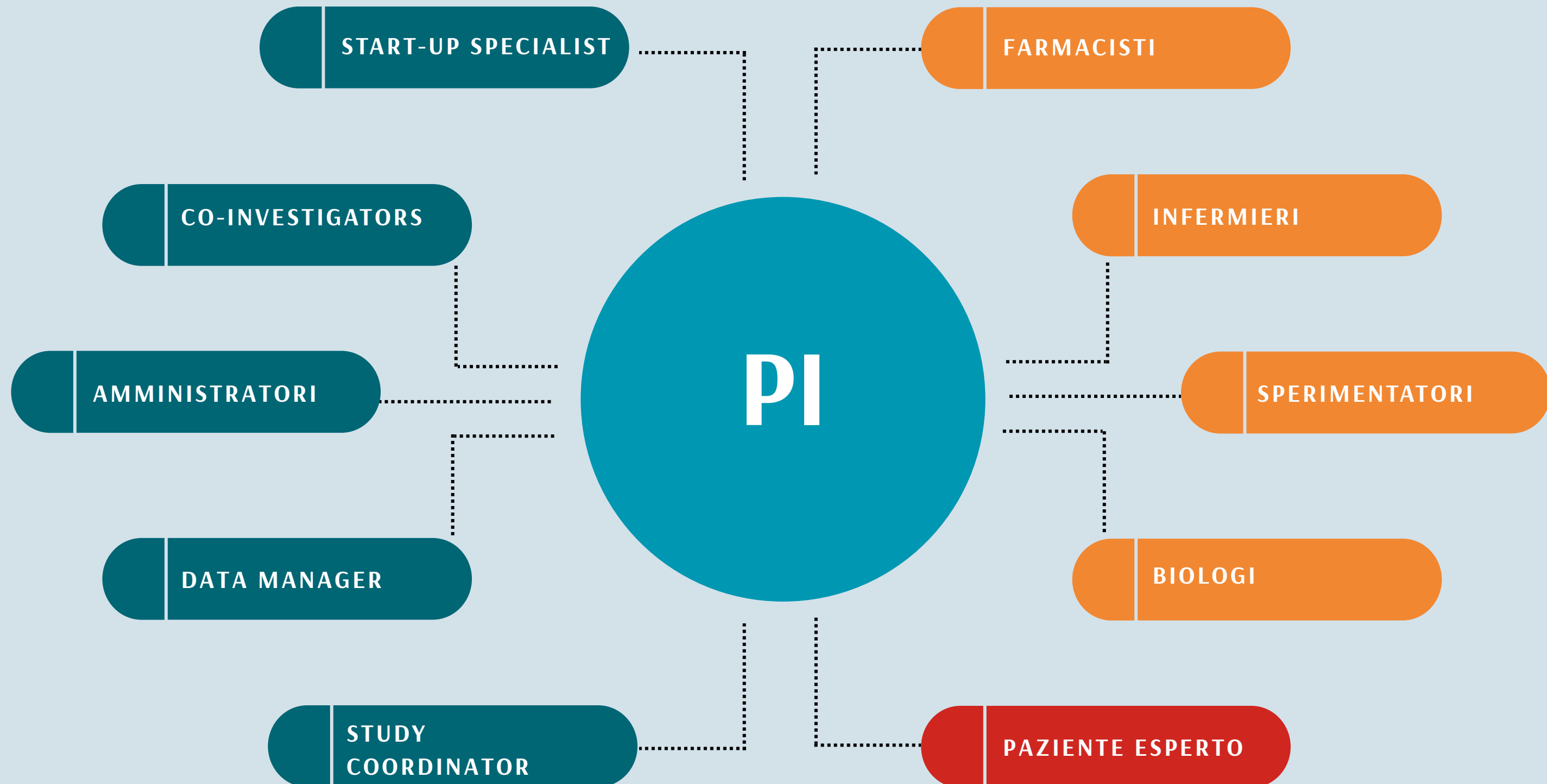
Regolamento Europeo 536/2014

- Tutela principalmente il benessere dei partecipanti
- È progettato per generare dati affidabili e robusti.

Il complesso mondo dei CTS



Il complesso mondo dei CTS



Obiettivi del progetto

01



**SVILUPPARE UNA
METODOLOGIA CHE
ANALIZZI I VARI
ASPETTI LEGATI ALLA
QUALITÀ DEI CTS**

02



**CREARE UNO
STRUMENTO CHE
PERMETTA AI CTS DI
MIGLIORARE
INTERNAME**

03

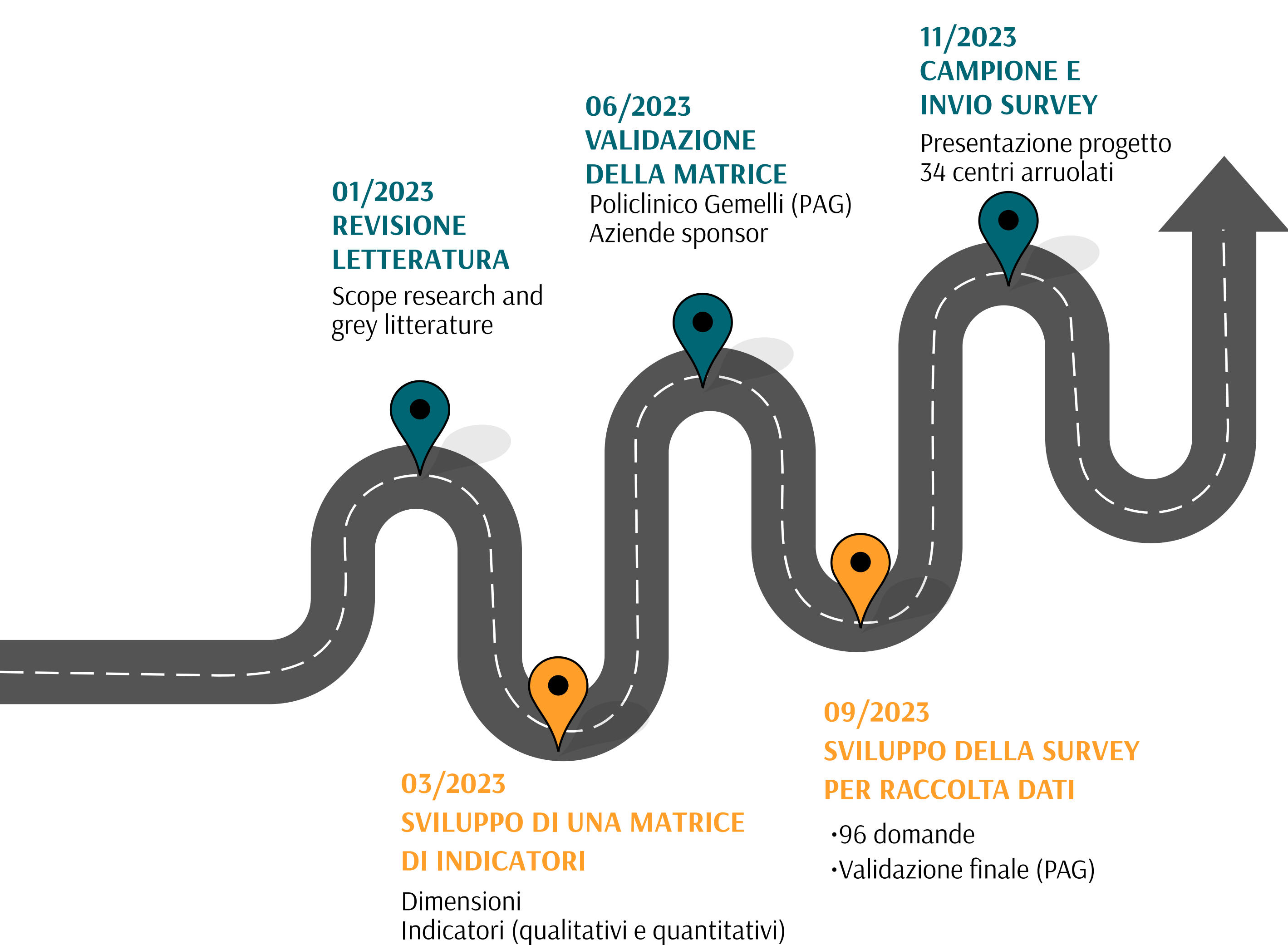


**CONSENTIRE AGLI
SPONSOR
L'IDENTIFICAZIONE
DI SITI DI ALTA
QUALITÀ**

04



**PROMUOVERE UNA
CULTURA BASATA SUI
STANDARD DI
QUALITÀ PER
AUMENTARE
L'ATTRATTIVITÀ DEL
PAESE**



Timeline del progetto

- La metodologia verrà aggiornata ogni anno (per un minimo 3 anni) per poter sviluppare uno strumento che raggiunga gli obiettivi del progetto.
- La metodologia dovrà essere applicabile a tutti i Clinical Trial Sites, indipendentemente dalla dimensione, dal tipo di organizzazione e di area terapeutica.
- E' stato sviluppato un piano statistico per analizzare gli indicatori qualitativi e quantitativi e correlarli agli output di qualità.
- Il progetto è iniziato con una prima raccolta dati relativi al 2022.
- La survey sviluppata riguarda solo i studi clinici interventistici con promotore profit

Punti metodologici

- Guidelines: GCP standards, nuovo regolamento EMA
- Pubblicazioni scientifiche
- Articoli e paper di conferenze
- Position papers
- Clinical Trials journals

Revisione della letteratura

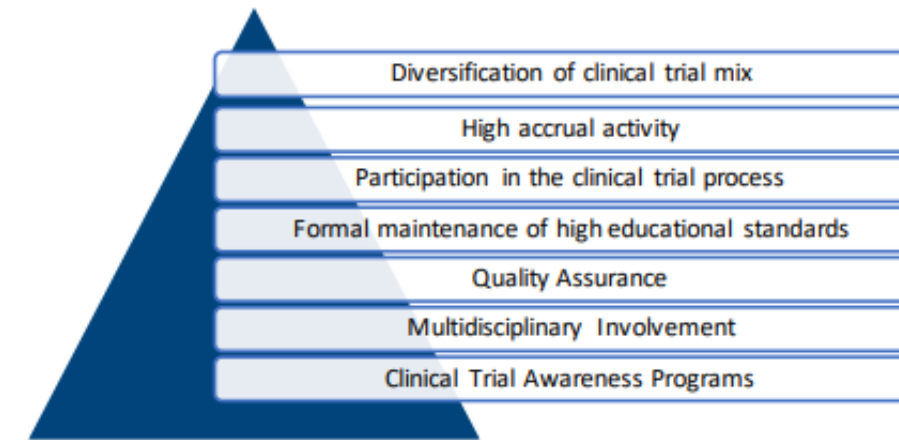
QUALITY ASSESSMENT OF CLINICAL TRIAL SITES

— AT A GLANCE —

KEY CONSIDERATIONS, TIPS, AND BEST PRACTICES



Quality management in clinical research ensures the protection of participants' rights and well-being; the accuracy, completeness, and verification of trial data; and clinical trial adherence to protocol/amendment(s) and federal regulatory requirement(s) and guidelines.² Well-designed, high-quality clinical trials also increase research participant access to state-of-the-art medical care.² ASCO released a statement in 2008 to provide recommendations on developing and implementing high-quality clinical trial programs.³ The ASCO Research Program Quality Assessment Tool is available to help sites establish or enhance internal quality assessment programs and exceed the minimum standards of conducting clinical research.⁴



Attributes of an exemplary clinical trial site.²

Minimum Standards

For minimum standards of research site quality, consider the following:



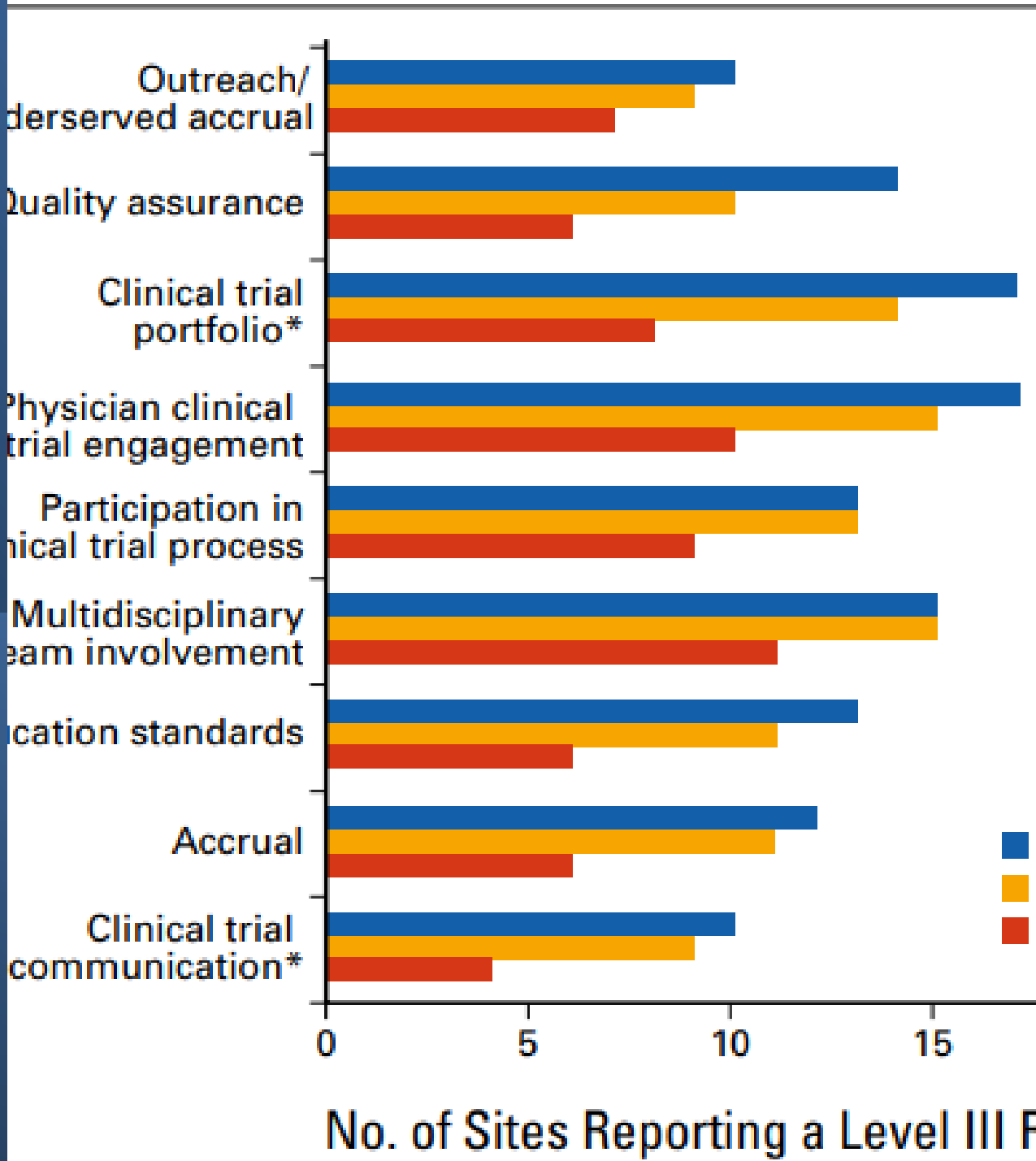
- ❑ A quality clinical trial research site, at a minimum, fully complies with the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) [guidelines](#) for designing, conducting, recording, and reporting trials that involve human participants. The responsibility of compliance is shared by the trial sponsor, investigator(s), and institution(s).³ Depending on the specific nature of the trial, the specific regulations and accepted standards for GCP will vary.³
- ❑ Standard operating procedures are a way to facilitate consistent quality in site performance, protection of participant rights, and compliance with GCP.³ Refer to [Zon et al., 2008](#) for a list of suggested topics for SOPs.

