



Bambino Gesù
OSPEDALE PEDIATRICO

Sustainability Report

& Scientific Research
and Clinical Care Activity



2024

**Sustainability Report
&
Scientific Research
and Clinical Care Activity**

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Bambino Gesù
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Summary

Sustainability Report	4
Overview of the Sustainability Report and methodological note	4
01 OPBG identity	6
02 The resilient management model of OPBG	24
03 The care of children and adolescents	38
04 Care-oriented research	50
05 OPBG academic activity	62
06 Hosting and solidarity initiatives	70
07 Worker safety and well-being	88
08 Environmental protection	104
09 Economic sustainability and financial independence	112
10 Technology and digital transition	118
11 Attachments	124
Scientific research and clinical care activities	133
01 Research Areas	134
02 Clinical care activities	166

Overview of the Sustainability Report and methodological note

Bambino Gesù Children’s Hospital (the **Hospital** or **OPBG**) draws up on a voluntary basis its Sustainability Report, which anticipates the publication of the annual Sustainability Statement (also on a voluntary basis) according to the *Sustainability Reporting Standards of the Global Reporting Initiative 2021 (GRI Standards or GRI)*.

The promotion of sustainability in its different dimensions is a key factor for the strengthening of the Hospital’s strategic path, which is focused on sustainability aimed at innovation, knowing that “Sustainable Development is the one that allows the present generation to meet its needs without compromising the ability of future generations to meet their own” (Brundtland Report, 1987). The Sustainability Report 2024 covers the period from January 1st to December 31st, 2024, also including the more significant developments that occurred in the first months of 2025. The document is divided into two sections: the Sustainability Report 2024 and the 2024 Report on Scientific Research and Clinical Care Activities.

Relevance of the Agenda 2030 in the analysis of material topics and in the identification of impacts

The analysis of material topics and impacts, in the context of the Hospital’s Sustainability Report, is based on the Sustainable Development Goals (SDGs) of the UN 2030 Agenda, that provide global guidance for addressing social, environmental, and economic challenges in an integrated manner. The Hospital is

committed to meeting these goals, also taking into account the fundamental principles of the *Laudato Si*, Pope Francis’ encyclical letter on the care for our “Common Home,” which fits perfectly into the sustainability methodology.

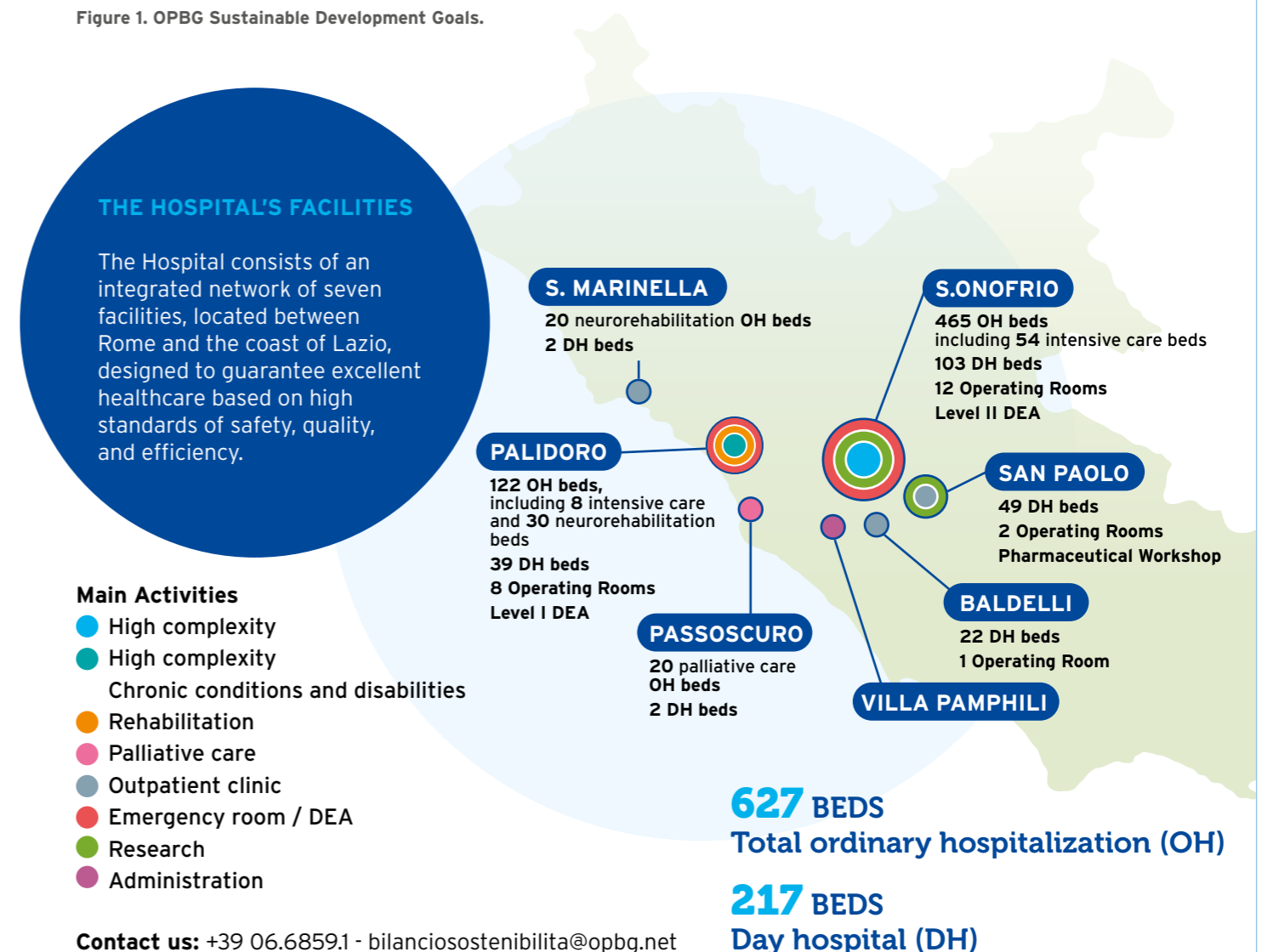
Laudato Si, emphasizes a new paradigm of development that is not limited to pursuing economic well-being but promotes a broader vision of “progress” based on social inclusion, respect for the environment, and the well-being of people, especially the poorest and most vulnerable. The encyclical letter calls for a concrete commitment to care for our environment, highlighting the connection between the health of the planet and that of humanity, as well as the urgent need for collective action to halt ecological and social degradation (LS 13). *Laudato Si*, in point 49, recalls the importance of a development model that recognizes the dignity of every individual, from a perspective of solidarity and social justice. The Hospital, in line with its Code of Ethics, is therefore committed to promoting a model of care that is in tune with these values, integrating care for the environment and human well-being into its sustainability objectives.

Goal 3 of the 2030 Agenda, “Good Health and Well-Being,” aimed at ensuring health for all, at all ages, is at the heart of the Hospital activity. In line with this goal and with the recommendations of *Laudato Si*, the Hospital is committed to ensuring access to quality care, promoting prevention, and improving the well-being of the communities it serves, always bearing in mind the need to protect our natural environment. This approach translates into a vision of an integrated sustainability system that guarantees continuity, as well as the maintenance and development of quality standards in care and research.

The Hospital contributes to the achievement of the following Sustainable Development Goals set out in the 2030 Agenda:



Figure 1. OPBG Sustainable Development Goals.



01



OPBG identity

Legal status

Bambino Gesù Children's Hospital was established by a Chirograph of Pope Pius XI on January 24, 1924, as an institution, with all its appurtenances and dependencies, owned by the Holy See.

The Hospital, which has no legal personality, is located in Rome, in Piazza Sant'Onofrio 4, in one of the extraterritorial areas recognized by the Lateran Treaty of 1929 which enjoy specific immunities. Its tax code is 80403930581. The Hospital does not have a VAT number.

Bambino Gesù Children's Hospital reports directly to the Holy See and is subject to its supervision and guidance; it is on the General List referred to in Article 1§1 of the Statute of the Council for the Economy and, as such, is one of the institutions subject to the supervision of the Council for the Economy and of the Secretariat for the Economy, in accordance with the powers of these bodies under Vatican law.

Italian Law No. 187 of May 18, 1995 - which ratified the international agreement between the Italian Government and the Holy See of February 15, 1995, and therefore regulated, in the context of Article 4, paragraph 13, of Legislative Decree No. 502 of December 30, 1992, the relations between Bambino Gesù Children's Hospital and the Italian National Health Service (SSN) - confirmed the formal legal status of the Hospital (including its subordinate structures), without prejudice to the relevant provisions of the Lateran Treaty.

Bambino Gesù Children's Hospital is authorized to operate with the National Health Service and to provide services under the SSN by virtue of the aforementioned Law. Law No. 187 of May 18, 1995, also classified the research activity carried out by Bambino Gesù Children's Hospital as a Scientific Institute for Hospitalization and Care (IRCCS) within the frame-

work of Legislative Decree No. 269 of June 30, 1993, subsequently replaced by Legislative Decree No. 288 of October 16, 2003, as supplemented and amended by Legislative Decree No. 200 of December 23, 2022, concerning the reorganization of the regulations governing IRCCSs.

The recognition of the Hospital as a Scientific Institute for Hospitalization and Care, on the basis of the aforementioned regulations, is subject to periodic confirmation, at intervals specified by the applicable legislation, following a positive verification of the existence of the relevant requirements.

Within the framework of Italian law, Bambino Gesù Children's Hospital is therefore a private law entity belonging to (and therefore owned by) the Holy See and, as such, subject to specific regulations, also relating to its purposes.

In this context, the Hospital, as an institution of the Holy See, is subject to the relevant regulations; among others, the following apply to the Hospital, within the limits and in the manners defined by the competent Vatican authorities: the rules on transparency, control, and competition in public contracts of the Holy See and the Vatican City State (NCP Regulation), the regulations governing the assets of the Apostolic See referred to in the Apostolic Letter in the form of a *Motu Proprio* of His Holiness Pope Francis dated February 20, 2023, as well as those relating to the Financial Statements included in the aggregate perimeter of the Financial Statements of the Holy See with the related indications provided by the Secretariat for the Economy.

Acts performed towards third parties, for all matters not expressly regulated by the laws of the Vatican City State, also in reference to the Hospital, are governed by Italian law unless the parties agree to refer to the legislation of the Vatican City State.

Management and control bodies

The management bodies of Bambino Gesù Children's Hospital are the President and the Board of Directors. The Board of Auditors is the control body.

The President is appointed by the Holy See by act of the Secretary of State. The President of the Board of Auditors is appointed by the Prefect of the Secretariat for the Economy. The Secretary of State also appoints Directors and Auditors.

The composition of the Board of Directors in office as of the date of approval of the Financial Statements 2024, expiring on the date of the approval of the Financial Statements 2026 is as follows:

- President: **Tiziano Onesti**
- Directors: **Renato Balduzzi, Maria Bianca Farina, Rev. Mons. Piero Gallo, Fabio Gasperini, Sergio Gatti, Agostino Miozzo, Alessandra Perrazzelli, Duchess Maria Grazia Salviati.**

The composition of the Board of Statutory Auditors in office as of the date of approval of the Financial Statements 2024, expiring on the date of approval of the Financial Statements 2026 is as follows:

- Chairman: **Salvatore Sardo**
- Full members: **Gianni Artegiani, Francesco Capogrossi Guarna**
- Alternate members: **Antonio Di Iorio, Guido Paolucci.**

The President, who also chairs the Board of Directors, is responsible for the strategic direction of the Hospital and its humanitarian and care mission, ensuring the continuous involvement of the Board of Directors in the sharing of strategic objectives and all relevant initiatives, in line with the Vatican regulatory framework. Specifically, the President, who has strategic oversight of all areas of the Hospital, submits proposals to the Board of Directors for the approval of: (i) the multi-year plan; (ii) the annual budget; (iii) the Financial Statements and Sustainability Statement; (iv) the appointment of Directors; (v) acquisitions exceeding 500,000 € per year that are not included in the an-

nual budget; (vi) acquisitions and sales of real estate regardless of their value; (vii) works on real estate exceeding 500,000 €; (viii) the Hospital shareholding in corporate vehicles formally equipped with their own management bodies for initiatives exceeding 500,000 €; (ix) the granting of unsecured loans or loans secured by collateral by banks in favor of the Hospital for amounts exceeding 500,000 €.

The annual Budget and Financial Statements approved by the Board of Directors are then submitted by the President to the Secretariat for the Economy for assessment and approval, also in relation to the fact that the Hospital's Financial Statements are included in the aggregate perimeter of the Holy See's Financial Statements.

The President approves the Annual Audit Plan and validates the results of the Risk Assessment presented by the Control Systems function, defines the priorities for action and approves the strategies to address the Hospital's main risks, providing information on these matters to the Board of Directors. The President also provides periodic reports to the Board of Directors on the economic, operational, and financial performance of the Hospital and on the initiatives that, in his sole discretion, he deems appropriate to propose, including in the context of the overall assessment of the adequacy of the Board's organizational, administrative, and accounting structure.

The President is also the Employer for matters relating to health and safety in the workplace and, in this role, he approves the related Risk Assessment Document.

The President is the legal representative of the Hospital. The Board of Auditors is an independent body that monitors the overall compliance of the Hospital's activities with the applicable regulatory framework, as well as with the principles of good governance and the adequacy of the organizational, administrative, and accounting structure and its actual functioning. The Board of Auditors is also in charge of accounting control. By virtue of its nature, the Board of Auditors also monitors the compliance with the Code of Ethics and handles the related reports.

Purpose, ethics, and scope of action

The activities of Bambino Gesù Children's Hospital are based on the guiding principles - emphasized in Pope Pius XI Chirograph - of hospital care provided to poor children as part of the Ministry of the Church.

In this context, and in accordance with the provisions of the aforementioned Apostolic Letter in the form of a *Motu Proprio* by His Holiness Pope Francis on February 20, 2023, the institutional goals pursued by the Hospital, as well as those of the other institutions of the Holy See, serve the common good and the universal Church.

The Hospital's activity is rooted in the essential ethical principles of Catholic morality and of the sacredness of life, knowing that life is always a good, for the purposes of both spiritual and material charity. All this is done to respond to the broader mission entrusted to the Hospital by the Pope: to support the poorest in order to build a world in which there is no longer an unbridgeable gap between those who have much and those who have little, between those who can take care of themselves and those who cannot. In this way, the teaching of Christ to care of the sick and serve the infirm, that is the mission on which the entire activity of the Bambino Gesù Children's Hospital is based, is fully applied.

The Code of Ethics, available at www.ospedalebambinogesu.it, details the values, principles, and rules of conduct that, in the context of the mission pursued, characterize and shape the Hospital's activities both internally and in its relations with external stakeholders. In addition to human life and dignity, both physical and spiritual, the core values and principles of the Hospital are legality, ethics of scientific research activities, solidarity, people's safety and health, protection of the environment, and confidentiality. In this context, OPBG values (as well as its Code of Ethics) are an essential prerequisite to ensure transparency, thus consolidating the trust between the Hospital and its stakeholders.

The Code of Ethics has strategic value for the Hospital, as it is an integral part of the internal control system for the prevention of unlawful conduct and, more gen-

erally, of potential mismanagement, and for the consolidation of a culture that increasingly values ethics, fairness, and compliance with the rules.

In this regard, among the general and specific rules of conduct with which the staff must comply, the provisions of the Code of Ethics on potential conflicts of interest are of great importance, with the obligation for everyone to refrain from any situation or activity that may, even only potentially, favor a personal interest to that of the Hospital, or that may interfere with the ability to make impartial and objective decisions in the Hospital's best interests.

A key component provided for in the Code of Ethics is the reporting system managed by the Board of Auditors, that adopted specific regulations, with the support of the authorized personnel from the Control Systems-Internal Audit Function.

In this regard, the Hospital makes available its own internal reporting channels, which can only be accessed by the members of the Board of Auditors and the staff of the Control Systems-Internal Audit Function. These channels guarantee, also with the use of encryption tools, the confidentiality of the identity of the person who is reporting, of the person involved, and of any other person mentioned in the report, as well as of the content of the report and the related documents. The provisions of the applicable legislation regarding the right of whistleblowers to use external channels, if the conditions are met, remain unchanged. As in the previous two years, no reports of corruption were filed in 2024.

In this context, and with constant reference to the Catholic values and principles that inspired its creation and ensure its development, the Hospital, which never pursues profit, focuses its activities on clinical care in the pediatric field and on translational research, providing highly specialized and complex services.

Another distinctive feature is the institutional training activity carried out by the Hospital which, according to the interregional agreement for the compensation of health mobility, falls within the so-called mixed companies, as the Hospital provides three-year clinical training in pediatrics at the Faculty of Medicine and Surgery, based on the agreement with the University of Rome "Tor Vergata". The Hospital is also accredited

as an Academic Hospital by *Joint Commission International (JCI)*, which adds to the other certification and accreditation programs that Bambino Gesù Children's Hospital undergoes to ensure effective, safe, and patient-centered care.

The Hospital and its facilities (sites and buildings) operate throughout Italy, also supporting local health authorities and regions through specific agreements, and internationally, participating in network projects and playing a leading role in international cooperation initiatives implemented in cooperation with institutional bodies, according to specific agreements aimed at responding to the need for medical and scientific training, and providing highly qualified or complex services to local communities.

Values and principles of the Hospital

Legality

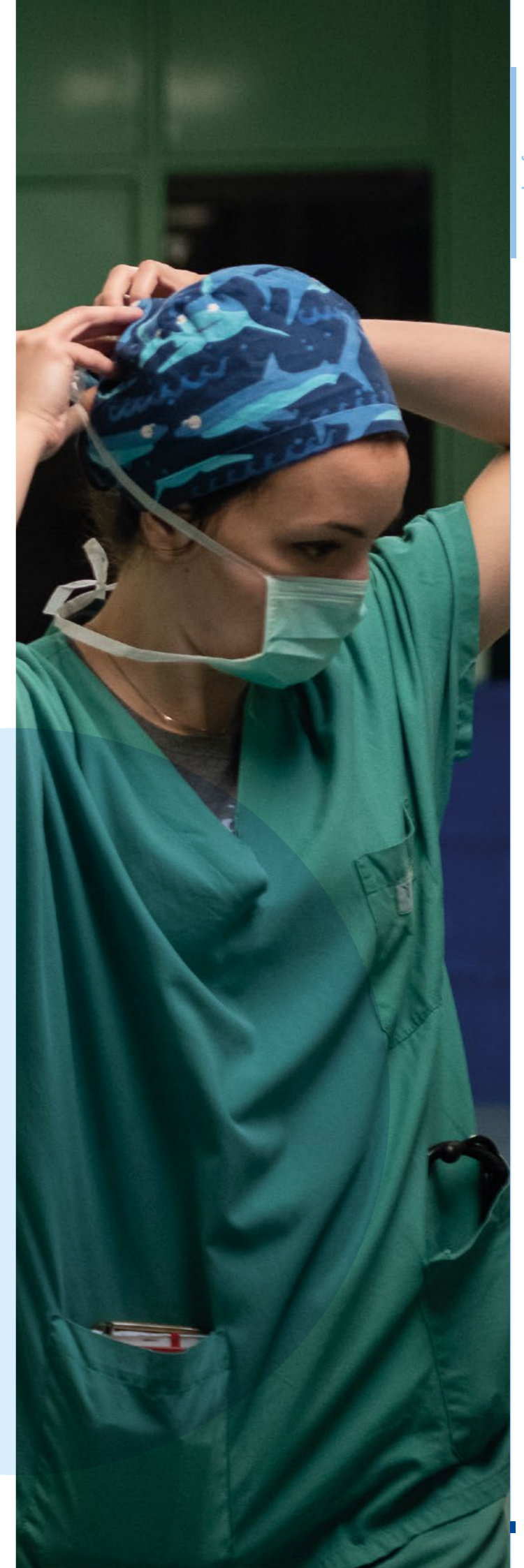
Ethics of scientific research activities

Solidarity

People's safety and health

Protection of the environment

Confidentiality



Clinical ethics

“What is the right thing to do in this situation?”

The ethical question posed in the introduction to the Trento Document (see “Clinical Ethics Consulting in Italy. Features and Prospects”, Padua: Piccin; 2016) is unavoidable for all those involved in the care relationship, from the patient to the healthcare professional (doctor or nurse), and from the parent to the healthcare institution itself. The more critical and complex the circumstances, the more urgent the question becomes; but the greatest difficulty arises when decisions must be made for someone who cannot decide for themselves, as in the case of pediatric patients. For this reason, clinical ethics cannot be considered as optional; it is rather an integral part of the decision-making process that guides the patient’s clinical pathway.

Bambino Gesù Children’s Hospital answers this complex ethical question by supporting healthcare professionals who are faced with complex decisions that go beyond the Hippocratic ethics taught in university classrooms and their own values, and which often seem insurmountable.

In 2024, requests for consultation increased, involving dedicated staff on a biweekly basis, and increasingly involving the Clinical Ethics Committee, which was convened on an extraordinary basis to discuss specific cases. Compared to previous years, the statistical increase in requests for consultation by the Hospital’s Complex and Simple Operating Units has made it possible to focus clearly on recurring ethical dilemmas. For example, some of the main issues on which it was deemed necessary to set up study and analysis groups are:

- unequal treatment in similar clinical situations due to differences in parental preferences
- standard of care as an ethical criterion
- ethical criteria for the withdrawal of life-sustaining devices
- allocation of resources.

Upon completion of this work, guidelines and protocols will be drawn up and scientific articles will be published to support not only all healthcare professionals but the entire Hospital as well. For several years now, the Hospital has been evaluating new procedures from an ethical perspective, in addition to individual cases.

One example is the Protocol “Obstetric-gynecological clinical care pathway for patients with cystic fibrosis”, which is the result of the collaboration between the Bioethics Function and the Pulmonology and Cystic Fibrosis Unit, and the Fetal and Perinatal Medicine and Surgery Unit.

In 2024, the Hospital promoted an event in the field of Medical Humanities entitled “Spirituality in the grieving process in the Jewish and Christian communities”, with the participation of the Chief Rabbi of Rome, Dr. Di Segni; it also provided annual training in bioethics at the Pediatric Palliative Care Center in Passoscuro. Ad hoc training modules were also provided, focusing on therapeutic obstinacy in pediatrics, shared care planning, and ethics of pain management.

The Good Practice Project 2024 was promoted at the Pediatric Palliative Care Center in Passoscuro, following up on the bioethics research project launched in 2023 and entitled “The best quality of life in pediatric palliative care: ethical criteria for patients at the end of life and their families in pediatric hospices. From quality of life to quality of life-relationships”. The Good Practice Project has made it possible to recognize the quality of life-relationships as a new ethical criterion in clinical ethics counseling and to integrate clinical bioethicists as essential members in the transdisciplinary team.

What is the advantage of clinical ethics? It makes those involved in the care relationship aware observers of the patient’s condition and quality of life, making their assessment as objective as possible. This gives clinical ethics the merit of conducting appropriately formulated ethical reasoning that is free from prejudice and discrimination regarding the patient’s quality of life and from misconception of their dignity.

Every observer of a patient’s life story, each from their own perspective, is supported in their medical choices and has the opportunity to observe their patient with a fresh perspective, placing them at the center of their ethical reasoning, recognizing them for their uniqueness and irreplaceability, and investigating as accurately as possible what is best for them, in order to reach a thorough ethical judgment. The experience of recent years seems to confirm that the tool of Clinical Ethics can make a decisive contribution to the quality of healthcare.

The Hospital’s stakeholders

The activities of Bambino Gesù Children’s Hospital are grounded in the awareness of the importance of its stakeholders, i.e., all the actors, inside and outside the organization, who have an interest in the Hospital and are actively involved in the wider context of its processes and relationships.

The main groups of stakeholders are:

- Patients and families
- Hospital staff
- Institutions and regulatory bodies
- Universities, scientific institutions and societies
- Local and international communities
- Voluntary associations
- Donors and benefactors
- Suppliers, contractors, consultants, and partners
- Media and social networks.

By reason of this awareness, the Hospital involves its internal and external stakeholders also in the assessment of the material topics. In particular, with regard to 2024, the questionnaire for impact assessment was sent to 26 representatives of voluntary associations that collaborate with the Hospital, as well as to top managers and representatives from all areas of the Hospital.

The purpose of this involvement is to perform a materiality analysis that is more representative and takes into account the expectations, perspectives, and priorities of both internal and external stakeholders.

Patients and families



Hospital staff



Institutions and regulatory bodies



Universities, scientific institutions and societies



Local and international communities



Voluntary associations



Donors and benefactors



Suppliers, contractors, consultants, and partners



Media e social network



Relevant issues

As already mentioned, in 2024 the Hospital updated its materiality analysis to identify the sustainability issues relevant to the Organization and its stakeholders, which are described in this Report.

This analysis is a useful tool for guiding the Organization in identifying and assessing the most significant topics, i.e., the so-called “material topics”, related to the current and potential positive and negative impacts on the economy, the environment, and people, including human rights.

The analysis was carried out in accordance with the principles set out in the GRI *Sustainability Reporting Standards* published and updated in 2021 by the *Global Reporting Initiative*. Based on the provisions of the *Standard*, the identification of material issues included the following steps:

Understanding the context of the organization

Review of the reference context and of the main national and international trends in the healthcare sector, and benchmarking against companies comparable to the Hospital.

Identification of impacts

Based on the analyses described above, the main positive/negative and current/potential impacts attributable to the Hospital's activities were identified.

Assessment of the significance of impacts






Impacts were assessed through a questionnaire administered to Directors, Managers representing all areas of the Hospital, and a cluster of representatives from voluntary associations. Each stakeholder was asked to assign a score from 1 to 5 (1 being the least significant and 5 the most significant value) based on the perceived degree of relevance to the activity carried out in the Hospital. Furthermore, in the case of potential impacts, they were also asked to assess the likelihood of the impact occurring.





Prioritization of impacts and identification of material topics






Based on the outcome of the previous phases, the impacts were prioritized and linked to the material issues on which this Sustainability Report is based.

List of material topics

The result of the above process is detailed in the following list of material topics.

Material topics	Associated impacts	Description of impacts	Type of impact
 Appropriate and highly qualified care	Access to appropriate, high-quality care for all patients	Provision of a qualified care pathway to all patients, even to those with the most complex conditions, through highly specialized staff and innovative technologies	Current
 Patient safety	Patient safety	Promotion of practices, procedures, and staff training activities aimed at ensuring the best care and the safety of patients	Current
 Continuity, transition of care, and management of chronic conditions	Continuity of care for patients with chronic conditions	Ensuring the continuity of an integrated care pathway for patients with chronic conditions by connecting with other hospitals and territorial services	Current
 Research, clinical trials, and translational medicine	Support and contribution to scientific research	Support and contribution to scientific research through the activities of the Hospital and by interacting with research institutions and universities to create innovative solutions and projects	Current
 Technological innovations and digitalization	Improvement of the service provided	Improvement of the quality of work and service provided through the use of appropriate equipment and technological advances; for example, digital tools for remote visits and care	Current

Material topics	Associated impacts	Description of impacts	Type of impact
 Hosting and support for patients and families	Support for patients and families	Support the patients' families by identifying their social needs, such as language mediation, housing needs, or residence permits	Current
	Failure to handle complaints	Reduction in the quality of the service provided to patients due to poor complaint management by the Hospital	Potential
 Training, development, and enhancement of staff	Development of employees' skills	Improvement of workers' skills and development of the company know-how through the provision of training courses for employees	Current
 Transparent communication	Transparent communication towards the community	Transparent communication of the Hospital's activities towards the community through internal and external communication activities	Current
 Well-being at the workplace and inclusion of workers	Employee satisfaction and well-being	Working conditions and hours that ensure a work-life balance with a positive impact on the physical and mental health of employees	Current
	Fair remuneration policies and equal pay	Compliance with wage agreements or employee expectations in terms of fair remuneration policies that guarantee equal pay for men and women	Current
	Episodes of discrimination, harassment, and abuse in the workplace	Work environment that does not respect the diversity of the company's workforce due to episodes of discrimination (related to gender, religion, ethnicity, generation, etc.), harassment, and abuse	Potential

Material topics	Associated impacts	Description of impacts	Type of impact
 Resilient management model	Proper risk management	Proper management and assessment of economic, financial, social, environmental, and health risks to ensure the operational continuity of the Hospital's activities	Current
 Waste management	Waste generation	Environmental impacts related to the production of hazardous and non-hazardous waste and to its inadequate disposal	Current
 Solidarity initiatives	Development of solidarity initiatives for local and international communities	Development of solidarity initiatives aimed at providing local and international communities with highly specialized healthcare services	Current
 Sustainable supply chain management	Positive impacts on the environment and society due to proper supply chain management	Increased environmental and social benefits generated along the supply chain through the adoption of fair and transparent procedures and policies for the selection of suppliers, contractors, and commercial partners that include ESG criteria	Current
 Water management	Water consumption	Negative environmental impact from water withdrawals that may affect water scarcity	Current






Tematiche materiali	Impatti associati	Descrizione degli impatti	Tipologia d'impatto
 Climate change and energy efficiency	Direct and indirect greenhouse gas emissions	Contribution to climate change due to direct and indirect GHG emissions related to the Hospital's activities	Current
	Energy consumption	Negative impact on the environment due to the purchase of energy from non-renewable sources	Current
 Creation of value and economic and financial sustainability	Generation and distribution of economic impacts on local communities and on the territory	Contribution to the development of professional and social opportunities in the territory with consequent direct/indirect economic impacts on local communities and the territory	Current
 Health and safety in the workplace	Accidents in the workplace	Accidents in the workplace, with negative consequences for the health of direct employees or external collaborators	Potential
	Occupational diseases	Increase in cases of occupational diseases among healthcare professionals related to the working environment in which they operate	Potential
 Privacy and data security	Incidents of privacy and cybersecurity breaches	Incidents of privacy and cybersecurity breaches threatening the security of critical infrastructure and leading to the loss of sensitive patient data	Potential
 Ethics and integrity	Violation of the Code of Ethics and episodes of corruption	Unethical behavior in the workplace that may lead to episodes of corruption with negative impacts on people and economic systems	Potential

Table 1. List of material topics 2024.



Hospital events

Every year, the Hospital organizes and participates in numerous events and initiatives to offer valuable life experiences to its patients and raise awareness in the community about the diseases and suffering that children and families face every day.

Bambino Gesù Children's Hospital is received in audience by Pope Francis for the 100th anniversary of the donation of the Hospital to the Holy See

On Saturday, March 16, in the Paul VI Audience Hall, the staff of Bambino Gesù Children's Hospital, patients, and their families were received in audience by the Holy Father. The audience was held on the 100th anniversary of the donation of the Hospital to the Holy See by the Salviati family, who founded it in 1869.



A delegation from the Italian soccer team visits OPBG

On October 9, on the eve of the match between Italy and Belgium, the FIGC President Gabriele Gravina, together with coach Luciano Spalletti, the Head of the delegation Gigi Buffon, and players Riccardo Calafiori, Giacomo Raspadori, and Gianluigi Donnarumma, visited the facility of Piazza Sant'Onofrio, two days after the visit to Coverciano by seven children and teenagers treated at the Hospital.



Visit by the Vatican Secretary of State Cardinal Pietro Parolin

On December 20, the Secretary of State of the Holy See visited the facility of Piazza Sant'Onofrio. Cardinal Parolin stopped at the Chapel where, together with a delegation of doctors, nurses, patients, and families, he presided over a moment of reflection together with the Hospital's religious staff. Furthermore, as is tradition, he extended Christmas greetings to the entire OPBG community.

New season of *Dottori in Corsia*

Rai3 aired the second part of the sixth season of the docuseries on the care pathway of some patients of the Hospital. The first episode was broadcast on Monday, February 19, and followed by five more episodes, also aired on Mondays in the late evening.



Communication and sharing

Media presence

Through its media coverage, the hospital builds and consolidates its position as a national and international center of excellence for clinical care and scientific research, with a particular focus on humanitarian and hosting activities in line with its mission and institutional nature.

In 2024, media focused on various topics concerning the Hospital, including research, particularly CAR-T cell gene therapy for autoimmune diseases and studies on genetically modified skin for patients with epidermolysis bullosa; clinical care, with the dissemination of data on neuropsychiatric emergency, child abuse, seasonal influenza management, and tips for preventing drowning, as well as the surgical activity, with summary data from 30 years of transplantation released during a press conference attended by Reginald Green, and significant activities such as the life-saving "EXIT to ECMO" procedure for a 37-week fetus, and the birth of twins from a mother with "half a heart".

Media discussed the hosting of families and the care of children fleeing from the Middle East conflict. The stories of the Hospital's patients were the focus of the new edition of the docuseries Dottori in Corsia (Doctors on duty) broadcast on Rai3.

Other initiatives that attracted media attention were the chat with astronaut Walter Villadei connected from space during Pope Francis audience with the Hospital community in the Paul VI Audience Hall, in the Vatican. On that occasion, the Pontiff referred to the Hospital's great capacity for care and scientific research.

In detail, the figures for the Press Office activity for 2024 are:

- **18,350** mentions in different media, including **2,800** in newspapers and magazines
- **14,200** mentions on websites and online publications
- almost **1,350** mentions on radio and TV stations, with an average of over **25** reports per week
- approximately **650** interviews with the Hospital staff.

Portal - Social

The portal plays an important role in informing and guiding users, as confirmed by traffic data for 2024, that are in line with those from the previous year:

- visits: **16.8 million**
- users: **9.2 million**
- pages viewed: **20.5 million**
- users from Google Search: **8.4 million**
- social media users: **over 54,000**.

Also, "Pillole di salute" (Health tips), written by doctors on health-related topics, are particularly popular. Over 1,700 pieces of content are constantly updated and revised, representing over 45% of the portal's total traffic.

Social network

Social media activities build loyalty within the Hospital community, engaging families and stakeholders through the sharing of stories and initiatives, and disseminating news and insights on the health of children and teenagers. In synergy with the profiles of Fondazione Bambino Gesù Philanthropic Institution, they strengthen the relationship with donors, making them key players in the Hospital's growth.

Here are the figures for 2024:

- Facebook (official page) - Followers: **245,778** (+3.5% compared to 2023)
- Instagram - Followers: **87,928** (+10% compared to 2023)
- LinkedIn - Followers: **49,808** (+21.5% compared to 2023)
- Twitter - Followers: **16,270** (+0.5% compared to 2023).

Landing Page

The Landing Page is the digital platform dedicated to employees, published on the Hospital intranet, aimed at informing on the initiatives and latest news of interest to those working at OPBG. In 2024, it received **1.7 million views**, with **579 articles published**.

Press Office

18,350

MENTIONS IN DIFFERENT MEDIA, INCLUDING 2,800 IN NEWSPAPERS AND MAGAZINES

14,200

MENTIONS ON WEBSITES AND ONLINE PUBLICATIONS

Almost 1,350

MENTIONS ON RADIO AND TV STATIONS, WITH AN AVERAGE OF OVER 25 REPORTS PER WEEK

Approximately 650

INTERVIEWS WITH THE HOSPITAL STAFF

Landing Page

1.7 million

VIEWS

579

ARTICLES PUBLISHED

Portal

16.8 million

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9.2 million

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USERS FROM GOOGLE SEARCH

Over 54,000

SOCIAL MEDIA USERS

Social Network

245,778

FACEBOOK - FOLLOWER: (+3.5% COMPARED TO 2023)

87,928

INSTAGRAM - FOLLOWER: (+10% COMPARED TO 2023)

49,808

LINKEDIN - FOLLOWER: (+21.5% COMPARED TO 2023)

16,270

TWITTER - FOLLOWER: (+0.5% COMPARED TO 2023)

02

The resilient management model of OPBG



Promote peaceful and inclusive societies for sustainable development, provide access to justice for all and build effective, accountable and inclusive institutions at all levels

The organizational model

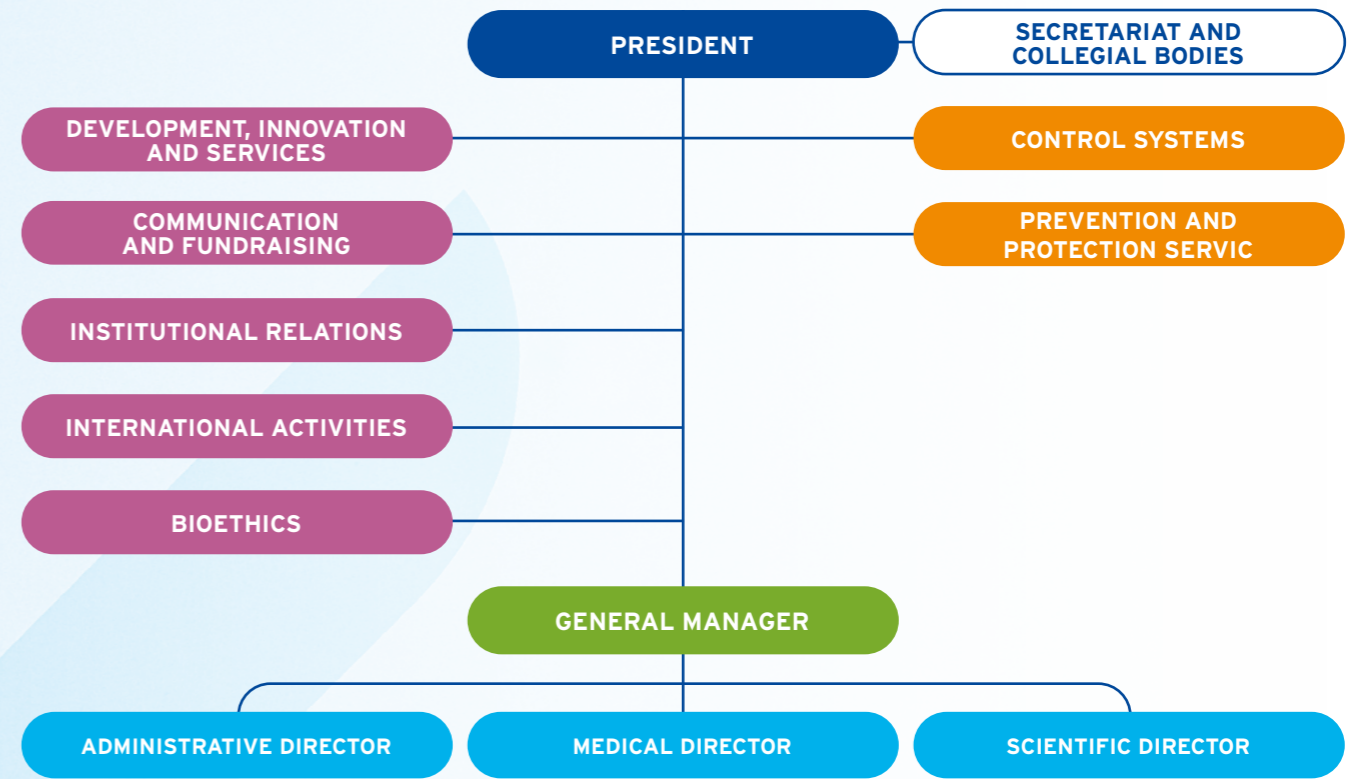
The Hospital's organization ensures the President strategic oversight of all areas, within the framework of an organizational model designed to consolidate - in line with the Hospital's strategic focus defined by the Board of Directors and the President, as well as with its humanitarian and care mission - the achievement of clinical, care, and scientific research objectives within an organic system of integrated sustainability, while ensuring the Hospital's continuity and promoting its excellence through the effective integration of care and training activities with translational research, thus promoting innovation and technology transfer.

Reporting directly to the President are:

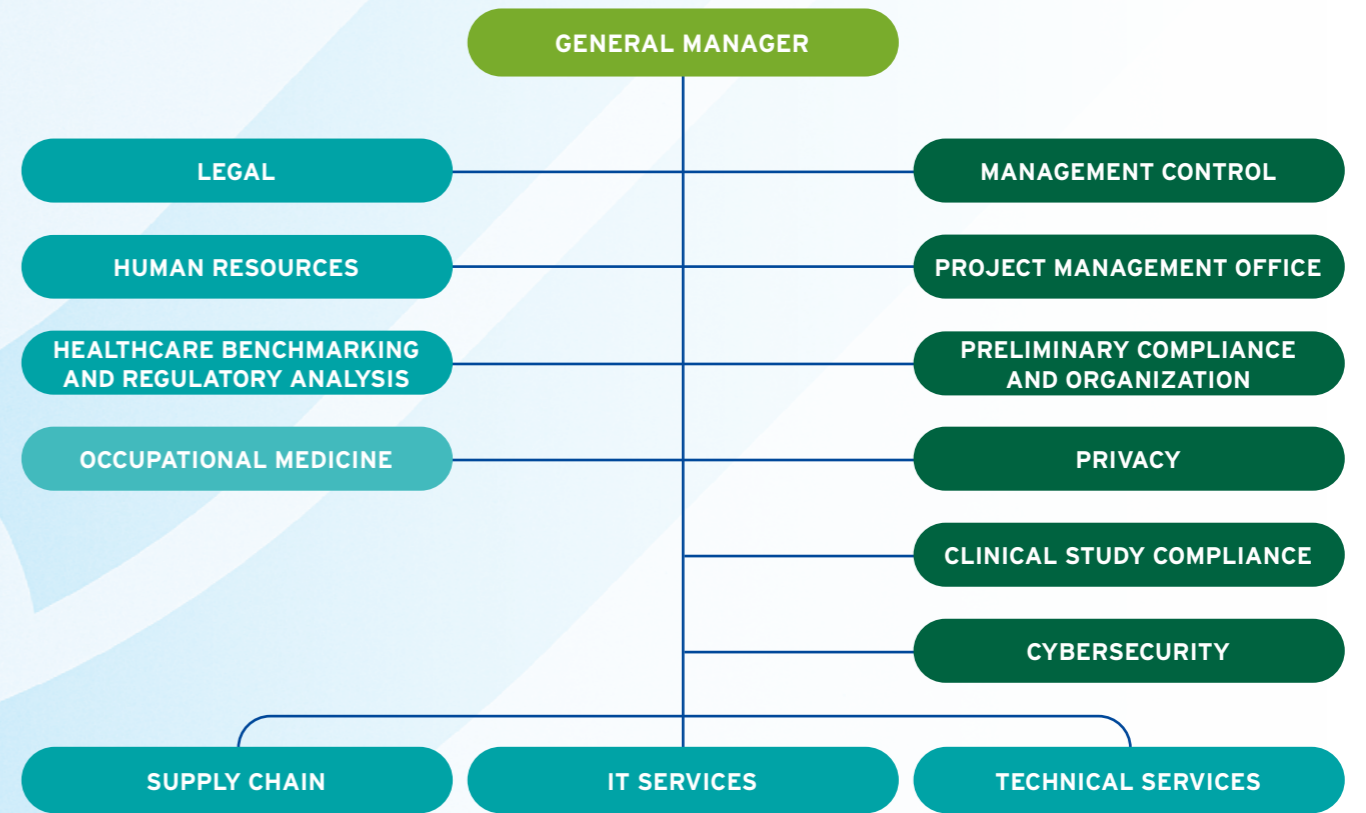
- the General Manager, who ensures - in line with the objectives defined by the President and in constant communication with him - the coordination of the operations management of all areas (administrative, healthcare, and scientific) of the Hospital in the framework an integrated sustainability system
- staff organizational units, in charge of coordinating specific cross-cutting areas, as well as independent organizational units that support the Employer in preventing and protecting against health and safety risks in the workplace, and in monitoring the adequacy of the Hospital's internal control and integrated risk management system.

Reporting directly to the General Manager are:

- the Administrative Director, who oversees the promotion and implementation of administrative objectives that are essential for the effective management of financial and administrative flows and for the drafting of the Financial Statements and the Sustainability Report
- the Medical Director, who oversees the promotion and implementation of clinical and healthcare objectives to ensure the maintenance and development of quality standards of care
- the Scientific Director, who oversees the promotion and implementation of scientific research objectives to ensure the maintenance and development of research quality standards.



Staff organizational units, including supervisory units, also report to the General Manager. These units are responsible for the systematic coordination of the effectiveness and efficiency of the Hospital's operations, of the economic, financial, and asset reporting, of regulatory and labor protection, and of the resulting regulatory and procedural design for operational and functional risk management purposes. A specific organizational unit is responsible for health surveillance with regard to health and safety in the workplace.



Furthermore, more detailed organizational structures report to the Administrative, Medical, and Scientific Directors, as well as to the aforementioned staff organizational units.

The hierarchical organizational structure of the Hospital is integrated with a procedural structure aimed at promoting convergence between clinical practice and translational research, also considering academic activities and monitoring of integrated sustainability.

In this context, the overall organizational model ensures: (i) strategic orientation of the Hospital and strategic oversight by the President in all areas; (ii) sharing of the objectives defined by the President with and among Directors; (iii) collegiality of the top management; (iv) systematic implementation and monitoring by the Directors of ordinary cross-cutting activities; (v) constant dialogue between the General Manager and the President, and systematic involvement of the President in the most significant initiatives.



All of this is supported by technical analyses specific to each function, consistent with the responsibilities assigned and always within a process-based framework.

More specifically, the President defines the strategic objectives of the Hospital in coordination with the Directors. The Directors identify specific actions, ensuring their implementation through direct supervision of their respective areas of competence and collective involvement through the Committee of Directors, which is an internal advisory and operational body, coordinated by the General Manager and responsible for ensuring the systematic implementation and monitor-

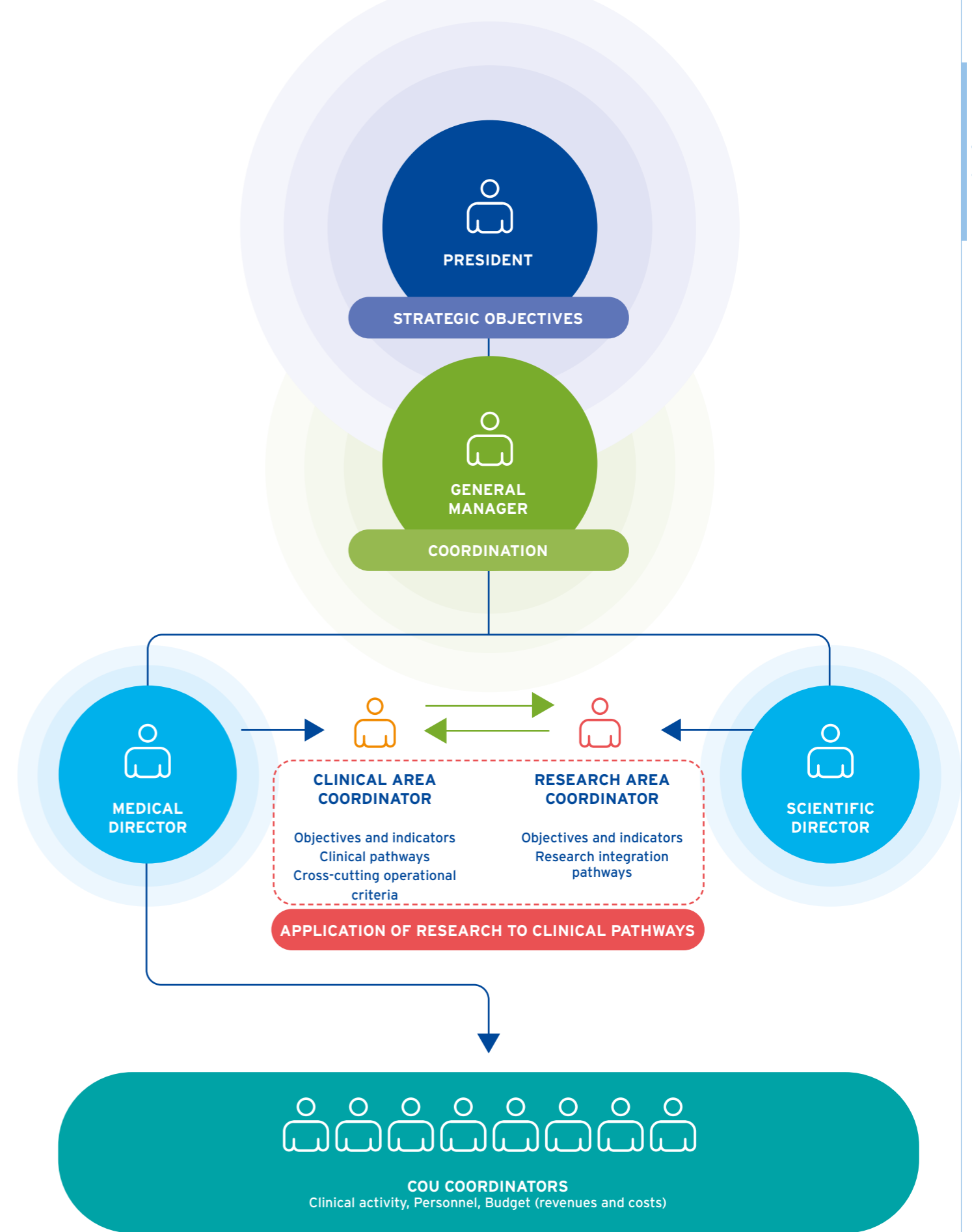
ing of ordinary cross-cutting activities, to guarantee the development of the Hospital's quality standards in terms of care and research within a system of integrated sustainability.

The General Manager maintains constant communication with the President, including on the results of the activities of the Committee of Directors, to ensure the periodic sharing of the operational guidelines adopted and performance monitoring, in an overall framework of coordination with the President such as to guarantee the latter's strategic oversight of all areas of the Hospital.

The most significant initiatives requiring the systematic involvement of the President are also submitted to the Presidential Committee, which is an internal advisory body comprising the President and the Directors, as well as the Coordinators of Functions reporting to the President, who are invited by the latter. All initiatives of strategic importance or not related to the ordinary activities of the Hospital or not falling within the scope of the powers granted by the President are always submitted to the President for approval.

With regard to the more specific aspects of the organizational model for clinical, care and scientific research.

- Reporting directly to the Medical Director are:
 - the Complex Operating Units (COUs, to which the Simple Operating Units - SOUs - belong), which have clinical, management, and budgetary responsibility for their own scope of activity
 - the functional coordinators of the clinical areas to which several Complex Operating Units report for their main clinical pathway activities; this is to promote multidisciplinary, integration, and optimization of cross-cutting clinical pathways. Therefore, these coordinators have no hierarchical responsibility over the Complex Operating Units, but provide specialist clinical expertise to support the Medical Director in identifying objectives and specific projects, ensuring the monitoring of results
 - Complex Operating Units, Simple Operating Units, and other staff organizational units, which are responsible for overseeing cross-functional activities within the scope of the Department.
 - In this context, dedicated coordination is ensured for academic activities and, more generally, for training activities for third parties.
- Reporting directly to the Scientific Director are:
 - the research areas to which the relevant research units belong
 - research areas and/or units and other staff organizational units, which are responsible for overseeing cross-functional activities within the scope of the Department
 - In this context, dedicated monitoring is provided for clinical studies in a functional relationship with the trial centers reporting to the Medical Director, given their clinical value.



Overall, the functional relationship between the coordinators of the research areas and the coordinators of the clinical areas facilitates the application of research to clinical pathways.

The regulatory framework

The Hospital's regulatory model is a systemic framework of internal rules (regulations) that are binding on staff, in the same way as external regulations, and are a key prerequisite for the achievement of its objectives, as they are essential for ensuring legality and transparency in the conduct of activities - in reference to the nature of the Hospital, its institutional purposes, and its values - as well as an essential lever for ensuring the systematic implementation of initiatives with a view to operational efficiency and risk management.

In this context, the overall regulation of the Hospital is defined to ensure: (i) process-based management of activities consistent with the organizational structure and the related responsibilities assigned to Management, with the relevant systemic risk management; (ii) an evolving design approach with a systemic improvement perspective, based on rationalization and simplification; (iii) compliance with the regulations applicable in the Vatican and, therefore, also with the guidelines of the competent Vatican authorities; (iv) effectiveness, efficiency, and transparency of the overall activity carried out in line with the objectives defined and the related management plan adopted. A noteworthy feature of the Hospital's regulatory model is the hierarchy of the regulatory sources themselves,

as this is necessary to ensure the definition of the essential measures to be implemented in the Hospital's procedural actions in accordance with the hierarchy of decision-making sources, while ensuring uniformity of conduct, rationalization, and simplification.

In addition to the Regulations defining the structure and governance of the Hospital as a Scientific Institute for Hospitalization and Care, and the Code of Ethics, primary internal regulatory sources are the strategic regulations formalized by the President or with the involvement of the competent Vatican authorities, including the guidelines and recommendations formulated by them, as well as the technical and management regulations with a cross-cutting impact formalized by the General Manager.