Exemplary Attributes

Consider the following key attributes for a quality clinical trial site that exceed GCP compliance³:

- ❑ Diversification of clinical trial site portfolio – A diverse portfolio offers patients a broad range of options and fully utilizes site resources.
- ❑ High accrual activity – Establishing site benchmarks for accrual can help measure progress and facilitate goal setting.
- ❑ Participation in the trial development process – Involvement of all stakeholders in the research process can increase communication among stakeholders and facilitate understanding of the trial process and sharing of resources and support.
- ❑ Formal maintenance of high educational standards – Maintenance of certification, as available, and continuing education for research staff (e.g., specialty board, certification, etc.) demonstrates staff qualifications and ability to perform to an exemplary standard.
- ❑ Quality assurance – An internal quality assurance process and routine self-audits are key parts of site quality assurance. Utilization of tools for continuous improvement, including the plan-do-check-act cycle—a four-step quality model⁵—Six Sigma, Lean, and Total Quality Management can help in developing and maintaining a site quality assurance process.⁶ The ASCO Research Program Quality Assessment Tool is helpful for internal quality assessment programs and establishing a proactive approach to quality control.⁴
- ❑ Multidisciplinary involvement in the clinical trials process – Engaging physicians and non-physicians outside of oncology (e.g., surgery, radiology, radiation oncology, pathology, primary care, etc.) could increase a site's capacity for trials.
- ❑ Clinical trial awareness program – Developing awareness programs can increase physician and lay knowledge of clinical trials.

Dimond et al.
01/2016 Clinical
Trial Assessment
of Infrastructure
Matrix Tool to
Improve the
Quality of
Research Conduct
in the Community



Level-three reporting for 2011, 2012, and 2013 for 21 National Cancer Institute Community Cancer Centers Program sites. Although all sites completed self-assessment each year, bars do not add to 21 because some sites did not report a level-three score in each year. Increase in level-three scores over time across all attributes combined was significant at $P < .001$. (*) Significant F test over time (clinical trial communication, $P = .0281$; clinical trial portfolio, $P = .0228$).

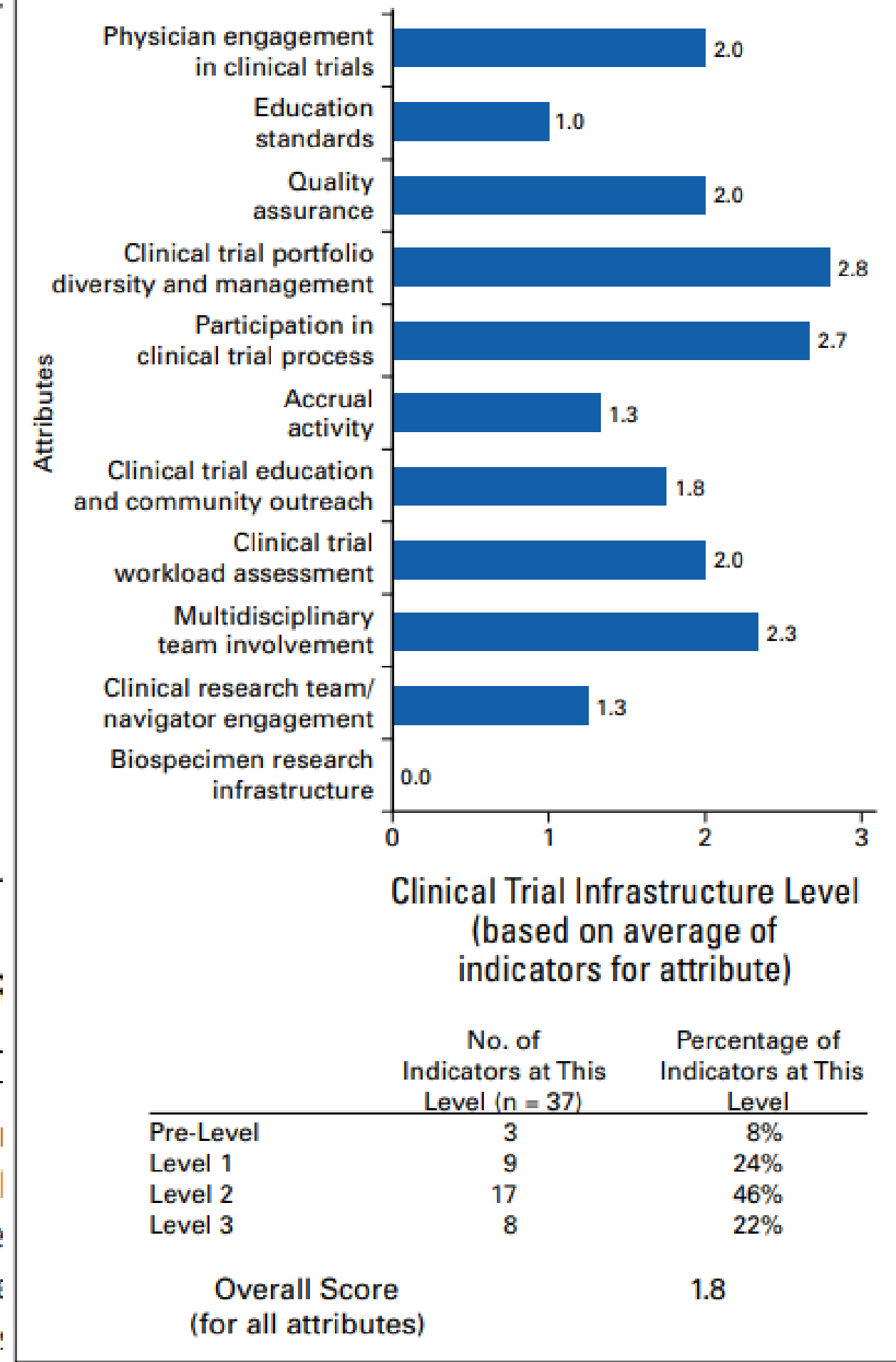


FIG 3. Example of Clinical Trial Assessment of Infrastructure Matrix (CT AIM) scoring report. The scoring report shares three pieces of information: the attribute level (range 0-3), an overview of how many indicators fall at each

Snyder et al.
04/2016
Retooling
institutional
support
infrastructure for
clinical research

Table 1
Study startup metrics for fiscal years 2011–2015.

Fiscal year	Number of protocols approved	Median days from IRB submission to institutional approval	Median days from institutional approval to first participant consented	Median days from IRB submission to first participant consented
2011	306	86	74	182
2012 ^a	352	93	69	180
2013 ^b	292	101	68	194
2014	296	92	52	161
2015	313	100	50	171

Note: Data are for clinical research studies that scheduled, ordered, or charged through the Duke University Health System.

^a Transition to unified research support office.

^b Electronic health record implemented at Duke.

Table 2
Study closure metrics for fiscal years 2011–2015.

Fiscal year	Median days from institutional approval to study closure ^a	Number of protocols closed with no consent	Number of protocols closed (total) ^b	Percentage of studies closing with no consented patients
2011	561	73	246	30%
2012 ^c	449	67	323	21%
2013 ^d	469	63	330	19%
2014	592	68	393	17%
2015	532	44	304	14%

Note: Data are for research studies that scheduled, ordered, or charged through the Duke University Health System.

^a Shorter time from institutional approval to study closure is considered more efficient.

^b These protocols did not necessarily open in the fiscal year indicated.

^c Transition to unified research support office.

^d Electronic health record implemented at Duke.

Table 3
Duke University School of Medicine active research studies and participants enrolled for fiscal years 2011–2015.

Fiscal year	Total active studies	NIH-sponsored studies	Other federal studies	Industry-sponsored studies	Internal studies	Total enrolling studies	Total patients enrolled on studies	Average patients enrolled per enrolling study
2011	4988	1114	844	1136	1894	2171	18,371	8.5
2012 ^a	5362	1170	887	1195	2110	2187	18,321	8.4
2013	5628	1230	933	1251	2214	2184	22,707	10.4
2014	5749	1250	965	1265	2269	2167	24,500	11.3
2015	5757	1239	1000	1292	2226	2104	24,355	11.6

^a Transition to unified research support office.

Johnston et al. 10/2017 It's Time to Harmonize Clinical Trial Site Standard



Figure 1 | Performance Domains and Subdomains for Clinical Trial Site Standards
SOURCE: Johnston et al., "It's Time to Harmonize Clinical Trial Site Standards," National Academy of Medicine.

Johnston et al. 10/2017

It's Time to Harmonize Clinical Trial Site Standard

- For **clinical trial sites**, voluntary accreditation could provide consistent and transparent application of baseline standards for core competencies, reduced administrative burden, recognition for high-quality performance, and a competitive edge. “Add-on” certification options beyond baseline accreditation could attest to a clinical trial site’s unique expertise and ability to conduct research in a particular therapeutic area or patient population.
- For **research participants**, voluntary accreditation could provide greater confidence in the quality of clinical trials conducted at accredited sites. Such confidence could help encourage volunteers to participate in clinical trials, thus improving treatment options in the future.
- For **research sponsors**, the consistent and transparent application of clinical trial site standards in an accreditation system could allow for easier identification of high-quality sites for various types of studies, faster study start-up, and a reduction in the administrative burden from conducting repetitive site evaluations.
- For **regulators of clinical research**, an accreditation program could provide greater reliability of—and confidence in—the evidence generated for a medical product.

Williams et al.
09/2020
Clinical trials best
practice checklist:
Guidance for
Australian clinical
research sites
from CT:IQ



CT:IQ
Clinical Trials:
Thinking Smarter

Early Phase Trials Best Practice Checklist

This checklist and toolkit provides a summary of recommendations, considerations and resources for clinical research sites in the conduct of clinical trials, particularly those sites conducting early phase studies. For existing clinical trial sites it will validate your current practices, for new sites it will guide you in your set up.



**HOW TO USE THIS
CHECKLIST**



**FREQUENTLY ASKED
QUESTIONS**

Clicking on an icon below will lead you to that respective section of the best practice checklist for the conduct of clinical trials. Work through the relevant section (tabs) of the checklist in your preferred order, filtering by either IP (Investigational Product) or DEVICE. You can also filter on the SUMMARY page to show only your NO responses, to see what areas your site needs to focus on to meet best practice standards.



Buse et al.
05/2023
A framework for
assessing clinical
trial site
readiness

Journal of Clinical and Translational Science

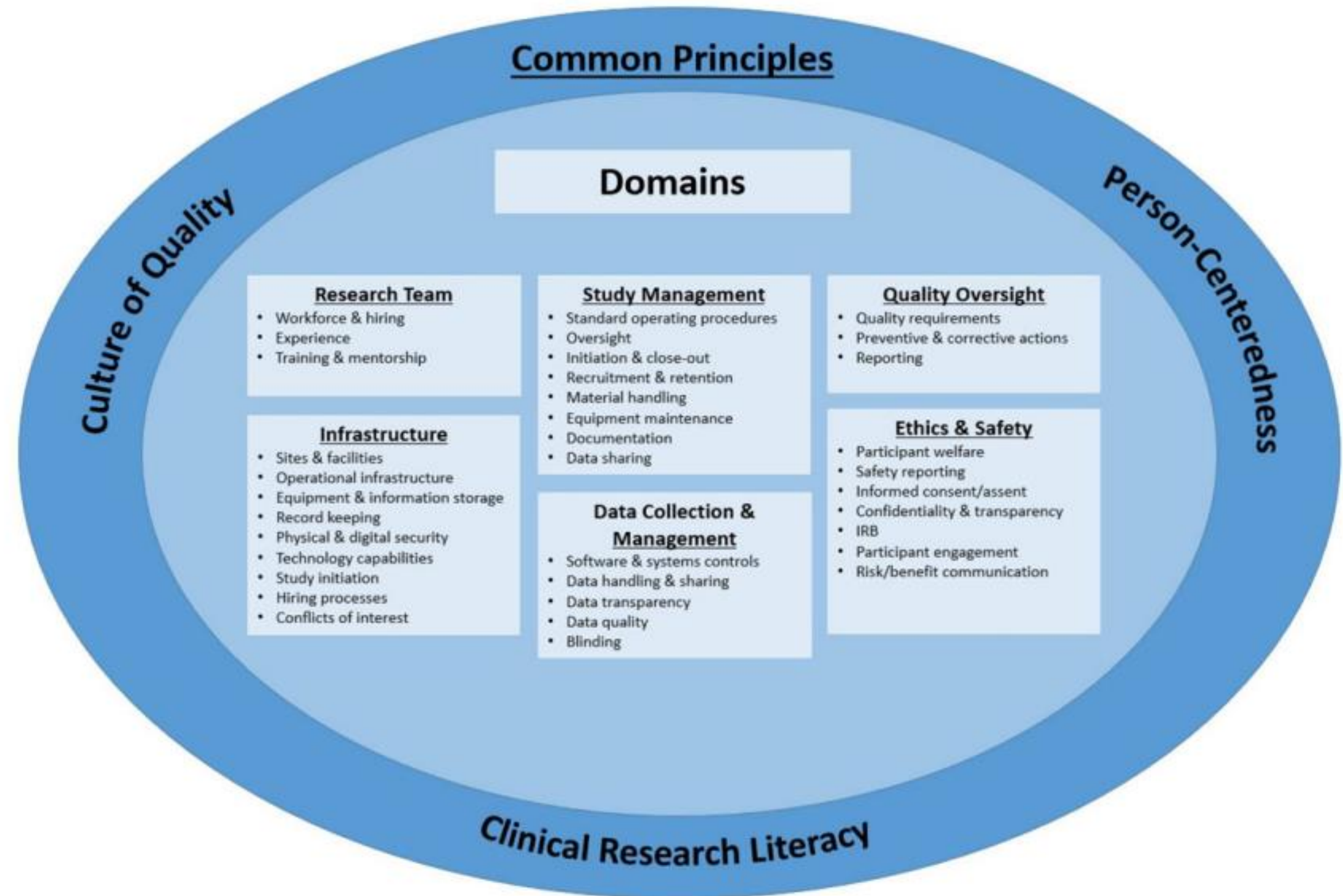
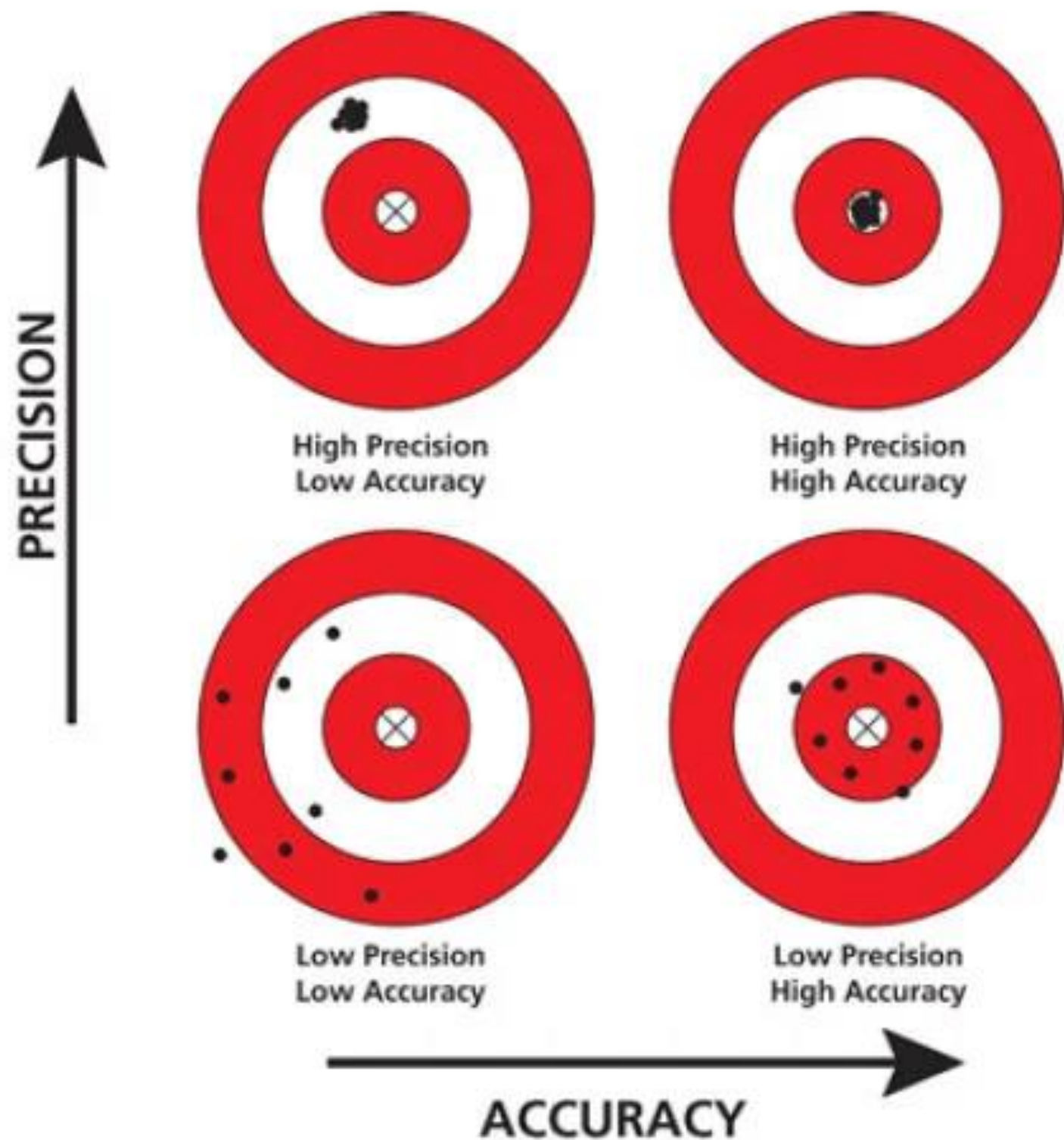


Figure 1. Common principles and domains for site readiness practices for clinical trial site readiness.