In compliance with the provisions of applicable legislation and the aforementioned regulations, Bambino Gesù Children's Hospital adopts internal technical and management regulations relating to specific areas and formalized by the Director responsible for them, as well as additional regulations containing detailed elements of specific areas of competence which are the responsibility of the Manager(s) in charge.



Operational management criteria and operating organizational model

The Hospital's activities - within the framework of the organizational and regulatory model mentioned above - are implemented according to short - to medium-term objectives.

The Hospital adopts the Budget - economic, ordinary investments, financial, and asset - as a tool to carry out annual planning, measure results, and implement corrective measures.

The Budget is divided into two parts:

- preparation of forecasts of operating costs and revenues by the Coordinators of clinical, scientific and administrative functions
- identification and definition of specific projects aimed at ensuring effectiveness and efficiency in an integrated sustainability system.

The implementation of the projects is monitored periodically.

In this context, the Directors, with the involvement of Management Control and the support of the Project Management Office, identify projects relating to the various dimensions of integrated sustainability (revenues, costs, digital, environment, social), each of which is carried out under the supervision of a Project Manager and with the involvement of the different organizational units for their respective impact profiles.

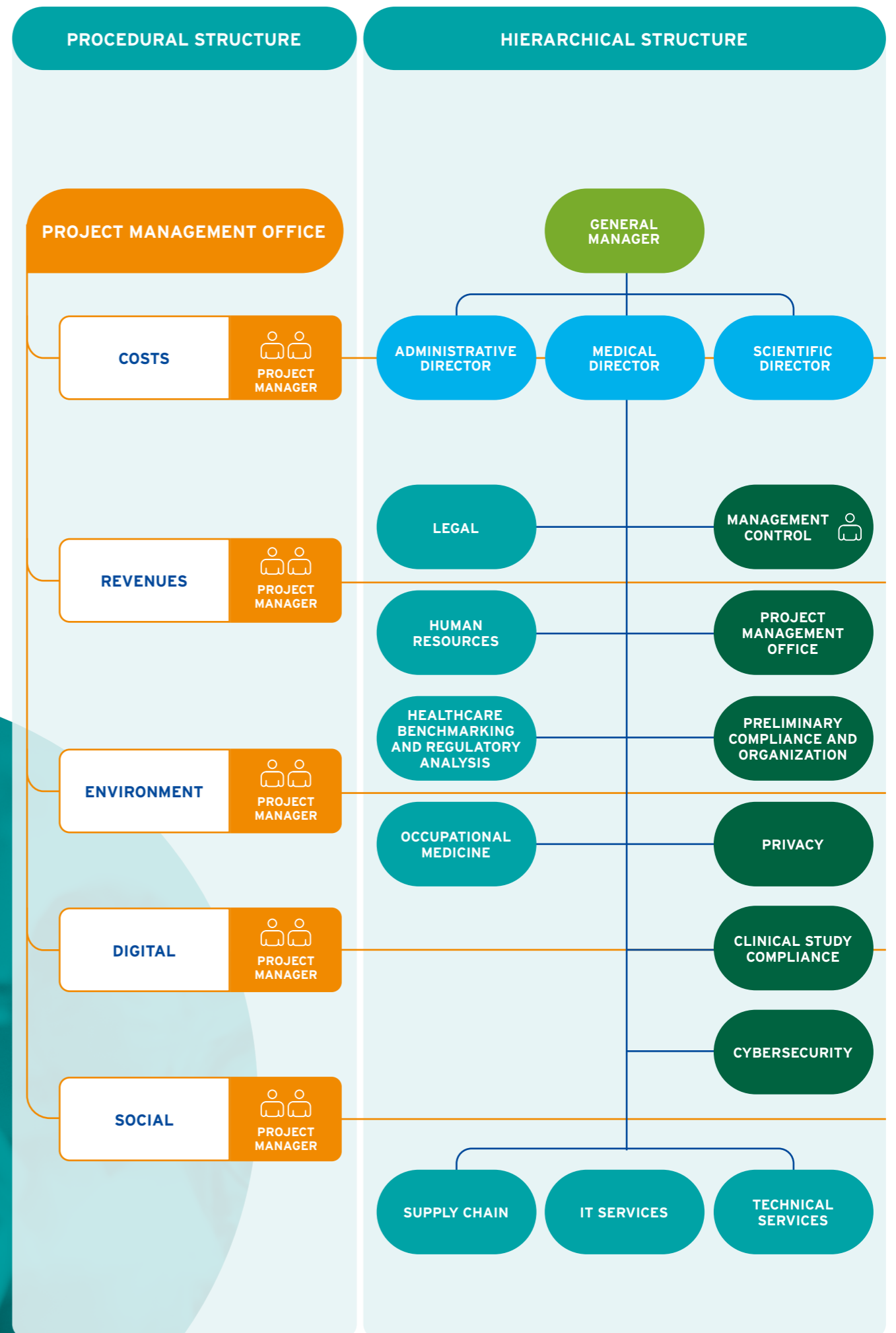
The Management Control Function also validates individual projects from an economic and financial point of view, ensuring overall economic control and reporting; the Project Management Office Function provides project management methodology and analysis support.

Systematic monitoring of relevant cross-functional initiatives is also ensured by the Committee of Directors, including for the implementation of the necessary technical and management actions to guarantee effectiveness and efficiency.

The Administration Department ensures correct accounting. Any initiative of strategic importance or

not included in the Budget is submitted, as already mentioned, for direct evaluation by the President, who constantly communicates with the General Manager regarding major ordinary initiatives.

The results of the financial year are summarized in the annual Financial Statements drafted under the coordination of the General Manager and drawn up in accordance with the directives of the Holy See and in line with the international standards for the public sector (IPSAS) issued by the International Public Sector Accounting Standards Board (IPSASB). The Financial Statements are audited by an independent company which issues its report prior to approval by the Board of Directors.



The Internal Control and Risk Management System (SCIGR)

In order to ensure effective integrated risk management, the Hospital has been implementing an Internal Control and Risk Management System (SCIGR) for several years, involving all levels of the organization to guarantee a coordinated, synergic, cross-cutting, and interdependent contribution from all the organizational structures of the Hospital.

The Hospital SCIGR is based on a three-level control model, within which the corporate bodies, control functions, and line functions have a clear position and perform well-defined roles to achieve effective and efficient risk management, also contributing to the achievement of the company's objectives.

To support the Top Management (President, General Manager) and Senior Management (Medical Director, Scientific Director, Administrative Director) in the monitoring of the Hospital's SCIGR, the following levels of control are established:

- a first level, overseen by operational management, which defines and manages the so-called line controls inherent in operational processes
- a second level, which oversees the risk assessment and control process, ensuring consistency with corporate objectives and meeting organizational segregation criteria to enable effective monitoring. This area is handled by a series of central monitoring and control functions, such as Risk Management, Prevention and Protection Service, Management Control, Project Management Office, Preliminary Investigation and Organization Compliance, Privacy, Clinical Study Compliance, IT Security, and Clinical Risk Certification
- a third level, overseen by Internal Audit, which provides fully independent assessments by verifying the structure and functionality of internal controls.

The interaction between the three levels of control aims to provide the Governance and Control Bodies and Management with an integrated and holistic view of the control and monitoring activities (carried out by the same three levels) and of their effectiveness and efficiency.

In this context, the Control Systems Function has been established, reporting directly to the President, in order to oversee independent control activities in terms of assessing the adequacy of the Hospital's control and integrated risk management system, also ensuring the necessary internal specialist consultancy.

In this context, it is specifically responsible for ensuring:

- the preparation and execution of the annual Audit Plan to be submitted for approval by the President, with related progress monitoring

- the implementation of planned verification projects and ad hoc audit activities requested by the President
- the implementation and management of an integrated risk management system through preventive and proactive measures to assess the main risks to which the Hospital is exposed, reporting the results to the President, including proposals for intervention priorities and response strategies
- preparation of periodic reports to the President, Management, and Corporate Bodies, to whom it provides support for the management of reports in compliance with the Code of Ethics and, more generally, for the relevant verifications.

Internal Audit and Risk Management report directly to this Function. The Internal Audit oversees the assessment of the suitability and the correct implementation of the Internal Control System, also to ensure that resources are acquired economically, used efficiently, and preserved adequately. In this context, it is specifically responsible for:

- the preparation, in accordance with the guidelines received from the Control Systems Function, of the Annual Audit Plan to be submitted, together with the Control Systems Manager, to the President for approval
- the implementation of the planned verification projects and ad hoc audit activities requested by the

- President to the Head of Control Systems according to specific information requirements
- follow-up monitoring of the progress of implementation, by process managers, of the Corrective Action Plans identified during the audit activities carried out
- providing training and specialist consultancy on internal control.

Risk Management oversees the integrated management of risks relating to the Hospital's relevant processes and, in this context, it is specifically responsible for:

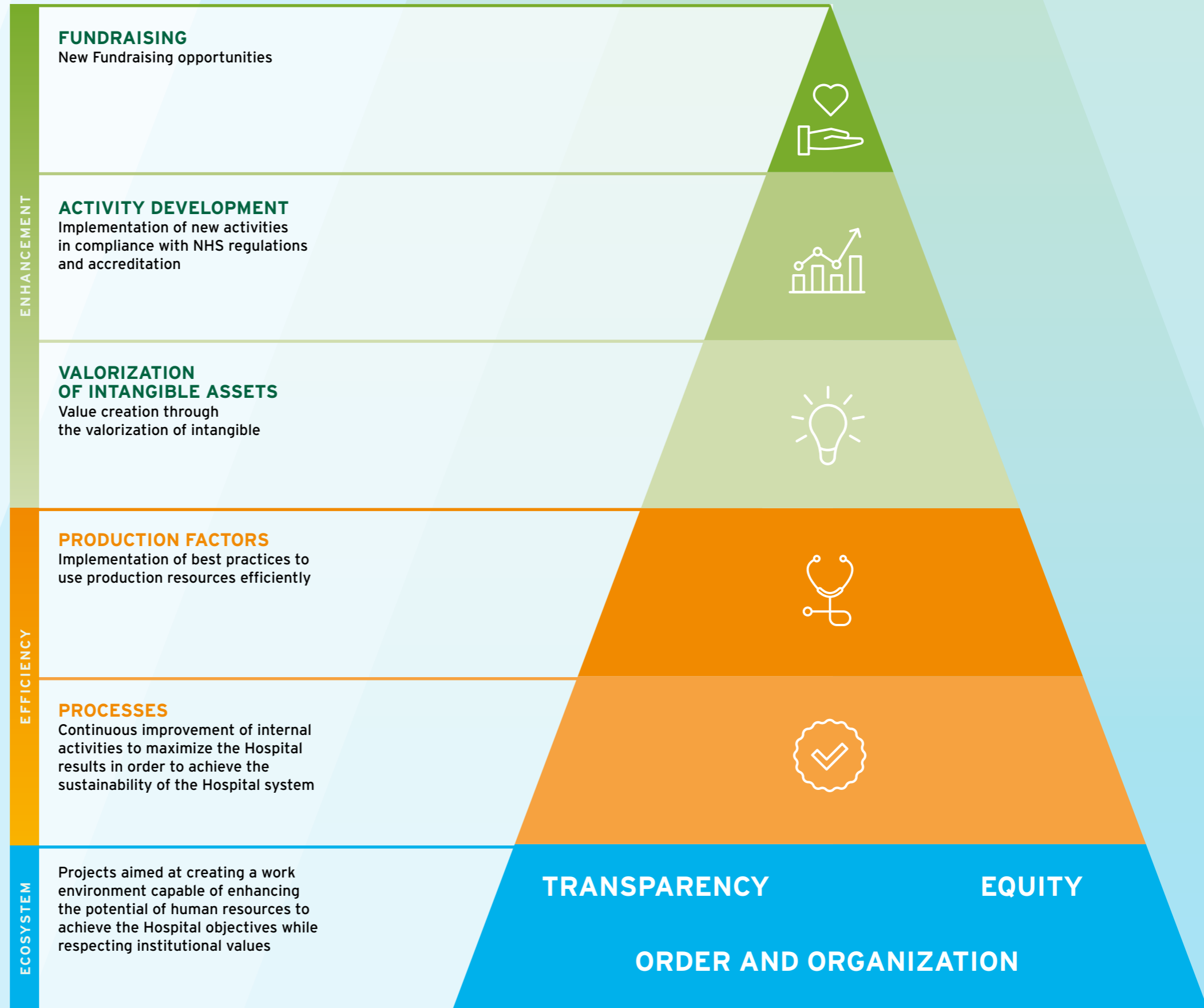
- the development of an Enterprise Risk Management model for all Hospital processes
- the definition of an annual risk assessment plan, in line with the guidelines received from the Control Systems Function
- the identification, analysis, assessment, and monitoring - with the involvement of the managers of the functions concerned - of risks relating to areas potentially detrimental to the Hospital's strategic and sustainability objectives
- the involvement of additional independent control functions and of the functions that oversee process activities to implement the necessary actions related to integrated risk management
- updating the Hospital's risk profile and Risk Register.



The Multi-Year Strategic Plan

In 2024, the Hospital launched a new Multi-Year Strategic Plan based on five lines of action, including specific project clusters.

The lines of action of the Multi-Year Strategic Plan are set out below. Pending the consolidation of the strategic pillars of the Multi-Year Strategic Plan, projects in line with the identified areas of intervention were started and carried out during 2024.



03

The care of children and adolescents

98,598

EMERGENCY ROOM VISITS

3,335

OUTPATIENT SURGERIES

2,845,451

OUTPATIENT SERVICES

18,325

PATIENTS ENROLLED IN THE RARE DISEASES NETWORK

30,409

HOSPITAL ADMISSIONS (including 610 for rehabilitation)

33,777

SURGICAL AND INTERVENTIONAL PROCEDURES

359

ORGAN, CELL, AND TISSUE TRANSPLANTS

20

ERN NETWORKS IN WHICH THE HOSPITAL IS A PARTNER



Ensure healthy lives and promote well-being for all at ages



Promote peaceful and inclusive societies for sustainable development, provide access to justice for all and build effective, accountable and inclusive institutions at all levels

Clinical care activities

In 2024, the total number of ordinary admissions to Bambino Gesù Children's Hospital was 30,409, including 610 for rehabilitation. The table shows the trend in

the main specific indicators of the care and assistance services provided by the Hospital in 2024 compared to 2023 and 2022.

CRUSCOTTO INFORMATIVO				
	2024	2023	2022	
No. of beds	627	627	627	
No. of admissions	30,409	29,815	28,980	
<i>including rehabilitation</i>	610	612	632	
ACUTE CARE HOSPITALIZATIONS	Average load	1.09	1.11	1.11
	Average lenght of stay	6.36	6.43	6.54
REHABILITATION	Average lenght of stay	29.01	28.57	28.10
DAY HOSPITAL AND REHABILITATION DH	Visits	72,049	72,832	69,761
DAY SURGERY	No. of cases	4,443	4,158	4,110
OUTPATIENT SURGERY	No. of cases	3,335	3,421	3,139
EMERGENCY ROOM	Visits	98,598	94,700	95,351
OUTPATIENT CLINIC	No. of services	2,845,451	2,710,400	2,512,689
SURGICAL ACTIVITY	No. of surgical and interventional procedures	33,777	33,090	32,009
TRANSPLANTS	No. of transplants	359	348	338

Table 2. Information dashboard. Years 2022-2024.

Overall, the indicators show a slight increase in ordinary acute admissions (+2% compared to 2023), whose average burden (indicator for the level of care intensity/complexity) did not change significantly compared to the previous year. Medical daily hospitalization remained at the same levels as in 2023 (-1%), while the outpatient activity increased (+5% compared to 2023).

Overall access to the Emergency Department increased compared to 2023 (+4%), including the increase at Palidoro facility (42% of total access rate, compared to 58% of Piazza Sant'Onofrio facility). 84% percent of admissions resulted in discharge, while only 11% of patients were hospitalized. As for the

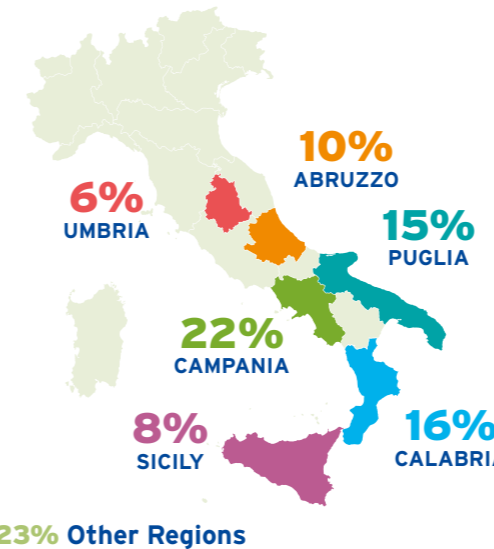
prevalence based on triage color codes, most patients were assigned a "green code - not critical, no risk of deterioration, treatment can be postponed" (61%). In 2024, 155 helicopter rescues were performed, thanks to an agreement with the Governorate of Vatican City State allowing for the use of its heliport.

In terms of the Hospital's capacity to attract patients, in 2024 a significant proportion of ordinary admissions (31% of total admissions) were from regions other than Lazio, mainly Campania, Puglia, and Calabria. The following table provides evidence of the regions of origin, other than Lazio, with the relevant incidence rate.

The complexity of hospitalizations of patients not com-

ing from Lazio region (measured based on DRG-specific relative weight) is on average 26% higher than the total number of hospitalizations, highlighting the considerable capacity of the Hospital to attract patients due to its specialization in numerous diagnostic and therapeutic fields. A similar phenomenon also emerg-

es from the analysis of the number of hospitalizations of patients coming from abroad and not resident in Italy (Table 4 - International mobility. Years 2022-2024), with 792 ordinary admissions in 2024. The complexity of the conditions treated in these patients was 35% higher than that of children coming from Lazio region.

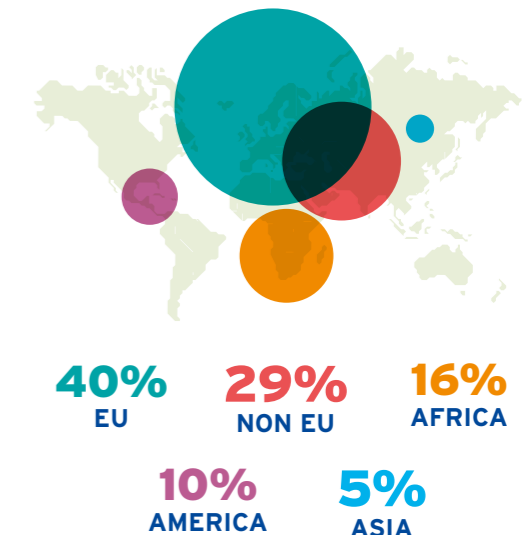


REGION	INTERREGIONAL MOBILITY					
	2024		2023		2022	
	N°	%	N°	%	N°	%
Abruzzo	947	10%	925	10%	919	10%
Campania	2,049	22%	2,063	22%	1,954	22%
Calabria	1,482	16%	1,496	16%	1,314	15%
Sicily	800	8%	854	9%	853	10%
Puglia	1,459	15%	1,567	16%	1,394	16%
Umbria	539	6%	554	6%	463	5%
Other Regions	2,233	23%	2,100	22%	1,963	22%
Total	9,509	100%	9,559	100%	8,860	100%

Table 3. Interregional mobility. Years 2022-2024.

GEOGRAPHICAL AREA	INTERNATIONAL MOBILITY					
	2024		2023		2022	
	N°	%	N°	%	N°	%
Africa	123	16%	110	19%	145	25%
America	77	10%	34	6%	41	7%
Asia	40	5%	65	11%	47	8%
European Union	318	40%	248	43%	230	40%
Non EU	231	29%	118	20%	116	20%
Oceania	3	0%	2	0%	2	0%
Stateless	0	0%	0	0%	2	0%
Total	792	100%	577	100%	583	100%

Table 4. International mobility. Years 2022-2024



OPBG: AN INTERNATIONAL REFERENCE POINT FOR THE MOST ADVANCED CARE

Every year, patients from all over the world are treated in the six OPBG hospital facilities. In 2024, a total of 728 foreign patients not resident in Italy were admitted, coming from 107 countries, including 37 European, 31 African and 24 Asian countries, 1 Oceania country, and 14 American countries.

Highly qualified and appropriate care

Bambino Gesù Children's Hospital, a nationally and internationally recognized center of excellence, is now the largest pediatric teaching hospital and research center in Europe, connected to major international centers in the field, and a point of reference for the health of children and adolescents from all over Italy and abroad.

The Hospital's healthcare services cover all medical specialties. Transplantation, genetic and metabolic diseases, medical and surgical cardiology, neuroscience, onco-hematology, and rehabilitation are among the areas of care and research of excellence.

In particular, OPBG is the only European center capable of meeting all pediatric transplantation needs: heart, heart-lung, bone marrow, cornea, as well as living donor liver and kidney transplants. The 359 transplants performed in 2024 included: kidney (37), liver (26), heart (8), lung (1), bone marrow (198) and tissues transplants (65 homograft, 12 cornea, and 12 amniotic membrane). 14 artificial hearts were implanted. Below are some examples of the excellence that characterizes the clinical care activities of the Hospital.

Rare Diseases

Rare diseases (RD) are a group of conditions that are heterogeneous in terms of their etiopathogenesis, clinical features, and therapeutic and/or rehabilitative approach, requiring a significant clinical commitment both in the diagnostic phase, which is generally long and sometimes associated with uncertain outcomes, and in the management phase. Due to its importance and complexity, the latter must be carried out based on multidisciplinary, multi-professionalism, and constant interaction between the specialized hospital center and local and school health services.

OPBG has a long-standing tradition in the diagnosis and management of patients with suspected or confirmed rare diseases. The availability of the most advanced biochemical and genetic diagnostic techniques, the presence of experts from various pediatric specialties, the possibility for patients to receive all the traditional and experimental therapies used in these conditions, the wide and well-established network of collaborations with local services within the Regional Healthcare System, and the presence of a research center with an area dedicated to RDs, are all factors that underpin its position of excellence at the national and international level.

At European level, the Hospital is fully integrated into the European Reference Networks (ERNs), launched by the European Commission in March 2016, and aimed at promoting collaboration between centers with greater clinical and research experience. In 2017, the Hospital achieved full member status in all 15 ERNs for which it had applied. With the reopening of the application deadline in autumn 2019, the Hospital was recognized as a member of five more ERNs at the end of 2021, for a total number of 20 (Table 5 - ERNs in which OPBG participates). In terms of the number of ERNs in which it participates, the Hospital ranks first among pediatric hospitals in both Italy and Europe.

ERN
ERN BOND European Reference Network on rare Bone Diseases
EpiCARE * European Reference Network on Epilepsies
ERKNet * European Reference Network on Kidney Diseases
ERNICA European Reference Network on Inherited And Congenital Anomalies
ERN-EuroBloodNet European Reference Network on Haematological Diseases
ERN eUROGEN * European Reference Network on Urogenital Diseases and Conditions
EURO-NMD * European Reference Network on Neuromuscular Diseases
ERN-EYE * European Reference Network on Eye Diseases
ERN GENTURIS European Reference Network on Genetic Tumour Risk Syndromes
ERN GUARD-Heart * European Reference Network on Diseases of Heart
ERN-ITHACA * European Reference Network on Congenital Malformations and Rare Intellectual Disability
ERN-LUNG * European Reference Network on Respiratory Diseases
MetabERN * European Reference Network on Hereditary Metabolic Disorders
ERN PaedCan * European Reference Network on Paediatric Cancer (haematology)
ERN RARE-LIVER European Reference Network on Hepatological Diseases
ERN RITA * European Reference Network on Immunodeficiency, Autoinflammatory and Autoimmune Diseases
ERN-RND * European Reference Network on Neurological Diseases
ERN-Skin * European Reference Network on Skin Disorders
ERN TRANSPLANT-CHILD * European Reference Network on Transplantation in children
VASCERN * European Reference Network on multisystemic Vascular Diseases

* riconosciute nel 2017

Table 5. ERNs in which OPBG participates

During the planning phase of the ERNs, particular attention was paid to the periodic evaluation of the results achieved, both by the entire ERN and by each clinical center involved. The two European Commission acts of March 10, 2014, and the executive act of July 26, 2019 (2019/12697 EU) defined the evaluation process, to be carried out every five years, based on information contained in a self-administered questionnaire and, for a randomly selected sample of clinical centers, on a direct visit by a group of experts. The entire assessment process was managed by an independent third party (Independent Evaluation Body-IEB). In 2023, the 15 ERNs recognized in the first phase underwent their first five-year assessment; of these, two ERNs (EURO-NMD and ERN RITA) also underwent an on-site visit. As already described in the 2023 Sustainability Report, all 15 ERNs assessed in 2023 were evaluated positively, with an overall score of 91% in achieving the 64 "Measurable Elements" of the questionnaire.

In 2024, the ERNs continued their work by drawing up guidelines (Clinical Pathways) and, in some cases, feeding Disease Registries. Of note was the presentation of complex clinical cases on the Clinical Patients Management System (CPMS) platform, with version 2.0 released in December 2024.

Intensive care

OPBG has 5 Intensive Care Units, one of which is dedicated to cardiac surgery patients and one to newborns with both medical and post-surgical conditions, for a total of 62 beds. Four wards are located at Piazza Sant'Onofrio facility and one at Palidoro facility. With Regional Council Resolution No. 869 of 12/7/2023 (Hospital network planning for 2024-2026 in accordance with the standards set out in Ministerial Decree 70/2015), the Hospital's role as a reference center within the regional medical and surgical emergency network, both pediatric and neonatal, was confirmed. OPBG is the only hub for cardiac surgery, while it shares with Policlinico Gemelli and Policlinico Umberto I the function of hub for Pediatric Intensive Care; the role of hub for Pediatric Surgery with San Camillo-Forlanini Hospital, and the function of Highly Specialized Trauma Center (CTS) in the Pediatric Severe Trauma Network with Policlinico Gemelli. Regarding the Perinatal Network, which consists of 11 level II facilities and 18 level I facilities, the Hospital performs level II function mainly for newborns requiring post-surgical neonatal intensive care and for those coming from other regions.

Neonatal Transport Service

Proper and adequate care for pregnant women and their baby must be aimed at providing expectant mothers with the birth facility that best meets the level of care required, ensuring the transport of newborns in cases where unforeseen risks or true emergencies require their transfer to facilities with the adequate medical and/or surgical expertise. OPBG is

an integral part of the Neonatal Emergency Transport Service (STEN), which is organically integrated into the Regional Emergency Health Service (ARES 118). The Transport Coordination Center, headed by ARES 118, uses the OPTIN (Bed Occupancy in Neonatal Intensive Care Centers) IT system, which allows transport to be managed based on real-time knowledge of the beds available in the region.

The STEN Managers are responsible for: (i) maintaining operational relations with the Hospital and Specialist Network Area of the Regional Health and Social Integration Directorate of Lazio Region and with the birth centers; (ii) managing the Information System; (iii) identifying service performance indicators; (iv) developing diagnostic and care guidelines; (v) ensuring the adequacy of means of transport; (vi) managing the theoretical and practical training and refresher courses for the staff.

The Service ensures the assisted transfer of sick newborns or infants up to two months of age, weighing 5.5 kg or less, from all hospitals and clinics in Lazio Region to the centers equipped with neonatal intensive care and sub-intensive care operating units. The 309 transports carried out by OPBG in 2024 accounted approximately for 32% of all transports performed by the regional STEN of Lazio region.

The pediatric transplant center

Procurement activities

In the case of pediatric patients, the possibility of organ donation involves delicate approach to the families of deceased patients, based on professionalism and empathy. In the case of minors, the decision to consent to organ donation requires the unanimous consent of both parents, who are facing the traumatic and dramatic experience of losing a child. Procurement is organized according to a multidisciplinary and interfunctional model involving various Operating Units, such as Cardiac Surgery, Hepato-Biliary-Pancreatic and Liver and Kidney Transplantation Surgery, Ophthalmology, Gastroenterology and Nutrition, Nephrology, Oncohematology, Cell Therapy, Gene Therapy, and Hematopoietic Transplantation Clinical Area. The organizational model provides for systematic monitoring of cases of brain injury in intensive care units and close links with regional facilities.

Transplantation activity

Transplantation activity is one of the Hospital's strengths as a center, the only one in Europe, capable of performing all types of pediatric transplants, from cells to tissues, to all solid organs: kidney (from cadaveric and living donors), liver (from cadaveric and living donors), heart, lung, and heart-lung. The Hos-

pital has been performing pediatric heart and heart-lung transplants since 1986, kidney transplants since 1993; and liver transplants since 2008. The living donor transplant program has been active since 1996 for kidneys and since 2011 for liver.

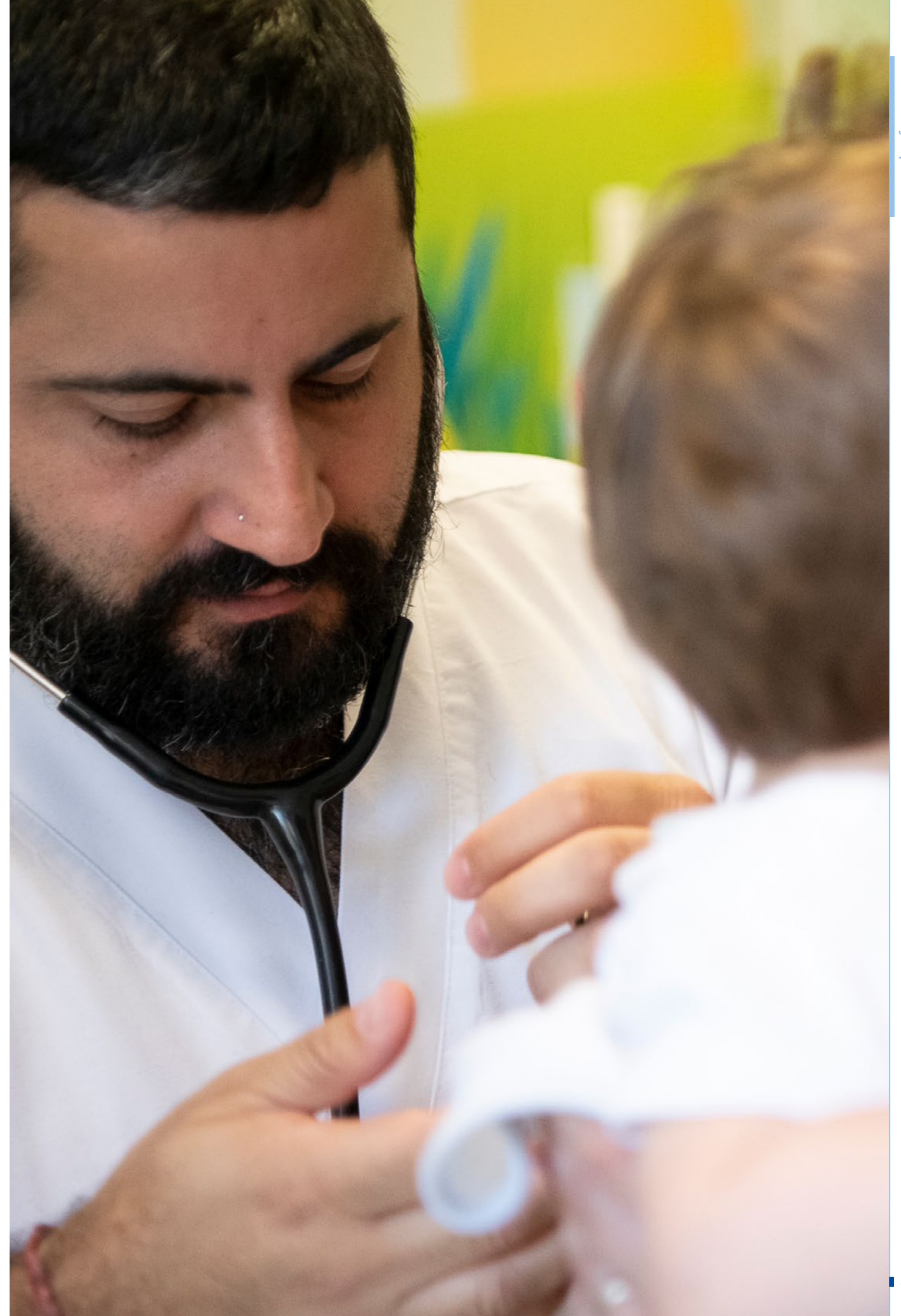
The Regional Poison Control Center

The OPBG Poison Control Center has been recognized by Lazio Region as a Reference Center, together with the centers of Policlinico Umberto I and Gemelli (Decree of the Commissioner Ad Acta No. 00073 of 09/29/2010). In its capacity to respond to urgent/emergency situations, the OPBG Poison Control Center is part of the Regional Emergency Network. As the only Pediatric Poison Control Center in Italy, its Clinical Toxicology activity is carried out exclusively for patients under the age of 18, both through telemedicine consultations and the direct management of intoxicated patients transferred from other facilities.

Care of pediatric patients with HIV/AIDS and STDs (sexually transmitted diseases)

Bambino Gesù Children's Hospital has been identified as a regional reference center for HIV infection and the prescription/dispensing of antiretroviral drugs (Decree of the Commissioner Ad Acta of Lazio Region U00030 of 01/30/2018). The services provided include diagnostic assessment, treatment, family counseling, and follow-up, and are delivered in various settings (Day Hospital, Outpatient Clinic, and telemedicine) for better management and follow-up of the clinical case. The Hospital manages children and adolescents with HIV infection acquired at birth or later, as well as individuals exposed at birth as they were born from HIV-positive women but were not infected with HIV. Foreign patients from highly endemic areas are also managed for infectious disease assessment and identification of resistant variants and alternative treatment options. The services provided are based on the best options available to manage the clinical case and its follow-up (Day Hospital, Outpatient Clinic, and telemedicine).

Upon reaching adulthood, the pediatric population with HIV infection managed over the years is referred to local adult care facilities (in recent years, over 80 patients have been referred). The Center also provides second opinion services to other hospitals, both in and outside Lazio region, on the management of antiretroviral therapy in newborns, children, and adolescents. On average, each year one/two new cases of HIV infection are diagnosed in children, despite the current prevention measures. The Unit participates in clinical studies and trials on new drugs; two trials on the use of new antiretroviral drugs are ongoing.



Patient safety

The Hospital has been implementing the Program for the Continuous Improvement of the Quality of Care for years, which is updated annually under the coordination of the Medical Director, involving the other Directorates and Functions, as well as relevant clinical and care areas.

The multidisciplinary Health Committees participate in the implementation of the Program in their respective areas of competence, for uniform risk assessment.

Each year, the Program identifies priority areas in the processes to be measured and in the improvement activities to be implemented, also analyzing the results achieved during the previous year. It then selects specific indicators grouped by specialty area, with analytical evidence of the rationale, the related objective to be achieved during the year, and the relevant reference. The indicators collected, validated, analyzed, and disseminated within the Program are derived from routine data sources (e.g. hospital discharge records, electronic health records, and the computerized incident reporting system) or from ad hoc surveys, such as annual surveys on the prevalence of healthcare-associated infections and antibiotic use.

The continuous improvement of the quality of care is further guaranteed by a comprehensive Health Risk Management Program, as well as by the Hospital's institutional and voluntary Accreditation and Certification pathways.



Clinical risk management

In 2024, the Health Risk Committee (CRS) was established at OPBG as an internal advisory and operational committee reporting directly to the Medical Director, with the aim of supporting them in the assessment and integrated management of health risks and, in this context, monitoring the full implementation of the Annual Health Risk Plan (PARS). The CRS acquires, on a quarterly basis, the results of the activities of the individual interdisciplinary committees within the Health Department: data collection and analysis, as well as identification of corrective actions, also with systemic proposals. The CRS then periodically reviews the results of its assessments with the Accident Assessment Committee and the Risk Management Service, sharing information to achieve comprehensive health risk management.

Within this framework of healthcare risk management, the CRS monitors data from reports of avoided and sentinel adverse events, complaints, related analyses by the interdisciplinary committees and the Accident Assessment Committee. The CRS assessment is reported every six months by the Medical Director to the Committee of Directors and the Presidential Committee. Specific activities of analysis of data on the safety of care and a proactive approach to risk reduction are coordinated by the Clinical Risk Committee. Established in 2016, the CRC is a multidisciplinary and multi-professional group chaired by the Medical Director, also including a representative of patient and family associations, which analyses data on the safety of care and implements a proactive approach to risk reduction. The CRC shares data from various sources on health risks, including the analysis of deaths and consultations with the Legal Medicine Department for events that could potentially be classified as sentinel events, with subsequent investigations by the Legal Function. The Clinical Risk Committee also carries out multidisciplinary and multi-professional activities for the prevention and control of Legionella.

A weekly report is drawn up containing reports, proposals for further investigation, and root cause analyses. Every month, reports and improvement actions are shared at CRC meetings. A proactive risk analysis (Failure Mode Effect Analysis - FMEA) is carried out on an annual basis. Regarding the reporting of adverse and avoided events, 928 reports were submitted in 2024, 855 of which were reports of adverse events and 73 of avoided events. The reporting rate was 4.20 reports per 1,000 hospital days (compared to a rate of 3.9 events/1,000 in 2023, 3.8 events/1,000 in 2022, 4.6 events/1,000 in 2021, and 4.5/1,000 in

2020). Most of the events consisted of falls (16%), followed by medications (14%) and laboratory diagnostics (12%). In 2024, 565 investigations were carried out into adverse and avoided events, covering 60% of total reports, compared to 21.5% in 2023. The 565 investigations conducted resulted in 585 improvement actions aimed at reducing the risk of recurrence. In 2024, nine Root Cause Analyses (RCA) were conducted, and a proactive risk analysis was carried out using the FMEA method, which concerned the transport of patients from the Emergency and Admission Department (DEA) to the Diagnostic Imaging Department.

Accreditation and certification programs

The accreditation and certification of healthcare facilities are tools used to assess the quality of care, based on the systematic verification of facilities against shared and explicit standards, carried out by the National Health Service (institutional accreditation) or by independent bodies (voluntary accreditation and certification).

For over 20 years, OPBG has undertaken various excellence accreditation programs (*Joint Commission International - JCI*; *Joint Accreditation Committee Isct Ebmt - JACIE*; *European Federation for Immunogenetics - EFI*) and certifications of excellence (ISO Quality Management System), coordinated by the Health Department and integrated with each other to promote the quality and safety of care. During 2024, activities continued for institutional accreditation, JCI accreditation, ISO Quality System certification according to UNI EN ISO 9001:2015 standard, JACIE accreditation for the Transplant Program, EFI (European Federation for Immunogenetics) accreditation for hematopoietic stem cell transplants and solid organ transplants, and AIFA certification of the Phase I Units established at OPBG.

Joint Commission is the largest and most experienced healthcare accreditation body in the world. To date, through a voluntary accreditation process, more than 20,000 healthcare organizations and programs have been accredited by JCI in over 80 countries. In Sep-

tember 2024, JCI carried out the accreditation visit, taking place every three years, which ended positively with OPBG confirmed as an “Academic Medical Center” until 2027. The four members of the JCI international team assessed the Hospital against a total of approximately 300 standards and 1,250 measurable elements, confirming OPBG efforts to ensure the quality and safety of care. The Hospital obtained its first JCI accreditation in 2006, which was confirmed every three years in 2009 and 2012; in 2015, OPBG obtained the JCI certification as an “Academic Medical Center” for the first time, for its activity in the field of medical training and clinical research, thanks to its collaboration with the University of Tor Vergata, whose School of Pediatrics is located at OPBG. Following the JCI accreditation visit in 2021, which confirmed OPBG as an “Academic Medical Center” for the three-year period 2022-2024, the clinical procedures and protocols containing recommendations for meeting the standards and measurable elements set out in the current version of the Manual for the Accreditation of Academic Hospitals and Medical Centers (version VII) were reviewed and updated in 2023.

In May 2024, the National Transplant Center assessed the compliance with the technical and organizational requirements of the National FMT Program at the Microbiome Simple Operating Unit at the facility of San Paolo Fuori Le Mura, with very positive outcomes. In October 2024, the EFI Board renewed the certification of the Transplant Immunogenetics Laboratory for hematopoietic stem cell transplants and solid organ transplants. In November 2024, the compliance of OPBG Quality Management System with UNI EN ISO 9001:2015 standards was renewed, successfully passing the last audit of the three-year accreditation period carried out by the International Certification Body DNV on the organizational elements of the certified healthcare, scientific, and administrative areas. In April 2024, the CME-accredited (Continuing Medical Education) training course “ISO Certification: Quality System according to UNI EN ISO 9001:2015 standards” was held for all OPBG professionals, with a significant participation.

Infectious risk control

In 2024, actions to fight infectious risk focused on the prevention and control of healthcare-associated infections and multi-drug resistance through the promotion of standard precautions, primarily hand hygiene, of precautions based on the route of transmission, and of bundles for the prevention of infections associated with invasive procedures such as surgical site infections and central vascular catheter-associated bacteremia, on the monitoring of environmental sanitation, on the control of water systems, on food safety,

and on staff vaccination. Healthcare-associated infection control activities are coordinated by the Healthcare-Associated Infection Control Committee (CCICA), established in 1999. The Committee is chaired by the Medical Director, is made up of various professionals coming from different disciplines and involves family and patient associations. The Committee's objective is to identify and reduce the risks of acquiring and transmitting infections among patients, healthcare professionals, students, volunteers, and all those who visit the Hospital. Each year, the Committee draws up a Plan identifying potential infectious risks and assessing priorities for action based on the probability of each risk occurring, its potential severity, and the possibilities for prevention.

The Committee also carries out specific activities to combat antibiotic resistance, with the aim of promoting the correct use of antibiotics in different care settings. This activity is coordinated by a dedicated group, including pediatric infectious disease specialists, pharmacists, microbiologists, and clinicians from the Health Department with epidemiological expertise.

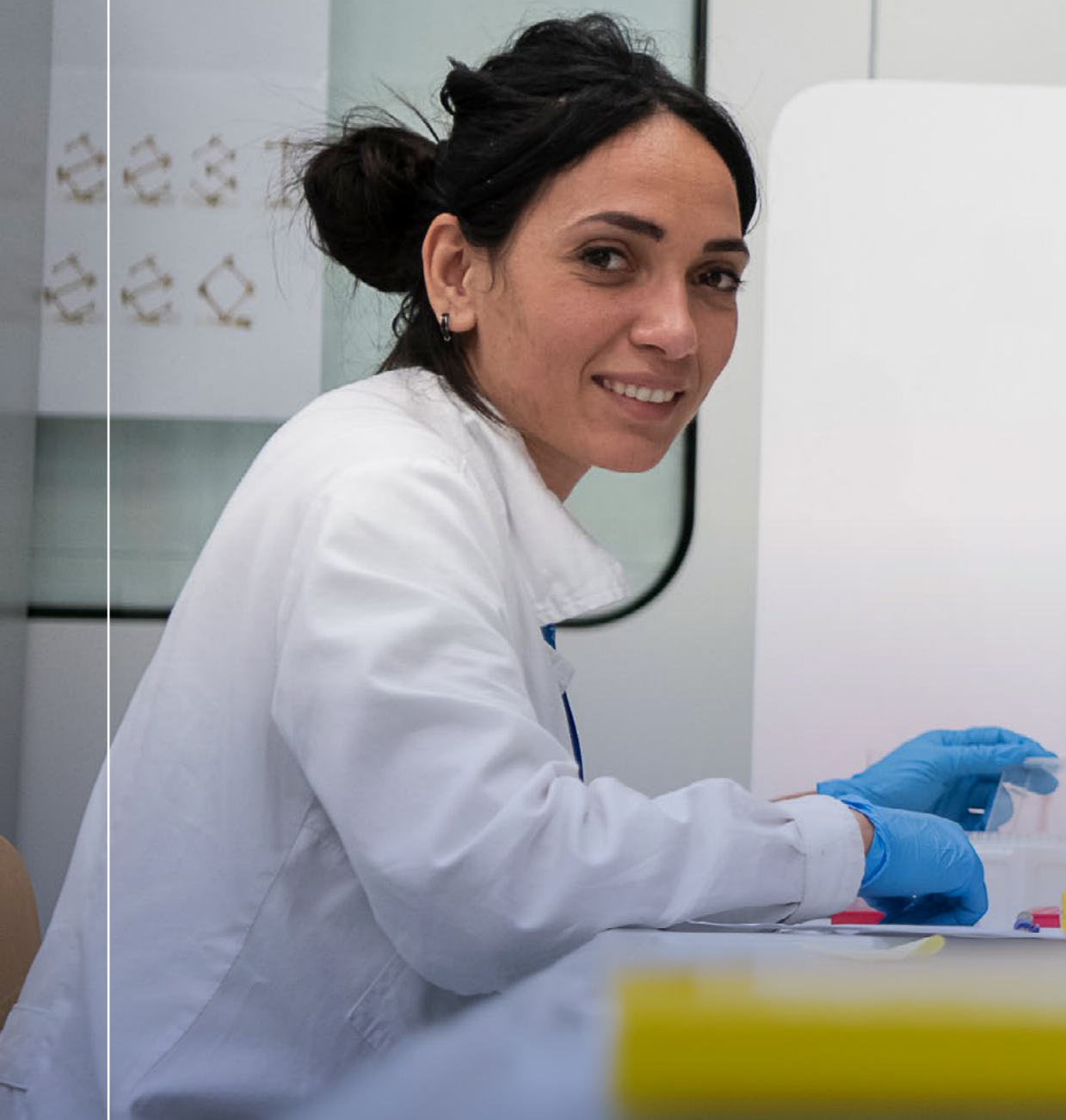
The activities of CCICA are based on current scientific knowledge, guidelines, and applicable laws and regulations, and are integrated with the Program for the Continuous Improvement of the Quality of Care. The documents produced by CCICA (annual plan, quarterly meeting minutes, procedures, and protocols) are published in the Intranet section dedicated to the Committee. Upon hiring, healthcare professionals are trained in infection prevention measures. The same training is provided for third-party staff, volunteers, students, and visitors.

In 2024, staff compliance with hand hygiene was 92%, in line with the results of the previous two years (93% in 2023 and 92% in 2022). The consumption of alcohol-based hand sanitizer was 38 liters/1,000 hospital days, compared to 25 liters/1,000 hospital days in 2023, and the World Health Organization standard of 20 liters/1,000 hospital days. The compliance with contact precautions, actively monitored in cases of infection or colonization by multi-drug-resistant germs, was 100%.

The point prevalence of healthcare-associated infections was 1.7%, compared to 1.8% in 2023 and 2% in 2022, consistently lower than the figures reported for the European pediatric setting (4-6%). (Zingg W et al. *Health-care-associated infections in neonates, children, and adolescents: an analysis of pediatric data from the European Centre for Disease Prevention and Control point-prevalence survey. Lancet; 2017; Point prevalence survey of health care associated infections and antimicrobial use in European acute care hospitals.* Stockholm: ECDC; 2024).



04



Care-oriented research

1,999

PEOPLE ENGAGED IN VARIOUS ROLES IN SCIENTIFIC RESEARCH IN 2023

4,651

CORRECTED IMPACT FACTOR

APPROX. 38,000

GENETIC ANALYSES

550

CLINICAL STUDIES MANAGED INCLUDING 213 FOR-PROFIT CLINICAL STUDIES 337 NON-PROFIT CLINICAL STUDIES

25.9 €/MLN

SCIENTIFIC RESEARCH FUNDING

28

PATENT FAMILIES

1,293

SCIENTIFIC PUBLICATIONS

1,686

NATIONAL AND INTERNATIONAL INSTITUTIONS INVOLVED IN SCIENTIFIC COLLABORATIONS

458

RESEARCH PROJECTS ACTIVE IN 2024



Ensure healthy lives and promote well-being for all at ages



Build resilient infrastructure, promote inclusive and sustainable industrialization and foster innovation

Scientific Research: Vision, Transformation, New Structures



The scientific activity of Bambino Gesù Children's Hospital is a key factor for the promotion, coordination, and enhancement of clinical and experimental research, and a distinctive feature of a Scientific Institute for Research, Hospitalization, and Care (IRCCS).

The goal is to promote the integration of research and care, with a strong focus on innovation, translational research, and continuous improvement of diagnostic and therapeutic pathways for children and adolescents. The organizational structure aims to make research governance more efficient and effective by simplifying structures, further integrating skills, and strengthening technical and administrative support for researchers.

In this perspective, the Research Areas have been reduced from five to four, with the existing Research Units redistributed into the four new Areas according to their specific clinical and scientific characteristics.

At the same time, three new Research Units have been established to meet emerging and strategic clinical and scientific needs. The organizational model also provides for the strengthening of the structures reporting to the Scientific Director that support research, through the establishment of four new Functions that operate in close synergy with the Scientific Department: Grant Office, Research Support, Technology Transfer, and Technology Platforms for Research and Biobank. These are fundamental tools that facilitate access to funding, support planning, promote applied innovation, and leverage the most advanced technological expertise.

The scientific activity, led by the Scientific Director and supported by these and other structures reporting to the Scientific Director, keeps promoting a vision based on collaboration, empowerment, interdisciplinarity, and fair competition as key tools for the growth of the Hospital's human and scientific resources. The definition of strategic guidelines, the independent management of funds by the Units, participation in competitive calls for proposals, and the evaluation of activities by the Technical Scientific Committee are key factors to ensure excellent, sustainable, transparent, and increasingly quality-oriented research.

Scientific research activities

gy, cell biology, and genetics. The laboratories' technological platforms include state-of-the-art instruments that enable researchers to carry out complex and advanced analyses.

The integration of biological sample collection and storage with the use of cutting-edge technological platforms allows for the effective management of data and materials in compliance with the highest international standards. The monitoring of these processes ensures the quality, traceability, and valorization of samples, thus facilitating collaboration with the national and international scientific community. This is a key element for the development of translational research and for the transfer of scientific discoveries to clinical practice.

The equipment in the research laboratories allows for complex analyses in the field of molecular, cell, and genetic biology, and is part of an integrated research model that spans over 5,000 square meters across multiple facilities. This model promotes continuous dialogue between research and clinical practice, improving the understanding of pediatric diseases, the identification of new diagnostic and therapeutic approaches, and the Hospital's ability to respond to the challenges of personalized medicine.

Bambino Gesù Children's Hospital has an advanced technological infrastructure that makes a fundamental contribution to scientific, clinical, and translational research.

The Biobank takes care of the collection, storage, and distribution of biological material and ensures the quality and traceability of samples, promoting collaboration between the Hospital and the international scientific community. It is a key element in translational research, supporting innovative studies aimed at turning scientific discoveries into concrete clinical applications. To this end, it coordinates the activities carried out in the laboratories and by the Management Committee, while planning and supervising initiatives in support of the Technical Scientific Committee (CTS). This crucial role allows the Biobank not only to consolidate itself as a strategic resource for the entire scientific community, but also to contribute significantly to the Hospital's research activities. Alongside the Biobank, the Hospital's Research Center is equipped with cutting-edge technological instruments, dedicated to in-depth investigations in the fields of molecular biolo-

Alongside the technological infrastructure, the Scientific Department avails itself of strategic support for research activities, focused on obtaining and managing national and international funding. The main objective is to promote and optimize access to competitive funds, providing researchers with the tools and expertise to develop innovative projects in the field of pediatrics. This support includes constant monitoring of funding opportunities, help in designing research proposals, and handling the administrative issues related to calls for proposals. The team supports the drafting of funding applications, reviews documentation, and carries out close monitoring and project management to ensure optimal management of project activities and compliance with the rules established by funding programs.

A fundamental role is played by the promotion of training and consulting through workshops and meetings dedicated to improving researchers' skills in project writing and management. Thanks to this approach, the Grant Office contributes to the growth of scientific

research at the Hospital, fostering collaboration with national and international institutions and promoting an increasingly innovative and competitive research environment.

Great attention is paid to the protection of intellectual property to enhance and promote the results of scientific research, transforming them into concrete applications to improve the health and well-being of patients. This is achieved through the protection of intellectual property, patent management, and collaboration with industrial, academic, and institutional partners. This process includes the identification of opportunities for development and support throughout the technology transfer process.

To support all the activities described above, the tools promoting efficiency, quality, and innovation have been strengthened, including monitoring of scientific production, support in the publication of articles and in the assessment of the impact of research, to ensure compliance with guidelines and continuous improvement of processes. Computerized tools were also developed to facilitate the management of contracts and training, including internships and doctorates, and to support the drafting of scientific and institutional documents, including the Sustainability Report and reports for partners and accreditation bodies.

Finally, scientific collaboration with universities and research institutions has been promoted, maintaining long-term relationships with the Ministry of Health and confirming commitment to share research results through events and dissemination initiatives.