Dimensioni di analisi



Meglio una misurazione precisa o accurata?



Accuracy

Precision

Numero di dimensioni

Rappresentatività del Campione

Effetti di correzione

Numerosità del campione

Variabilità del campione

Effetti di correzione

Sfide Metodologiche

Autoselezione
del campione

Limitazione del
campione

Variazioni
temporali

Errori nelle
risposte

Incertezza
nelle risposte

Interpretazione
della domanda

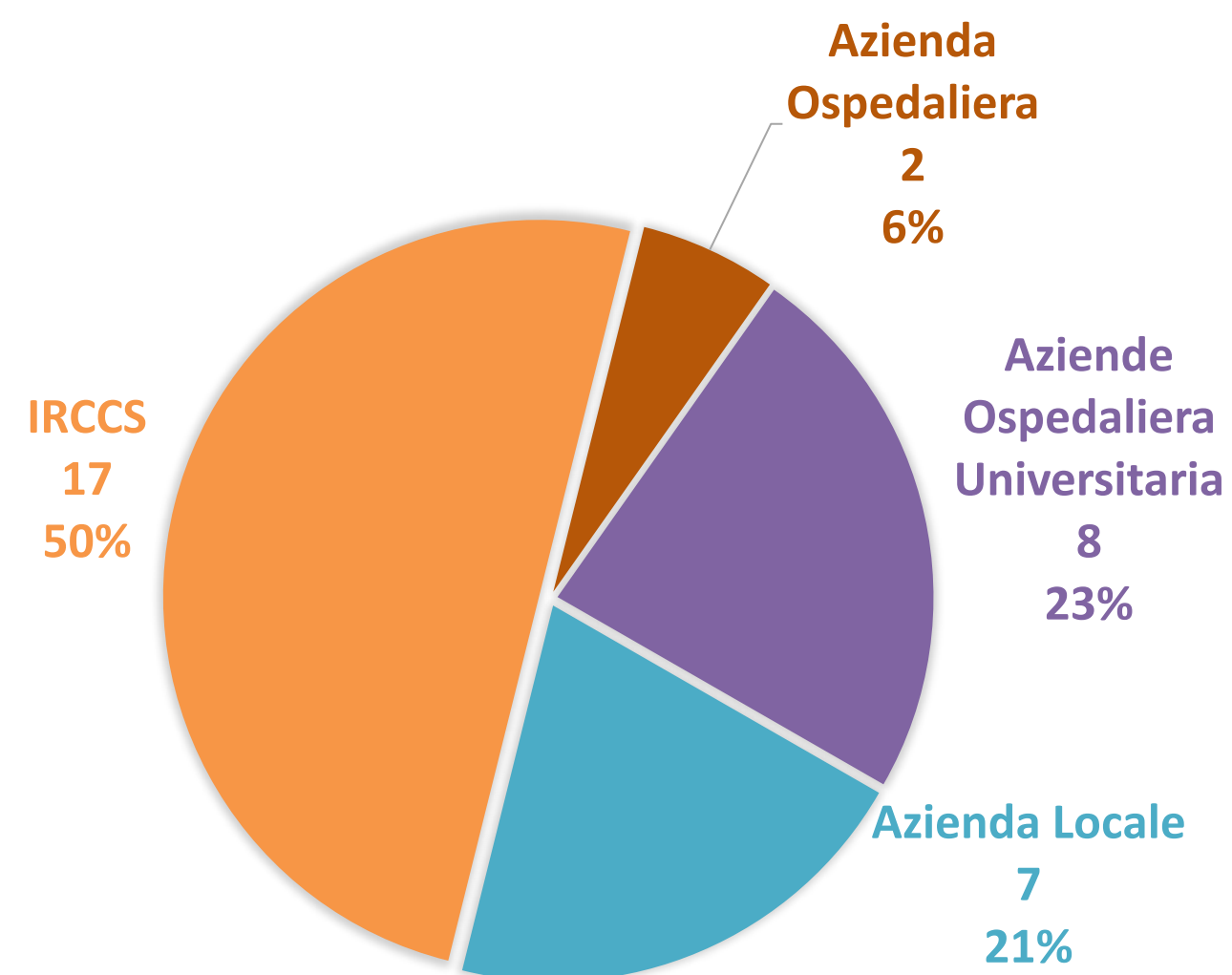
Sfide Organizzative

Difficoltà nel reperimento delle informazioni

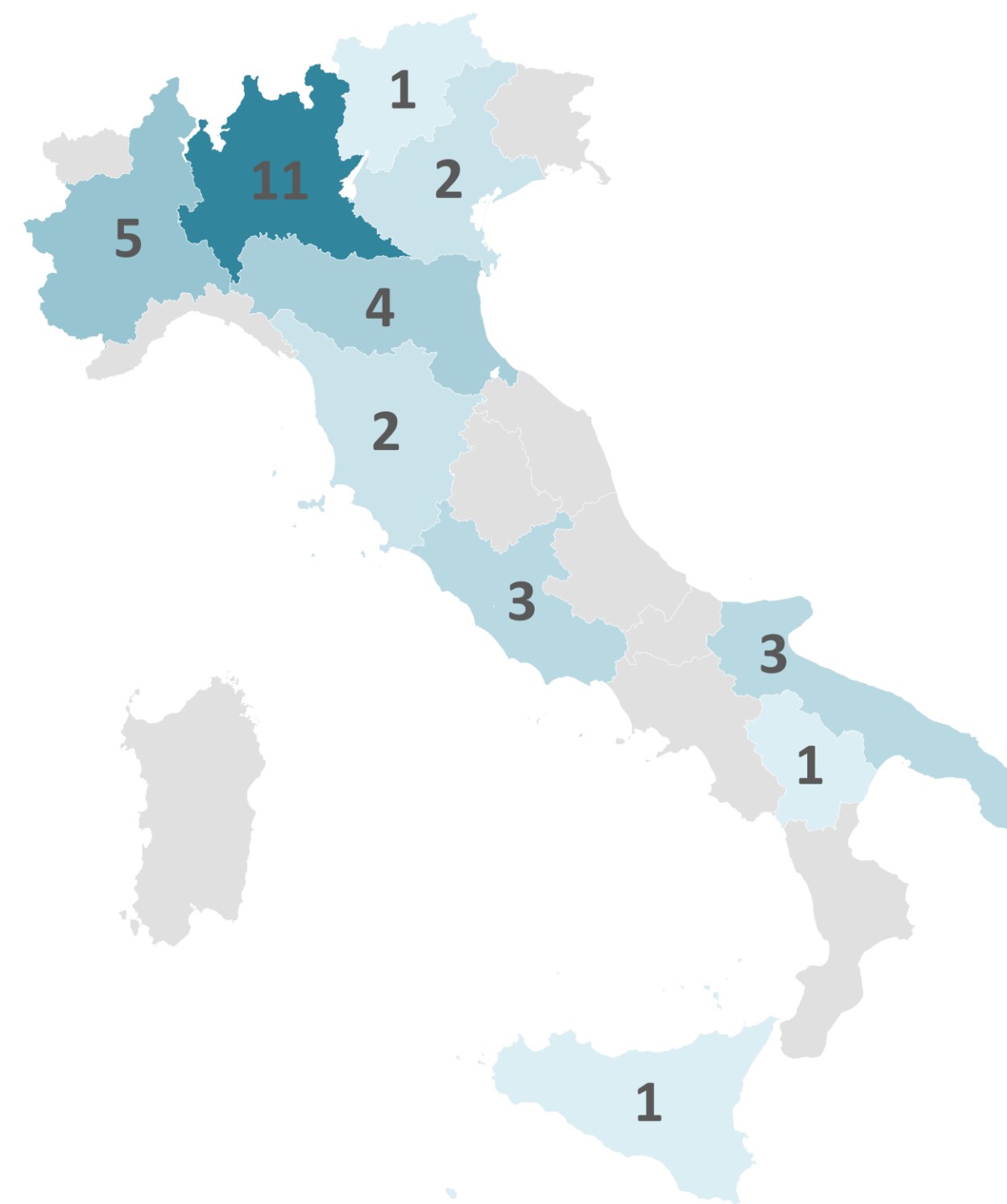
Difficoltà nel rispondere alle domande

Campione

☐ 34 CTS relezionati per il progetto pilota del 2023



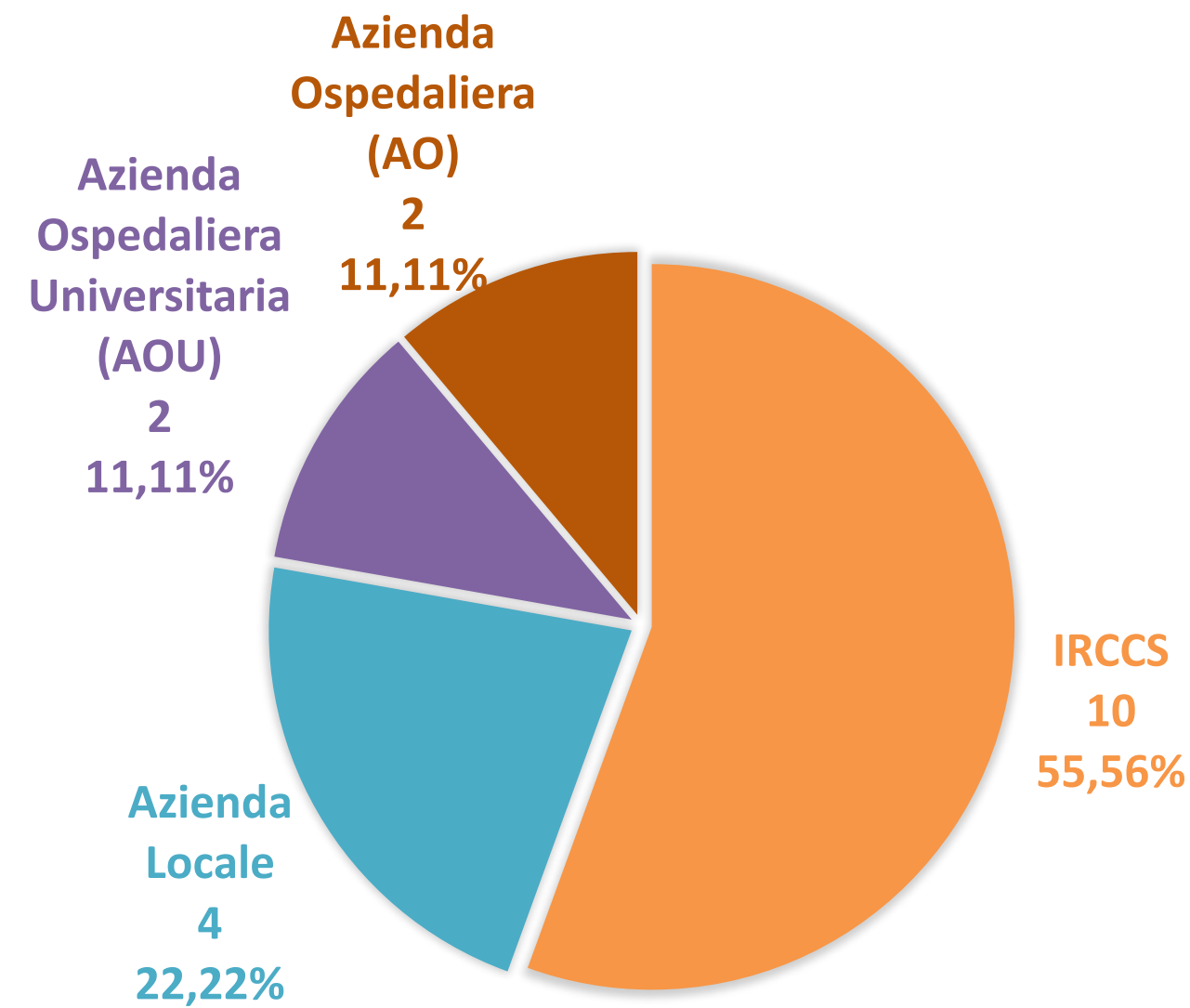
*Azienda locale include ASL, AUSL, ASST, AO controllo ASL



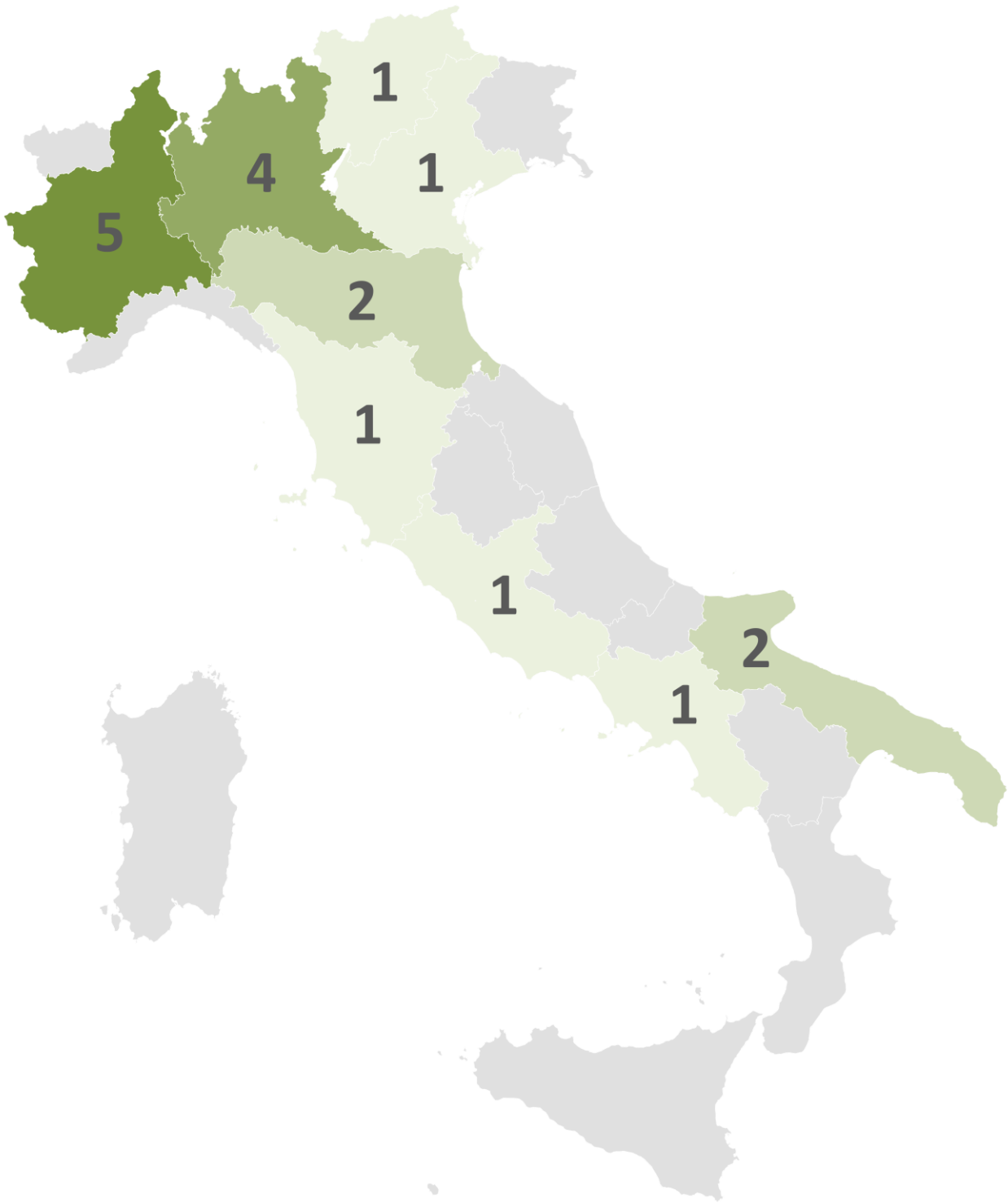
Numero Centri 1 11

Rispondenti Survey

☐ **18** su 34 CTS hanno completato il questionario fin'oggi con un tasso di partecipazione del **52,94%**.