Medical Library

The Medical Library of Bambino Gesù Children's Hospital, specialized in biomedical sciences, plays a strategic role in ensuring access to up-to-date scientific literature and in promoting a culture of research. It serves all the Hospital professionals, from doctors to researchers and university students, offering constant support for bibliographic consultation and bibliometric analysis.

Besides ensuring the preservation and updating of its collections, the Library provides access to the main bibliographic, bibliometric, and evidence-based medicine databases and facilitates the sharing of scientific articles through the NILDE (*Network InterLibrary Document Exchange*) and DocLine (*National Library of Medicine - USA*) circuits, even for material not available in Italian libraries.

Users have access to a continuously updated collection, both in paper and electronic format, which includes specialist journals, books, databases, and bibliography managers. The Library actively promotes the dissemination of high-quality scientific literature, guid-

ing researchers in the selection of journals in which to publish and in the retrieval of bibliometric indicators.

Equipment 2024

- > 7,000 electronic journals
- Numerous biomedical databases (including EBM databases)
- Bibliography managers
- Article sharing services with NILDE and DocLine.

The Library is part of the national BiblioSan network, which connects the libraries of Italian biomedical research institutions, allowing for the continuous sharing of scientific and management resources. In 2024, despite the wide availability of open access resources, the overall exchange of articles increased compared to the previous year.

Documentary activity in 2024

- 803 articles shared, of which:
 - 518 requested by internal users
 - 285 requested by other institutions.

As the Library was moved to new premises, the reading room was closed for eight months (February-September 2024), resulting in a significant drop in visits, which had historically been very high due to the need for space dedicated to study. However, during the four months it was open, attendance was in line with the figures for the previous years.

Reading room visits

- 2024: 854 visits in 83 days
- 2023: 2,456 visits in 240 days.

The Library organized two CME courses - "Scientific publishing: news, risks, and opportunities" and "Making the best use of bibliographic databases" - which were attended by 65 professionals. In-person seminars on specific resources (e.g. the *Uptodate* database) and thematic meetings were also offered, such as the presentation of the book "On publishing in medicine" (Il Pensiero Scientifico, 2024). The webinar organized by the BiblioSan network entitled "Reconciling open science with personal data protection" attracted great interest.

Among the most significant activities in 2024 was the qualified assistance provided by the Library staff in combating predatory journals - which send invitations to publish to many healthcare professionals and researchers - and in selecting reliable scientific journals. Support was also provided to identify the bibliometric indicators required for access to research calls, both for individual researchers and groups. Collaboration with the Research Support Function remained constant and fruitful, particularly regarding the annual reporting of scientific output to the Ministry of Health.

Scientific output

In 2024, OPBG researchers published a total of 1,293 articles, with a raw Impact Factor (rIF) of 6,915 points (Figure 2 - *Impact Factor and Total Publications. Period: 2017-2024*). Compared to 2023, there was an increase in the Impact Factor (IF), in line with the upward trend recorded since 2017. The extraordinary increase in both the number of publications and the IF recorded in 2021 and 2022 was presumably due to the SARS-CoV-2 pandemic, which allowed researchers to devote more time to data processing and writing.

Figure 3 - *Impact Factor and Publications recognized by the Ministry of Health. Period 2017-2024*. shows the trend in publications recognized by the Ministry of Health as eligible in relation to the Hospital's Area of Recognition (Pediatrics), which in 2024 accounted for 71% of total publications.

Even in this share of publications, i.e. 919, the IF corrected according to the criteria defined by the Ministry of Health grew compared to 2023, maintaining the upward trend from 2017 to date.

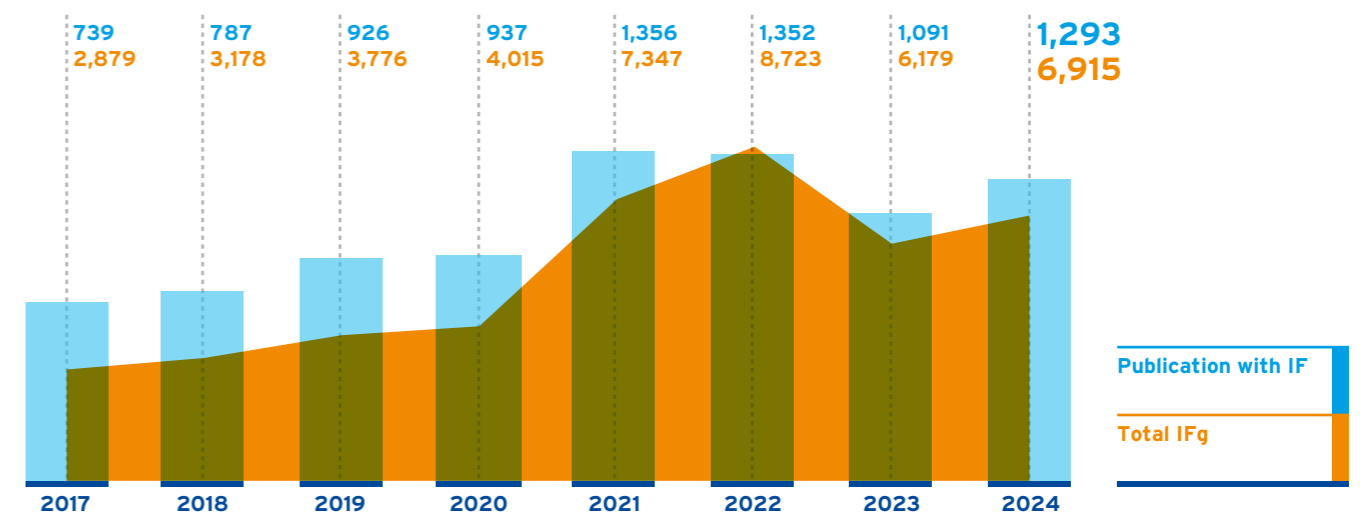


Figure 2. Impact Factor and Total Publications. Period: 2017-2024.

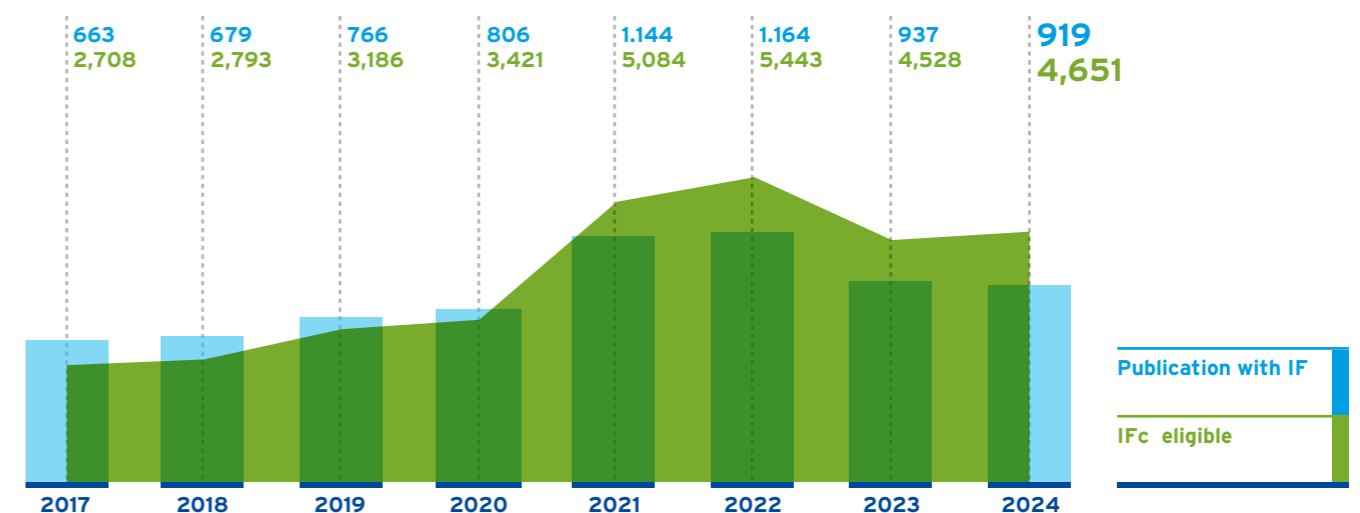
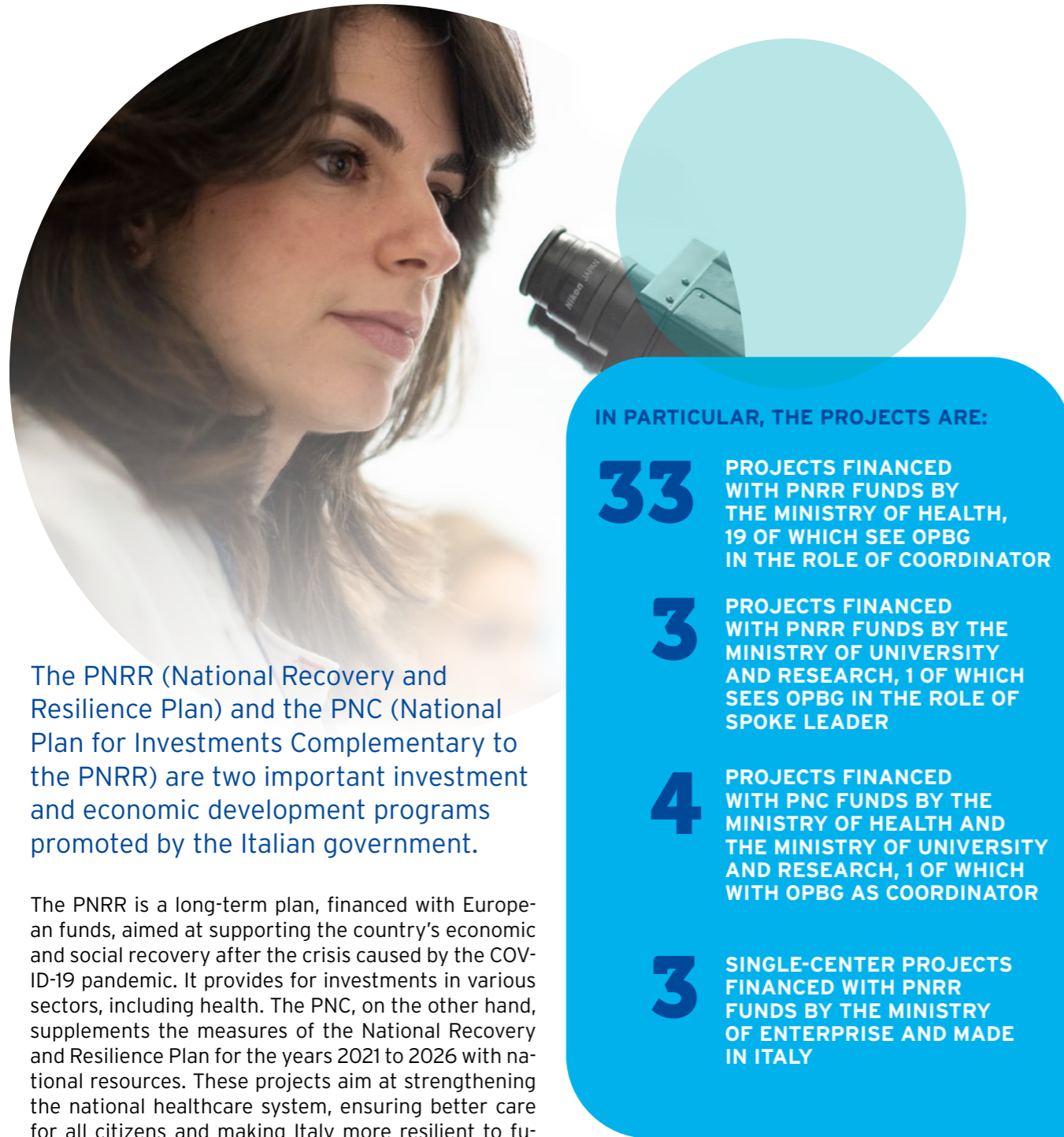


Figure 3. Impact Factor and Publications recognized by the Ministry of Health. Period 2017-2024.

National Recovery and Resilience Plan (PNRR) and National Plan for Complementary Investments (PNC)



The PNRR (National Recovery and Resilience Plan) and the PNC (National Plan for Investments Complementary to the PNRR) are two important investment and economic development programs promoted by the Italian government.

The PNRR is a long-term plan, financed with European funds, aimed at supporting the country's economic and social recovery after the crisis caused by the COVID-19 pandemic. It provides for investments in various sectors, including health. The PNC, on the other hand, supplements the measures of the National Recovery and Resilience Plan for the years 2021 to 2026 with national resources. These projects aim at strengthening the national healthcare system, ensuring better care for all citizens and making Italy more resilient to future challenges in the field of health.

In 2024, the Hospital launched 23 new projects financed by the Ministry of Health with PNRR funds, bringing to 43 the total number of projects underway in 2024 financed with PNRR and PNC funds, for a total funding value for OPBG of over 40 million euros.

IN PARTICULAR, THE PROJECTS ARE:

33 PROJECTS FINANCED WITH PNRR FUNDS BY THE MINISTRY OF HEALTH, 19 OF WHICH SEE OPBG IN THE ROLE OF COORDINATOR

3 PROJECTS FINANCED WITH PNRR FUNDS BY THE MINISTRY OF UNIVERSITY AND RESEARCH, 1 OF WHICH SEES OPBG IN THE ROLE OF SPOKE LEADER

4 PROJECTS FINANCED WITH PNC FUNDS BY THE MINISTRY OF HEALTH AND THE MINISTRY OF UNIVERSITY AND RESEARCH, 1 OF WHICH WITH OPBG AS COORDINATOR

3 SINGLE-CENTER PROJECTS FINANCED WITH PNRR FUNDS BY THE MINISTRY OF ENTERPRISE AND MADE IN ITALY

The projects, of which Table 6 - *PNRR projects underway in 2024* provides a complete list, are dedicated to Biomedical Research, Innovation Ecosystems, Rare Cancers, Rare Diseases, Innovative Technologies and Pathways in Healthcare and Care, and Programs for the Valorization of Patents or Patent Applications.

MINISTRY	TYPE	TITLE
Ministry of Health	PNRR	Impact of postbiotic administration on the immune-reconstitution and clinical outcome of bone marrow transplantation: a double-blind randomized interventional study
		SAPERRE. SARcomas in PEdiatric age, a molecular REgistry and network
		TAHyTi (Thresholds Allergen HYpoallergenic Therapeutic): Prospective evaluation of reactivity Thresholds for Allergens and HYpoallergenic food for potential Therapeutic applications
		I-HOPE PROJECT: Investigating Heart multi-Omics might influence Prognosis, Endpoints and survival in youngs.
		Preclinical validation of p53-reactivation peptides as a novel immunotherapeutic treatment in solid cancer
		Discovery of new anti-cancer immunomodulators to make high-risk neuroblastoma patients responsive to immunotherapy approaches
		Epitranscriptomic landscape and onco-transcriptomic/proteomic signature in cancer patients for better classification and therapeutic approaches
		Novel approaches for characterization and therapeutic targeting of T-cell acute lymphoblastic leukemia (TALL)
		The identification of microbial prognostic markers in Tuberous Sclerosis Complex-related Autism Spectrum Disorder
		COMBING REDox metabolism, oxidative proteomic and imaging techniques for the identification of Diagnostic markers and novel therapies against hypertrophic CARDiomyopathy (COREDICA)
		Nectin-1 as a new specific diagnostic and therapeutic marker for polymorphonuclear myeloid-derived suppressor cells (PMN-MDSC)
		EUCARDIS: Empowering mUltidimensional diagnostics and molecular prognostication of primary CARDiomyopathies and heart rhythm disorderS
		Emerging electrocardiographic, echocardiographic, biomarkers and genetic predictors of life-threatening arrhythmias in adult and paediatric patients with non-ischemic cardiomyopathy
		Optimizing noninvasive assessMent Of DYSmEtabolic compensated advanced Liver disease by integration of artificial intelligence model and omicS data (MODELS)
		Improving Cancer Immunotherapy responsiveness by inducing Tertiary Lymphoid structures via the activation of innate lymphocytes (ICI-TeL)
		Circulating miRNAs as innovative non-invasive biomarkers of pediatric intestinal failure-associated liver disease (IFALD)
		Validating the fibrosis-limiting activity of PF-03084014 (nirogaestat) and valproic acid in skin fibrotic disorders: towards novel therapeutic strategies to counteract fibrosis onset and progression in adult and paediatric patients
		Uncovering the Hidden Genetics Causes of Kidney Disease: A Whole Genome Sequencing Study. The ORIENTING Study
		New therapeutics targets with clinical intervention for both paediatric and adult Brain cancer
		A Collaborative Network for Advancing Research on Rare Tumors in Neurofibromatosis Type 1 and RASopathies (NET-RareT)
Development of an integrated tool based on genetic, epigenetic and clinical analysis to optimize the diagnosis, prognosis and treatment of myotonic dystrophies (GEPINDM)		
Home ultra-long-term EEG monitoring for rare epilepsies and developmental and epileptic encephalopathies. An open-label nonpharmacological interventional prospective study by means of minimally invasive wearable EEG device		
Digital diagnoSis of cardiac sOUNd in peDiatric patients [DI-SOUND study]		

Table 6. PNRR projects underway in 2024.

Research, Clinical Studies, and Translational Medicine

Scientific collaboration networks

The Hospital's scientific collaborations are an essential element of scientific research at an IRCCS. These collaborations consist in the participation in the Italian IRCCS Thematic Networks established by the Ministry of Health to promote scientific and technological research and training in specific fields, as well as in national and international networks made up of institutions of excellence both in the medical field and in other sectors aimed at enhancing results and improving knowledge.

The networks in which the Hospital actively participates are:

- IRCCS Thematic Networks, established by the Ministry of Health to promote scientific and technological research and training in specific areas:
 - Alliance Against Cancer - ACC
 - Association for the Study of Cardiovascular Diseases - Cardiology Network
 - Musculoskeletal Network - RAMS
 - Neuroscience and Neurorehabilitation Network - RIN
 - Italian Network for Health in the Developmental Age - IDEA

- Italian Advanced Translational Research Infrastructure* (IATRIS), Italian node of EATRIS - *European Advanced Translational Research Infrastructure in Medicine*, a network of institutions of excellence aimed at providing specific and complementary contributions in the field of translational medicine
- Biobanking and Biomolecular Resources Research Infrastructure of Italy* (BBMRI), part of the pan-European BBMRI-ERIC network
- NETVAL, Network for the Valorization of Research, whose activity is aimed at enhancing the results of scientific research
- Italian Network for Paediatric Clinical Trials* - INCiP-iT, the hub for Italy, which promotes the planning and conduct of all types of clinical trials carried out in Italy in the pediatric population
- PerfeTTO - *Life Science TTO Network* - an Italian network made up of the technology transfer centers of institutions of excellence, including Scientific Institutes for Research and Care (IRCCS), universities, and research institutions, promoting the enhancement of research and developing innovative solutions in the Life Sciences sector through the creation of services, tools, and resources instrumental to the technology transfer process
- EPTRI - *European Paediatric Translational Research Infrastructure*, a new research infrastructure aimed

- at increasing knowledge on child development and ontogenesis, as well as their impact on the effects and toxicity of drugs, and at implementing and providing services on basic, preclinical, and translational pediatric research
- European Reference Networks* (ERNs) for Rare Diseases.

In addition to the scientific collaborations established through the networks listed above, the national and international scientific collaboration network, made up of research institutions, universities, industries, and other institutions, is also crucial for the implementation of joint research projects whose results are documented through scientific publications. The numbers shown in the table below represent the affiliations of researchers who collaborated to the Hospital's scientific publications in the three-year period 2022-2024. The data were extracted from the InCites Clarivate © database in May 2025.

Clinical Studies

The Hospital places particular importance on clinical studies as a vehicle for consolidating research with a view to its functionality in clinical practice. To this end, the Hospital carries out clinical studies promoted and implemented both individually and in collaboration with its partners. As with all cross-cutting processes, the overall preliminary and administrative activities are performed within a structured organizational and procedural framework coordinated by the two Clinical Study Centers, which were established on November 1, 2024, reporting directly to the Scientific Director, and working in close collaboration with the trial centers assigned to the Health Department, given their clinical significance.

The Clinical Studies Compliance Function, also reporting to the General Manager, provides independent support to the Hospital's Ethics Committee and independent monitoring of the technical and administrative implementation of clinical studies. All of this is carried out in accordance with a plan that provides for a systematic multidisciplinary analysis approach, involving the technical functions in relation to the underlying risks and, therefore, collective assessment. The above is also functional to the complete presentation of Clinical Studies to the competent Ethics Committee, which performs the significant independent role of overall ethical, scientific, and methodological assessment. The clinical and scientific implementation is coordinated by the PIs with the support of the Trial Centers, for the relevant aspects, in compliance with the provisions of the applicable legislation and specific internal and contractual regulations.

In 2024, the Hospital carried out approximately 550 Clinical Studies including:

- 213 for-profit studies, 178 of which were pharmacological interventional; 2 were non-pharmacological interventional; 6 were clinical investigations on de-

- vices and 27 were observational studies
- 337 non-profit studies, 47 of which were pharmacological interventional, 23 were non-pharmacological interventional, 7 were clinical investigations on devices; 256 were observational and 4 were on healthcare professionals (not patients).

This area includes clinical trials on the use of drugs, vaccines, and devices, as well as oncohematology clinical trials.

Oncohematology Clinical Studies and Cell Therapies

The clinical studies in this field are coordinated and carried out, respectively, by the Center for Clinical Studies in Oncohematology and Cellular Therapies and the Complex Operating Unit of Oncohematology, Hematopoietic Transplantation, Cellular Therapies and Trials, to evaluate the efficacy and tolerability of new therapeutic options, particularly in the field of immunotherapy, cell and gene therapy, in children and young adults with hematological conditions that are refractory to conventional therapies. Clinical trials in this specialized field require the integrated work of the clinical staff and of the Oncohematology Trial Center, and encourages the involvement of a significant network of academic and industrial collaborators and the implementation of new products - new drugs, new treatments, and their stratification - that have been clinically tested, thus ensuring real benefits for patients and improving overall prognosis.

Specifically, the Trial Center also conducts Phase I trials in pediatrics, as it is a Phase I Unit accredited according to AIFA Resolution No. 809 of June 19, 2015. The CTQT (Clinical Trial Quality Team), based on the requirements set out in the document "Minimum requirements for participation in the AIFA project for the quality of non-industrial (non-profit) trials", with particular reference to Phase I studies, mainly aims to promote and ensure adequate quality standards for non-industrial trials, such as the principles of Good Clinical Practice (GCP) and Good Clinical Laboratory Practice (GCLP).

During 2024, over 157 single-center and multi-center clinical trials were conducted (66 for-profit clinical trials: 60 interventional pharmacological trials and 6 observational trials; 91 non-profit clinical trials: 35 interventional pharmacological trials, 4 interventional non-pharmacological trials, and 52 observational trials). For approximately 45% of clinical trials, the Hospital acted as a coordinating center at the national and international level. 58% of clinical trials were non-profit, largely of academic origin, while the remaining 42% were for-profit, thanks to fruitful partnerships with international pharmaceutical companies. 37% were observational studies and 63% were interventional studies, both pharmacological and non-pharmacological.

The total number of pediatric patients and young adults enrolled for the first time in a study protocol in 2024 was approximately 570 (105 of whom in in-

SCIENTIFIC COLLABORATIONS						
TYPE OF BODY	2024		2023		2022	
	N°	%	N°	%	N°	%
Research centers	552	33%	160	10%	158	10%
Hospitals	820	49%	526	34%	549	34%
Third sector	161	10%	742	48%	55	3%
Universities	100	6%	52	3%	774	48%
Other	53	3%	82	5%	91	6%
Total	1,686	100%	1,562	100%	1,627	100%
National	228	14%	227	15%	231	14%
International	1,458	86%	1,335	85%	1,396	86%

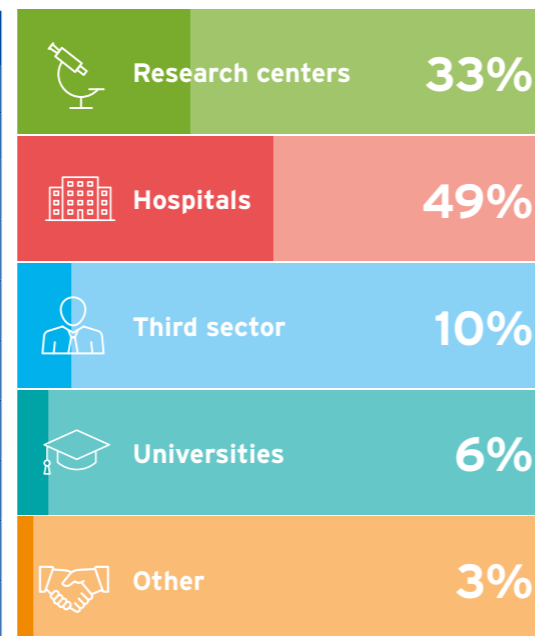


Table 7. Scientific collaborations 2022-2024.

terventional pharmacological trials), including interventional and observational clinical studies (including disease registries and biological sampling studies). In particular, in 2024, a total of 23 clinical studies on ATMPs (Advanced Therapy Medicinal Products) were carried out, including 4 newly activated studies, in compliance with Good Clinical Practice and Good Manufacturing Practice standards, with the following fields of application:

- pediatric subjects and young adults with hemoglobinopathies
- pediatric subjects and young adults with highly refractory leukemia and lymphoma
- pediatric patients and young adults with neuroblastoma and other highly refractory solid tumors
- pediatric patients with infectious complications following hematopoietic stem cell transplantation
- pediatric patients with metabolic diseases (adrenoleukodystrophy affecting the central nervous system).

In 2024, the number of hospital admissions of participants in these projects was 194 in the context of for-profit studies and 100 in the context of non-profit studies. Overall, approximately 33 patients were enrolled in these ATMP projects in 2024, benefiting from innovative, high-quality treatments.

Clinical studies carried out at the Center for Clinical Studies on Pediatric Drug Development and at the Trials COU

These clinical studies are coordinated and conducted by the Center for Clinical Studies on Pediatric Drug Development and the Trials Complex Operating Unit (Trials COU) and are aimed at developing drugs, vaccines, and medical devices for pediatric use in non-onco-hematological settings.