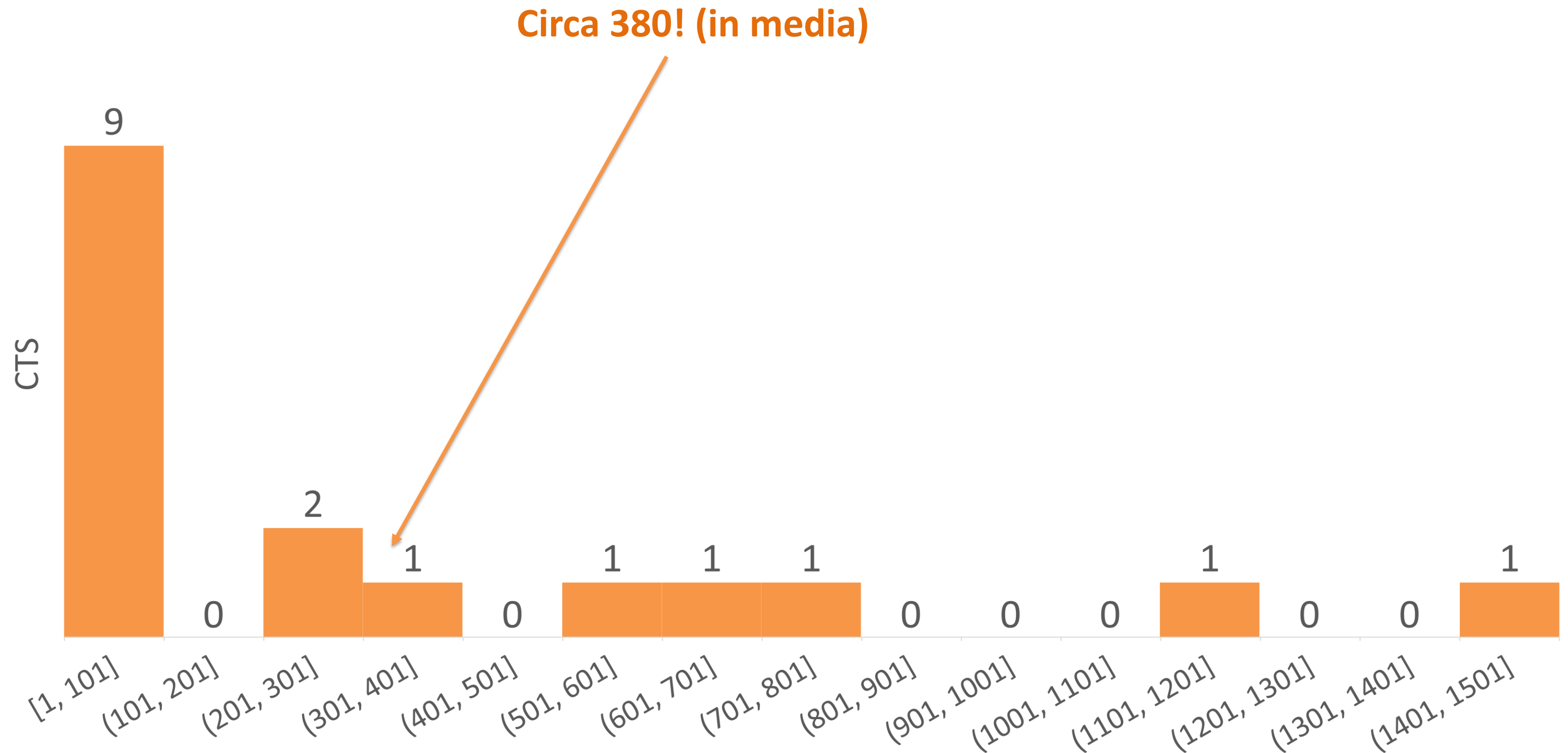
*Azienda locale include ASL, AUSL, ASST, AO controllo ASL



Risposte 1 5

Variabilità dei dati

➤ Quanti pazienti sono stati arruolati in ogni centro nel 2022?



Indicatore composito

Risposta Questionario

Quanti pazienti sono stati arruolati nel 2022?