Specifically, the Trials COU is also responsible for Phase I trials in pediatrics, as it is a Phase I Unit accredited according to AIFA Resolution No. 809 of June 19, 2015. Phase I studies, in which experimental therapies are evaluated for the first time in the pediatric population, are becoming increasingly numerous and fundamental for the treatment of rare diseases with onset in this age group. The center, one of the few in Italy organized as provided for in the Resolution, with its specialized staff and multidisciplinary approach, receives many proposals for Phase I studies.

Numerous studies have been conducted, leading to the approval of innovative medicines that have radically changed the evolution of the diseases studied. Among the most innovative experimental therapies are gene therapy, genetically modified organisms, antisense oligonucleotides and mRNA for the production of proteins that are lacking in genetic deficiency diseases. The Clinical Trials Quality Team (CTQT) Unit meets the requirements set out by AIFA in its Resolution No. 809 of June 19, 2015, for Phase I studies and in the document "Project for the quality of non-industrial trials" (revision of 2010). It provides support for all clinical

studies falling within its scope of competence in compliance with the Hospital Quality System, applicable clinical trial regulations (national and international), and Good Clinical Practice (GCP) standards, with the aim of ensuring quality in the conduct of non-profit clinical studies.

2024 Activities

- 143 studies (130 interventional pharmacological studies and 13 clinical investigations)
- 72 new patients enrolled in clinical trials.

The Pharmaceutical Workshop

The Pharmaceutical Workshop (OF - Officina Farmaceutica) - which, on November 1, 2024, was integrated into the new Development, Innovation, and Services Function reporting to the President - is dedicated to the generation of cell and gene therapy products falling within the category of advanced therapies (ATMP - Advanced Therapy Medical Products) in compliance with Good Manufacturing Practice (GMP) standards.

In the field of Cell Therapy, the OF is authorized by the Italian Medicines Agency (AIFA) to produce drugs based on antiviral T lymphocytes and mesenchymal stem cells. In the field of gene therapy, the OF is authorized by AIFA to produce genetically engineered CAR-T cells directed against various tumor antigens, both in clinical trials and for non-repetitive use (hospital exemption). The OF also develops and validates new production processes and analytical methods to expand treatment options with the use of ATMPs.

Results achieved

In 2024, the OF achieved the following results supporting the OPBG Oncohematology, Hematopoietic Transplantation, Cell Therapies, and Trials Units, as well as the OPBG Tumor Gene Therapy Research Unit, in collaboration with other regional and national hospitals.

- Extension of the phase III clinical trial using selected allogeneic T cells specific for viral antigens (CMV, EBV, AdV) for the treatment of patients with viral infections developing after hematopoietic stem cell transplantation (HSCT)
- Clinical production for the Phase I clinical trial authorized for the use of CAR-T cells directed against GD2 antigen in patients with central nervous system tumors
- Completion of production for Phase I, within the Phase I/II clinical trial for the use of CAR-T cells directed against CD7 antigen in patients with T-cell acute lymphoblastic leukemia
- Clinical production for Phase I/II clinical trial authorized for the use of allogeneic CAR-T cells targeting CD19 antigen in patients with B-cell acute lymphoblastic leukemia
- Production for Phase I/II clinical trial for the use of CAR-T cells directed against CD19 antigen in patients with autoimmune diseases (collaboration between OPBG and Policlinico Fondazione Gemelli)
- Validation of the gene therapy process using autol-

ogous hematopoietic stem cells (HSCs), genetically modified with a lentiviral vector for the expression of the functional beta-globin gene, for the treatment of beta-thalassemia (collaboration between OPBG and Associazione Telethon/S. Raffaele Hospital/Tiget)

- Contribution to scientific activities in the clinical application of Advanced Therapy Medicinal Products

- Contribution to regulatory activities in the clinical application of Advanced Therapy Medicinal Products (obtaining EMA PRIME Designation aimed at providing regulatory and scientific support to academic hospitals developing medicinal products for advanced therapies with Priority Medical Need, to accelerate the pharmaceutical development process in advanced clinical trial phases).



05

OPBG academic activity

316

RESIDENTS ON AVERAGE
PER MONTH

59

SPECIALIZATIONS IN THE
TRAINING NETWORK WITH
12 AFFILIATED FACILITIES

2

SPECIALIZATIONS IN THE
TRAINING NETWORK WITH
1 IN-HOUSE FACILITY



Ensure inclusive and equitable quality education and promote lifelong learning opportunities for all

OPBG academic activity

Bambino Gesù Children's Hospital promotes training and research, in collaboration with clinical and rehabilitation facilities, through agreements aimed at improving the quality of care in the medical treatment of young patients. The training activities under these agreements cover all the Hospital areas, in terms of clinical activity and healthcare, and in the field of clinical research as well.

The importance of agreements between universities and the Hospital is crucial for improving the quality of healthcare, professional training, and clinical research. These agreements help to integrate care with the most advanced findings of scientific research, thereby improving patient care. From an educational point of view, universities can exploit the Hospital's potential to offer practical training to future doctors, integrating theory and clinical practice. From a training perspective, these collaborations promote the professionalization of clinicians and the transformation of graduates into well-rounded professionals, thanks to the synergy between applied research, training, and clinical practice. Agreements between universities and hospitals are a fundamental pillar for the advancement of healthcare and medical education.



The agreement with University of Rome Tor Vergata

Bambino Gesù Children's Hospital, in collaboration with University of Rome Tor Vergata, offers an integrated system of training courses aimed at promoting and developing the School of Pediatrics. This project combines the teaching tradition of University of Rome Tor Vergata with the clinical and research experience of our Hospital, thus allowing for the training of medical students and for postgraduate courses in various specialist fields.

The School curriculum stems from the educational, clinical, and scientific partnership between these two entities, with the aim of supplementing theoretical knowledge with multidisciplinary clinical experience. Moreover, students have the opportunity to participate in national and international research projects in various disciplines of pediatric science. The concept of "School" is developed in an integrated system of multidisciplinary theoretical and practical training courses, that take students from "knowing" to "knowing how to do".

The School's teaching activities include:

- Specialization schools
- Master's and advanced courses
- Research doctorates
- Integrated course in Pediatric Sciences as part of the degree program in Medicine and Surgery.

Currently, the agreement between Bambino Gesù Children's Hospital and "Fondazione Policlinico di Tor Vergata" (Policlinico Tor Vergata Foundation) is being extended for the performance of integrated teaching, research, and care activities in the common interest of protecting public health, improving training, and developing biomedical and health research, in reference to the university training and research programs related to the facilities and specialized activities of OPBG, already authorized and accredited.

In compliance with current legislation, the University may assign training tasks to the Hospital's medical staff within the courses provided for in the teaching program. The personnel involved carries out various teaching activities, including teaching and tutoring, according to the organization defined by the relevant university departments. This commitment is carried out in full compliance with the regulatory and contractual provisions of the National Health Service and with the specific agreements concluded between universities and hospitals.

Specialists trained in the Training Network

The Hospital plays a key role in the training of young doctors, being part of the training network of numerous Italian universities. Thanks to the agreements signed, residents can apply the theoretical knowledge

acquired during their academic training to a practical context, thus improving their skills and preparing for the profession. Currently, the training network consists of 57 specialization schools, acting as affiliated centers, including the Hospital.

HEADQUARTERS	
UNIVERSITY	SPECIALIZATION SCHOOL
University of Rome Tor Vergata	Pediatrics
	Pediatric Surgery

CONNECTED FACILITIES	
UNIVERSITY	SPECIALIZATION SCHOOL
University Campus Bio-Medico	Allergology and Clinical Immunology
	Anatomical Pathology
	Anesthesia, Resuscitation, Intensive Care, and Pain Management
	Hematology
	Physical and Rehabilitation Medicine
	Plastic, Reconstructive, and Cosmetic Surgery
	Microbiology and Virology
	Internal Medicine
University Cattolica del Sacro Cuore	Otolaryngology
	Dermatology and Venereology
	Nuclear Medicine
	Hygiene and Preventive Medicine
	Radiological diagnostics
	Occupational Medicine
	Nephrology
	Child Neuropsychiatry
	Orthopedics and Traumatology
	Pediatrics
Audiology and Phoniatrics	
University La Sapienza	Forensic Medicine
	Anesthesia, Resuscitation, Intensive Care, and Pain Management
	Plastic, Reconstructive, and Cosmetic Surgery
	Maxillofacial Surgery
	Pathological Anatomy

CONNECTED FACILITIES	
UNIVERSITY	SPECIALIZATION SCHOOL
University La Sapienza	Endocrinology and Metabolic Diseases
	Nephrology
	Pediatrics - Policlinico Umberto I
	Pediatrics - Sant'Andrea
	Health Statistics and Biometrics
	Hospital Pharmacy
	Life Cycle Psychology
University of Rome Tor Vergata	Sports and Physical Exercise Medicine
	Anesthesia, Resuscitation, Intensive Care, and Pain Management
	Cardiac Surgery
	Plastic, Reconstructive, and Cosmetic Surgery
	Microbiology and Virology
	Medical Genetics
	Hygiene and Preventive Medicine
	Physical and Rehabilitation Medicine
	Child Neuropsychiatry
	Ophthalmology
	Clinical Pathology and Clinical Biochemistry
	Otolaryngology
	Urology
Medical Physics	
University of Ferrara	Medical Genetics
Vita-Salute San Raffaele University	Radiological diagnostics
University of Milan - Bicocca	Neurosurgery
University of Pavia	General Surgery
University of Turin	Medical Genetics
Humanitas University	Respiratory Diseases
	Anesthesia, Resuscitation, Intensive Care, and Pain Management
University of L'Aquila	Psychotherapy
	Pediatric Dentistry
	Orthodontics
Academy of Developmental Neuropsychology	Oral Surgery
	Psychotherapy

P. G. Frassati School of Health Professions

The evolution of the nursing profession has led to significant changes in the training system, redefining the cultural and professional profile of nurses. The growing complexity of healthcare, combined with new clinical and organizational requirements, has made it essential to provide training that guarantees not only sound theoretical knowledge but also advanced practical skills.

In this context, the Piergiorgio Frassati School of Health Professions, affiliated with the University of Rome Tor Vergata, offers a Bachelor's Degree in Nursing and a Bachelor's Degree in Pediatric Nursing, as well as various advanced courses and Level I Master's degrees, representing an effective tool for ensuring constant and organic integration between teaching/learning and care.

To this end, the School provides internships as a fundamental element in the training of nursing students, as they allow theory and practice to be integrated, progressively developing the skills necessary for professional practice. The quality of the internship experience has a direct impact on students' preparation and on their future ability to work in complex clinical settings, thus requiring constant monitoring and thorough assessment of the training program.

In 2024, a hybrid system for basic cardiopulmonary resuscitation and defibrillation (BLS-D) was implemented to respond to cardiac arrest (OHCA), a problem that affects more than 300,000 adults and approximately 7,000 children/adolescents in Europe and the United States each year. Early recognition of cardiac arrest and initiation of cardiopulmonary resuscitation (CPR), as well as early automated external defibrillation, are associated with improved patient outcomes. For this reason, CPR training in the general population remains an extremely important effort, associated with increased survival after OHCA.

In 2021, the *European Resuscitation Council* guidelines recommended the use of Virtual Reality (VR) learning environments as part of a blended learning and self-learning approach to CPR training. The VR BLS-D scenario, developed by the Interdepartmental Center for Research and Training of the University of Rome

Tor Vergata and the "Piergiorgio Frassati" School of Health Professions, created in *Unity* and installed on a *Meta Quest 2* headset, features an adult in cardiac arrest in an out-of-hospital setting. The virtual avatar is superimposed onto a real mannequin, so as to integrate it into the scenario before it begins.

The experience consists of guided performance of the entire BLS-D sequence, divided into individual steps. The user first reads the instructions for the task to be performed, then observes how to perform it, and finally performs it. If performed correctly, positive feedback appears and the next task is activated, and so on, until the entire sequence is completed.

Immersive technologies provide users with an engaging and enjoyable learning platform, training skills without compromising patient safety. The literature on virtual reality for first aid training supports the claim that this technology can be a powerful tool to increase public awareness and learn life-saving skills, mainly due to its high level of immersion, perceptual access to real-time scenarios, and sense of presence.

Thematic Days on International and Humanitarian Law (IHL)

International Humanitarian Law (IHL) governs relations between States, international organizations, and other subjects of international law during armed conflict. The International Committee of the Red Cross (ICRC) is the promoter and guardian of International Humanitarian Law. Considering the importance and relevance of this training for the entire community, but especially for civilian and military healthcare personnel directly involved in the protection provided by IHL, four thematic days on IHL were organized for third-year students of the Nursing and Pediatric Nursing Degree Programs.

The topics covered were: concepts and evolution of international Humanitarian Law; the International Red Cross and Red Crescent Movement; the role of the International Committee of the Red Cross in armed conflicts; the Red Cross emblem; healthcare personnel and their rights and duties; the evolution of armed conflicts in the international context; from classic conflicts to conflicts in the third millennium; Health Care in Danger; healthcare professionals in danger.



06

Hosting and solidarity initiatives

4,351

FAMILIES ACCOMMODATED
IN TEMPORARY HOMES

309

IN-PERSON
CULTURAL MEDIATIONS

21,153

CHILDREN AND ADOLESCENTS
WELCOMED INTO THE PLAYROOMS

952

TELEPHONE
MEDIATIONS

15

INTERNATIONAL
COOPERATION PROJECTS

27

COMPLAINTS RECEIVED
AND RESOLVED

61

HUMANITARIAN PATIENTS
ADMITTED TO THE HOSPITAL

104

PRAISES

Over 850

VOLUNTEERS IN THE HOSPITAL

4,476

STUDENTS ATTENDING THE
SCHOOL IN THE HOSPITAL



End poverty in all its forms everywhere



End hunger, achieve food security and improved nutrition and promote sustainable agriculture



Reduce inequality within and among countries

Accommodation of patients and families

Reception is part of care

The hospital experience for pediatric patients varies depending on several factors, such as age, type of treatment, and length of stay. However, what they all have in common is that the journey involves not only the child but also their family, that plays a crucial role in the care process. For this reason, reception is a key element in guiding and supporting families from the very first contact. Reception focuses on actively listening to the needs of families, such as logistics, accommodation, language mediation, the right to education, and recreational activities, with the aim of making the hospital experience as similar as possible to everyday life.

To this end, an online system has been developed that provides a complete list of available services, with information posters located at strategic points throughout the Hospital, which link to a dedicated page on the OPBG website containing useful information on the options available.

In 2024, the web page was viewed over **5,121** times by **3,469** users.

Welcoming patients and their families aims to:

- respond to their material and psychological needs
- guarantee access to services
- understand specific needs
- provide a channel for doubts and requests
- monitor satisfaction
- collect suggestions for continuous improvement of services
- promote relationships of mutual trust and collaboration.

Home away from home

Families who must move to Rome for their children's care face significant logistical and financial challenges. The need to adapt to a new city, manage living costs, and sometimes separate for work reasons or to care for other children can compromise family balance, placing a strain on the care process.

The Hospital supports these families by providing free accommodation, based on the specific care needs of the child, the family unit, and the distance between the "Home away from home" and the Hospital facility. This service is made possible thanks to the collaboration with associations, foundations, institutions, and private citizens who provide apartments or rooms with amenities, located near the Hospital or easily accessible by dedicated transportation.

Rooms/homes are assigned based on specific criteria:

- the patient's level of independence
- the level of care required
- the patient's condition, therapies, and treatments
- distance from the family home
- social and family vulnerability.

In 2024, **106,994** nights/person were provided free of charge, with **4,351** families hosted in **30** external facilities and **2** internal accommodations.



This considerable number of nights and families hosted is made possible by the solidarity of partner facilities, which support a fundamental aspect of the care pathway: keeping families together. This approach is fully in line with the principles of the Hospital's mission: "knowing, treating, taking care". Particular attention is paid to the reception of foreign patients, who account for over 65% of users requiring accommodation, for whom specific procedures are put in place to ensure adequate and timely support.

Attention to daily needs

Attention to children and their families involves understanding any social and economic difficulties and responding promptly to needs that arise during their stay at Bambino Gesù Children's Hospital. Reports are collected through the Reception Desk, the speak up service, social services, and thanks to the collaboration of healthcare professionals, who also play a fundamental role in identifying the non-clinical needs of families. Each family is then supported by a dedicated contact person who accompanies them throughout their stay.

An example of attention to daily needs is the "Lavanderia dei piccoli" (Children's laundry), a service created at the suggestion of a family and thanks to the generosity of donors, allowing families to manage their laundry independently, without waiting for outside help, thanks to the free washing machines and dryers.

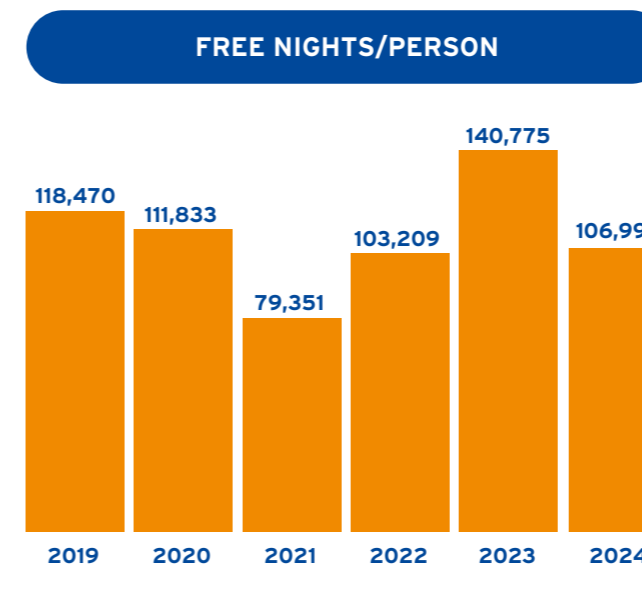


Figure 4. Free nights/person in the period 2019-2024.

School in the Hospital

Prolonged hospitalization or the need for frequent treatments and check-ups interrupt the continuity of schooling for children and young people. To protect the right to education during hospitalization, Bambino Gesù Children's Hospital offers a *School in the Hospital* service, which allows pupils to continue their education from primary school to high school graduation. Teaching is provided by approximately 80 teachers from five schools. The teachers travel to visit patients in their hospital rooms and create personalized teaching programs shared with the students' schools. Assessments are sent to the students' schools and contribute to their mid-term and final evaluation. Teachers work daily, from Monday to Saturday, identifying patients eligible for the service based on reports from head nurses and coordinators. At the request of the parent, the coordinating teacher of the hospital section officially contacts the school, plans the program in collaboration with the class board, and sends an assessment that contributes to the results of the mid-term and final evaluation.

The service is available at the following Hospital facilities, in collaboration with various educational institutions:

Piazza Sant'Onofrio:

- Elementary and middle school: Istituto Comprensivo Virgilio - Rome
- High school: Liceo Ginnasio Statale Virgilio - Rome

Palidoro and Passoscuro Pediatric Palliative Care Center:

- Elementary school: Istituto Comprensivo Fregene - Passoscuro
- Middle school: Istituto Comprensivo Pietro Maffi - Rome
- High school: Liceo Statale Vittorio Colonna - Rome

Santa Marinella:

- Elementary school: Istituto Comprensivo Fregene - Passoscuro

SCHOOL YEAR 2023/2024 IN NUMBERS

4,476 children and adolescents attended the *School in the Hospital*

12 pupils took their middle school final exam

11 children attended the *School at the Pediatric Palliative Care Center in Passoscuro*

The *School in the Hospital* service not only supports education but it also contributes to the psychological well-being and motivation of patients, preventing educational delays and school dropout. In addition, the service contributes to personalizing the educational plan and promotes continuity in schooling, also for the families of patients.

Literacy course for foreign families

In school year 2023/2024, 36 foreigners (29 adults and 7 patients) of 8 different nationalities attended a literacy course designed to meet the educational needs of families from countries where the school system is not recognized or from countries at war. The goal is to promote social and cultural integration by supporting parents in their participation in their child's care pathway.

PCTO (Pathways for Transversal Skills and Orientation)

In school year 2023/2024, 151 hours of PCTO were completed in collaboration with Liceo Ginnasio Statale Virgilio. This is the first national project designed for hospitalized students. It stems from the evident educational value that a demanding and complex treatment program can have when it requires a significant amount of time and takes place in unusual places. It consists of different modules that can be tailored to the student's field of study and personal inclinations, with the flexibility to reach students not only in the Hospital but also, for patients outside their region, in their temporary homes.

Online educational help desk

The Istituto Comprensivo Virgilio (Rome) has set up an online educational help desk to allow hospitalized patients and students staying in temporary homes to participate in afternoon classes from remote, integrating the activities carried out in person in the morning.

Projects carried out by Hospital school departments

Elementary and middle school (Virgilio):

- music workshop for DH patients
- art workshop for DH patients
- multilingual workshop for DH patients
- "Don't speak, I can hear you" project, on World Kindness Day
- "Con-tacto" project; sharing of iconographic material in the original language with María Zambrano Institute in Alcázar de San Juan, Ciudad Real, Spain
- participation in the "Atlante Italia Teacher Award" competition promoted by Repubblica@Scuola
- Science project, with live video lessons from Rome Bioparco (zoo)
- Interactive shadow workshops/shows
- Workshop "Cooking School"
- Educational field trips to "Casa di Ivana".

Palidoro Elementary School:

- "Together for the School in the Hospital" project
- "Together in the Nature Classroom" project.

Passoscuro Elementary School:

- "Together for Pediatric Palliative Care" project.

Palidoro High School:

- "WWF Nature Classroom" project
- Photography project in the WWF Nature Classroom and nature reserve
- "New Cinema Palidoro" film forum project
- Stereomicroscope project "Seeing the world with new eyes"
- "Telling stories with images: photographic narration" project
- "Flight Trajectories" project
- Sustainability project promoting the right to education for students hospitalized at the Pediatric Palliative Care Center in Passoscuro
- Project "Theological places in art"
- "Mathematics, music and... vice versa" project.

Through numerous educational and cultural projects, Hospital school departments contribute significantly to the well-being and growth of children and adolescents, supporting educational continuity and their integration into the care pathway.



The right to play and enjoy childhood

Play is a fundamental right for every child, as provided for in Article 31 of the UN Convention on the Rights of the Child. In a hospital setting, it plays a fundamental therapeutic role, supporting the psychological and social well-being of young patients. The Hospital offers numerous recreational and expressive activities, provided by professional educators in the playrooms and at the patient's bedside.

In 2024, **21,153 hospitalized patients** benefited from group play and expressive activities.

Time Out - space for adolescents

At the space for adolescents, which has been active for years at the facility of Piazza Sant'Onofrio, in addition to the usual creative activities, a workshop specifically dedicated to patients with eating disorders was launched in 2024 in collaboration with the healthcare staff of the General Pediatrics and Level II Emergency Departments. It includes artistic and narrative activities and a theater workshop twice a week. The workshops are the subject of an approved research project that is nearing completion.

The playroom at the patient's bedside

Thanks to collaboration with healthcare professionals, in 2024, counseling activities continued to support long-term hospitalized patients and those suffering from complex conditions, both in wards and in intensive care units. In particular, this year three sessions per week were held in collaboration with the neurosurgery team to support the development of social and learning skills in conjoined twins and to prepare them for separation surgery. Within the Child and Adolescent Neuropsychiatry Department, a weekly group workshop was held for adolescents with self-harming behaviors.

School-work program

Thanks to the collaboration with the contact person of Virgilio High School, teenagers from various departments took part in PCTO (Pathways for Transversal Skills and Orientation) projects.

Siblings

For the siblings of hospitalized children, a program of artistic and expressive activities was resumed in 2024, aimed at meeting the psychological needs of siblings, that are often neglected despite the significant emotional impact of the family context.

Horticultural therapy and the metamorphosis of butterflies

In Palidoro, the horticultural therapy project continues, allowing patients to grow vegetables and aromatic plants. The metamorphosis of butterflies, a symbol of transformation and growth, is used as a metaphor for improving well-being throughout the healing process.

Support for mothers from mothers

Listening spaces and initiatives dedicated to parents are always available. In particular, at the facilities of Palidoro and Santa Marinella, where hospitalizations in the neurorehabilitation ward are long and repeated, mothers have been supported through self-help activities, creating spaces for mutual support and sharing.

In time with music

Music therapy is an important service aimed at supporting the physical, emotional, social, and cognitive well-being of hospitalized patients. Thanks to its ability to influence mood, music is used as a complementary therapy to alleviate the challenges associated with hospitalization and to promote recovery. Music therapy sessions, both individual and in groups, can be relational, to process emotions, or rehabilitative, to support other therapies (physical therapy, speech therapy, etc.). Instruments such as guitars, keyboards, and maracas are used to personalize the therapeutic pathway according to the specific needs of each patient.

In 2024, approximately **4,000 music therapy sessions** were provided, involving approximately **1,600 patients** in the four Hospital facilities.

Reports on operational inefficiencies and complaints as opportunities for improvement

Listening to families allows us to analyze their needs and take targeted action, and to suggest changes to organizational and operational models to improve the efficiency and quality of services. Mapping the various needs identified on a daily basis allows us to constantly refine and monitor the quality of our services, thus promoting the image of an organization that is sensitive to the needs and feedback of its users. Reports and complaints are classified according to the specific characteristics of the communication received:

- a **report** concerns a problem or difficulty encountered by the user of a service. It certainly implies dissatisfaction, as it highlights a situation that does not meet expectations, but generally has no long-term implications, is quickly resolved or has minimal impact on the care pathway
- a **complaint** implies strong dissatisfaction on the part of the user, is not temporary or resolvable in a short time and/or has an impact on the treatment pathway. Complaints are submitted using a form, follow the steps defined by a Health Department Procedure, and have a maximum response time of one month

Complaints are the way in which families tell us how our care mission is going, and we must always bear in

mind that their involvement is a process that creates value for the entire Hospital. For this reason, specific surveys are carried out, also by directly contacting families who have been to the Hospital, to evaluate their experience through:

- an online questionnaire
- the analysis of reports sent to the email address of the Public Relations Office
- the analysis of complaints.

Patient satisfaction and the assessment of their experience is a key indicator to evaluating the quality of medical care and person-centered care. *sistenza medica e della cura centrata sulla persona.*

The results of the **customer satisfaction** monitoring show a positive level of satisfaction in all areas surveyed in 2024

The results are summarized as follows:

Total questionnaires:

- 6,646 questionnaires completed
- 8.29/10 average satisfaction rating

Hospitalizations:

- 6,466 questionnaires completed
- 8.34 average satisfaction rating

Outpatient services:

- 62 questionnaires completed
- 6.74 average satisfaction rating

Day Hospital:

- 104 questionnaires completed
- 6.71 average satisfaction rating

Blood collection center

- 14 questionnaires completed
- 6 average satisfaction rating.

The level of satisfaction among families is closely linked to the quality of care, the professionalism of staff, and the mutual trust that is established during the care process, with particular attention to individual needs. The completed questionnaires are a fundamental tool for the continuous improvement of evaluation processes and for strengthening dialogue with families, allowing any misunderstandings or inefficiencies to be addressed promptly.

Reports received via email, social networks, and telephone are an important source to ensure the excellence of services. They allow immediate critical issues to be resolved promptly and more complex issues to be investigated thoroughly, involving the relevant users and stakeholders.

In 2024, **230 reports** and **27 complaints** were submitted, which contributed to improving the care offered.

Praises

A dedicated section of the Hospital Intranet collects and publishes the praises of families who have expressed their appreciation for the services offered and for the staff. Due to their motivational value, they are shared with colleagues as examples of good practice and to promote the humanization of care.

In 2024, **104 formal praises** were received, testifying to the recognition and gratitude of families for the commitment and professionalism of our team.

Volunteer associations in the Hospital



In our societies, too enslaved to market logic, where everything risks being subject to the criterion of interest and to the quest for profit, volunteering is prophecy and a sign of hope, because it bears witness to the primacy of gratuitousness, solidarity and service to those most in need.

Pope Francis
Angelus, March 9, 2025

Throughout 2024, the Hospital continued to support the integration of volunteers in care, recognizing that volunteering and parents' associations are fundamental to the pediatric care system through support that goes beyond the clinical aspect and embraces the emotional and social well-being of patients and their families.

A dedicated structure oversees the organization of volunteer activities at all facilities, both for the planning and the organization of activities, and for the coordination of daily requests from across the Hospital. In 2024, 51 associations and over 850 volunteers provided approximately 89,000 hours of in-person activities. An invaluable gift. Alongside their noble contribution to research, the volunteers' daily activities were aimed at meeting the needs of patients and their families, falling into the following areas:

Reception and orientation

Approximately 70 volunteers welcomed patients at the entrance to the facilities of San Paolo Fuori Le Mura, Viale F. Baldelli, and Palidoro. Approximately 40 volunteers welcomed patients and their families at the Emergency Department (DEA) of the facilities of Piazza Sant'Onofrio and Palidoro.

Bedside assistance

In the wards, volunteers always supported parents in their daily needs, listening to them, and replacing them when necessary. In special cases of children without parents, great synergies were created among the associations, and volunteers took full responsibility for the children who were alone.

Play and entertainment activities

In all the Hospital facilities, numerous activities provided essential entertainment for children in the wards, waiting rooms, and playrooms, including games, clowning, storytelling, art and theater workshops, and clay modeling. These activities often help to distract children, relieve family members, and facilitate care, thus improving its quality. In this regard, the activity of clowns in blood collection centers and/or during complex clinical examinations is very important. By collaborating with the healthcare professionals, clowns facilitate the performance of the procedure and make it less traumatic for the child. Activities promoted by martial arts and pet therapy associations have also been greatly appreciated.

Emergencies

Groups of volunteers from various associations made themselves available to deal with situations that required immediate and, often, continuous assistance. The help of volunteers was fundamental in welcom-

ing children in need of medical care and their families fleeing wars around the world, in addition to their constant availability to assist children without parents.

Transport

Volunteers provided transportation between the different Hospital facilities and between the Hospital and external institutions (health facilities, police headquarters, temporary homes, etc.), train stations, and airports. Transportation was ensured by vehicles made available by one of the associations that support the Hospital.

Participation in Hospital projects

The valuable contribution of volunteers continued in projects promoted by the Hospital, such as:

- BLUD Project (Donor Human Milk Bank): collection of breast milk in Lazio region
- Forget-me-not Project: a mobile pediatric clinic for disadvantaged children living in the suburbs
- Monitoring of perceived quality: periodic surveys on perceived quality in the Hospital canteens.

The participation of associations was also ensured in some important Hospital committees.

Other activities

- 9,720 meals supplied to families in need
- purchase of basic necessities (linen, personal hygiene products, food, and other goods) for mothers or other caregivers staying at the Hospital, particularly at the Palidoro facility
- accommodation and, if possible, financial support for disadvantaged families (including the purchase of expensive medicines and rehabilitation therapies) and for specific Hospital projects (e.g., research grants for physical therapists, psychologists, and nurses).

Training

During 2024, basic and continuing training courses were promoted. The training provided an opportunity for volunteers from various associations to meet and share their experiences, motivating them to continue their fundamental and valuable work.

Specifically, the training was divided into:

- mandatory training on orientation and safety in the Hospital
- field training (particularly on care)
- training for the tutors dedicated to new volunteers
- refresher training sessions on specific topics of interest (child language, pediatric palliative care, the role of the caregiver, bereavement, and in-depth analysis of three topics already mentioned, including the issue of siblings).

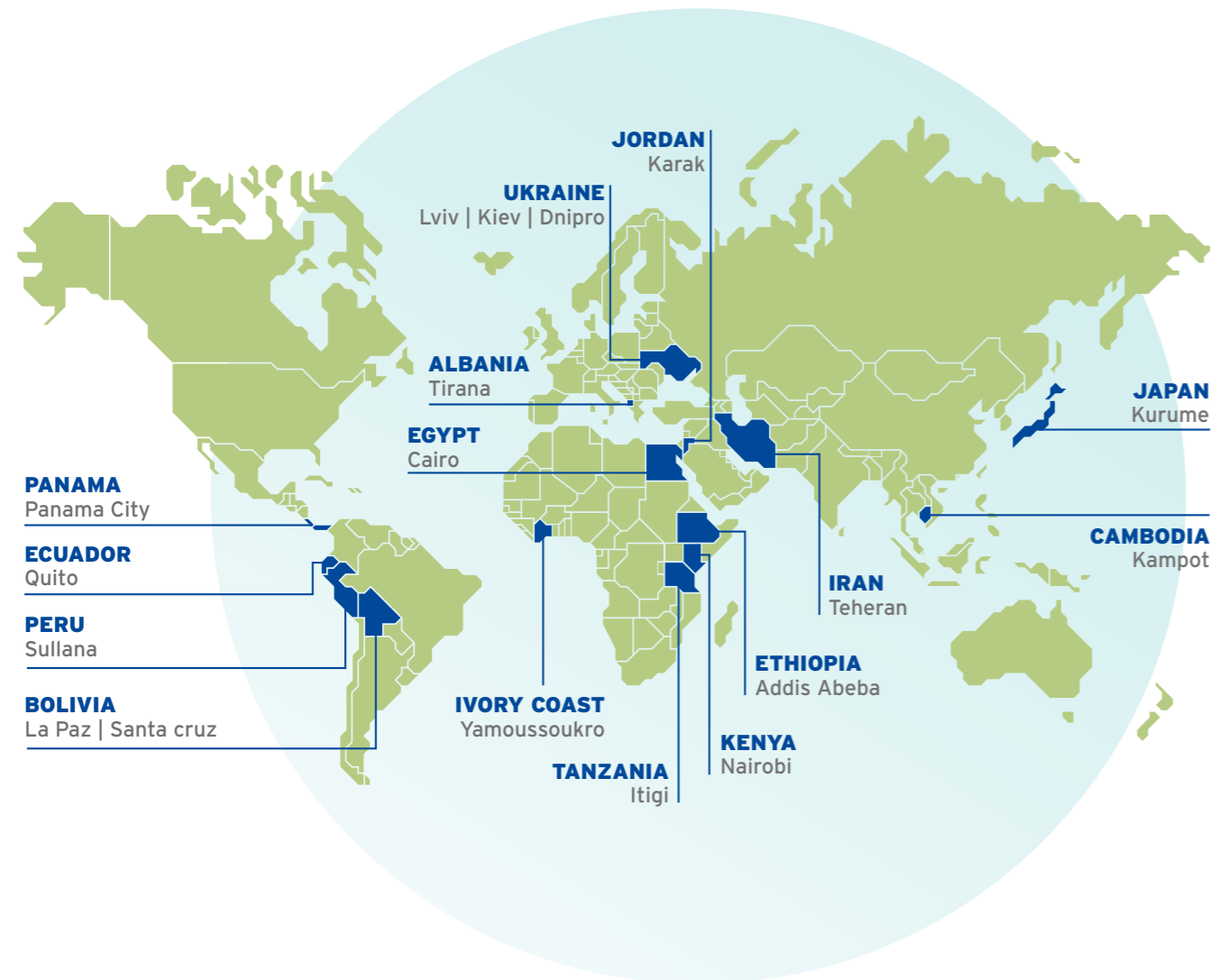
Seven training events were held with over 700 participants; approximately 4,700 hours of field training were also provided.

Solidarity initiatives

International cooperation projects

Over time, Bambino Gesù Children's Hospital has developed numerous solidarity initiatives to bring its clinical expertise to the world, where it is most needed, through the training of local healthcare staff. In line with its mission, OPBG has made "Donating knowledge" the focus of its cooperation projects, as research aimed at treatment is a modern form of charity. These projects are implemented through agree-

ments with governments, healthcare institutions, and international humanitarian organizations, providing distance learning, practical on-the-job sessions at partner hospitals, and residential training courses in Rome for local doctors and nurses. Thanks to the commitment of its specialists, OPBG offers clinical support and technological updates to healthcare professionals in different areas of the world, including Asia, the Middle East, Africa, Latin America, and the Balkans.



The international cooperation initiatives and activities implemented in 2024



CAMBODIA

OPBG continued its activity in Cambodia at the Son-ja Kill Memorial Hospital in Kampot. From November 22nd to December 1st, OPBG Urology and Neonatology teams worked on the ground, providing clinical support and training to local staff. From July 8th to 11th, a joint mission was also carried out with a team from St. Mary's Hospital in Kurume (Japan), strengthening international cooperation in improving pediatric care in the country. At the same time, healthcare was provided through the Mobile Clinic, the Pregnant Women program, dedicated to high-risk pregnancies, and a specific care program for patients living in poverty, thus contributing to the protection of maternal and child health in the most vulnerable areas.



JORDAN

OPBG strengthened its collaboration with the Italian Hospital in Karak (OIK) through a comprehensive training program for healthcare professionals in the fields of Neuropsychiatry and Neurorehabilitation. Particular attention was paid to the development of a training plan for the families of patients treated at OIK and for local therapists, to improve the approach to care and the support for children with neuropsychiatric disorders. In addition, a process has been launched to standardize data collection in line with OPBG standards, ensuring greater quality and consistency in clinical information. During the year, two field missions were carried out: Neuropsychiatry (June 20th - 28th) and Neurorehabilitation (July 9th - 15th). During these missions, an experimental phase was launched involving small groups of four families to test the most effective training model. This first phase provided key elements for the planning of a comprehensive and structured program fostering family involvement in the therapeutic process.



IRAN

OPBG has completed an important distance training and clinical consultation project in support of the Children's Medical Center (CMC), the leading center for the treatment of epilepsies in Iran, with over 600 cases treated each year. The initiative aimed at improving the quality of treatment and care for Iranian children with drug-resistant epilepsies, by providing local specialists with the tools and skills to manage the condition more effectively. Thanks to constant exchanges between OPBG experts and CMC medical staff, the project made a significant contribution to strengthening clinical skills in the country and was successfully completed in 2024.



IVORY COAST

OPBG has been collaborating with San Giuseppe Moscati Catholic Hospital to improve the medical services offered to the local population. The project was centered mainly on pediatric specialties, with a specific focus on pediatrics, governance, and the organization of health services. Following the signing of a Memorandum of Understanding (MoU) in 2025, OPBG intervention will focus on training, with particular attention to healthcare governance and the optimization of internal organization, to ensure more efficient and accessible management of resources and healthcare services.



TANZANIA

OPBG has implemented a distance learning program for medical staff at St. Gaspar Referral and Teaching Hospital in Itigi, which is located in one of the most disadvantaged areas of sub-equatorial Africa. The initiative aimed at strengthening the clinical skills of local healthcare professionals, meeting the specific training needs of the Hospital. During the year, distance learning modules were delivered on topics that are relevant to the management of critical patients, including non-invasive ventilation; head trauma; invasive ventilation in pediatric ARDS; hemodynamic monitoring; pediatric septic shock; and management of renal failure in intensive care settings. Through this program, OPBG has helped improve the quality of healthcare in a context characterized by limited resources, providing essential tools and knowledge for the management of pediatric emergencies.



KENYA

OPBG continued its collaboration with Ruaraka Uhai Neema Hospital in Nairobi, founded in 2008 by the *Amici del Mondo - World Friends* (WFK) Organization, with the aim of enhancing the skills of healthcare professionals. The project was developed with an integrated approach, combining distance learning, residential training, and on-the-job training missions, to improve diagnostic pathways and access to healthcare services by the vulnerable groups of the local population. From September 28th to October 5th, an on-the-job training mission took place, during which a multidisciplinary OPBG team, including a radiologist and a pediatrician, worked in collaboration with the local hospital. The main activities were: training local staff in the use of point-of-care ultrasound and CT scan in pediatrics, lessons on pediatric imaging techniques, implementation of care protocols, and consultation on complex clinical

cases. The importance of this mission was not limited to immediate assistance, as it laid the foundations for the implementation of a sustainable model ensuring a long-term impact on the quality of care. After the mission, online follow-up meetings were organized to monitor the learning and correct application of the concepts taught, further strengthening the growth of the local healthcare professionals.



ETHIOPIA

OPBG has continued its agreement with the Association San Vincenzo de Paoli for the Cardiology Center to be built at the facility run by the Vincentian Sisters of Charity. The agreement, signed in December 2023, provides for a cardiology training program for the local healthcare professionals, with the aim of enhancing their skills in the diagnosis and treatment of heart diseases. The project proposed by the Association San Vincenzo de Paoli involves the creation of a cardiology diagnostic clinic in the facility managed by the Vincentian Sisters in Addis Ababa, where patients can be diagnosed and, if necessary, referred to Black Lion Hospital for further treatment. The clinic will also offer eye examinations and laboratory tests. OPBG intervention will focus mainly on training medical and nursing staff, providing them with the skills necessary for the proper management of heart diseases and supporting the healthcare facility in setting up a sustainable care system for the local population.



UKRAINE

OPBG has started cooperating with Soleterre Foundation and two Ukrainian hospitals - First Lviv Territorial Medical Union and National Specialized Children's Hospital (Okhmatdyt) - of the Ukrainian Ministry of Health, in the field of neurorehabilitation. The partnership focused on training Ukrainian healthcare staff in the management of war trauma and injuries resulting from amputations, with a specific focus on pediatric rehabilitation. From November 26th to December 6th, 2024, 10 Ukrainian healthcare professionals participated in an intensive training program in Rome, completing practical training at the Neurorehabilitation Units in Palidoro and Santa Marinella. This initiative enabled Ukrainian professionals to acquire advanced skills in the treatment and rehabilitation of pediatric patients with traumas and neurological injuries, thus helping to improve the quality of care in war contexts.



ALBANIA

OPBG continued its commitment in Albania, collaborating with the Firdeus Foundation. Several healthcare professionals attended training sessions at our Hospital in preparation for the establishment of a Pediatric Polyclinic in Tirana, where OPBG specialists will provide on-site healthcare, assistance, consultation, and training in various pediatric disciplines.



PERU

OPBG continued its distance learning and residential training project for medical and nursing staff at the Apollo II Children's Hospital in Sullana. The project, in collaboration with the Italian-Latin American Institute (ILLA), covers various specialist areas, including pediatric and neonatal surgery, infectious diseases, onc-hematology, pediatrics, and neonatal critical area. The initiative also includes consultation on complex clinical cases to improve the skills of local professionals in the management of more serious and complex pediatric diseases. In 2024, six healthcare professionals arrived at OPBG, each trained for a two-month period, to complete the refresher course provided by the project. This program represents an important growth opportunity for Peruvian professionals, as it contributes to the improvement of the quality of pediatric care in Sullana region.



ECUADOR

OPBG continued its distance learning project for medical and nursing staff at the Baca Ortiz Children's Hospital in Quito. The project also includes consultation on complex clinical cases, to improve the management of heart diseases and health emergencies in the pediatric setting. In collaboration with the Italian-Latin American Institute (ILLA), the training of twelve local professionals in cardiac surgery started at OPBG in 2024. During 2025, these professionals will have the opportunity to spend a month at OPBG to complete their training, acquiring advanced skills to be applied in pediatric care in Ecuador, with a particular focus on pediatric cardiac surgery.



PANAMA

OPBG continued its distance learning project for medical and nursing staff in Panama City, supplemented by residential training periods and on-the-job training missions. The ultimate goal of the project is to set up the first reference center for epilepsy surgery in Panama, with the aim of improving the management and treatment of pediatric patients with epilepsy by offering advanced surgical treatment. The project is carried out in collaboration with the Italian-Latin American Institute (ILLA) and aims to develop the skills necessary for the setting up and management of a center of excellence for local patients.



JAPAN

OPBG has consolidated its collaboration with St. Mary's Hospital in Kurume, Japan, to promote mutual exchange and cooperation on the Catholic approach to medical ethics, to strengthen pediatric care in Southeast Asia. In November 2024, OPBG took part in an institutional mission to Japan and South Korea. The mission included meetings with the Nuncio to Japan and the Bishop of Tokyo, as well as a visit to St. Mary's Hospital in Kurume, where the "Charter of the Rights of the Incurable Child" was presented and the collaboration agreement was renewed and signed, with the inclusion of the Pontifical Institute for Foreign Missions (PIME) as a new partner. The delegation then attended the Congress of Catholic Hospitals of Southeast Asia in Seoul, where a meeting was organized between OPBG, St. Mary's Hospital of Kurume, and St. Mary's Hospital of Seoul, to explore potential three-way collaborations. The visit ended with a meeting with the Apostolic Nuncio to South Korea.



EGYPT

OPBG continued to offer its support in Egypt. An important development was OPBG involvement in the *Salus* project, which was blessed by the donation of two Mobile Clinics by Pope Francis. These clinics, designed to provide care for sick children and war victims in areas lacking healthcare facilities, are built in collaboration with OPBG and Gemelli Hospital, and bring vital pediatric care to the most vulnerable areas.



BOLIVIA

OPBG has launched a news project in Bolivia, in collaboration with the Ministry of Health and Santa Cruz Catholic Hospital, with the aim of strengthening and developing cooperation in pediatric care. The aim of the project is to improve the quality of pediatric healthcare in the country, by strengthening local skills and promoting access to high-quality pediatric care for Bolivian children.

MedTraining: the training platform dedicated to third countries and low-resource countries

The *MedTraining* platform is an online learning environment developed by OPBG to support distance learning in developing countries and in limited-resource countries. Designed in terms of content and technological infrastructure to adapt to contexts with insufficient IT infrastructure and equipment, it allows for access to courses from any device, including smartphones, without the need for advanced technologies. A browser and data connection are enough; it is also possible to download contents for offline viewing in areas with poor internet coverage. Thanks to this platform, pediatric training becomes accessible to a significantly larger number of professionals and healthcare facilities, thus offering free essential resources in fields such as healthcare organization, general pediatrics, neonatology, emergency care, and COVID-19 management. *MedTraining* is therefore an important initiative fostering the dissemination of medical knowledge in contexts where it is most needed.

Humanitarian patients

The Hospital is structured to respond to healthcare needs from all over the world, offering comprehensive and personalized support. Our organization effectively coordinates clinical, organizational, administrative, linguistic, and cultural needs, ensuring special attention to each child and their family.

The Hospital's goal is to provide integrated care that goes beyond the clinical aspect, including adequate human and cultural support, so that every care experience is not only more effective but also peaceful, in full compliance with internal policies and procedures.

The Hospital is founded on the principles of empathy, professionalism, and respect for diversity, constantly striving for excellence in every aspect of its activities. The integrated and personalized approach implemented accompanies the patient and their family in every

stage of the care pathway, with a particular focus on individual needs.

Management of care requests

From the very first contact, patients are offered support in managing their request, by verifying its feasibility, establishing contact with the relevant clinical facilities, and organizing its provision. The aim is to create a welcoming environment which, while maintaining the focus on medical care, helps to reduce the stress associated with journeys, logistics, and administrative issues, allowing families to concentrate exclusively on the care of their child.

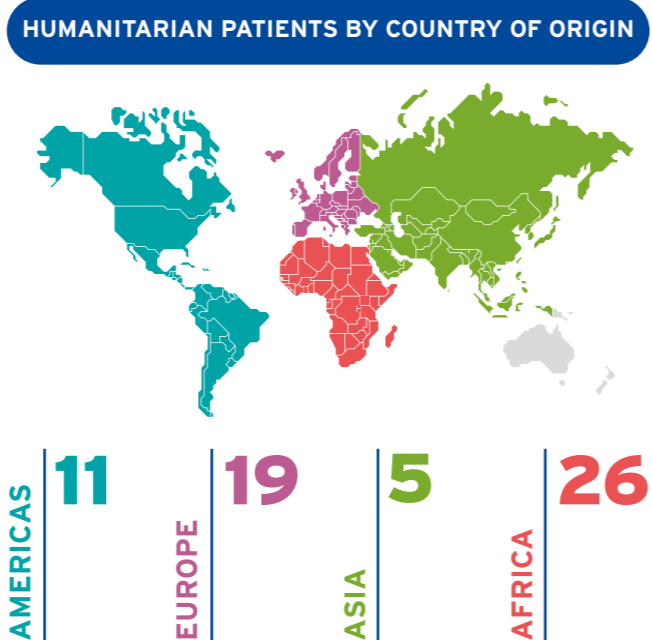
Collaboration between doctors and specialists from the Operational Units and offices involved allows for personalized treatment plans. Each intervention and treatment are constantly evaluated and adapted to specific clinical conditions and individual needs, thus ensuring personalized care.



Figure 5. Humanitarian patients. Year 2024.

Every year, the hospital manages many dozens of humanitarian patients who are not covered by the Italian National Health Service. In particular, in 2024, a total of 343 children were admitted, divided into patients with planned arrivals and financed by agreements, conventions, or specific initiatives by foundations, organizations, or benefactors (282), and humanitarian patients, i.e., children lacking any financial coverage and supported entirely by Bambino Gesù Children's Hospital (61); in 31 cases, their arrival was unplanned and their families made their own emergency trips to the Hospital.

Analyzing specifically the group of humanitarian patients, represented by country of origin and grouped by continent, 19 European, 5 Asian, 26 African, and 11 children from the Americas were admitted.



A multicultural Hospital

Communication is key to effective care. For this reason, the Hospital provides eight professional mediators for the most widely spoken languages. These specialists facilitate dialogue between patients, families, and medical staff, overcoming language barriers and helping to create mutual trust and understanding. In addition, thanks to the collaboration of some external partners, interpreters are also available for less common languages. A telephone mediation service is also available 24 hours a day, 365 days a year. In 2024, 330 in-person cultural mediation services were provided in 17 languages. In addition, 952 telephone mediation services were provided in 51 languages.

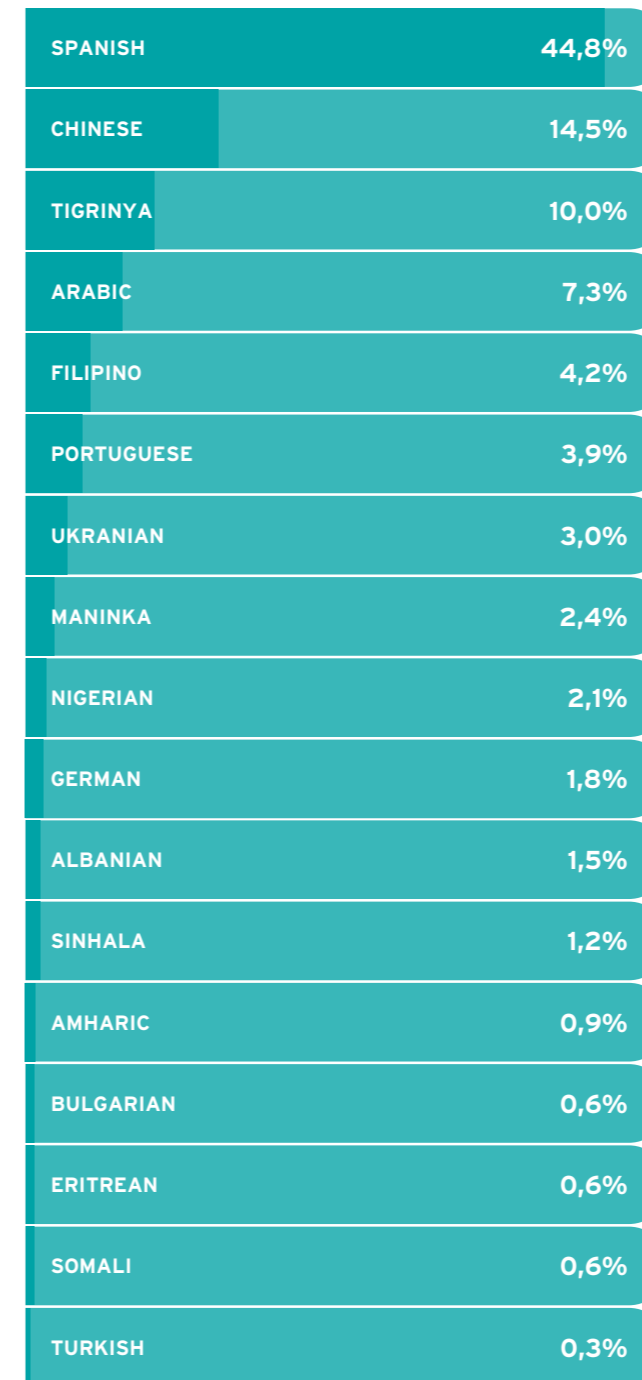


Figure 6. In-person mediation services provided. Year 2024

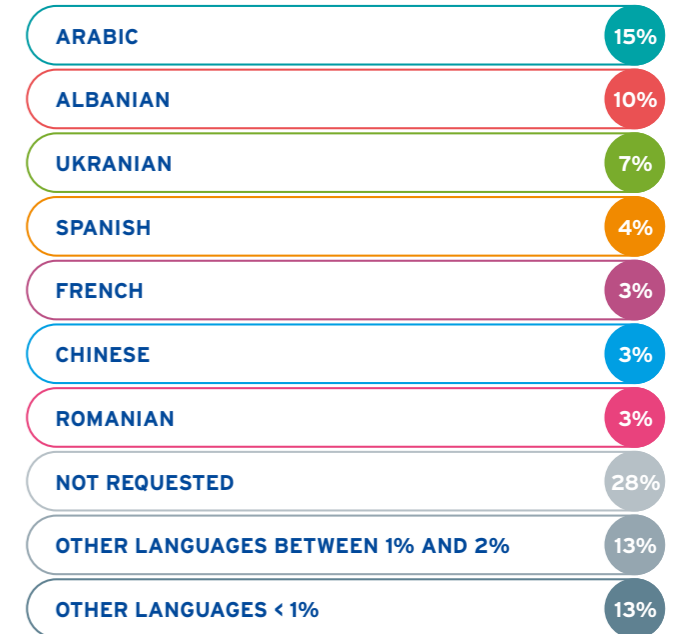
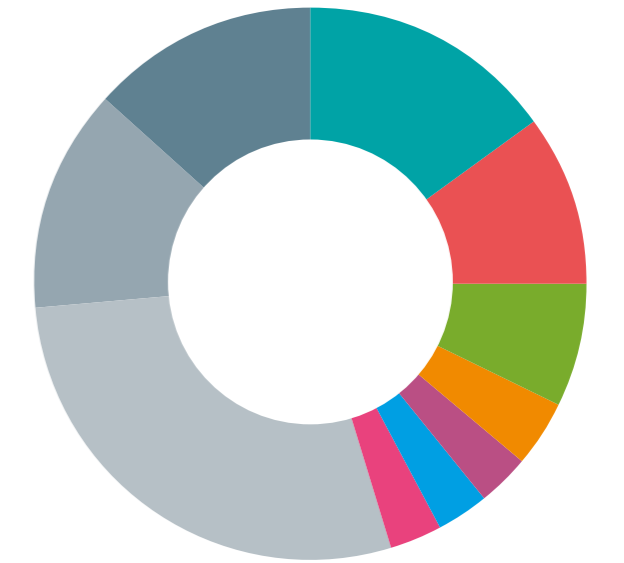


Figure 7. Telephone mediation services provided. Year 2024

A Bridge between Cultures and Continents

Cultural integration: our work aims to build a real bridge between different cultures, where the enhancement of diversity becomes a key element in creating a care environment that is inclusive and respectful of each person's uniqueness.