Indicatore semplice

Pazienti arruolati/pazienti dimessi nel 2022

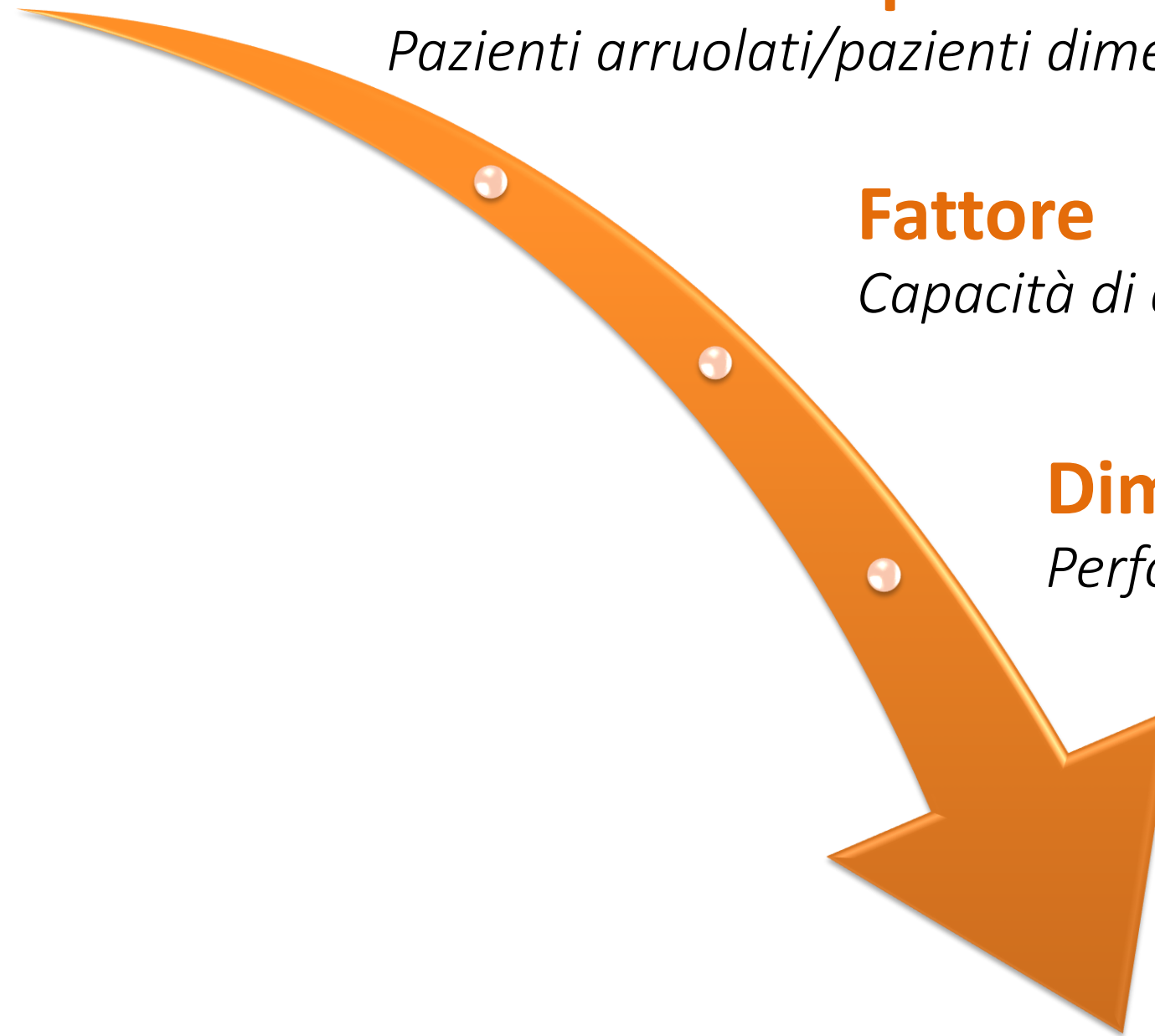
Fattore

Capacità di attrarre pazienti

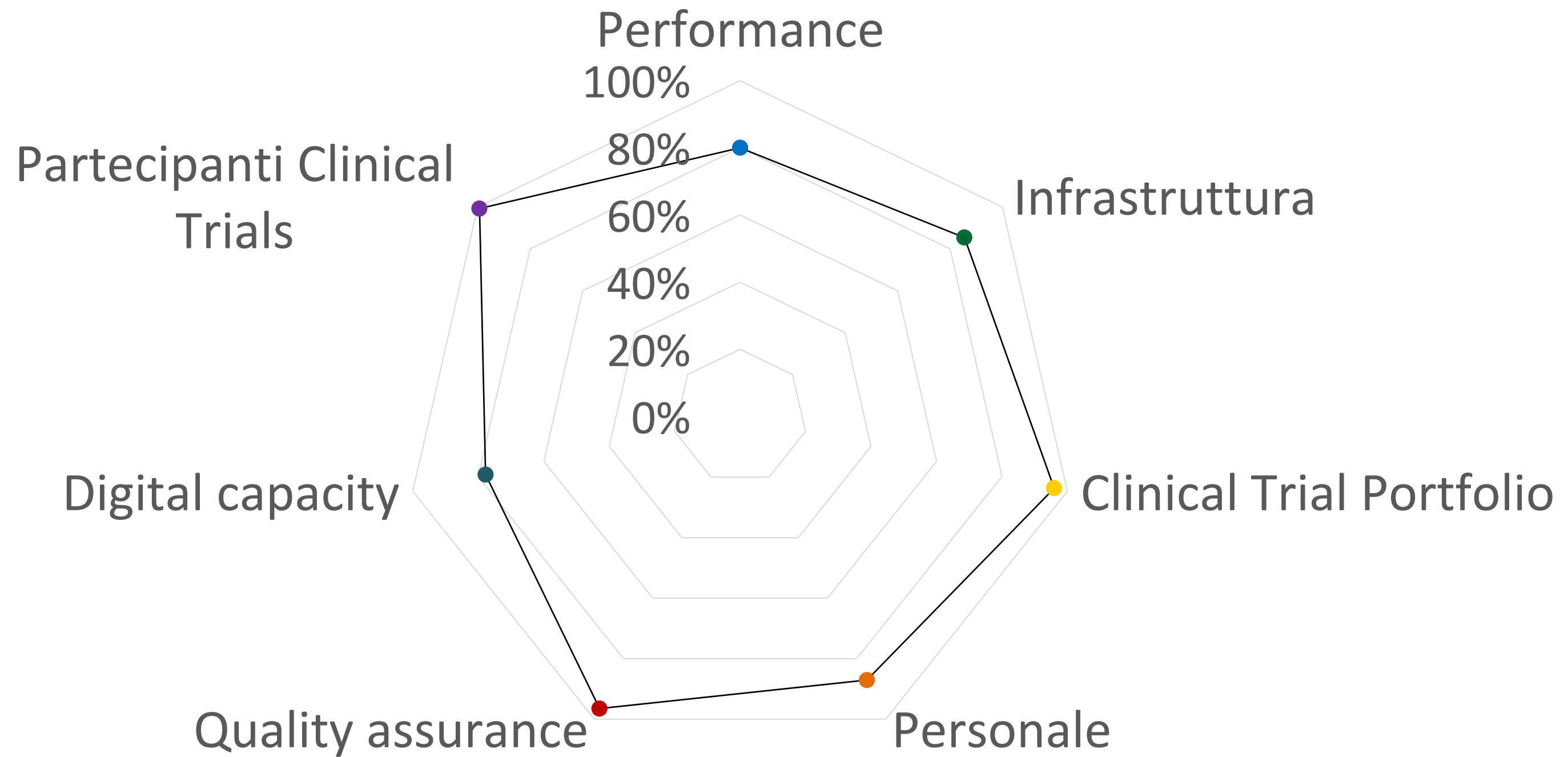
Dimensione

Performance

Indicatore composito

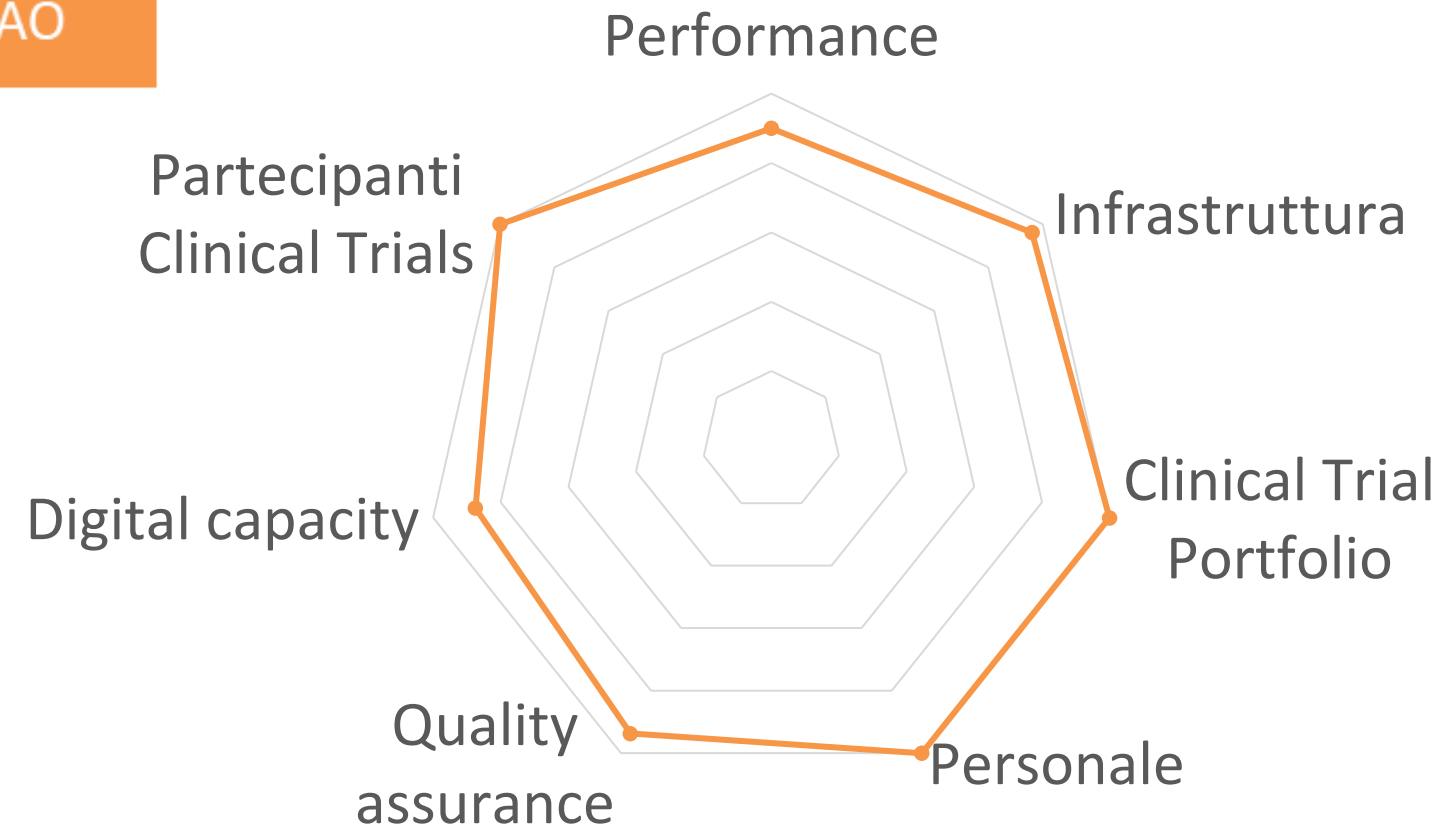


Tasso di risposta per dimensione

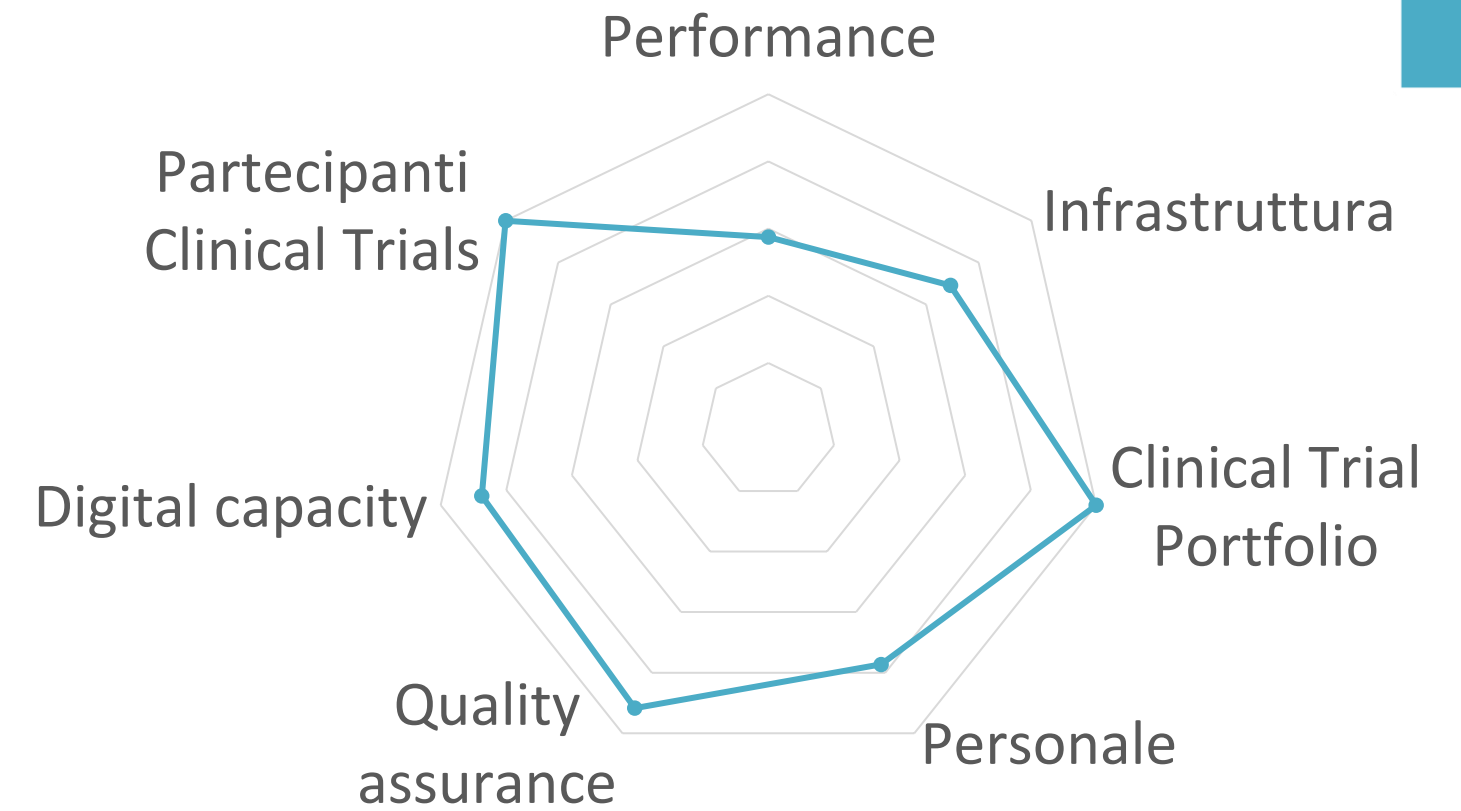


Panoramica risposte per tipo di organizzazione del CTS

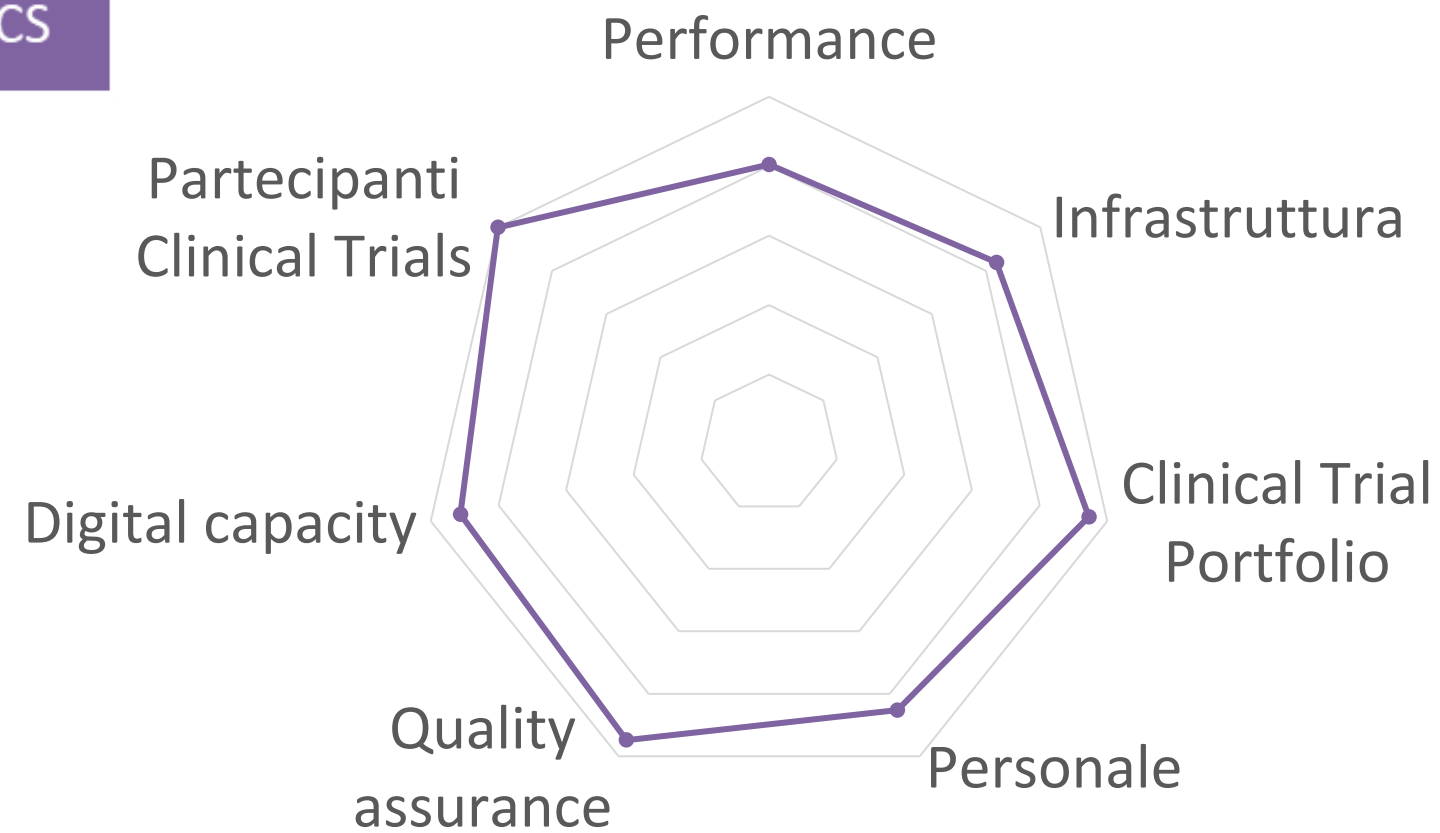
AO



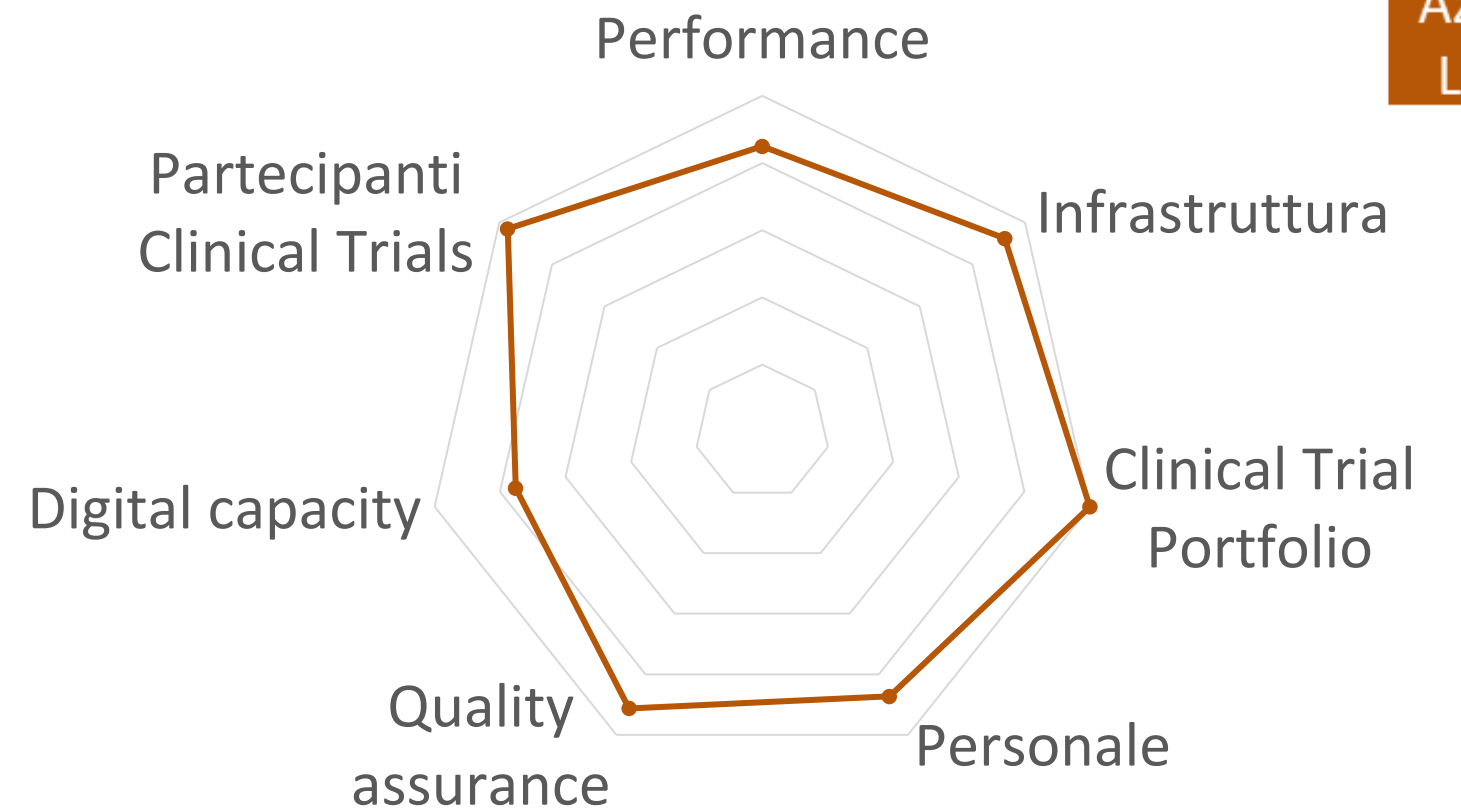
AOU



IRCCS



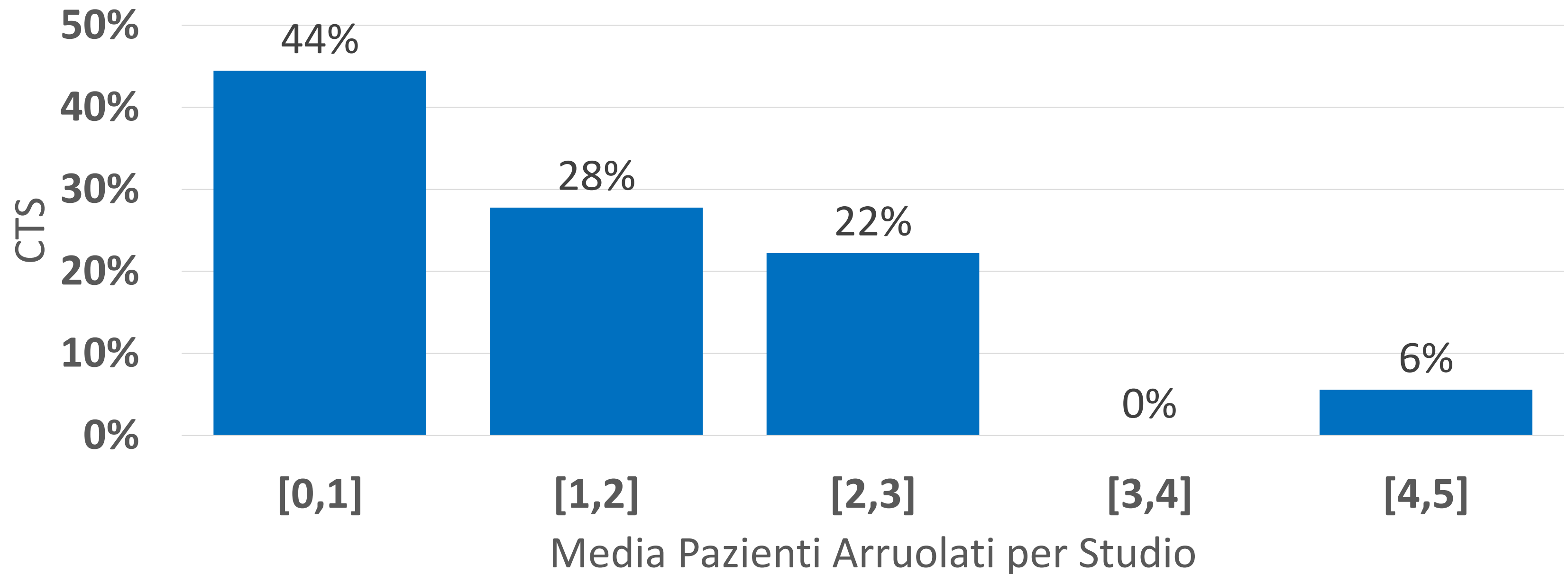
Azienda
Locale



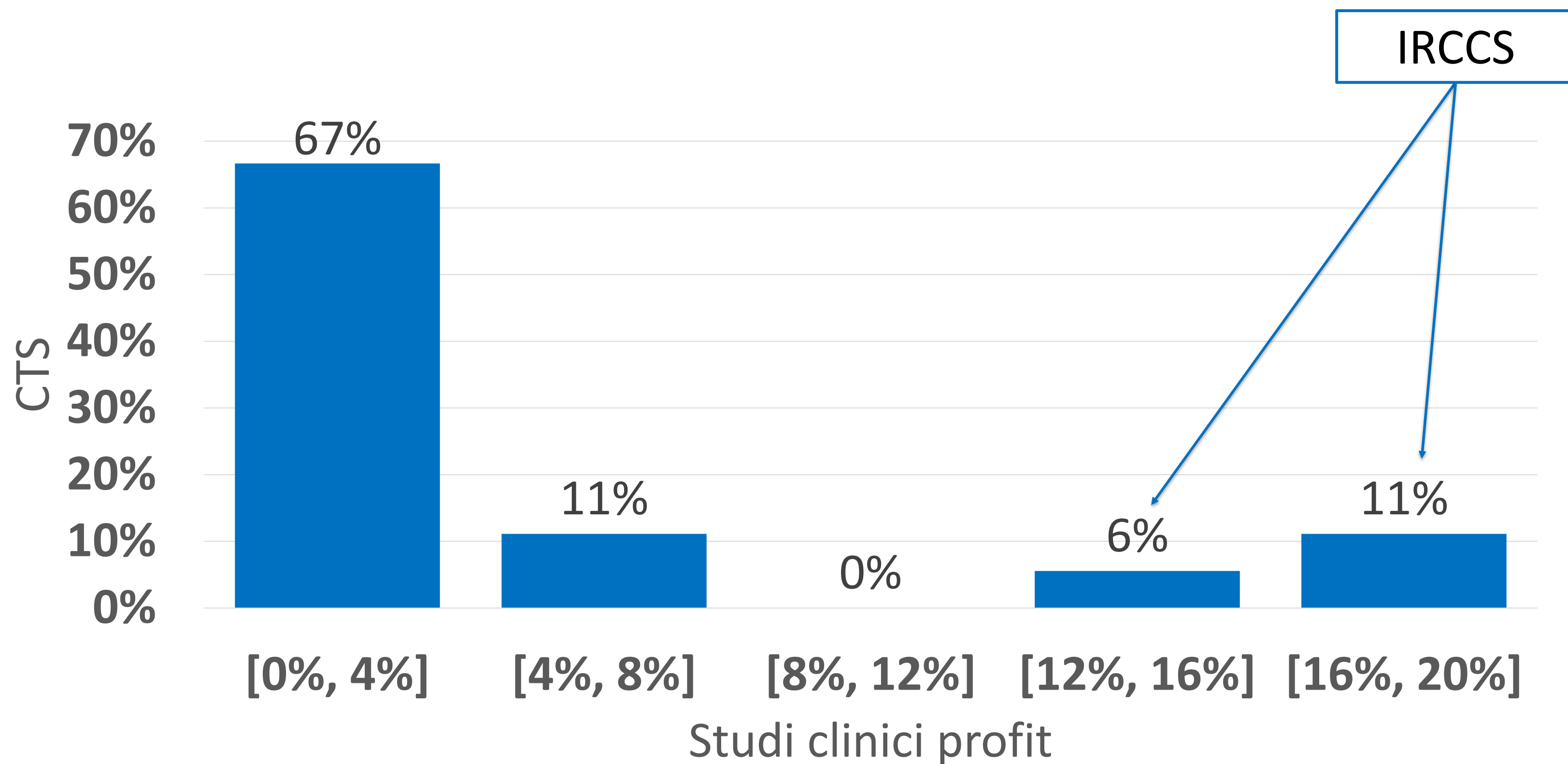
Arruolamento pazienti 2022

PERFORMANCE

□ La maggior parte degli studi attivi non arruola pazienti



❑ I CTS erano pronti al nuovo Regolamento EU 536/2014?



PERFORMANCE

Tipologia Struttura

Azienda Locale

IRCCS

AOU

AO

0 2 4 6 8 10 12 14 16

Media Giorni per l'invio di idoneità dalla richiesta dello Sponsor

Azienda Locale

IRCCS

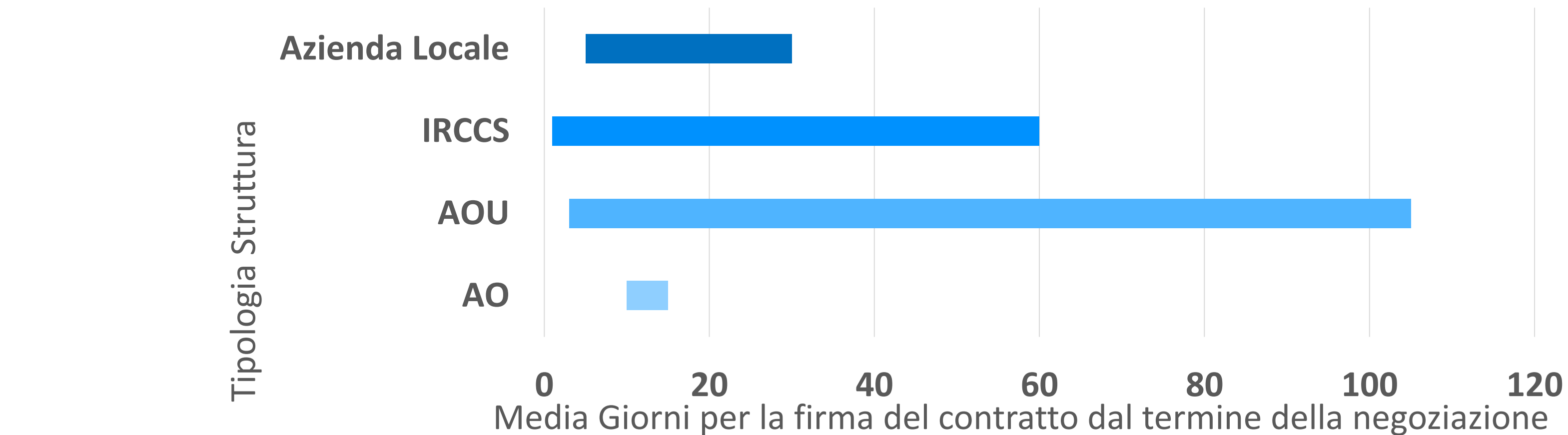
AOU

AO

Tipologia Struttura

0 20 40 60 80 100 120

Media Giorni per la firma del contratto dal termine della negoziazione



Alla domanda «*Le prestazioni sanitarie per studi clinici vengono erogate in spazi dedicati alla ricerca clinica*»:

IL 56% ha
risposto “Sì”

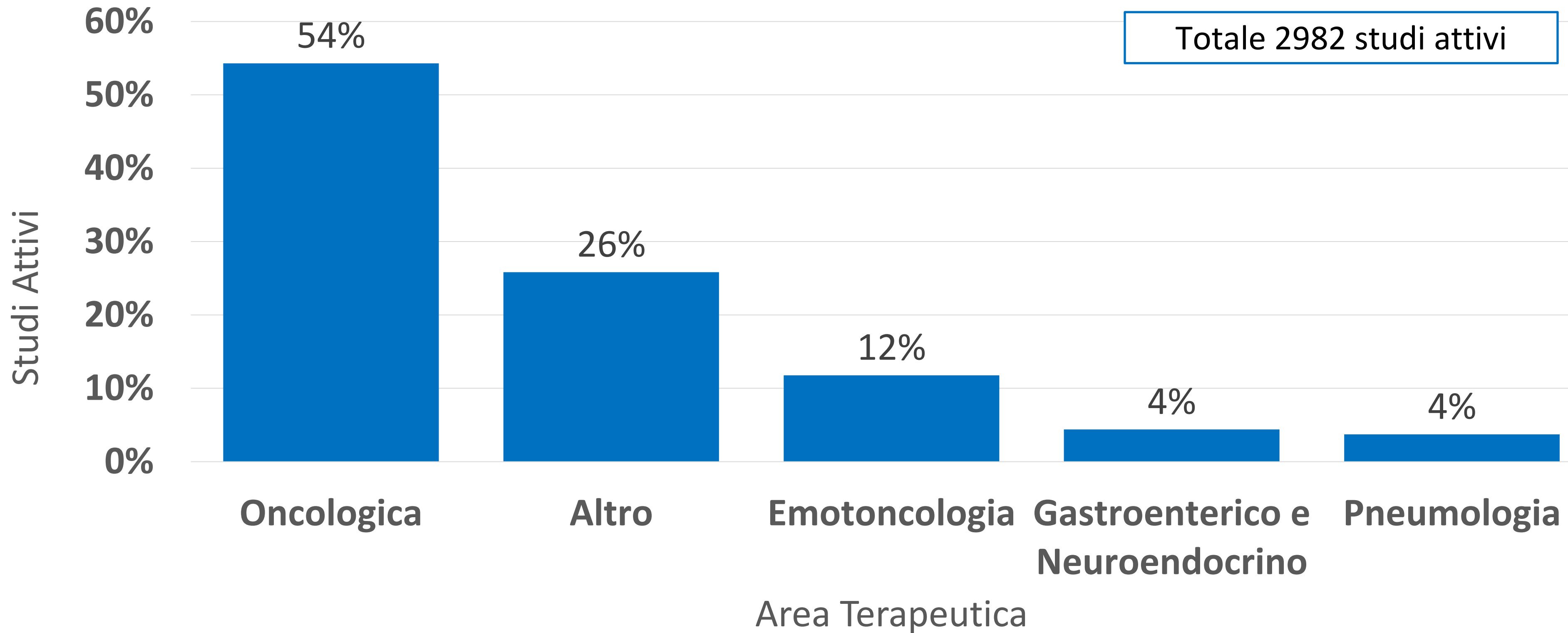
IL 28% ha
risposto “No”

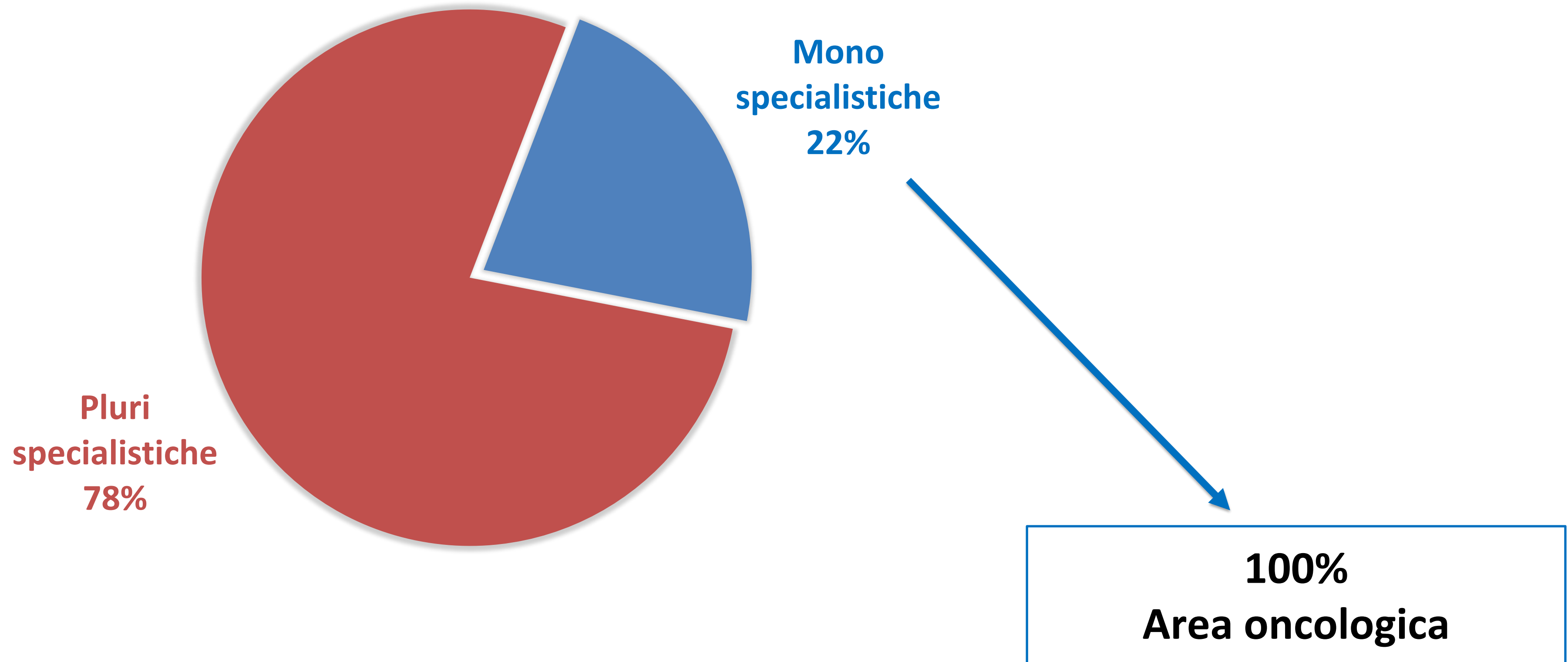
IL 16% ha risposto
“In parte”

- **89%** dei CTS ha **meno dell' 1%** dei posti letto Degenza Ordinaria dedicati alle sperimentazioni cliniche;
- **78%** dei CTS ha **meno dell' 1%** dei posti letto Day Hospital dedicati alle sperimentazioni cliniche;
- **67%** dei CTS ha **meno del 10%** dei slot per l'alta diagnostica (RSM + TAC) dedicati alle sperimentazione cliniche ;
- Slot ambulatoriali dedicati alle sperimentazioni cliniche sono quasi inesistenti nei CTS

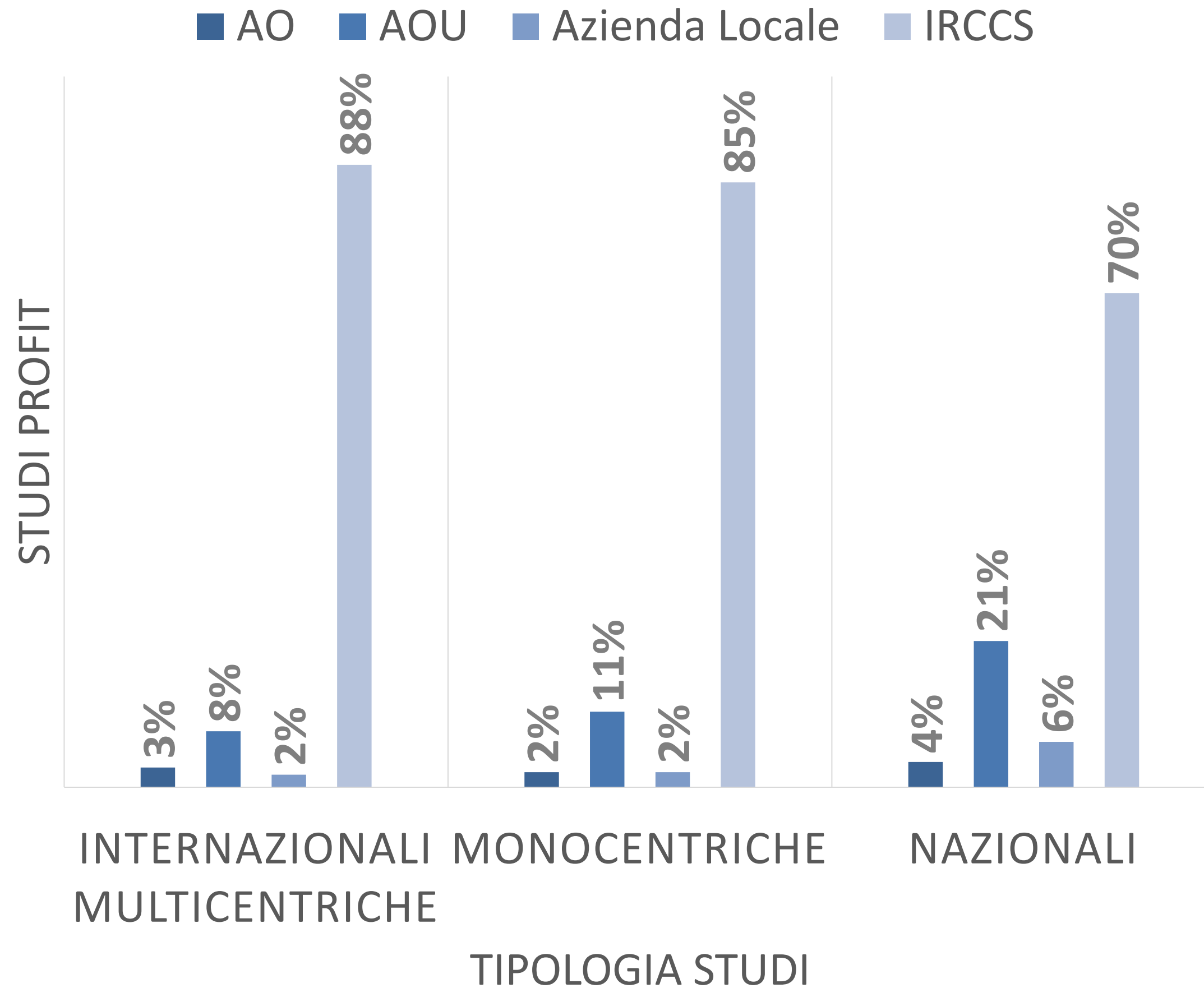
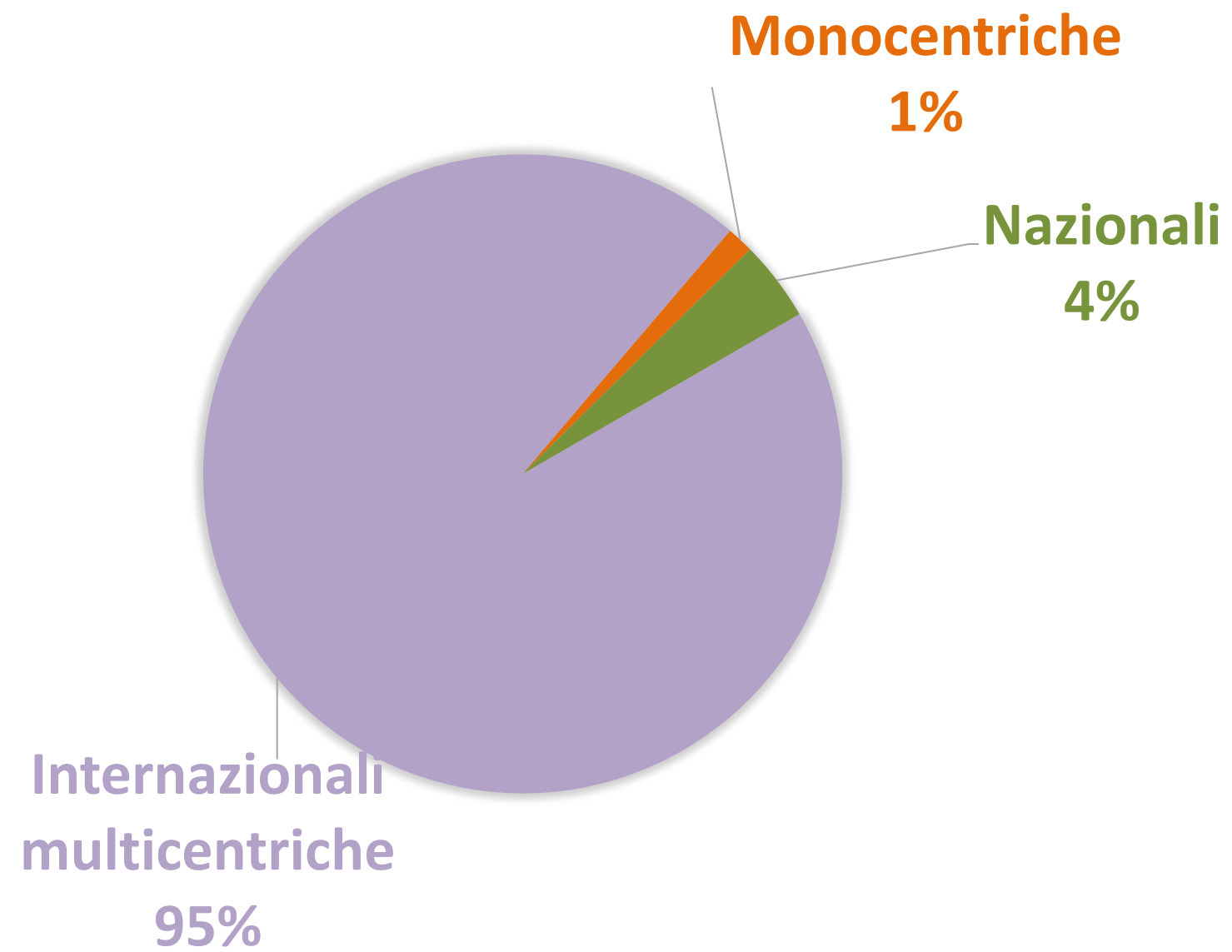


CLINICAL TRIALS PORTFOLIO

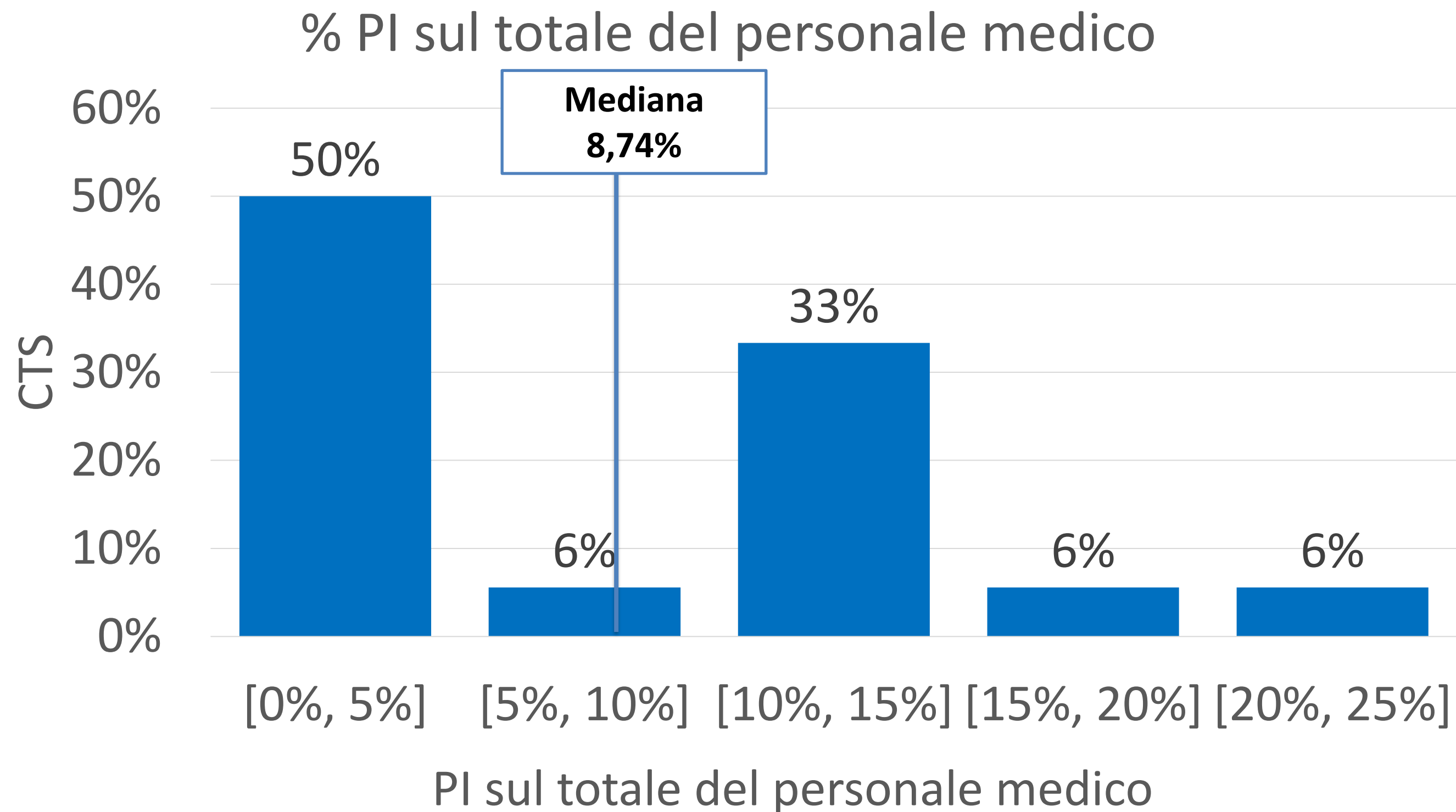




CLINICAL TRIALS PORTFOLIO

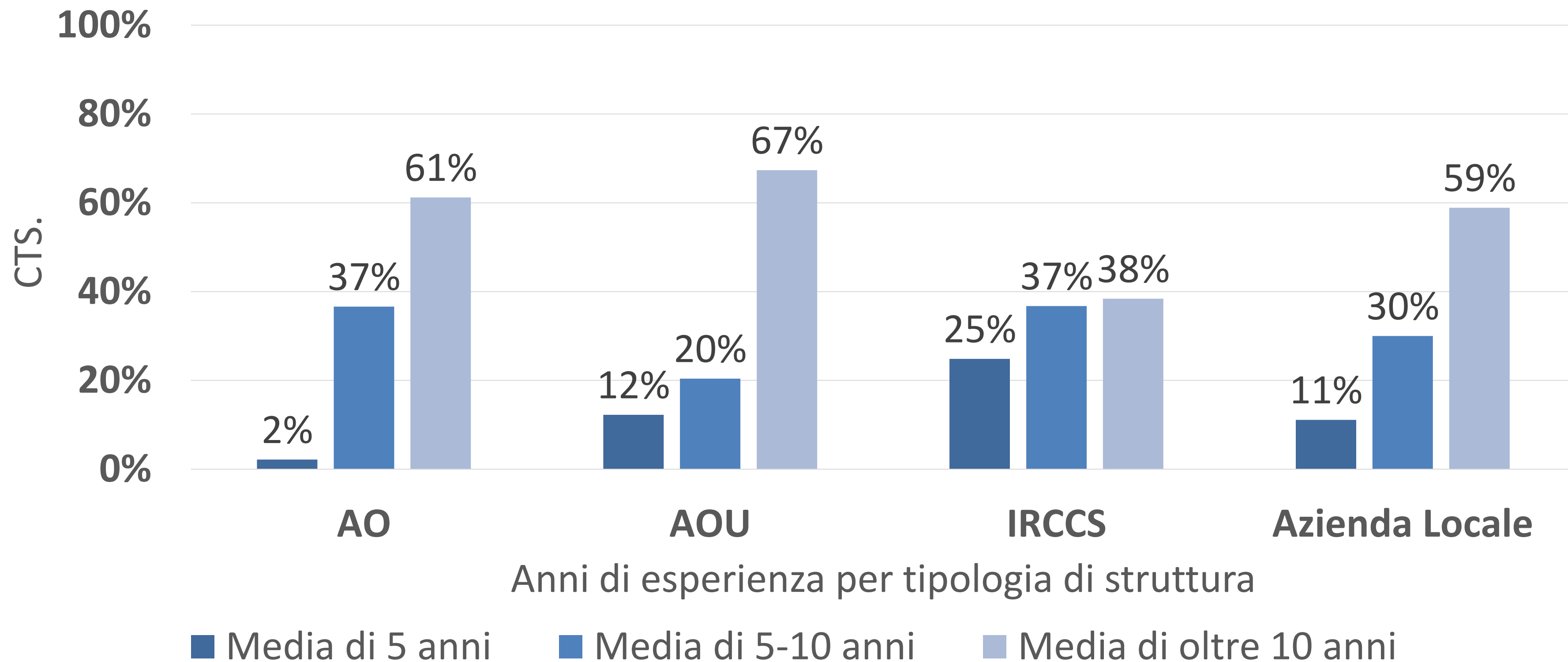


❑ Bassa percentuale di personale che svolge ricerca

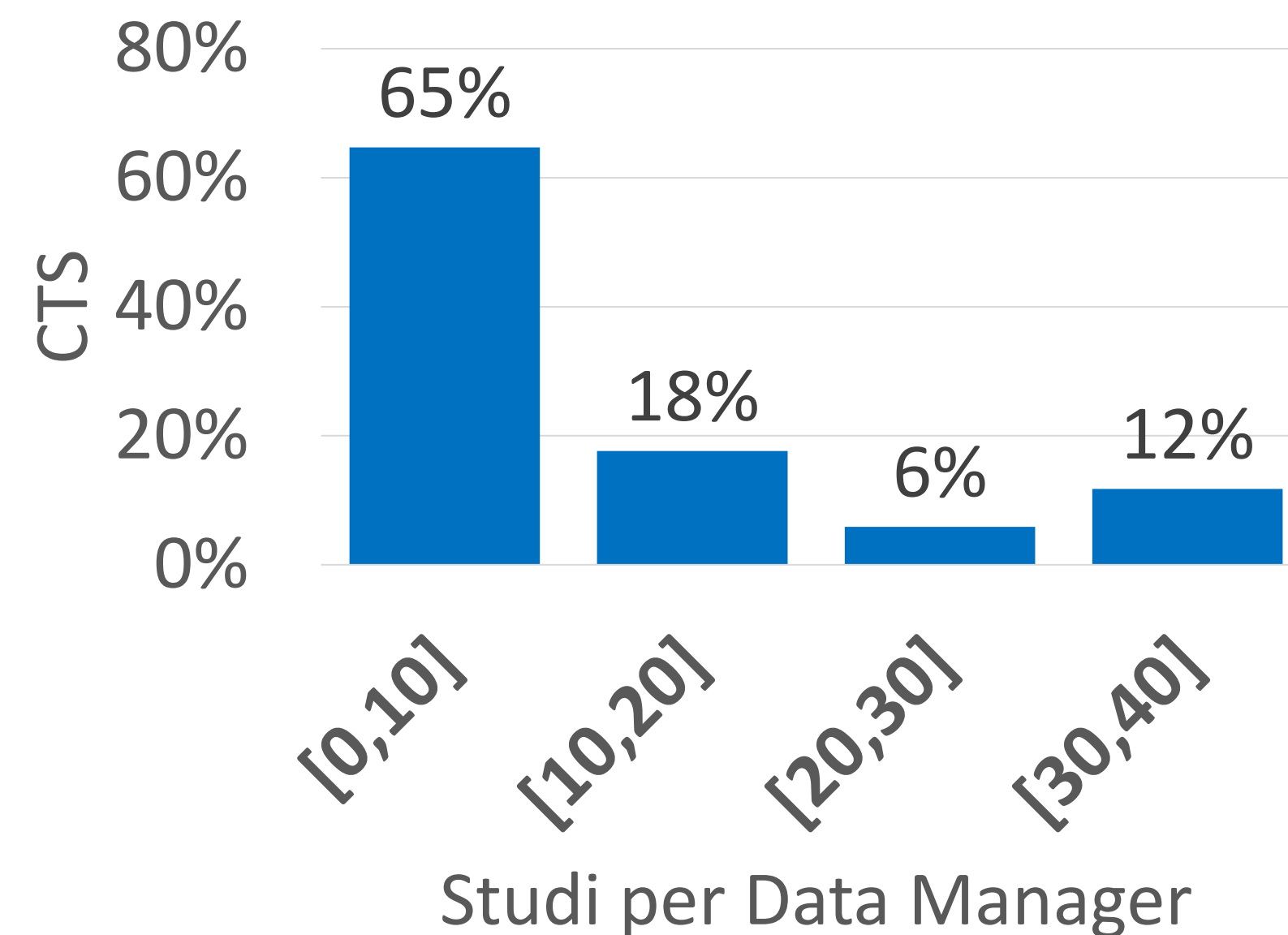
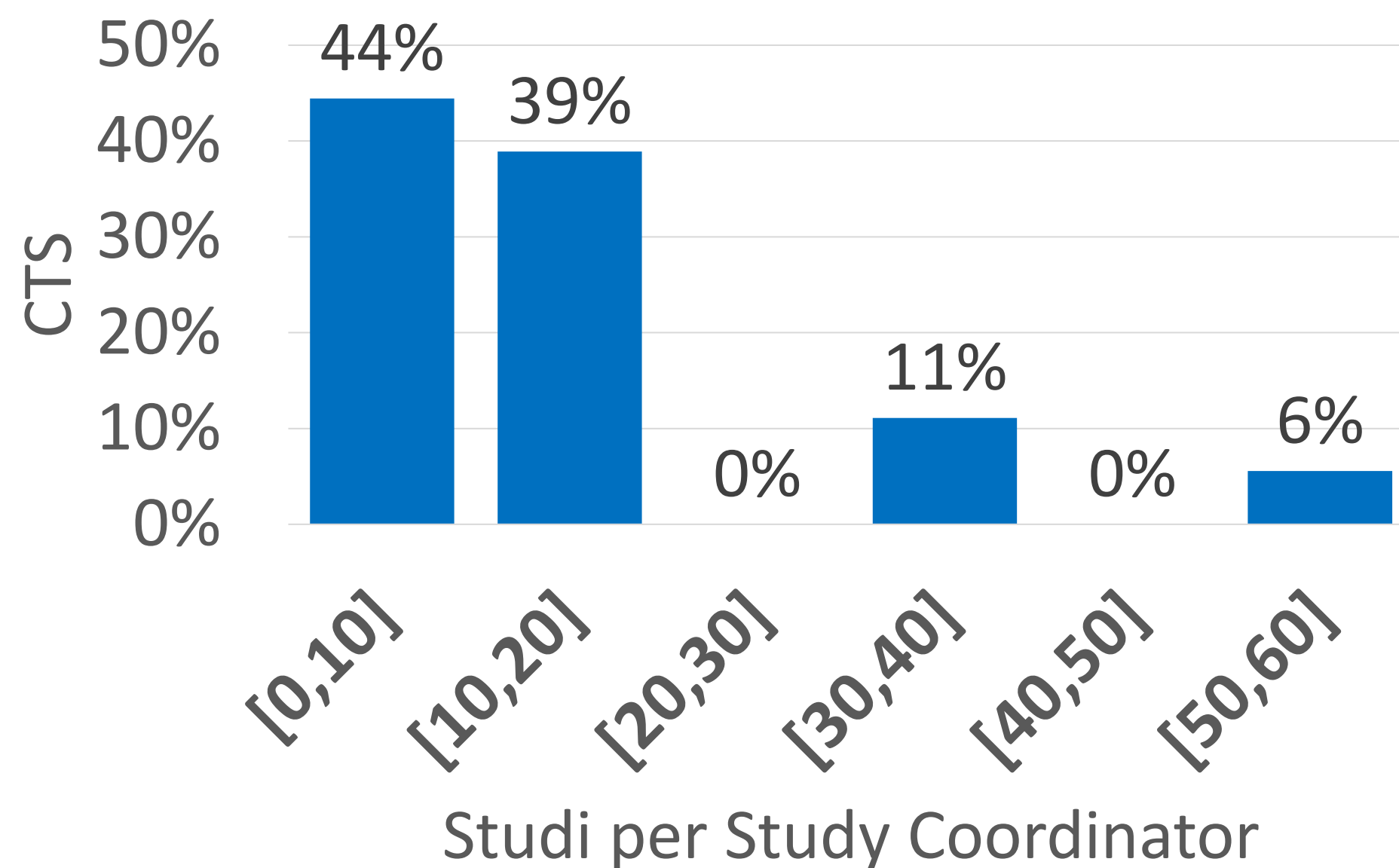


❑ **72%** dei CTS ha meno del 2% degli infermieri di ricerca

☐ > del **59%** dei **PI** ha più di **10 anni** di esperienza

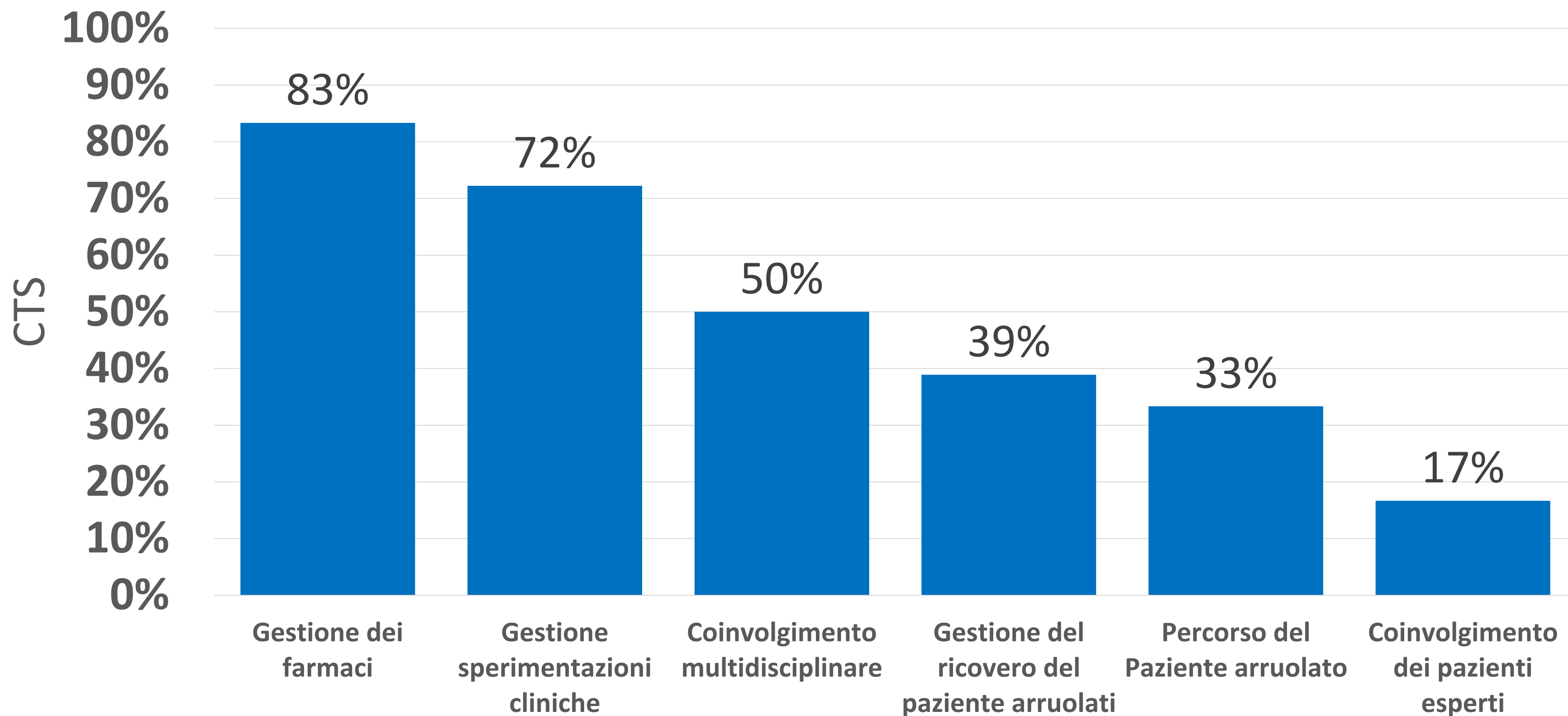


☐ Valorizzazione qualitativa del personale a supporto della ricerca



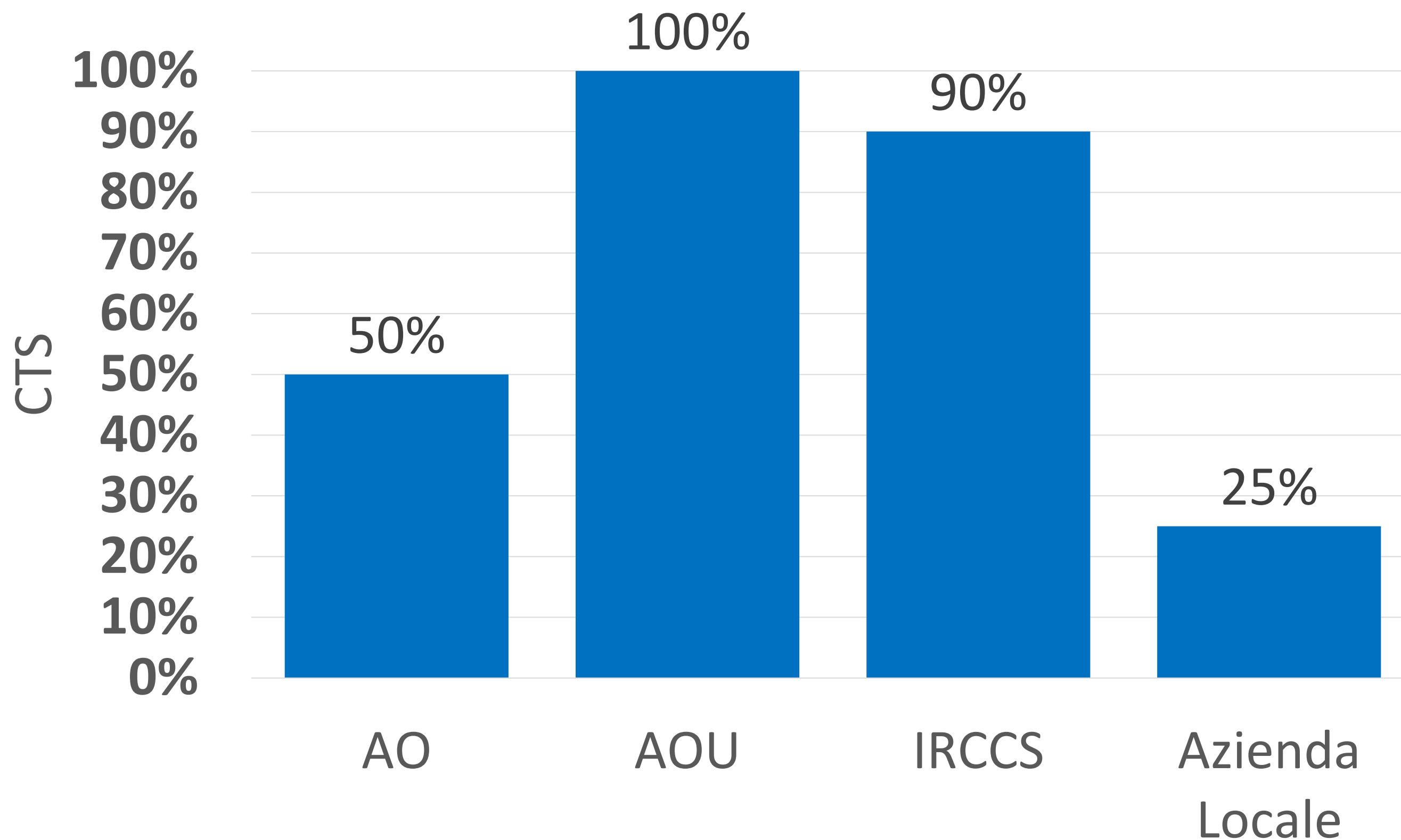
Overview SOP per

QUALITY ASSURANCE



Formazione Good Clinical Practice erogata dai CTS

QUALITY ASSURANCE



□ I CTS che hanno risposto che **erogano formazione GPC**, hanno in media il **19%** del personale formato.



L' **83%** dei CTS opera in una struttura dove si utilizza la cartella elettronica, ma sono nel **55%** dei casi è applicata in tutta la struttura



Il **50%** dei CTS utilizza software che sono dedicati agli studi clinici e per tutti gli studi clinici



Nel **17%** dei CTS il software per la ricerca è integrato con i sistemi informatici aziendali



Il **45%** dei CTS utilizza strumenti di telemedicina

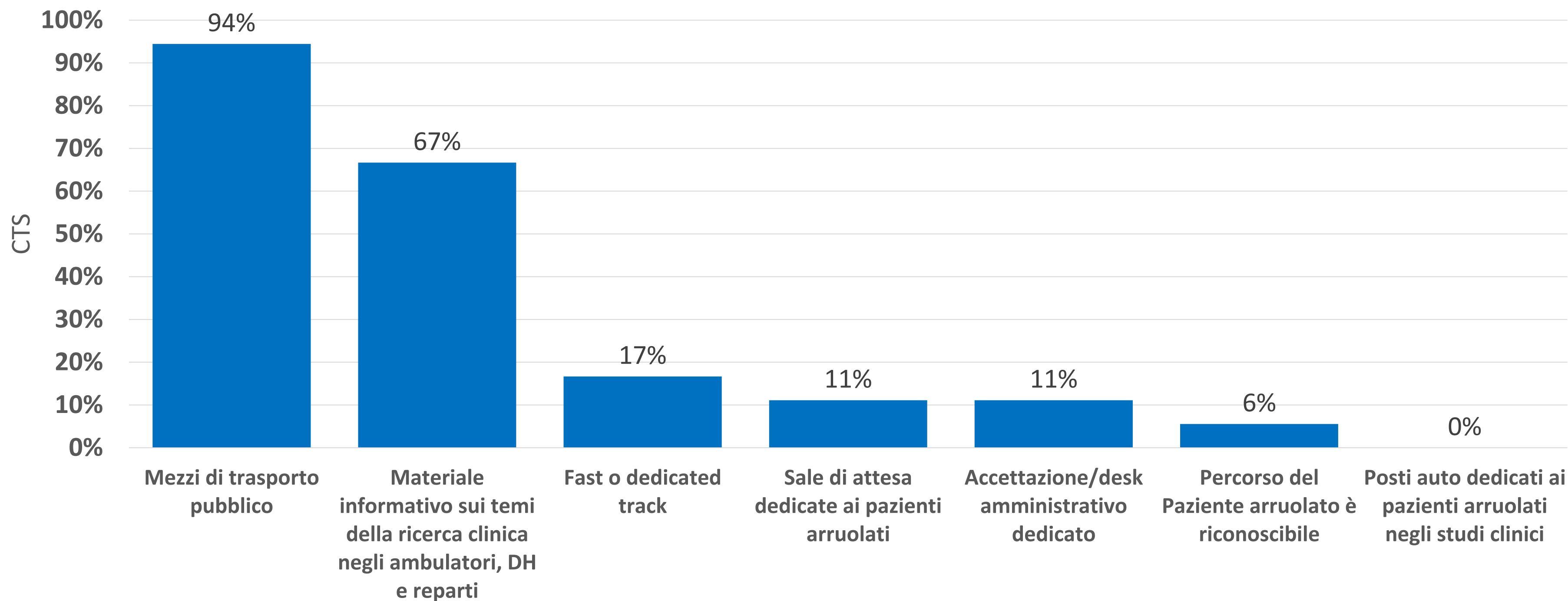


Il **33%** dei CTS ha la cartella elettronica validata secondo le normative

(i.e. EMA/INS/GCP/112288/2023)

Overview Digital Capacity

☐ Presenza di fattori che facilitano la partecipazione alla sperimentazione clinica



Prossimi passi anno 2024

- Chiudere la raccolta dati sollecitando i CTS che mancano
- Revisione delle risposte del 2022 e Validazione dei dati
- Revisione della metodologia, dimensioni, indicatori e domande del questionario
- Aumentare la dimensione del campione



“Torture the data and it will confess to anything.”

Ronald Coase, Economist and Author

Emmanouil.Tsiasiotis@unicatt.it



THANK YOU!!!