Global healthcare excellence: operating in an international context, Bambino Gesù Children's Hospital stands as a point of reference for healthcare excellence, attracting patients from all over the world and guaranteeing them the highest standards of care.

Our dedicated team combines medical, nursing, and administrative skills with knowledge of specific regulations, cultural mediation, and a strong humanitarian vocation.

Our stories

Priscilla a story of courage and hope

Priscilla, a 5-year-old girl, was born in Ghana in a context characterized by hardship and suffering. From an early age, her life has been difficult, as it was marked by painful events: first she was abandoned by her mother, and then she contracted a severe form of leprosy. Fortunately, a local religious foundation, the SVD Foundation¹ led by Rev. Fr. Andrew Campbell, took the child to heart, secured her legal guardianship in the person of Donna, and intervened with dedication to ensure she had the best chance of recovery and a more peaceful future.

Unfortunately, the treatment options in her country of origin were lacking, and for this reason, in August 2024, Priscilla was referred to our Hospital for management. She arrived at our Hospital with a complicated medical history, with the amputation of her left leg in her home country and a severe form of osteomyelitis in the residual stump.

Admitted to the infectious diseases ward, the little girl began a complex and delicate treatment pathway. Every day was a battle against pain and uncertainty, but also a small step towards recovery. Despite our efforts, the infection proved resistant, and in September 2024, plastic surgeons performed surgical curettage of the lesion, removing another bone segment from the stump to prevent the infection from spreading.

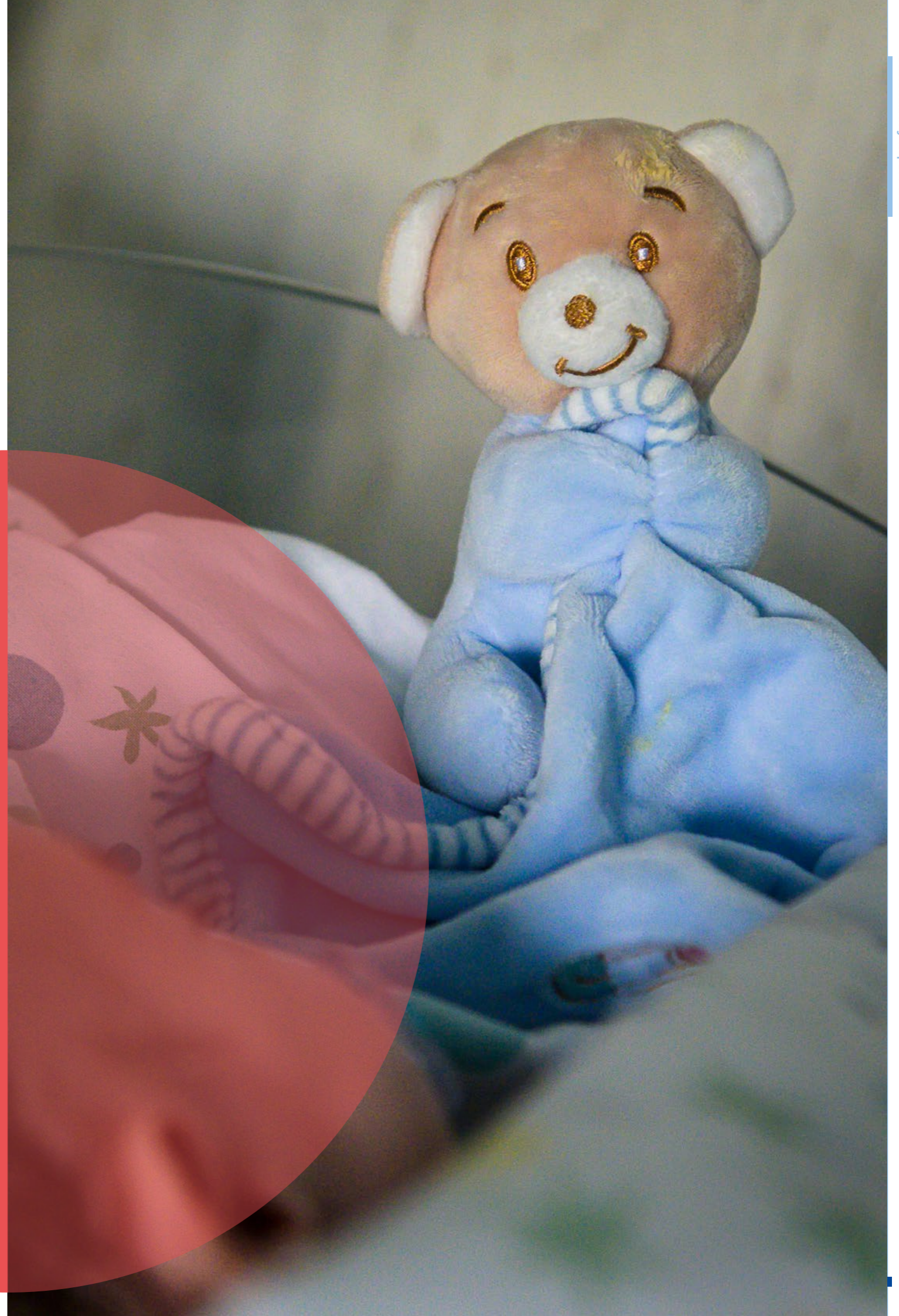
The constant support of all the healthcare professionals involved, as well as the cultural mediation of the Hospital interpreter, helped to make the Hospital environment less alien and more welcoming for Priscilla, creating a climate of solidarity and understanding.

Finally, once the infection was cured, the hope of walking again began to grow: Priscilla was transferred to the Neurorehabilitation COU - Rehabilitation Unit for Severe Developmental Age Disabilities (UDGEE) in Palidoro, where she was prescribed and fitted with a custom-made prosthesis and gradually taught how to use it. Every small step forward was a personal victory and a tangible symbol of Priscilla's amazing resilience. The little girl's determination, combined with the commitment and care of the entire team of professionals, led to surprising progress.

In December 2024, four months after her arrival, Priscilla was discharged and returned to her country. Her return was greeted with immense emotion and joy by the entire community. The news that followed told us of a little girl who had finally returned to school, walking on her "new little legs".

Priscilla's story is much more than a tale of suffering and pain: it is a testament to courage, determination, and love. Her experience reminds us that every step, every little progress, is a celebration of life and resilience, a message that urges us never to give up when facing adversities and to always believe in the possibility of a better future.

1. The SVD Foundation (Society of the Divine Word) is a charitable organization, legally registered in Ghana as a non-profit organization. It was established by Rev. P. Campbell in collaboration with the SVD community and the Catholic Archdiocese of Accra.



07

Worker safety and well-being

3,073
EMPLOYEES

279
COLLABORATORS

3,034
PERMANENT EMPLOYEES
39 FIXED-TERM EMPLOYEES

138 < 30
1,848 30 - 50
1,087 > 50
AGE GROUPS OF EMPLOYEES

577
PROFESSIONALS WHO
SUPPORTED RESEARCH
ACTIVITIES IN 2024

65,230
HOURS OF CME AND NON-CME
TRAINING FOR EMPLOYEES

620 Women
288 Men
MEDICAL AND NON-MEDICAL
HEALTH MANAGERS

305 Woman
216 Men
NON-HEALTHCARE SECTOR

9 Women
22 Men
ADMINISTRATIVE MANAGERS

1,272 Women
341 Men
HEALTHCARE SECTOR



Ensure inclusive and equitable quality education and promote lifelong learning opportunities for all



Achieve gender equality and empower all women and girls



Promote sustained, inclusive and sustainable economic growth, full and productive employment and decent work for all

Our people

For the Hospital, 2024 marked the beginning of new challenges: improving active listening, enhancing the uniqueness of each person, and supporting professional training focused on growth and emerging needs.

This challenge arose from the Hospital's desire to interpret the principles and values underlying a mission that, to be fully embraced, requires greater effort on the part of the entire OPBG community. OPBG workers represent its true wealth, because it is each individual who ensures that the whole truly participates in the shared ideal, even more than in the duty, of curing and caring for children. It is from these premises that specific concrete actions were launched, cornerstones of the ambitious project of everyone being part of a shared culture, that is not abstract, but rather a necessary tool for understanding that only through shared feelings and mutual collaboration a more peaceful, fair, and dignified reality can be built for all.

On December 31st, 2024, the total number of workers was 3,352, including 2,358 women and 994 men. The age distribution is concentrated in the age group 30-50. The number of employees is 3,073, of whom 3,034 are permanent. The largest professional category is direct care staff, comprising 1,613 workers, of whom 1,272 are women. The number of fixed-term employees is 39. In addition to them, there are 279 external collaborators.

In addition, 577 professionals supported research activities during 2024.



Workplace well-being and inclusion

Gender equality

The Hospital confirms its commitment to gender equality. In 2022, a regulation was adopted which, by enhancing internal regulatory sources that protect gender equality, including the Code of Ethics, defines the activities and the management and monitoring system of the Gender Equity Plan (GEP).

In the three-year period 2022-2024, awareness-raising and training initiatives on equal opportunities were carried out. The *Bias Lab and Gender Reflections* campaign involved senior management and groups of employees. Projects dedicated to new parents involved a limited number of employees; these initiatives were useful in preparing more structured pathways and drafting policies on working arrangements for new parents. Initiatives to implement agreements dedicated to employees and their families are ongoing.

In line with the management and monitoring system, in the first half of 2025, the Hospital updated its gender analysis on December 31st, 2024, and the dedicated action plan, extending it to the three-year period 2025-2027. In this context, evidence is also provided of the monitoring carried out on the previous action plan; all of this - which is also available on the website - constitutes another tool to identify trends, focus on critical issues, and set new objectives.

The actions taken are moving the Hospital in the right direction, although there is clear room for growth and development in relation to the important objectives set by the European Commission, particularly regarding certain specific indicators, such as gender equality in leadership and decision-making processes.

To this end, other initiatives are planned for the period 2025-2027 to raise awareness of the untapped potential of women to reach top positions and play a more significant role in the Hospital's decision-making process. At the same time, efforts will continue to support women in their daily attempt to balance family and work responsibilities.

Well-being at work

Facility Committees

Dialogue builds. This is the guiding principle behind the "Facility Committees" introduced in 2024 by the President and the entire management team as an open channel of communication with the Hospital. Forty representatives from all professional categories and all OPBG facilities gather and analyze suggestions for improvement and needs on a weekly basis in a systematic, critical, and constructive manner. An exchange of ideas, points of view, and new proposals.

The Facility Committees are not only a tool for identifying staff needs, but also for helping the Hospital provide concrete feedback. The findings are evaluated by the Committee of Directors, which monitors the analyses carried out during the meetings and determines whether improvement measures are necessary and how they can be implemented. The initiative has been positively received by the staff involved, not only in terms of the number of responses, but also in terms of participation, which is "heartfelt" by all those who take part in the weekly meetings. The approach is constructive, giving the impression, on several occasions, that participants are willing to bring to the attention of the Committees not only issues related to their work and individual needs, but also needs for improvement that would enable families and patients to experience hospital life in a less stressful way. These objectives also make the Facility Committees a tool to build a community that takes care of itself for the ultimate goal of being able to take care of others.

New Hospital Intranet

The "New Intranet" is one of the main innovations long awaited by all OPBG staff. Developed entirely within the Hospital, the platform was introduced in early 2025, replacing the previous Intranet and Landing Page, integrating them into a single tool that has been renewed both aesthetically and - most importantly - technically.

The "New Intranet" is the result of a project launched in April 2024, which saw the proactive involvement of staff from all areas of the Hospital with a systemic approach. Many new features have been integrated in the platform, which is essential for everyone working in the Hospital: from the responsive mode allowing the new Intranet to be navigated from all devices, including smartphones, to the search field for procedures and regulations, activated in the new and completely reconfigured document repository; from user-friendly staff search to the creation of macro-areas dedicated to Departments and Functions, to the possibility of accessing individual documents in the repository directly from the editorial areas.

All this is part of the priority objective of providing the Hospital staff with access to information in a simplified manner; further improvements will also be achieved as a result of the contribution that everyone can make by submitting their suggestions.

Welfare initiatives

The welfare initiatives promoted by the Hospital for employees and their families have the intrinsic goal of contributing to the harmonization of private and professional life. In 2024, new agreements were signed, or existing agreements were renewed to provide benefits in the following areas: education, culture and entertainment, sports and health, moving and transportation, personal services, financial services, online shopping, travel, and technology.

Among the most significant initiatives aimed at the well-being of employees and their families is the possibility of taking out a voluntary supplementary health insurance policy covering the following areas: hospitalization with or without surgery, caesarean section and natural childbirth, Day Hospital, outpatient surgery, extra-hospital expenses, cancer treatment, specialist visits and dental care. A total of 1,297 employees signed up for the scheme.

In order to guarantee the insurance package also for the following year and considering the need for economic sustainability, a market survey was conducted for 2025, which resulted in the renewal of the initiative for the new year and in the containment of costs.

Horizontal progression

From July 2024, Bambino Gesù Children's Hospital has granted to staff with five years' seniority on December 31st, 2023, within their own level of classification, the transition to the next horizontal pay bracket. This measure was applied in line with the horizontal pay progression measures implemented in March 2021. Regarding horizontal progression, the Hospital also informed the relevant Trade Unions of its willingness to negotiate a union agreement to review the regulations.

A.D.O.N.P. Agreement

In July 2024, two significant trade union agreements were signed between the Bambino Gesù Children's Hospital and the ADONP Trade Union (Non-Profit Association of Hospital Managers). The first agreement provides for the Hospital's adherence to the regulatory provisions of the ARIS - ADONP 2020-2022 National Collective Labor Agreement of September 17th, 2019, which will apply to managing (non-medical) staff in healthcare, professional, technical, administrative, and research roles. The second agreement, supplementing the financial agreement signed on July 18th, 2022, provides for the establishment of two new types of position: High Specialization, which refers to healthcare roles, and High Scientific Competence Research, in order to meet the organizational needs and the high complexity of the Hospital.

Another important provision is the legal recognition, starting from January 1st, 2025, of the Collective Incentive Fund for Healthcare Managers, which essentially confirms the provisions for the distribution of financial amounts applied to date. With the aim of identifying an incentive system that can ensure sat-

isfaction for all staff, a working group has been established involving the Parties. Over the coming months, it will examine and define the rules for incentives for employees in the Research Areas.

OPBG Pension Fund

The Fund, established in 2019 with *Rescriptum "Ex Audentia SS.mi"* by order of the Supreme Pontiff Pope Francis, also following agreements between the Hospital and Trade Unions, aims to provide supplementary pension benefits to employees. The amount of the Fund's pension benefits is determined according to the contributions paid and the management return. Enrollment in the Fund does not entail any costs for members; all costs for the management of the Fund are borne by the Hospital. The Fund is structured in two segments, differentiated by risk and return profiles.

On December 31, 2024, there were 3,053 members of the Pension Fund (including 2 pensioners), divided as follows according to the investment line chosen:

- 2,477 members in the bond sub-fund
- 576 members in the balanced sub-fund.

Remote working

From September 1st, 2022, in order to allow workers to achieve a better work-life balance, the Hospital and the relevant Trade Unions have signed an agreement for the introduction of remote working on an experimental basis. With this agreement, remote working is no longer simply linked to the pandemic emergency but is now a fully regulated work tool. It is implemented on a voluntary basis and requires the signing of an individual agreement only for employees whose activities can be carried out remotely. The Hospital and the Trade Unions have agreed to extend the experimental phase of remote working until December 31st, 2025.

Parental leave

In 2024, the new provisions of the Budget Law were implemented, which provide for 80% pay for parental leave, effective from January 1st, 2024, provided that the compulsory maternity leave has ended after December 31st, 2023. This leave must be taken within the child's sixth year of life (or within six years of the child joining the family in the case of adoption or foster care) and the months paid at 80% are two for both parents and can be taken alternately between them or by only one of them.

Data for 2024 show that 246 employees took 5,352 days of parental leave, 225 of whom were women (4,988 days) and 21 were men (364 days). In addition, in 2024, 106 employees (97 women and 9 men) also took parental leave days paid at 80% of their salary (157 days for men and 4,142 days for women).

A total of 9,651 days of parental leave were therefore taken by 246 employees. There was an increase in the use of parental leave paid at 80%, justified by more favorable conditions in the percentage of compensation applied.

Personal protection

Over the last year, the Hospital has continued to develop its workplace health promotion activities, which are increasingly integrated with those required by current legislation for the assessment and management of specific risks and are aimed at preventing and reducing not only work-related diseases but also the much more numerous chronic degenerative diseases, which are the main causes of morbidity and mortality in the population.

The Hospital increasingly takes overall responsibility for workers, going beyond occupational risk, recognizing that workers do not only suffer from occupational diseases and that lifestyle factors or problems outside work often make them more vulnerable to traditional exposures. All this inevitably has negative effects on both the health of individual workers and the Hospital as a whole. Health promotion in the workplace must aim at well-being in the workplace, i.e. the ability of an organization to promote and maintain the highest level of physical, psychological, and social well-being of workers, with a series of variables related to the risks inherent in the work activity, including those of an organizational nature.

Since human capital is a fundamental asset of the Hospital, it is necessary to maintain a constant focus on workers as individuals called upon to cooperate in achieving the Hospital's objectives, through actions that take into account the specific characteristics and needs of the individual, in line with the needs of the organization, and that can have an impact on improving the internal social system, interpersonal relationships, and, more in general, the health of the organization. The wellness tree, conceived and implemented in our Hospital since 2011, fits into this context, with its three branches projected towards the three horizons of organizational well-being:

- the perspective of *Disability Management*, aimed at the assessment and redeployment of staff with limitations and/or disabilities, while simultaneously identifying proposals for improvement
- the perspective of *Psychological Wellbeing*, aimed at removing organizational constraints that cause discomfort, conflict and, in the long term, system inefficiency
- the *Workplace Health Promotion (WHP)* perspective, aimed at initiatives promoting healthy lifestyles and preventing cancer and chronic degenerative diseases, which are the main causes of staff disability and unsuitability.

The model continues to show positive effects on business performance indicators, such as work suitability, occupational diseases, and absenteeism rates. The Hospital's method, called POP (parametric - (h)olistic - profitable), builds on the compliance with all regulatory obligations and takes into account clinical, administrative, and economic indicators that investigate individual well-being in terms of personal and profes-

sional health, as well as the well-being of the organization. This method is now considered a best practice, and Bambino Gesù Children's Hospital has received funding from the national PNRR-PNC project of the Ministry of Health, to set up a national Total Worker Health network for the dissemination of good practices. Health surveillance and promotion initiatives are implemented by qualified personnel in compliance with the current legislation, i.e. competent doctors and authorized physicians registered with the Ministry of Health and the Ministry of Labor and Social Policies. Competent doctors establish, update, and maintain, under their own responsibility, a health and risk file, protecting professional secrecy, in compliance with the provisions of the Privacy Guarantor.

Health promotion activities, such as *Disability Management*, programs to combat smoking (*Stop Smoking* seminars) and sedentary lifestyles (training courses, *Back School at work* courses, stretching tutorials, sporting events), to promote healthy lifestyles (training courses, vaccinations, *Food Education* programs) and proper sleep hygiene (specific training courses and OSAS risk assessment - Obstructive Sleep Apnea Syndrome), for cardiovascular risk prevention (specific cardiovascular protocol for workers at risk) and cancer prevention (screening for workers at risk) and psychological distress prevention (help points, empowerment, yoga), increasingly aim at personalized prevention with clear positive effects from a clinical and health standpoint, as well as on the economic and management levels, with positive results across all indicators: absenteeism due to illness, accidents, occupational diseases, and work limitations.

In 2024, the update of the work-related stress risk assessment was completed, in compliance with INAIL guidelines, based on a preliminary objective assessment of sentinel events and organizational constraints, and on a subjective assessment through the administration of the HSE questionnaire to workers. The results confirm a medium-high level of risk in the Hospital, as is the case of all highly complex healthcare settings, characterized by shift work, strong emotional involvement, the possibility of aggression, and emergency management. The importance of psychosocial aspects in managing the Hospital environment and the health of individual workers, in close connection with the quality of care, is becoming increasingly evident.

The Hospital has maintained and developed further actions to prevent distress and protect mental health, as recommended by the WHO. The goal of providing psychological or psychiatric support to workers is particu-

larly important in the current social context, especially when the worker's psychiatric disease and/or mental disorder is associated with a significant emotional burden and complex care, which is typical of healthcare professions. To this end, the activities planned in the Help Point protocol have continued, as a multi-level pathway to support workers, particularly women, with distress issues (whether work-related or not) that could potentially interfere with their mental and physical health and with the performance of their work.

In 2024, 585 assessments were carried out and the final results showed positive effects in terms of absenteeism and improvement of health, in its dynamic sense of strengthening resilience and maintaining integrity, balance, and mental and physical well-being. In addition to the guidelines issued by Lazio Region, in 2024, the health protocol approved by the Italian Society of Occupational Medicine for healthcare workers exposed to stress was published, which provides for psychological assessment and support in the frame of health surveillance activities. The model adopted by OPBG (Help Point for psychological support integrated in the Health Surveillance system) complies with the guidelines issued by Lazio Region and the Italian Society of Occupational Medicine, and has been incorporated in the Health Surveillance protocol adopted.

Among the measures to promote health in the workplace, the Hospital invests heavily in vaccinations, particularly the flu vaccination, which are offered free of charge also to non-healthcare workers in order to improve the culture of prevention. In 2024, vaccination initiatives were further implemented, such as open-access clinics with no need to make an appointment, vaccination during health surveillance visits, mobile teams in wards and offices with dedicated staff, communication campaigns, and involvement of workers. These activities led to a coverage rate of 57% in our Hospital, which represents the best coverage in healthcare facilities in Lazio Region and one of the highest at the national level.

One of the most recent areas of worker health promotion is sleep hygiene and the prevention of related subjective disorders and/or related diseases. A BRIC (Collaborative research call) project is underway in collaboration with INAIL to promote sleep hygiene, raise awareness of the issue and of the symptoms and signs that may be indicative of related diseases, that may cause accidents at work. The return on investment (ROI) for health promotion activities is consistently high, ranging from 189% for *Stop Smoking* seminars, aimed at helping people quit smoking, to 2,766% for *Disability Management* activities.



Staff training, development, and enhancement

Training as a lever for development

In the section dedicated to staff enhancement and protection, the Hospital's Code of Ethics states: *"The enhancement of staff skills and competencies is of great strategic importance, and high professionalism is a value that must be preserved and increased over time, as it affects the effectiveness of clinical and care outcomes and the quality of scientific research results"*. The Hospital's ongoing investment in training represents a constant commitment to ensuring the continuous professional development of its staff, in line with the Hospital's mission.

At the end of 2023, the Single Training Committee (CUF - Comitato Unico Formazione), coordinated by the systematic supervision of the Committee of Directors, launched a joint effort between the Functions responsible for organizing training, to ensure the cross-cutting identification of training needs across all professions, greater integration between training initiatives, and the development of a training plan that meets the needs of all areas of the Hospital, pursuing innovation, effectiveness, and efficiency of related processes.

In line with these objectives, 2024 saw the dissemination of the training plan through internal communication channels via the OPBG catalog, designed to provide all staff with an intuitive and user-friendly tool, divided into training areas, allowing immediate access to all internal training opportunities. The areas covered are: Clinical, Healthcare, and Scientific; Health and Safety; Cross-cutting Training, with CME training opportunities offering the possibility of direct access to the external CME platform through buttons associated with the courses themselves, linking to the dedicated page of the website formazione.ospedalebambinogesu.it.

For non-CME initiatives, a description summarizes the main information about the course (objectives, target audience, duration, logistical information, etc.). There is also a section dedicated to "instructions for use" containing useful information for staff on how to participate in training, in compliance with the Hospital regulations.

In 2024, the CUF confirmed its commitment to making the regulations for accessing internal and external

training increasingly clear and transparent, identifying specialist and cross-cutting training needs through a dedicated form and focus groups, to ensure the updating of skills, innovation, quality, and safety in order to "provide even better care, expand scientific knowledge, and welcome every child and every family with the love and dedication they deserve" (T. Onesti, OPBG Internal Magazine no. 1).

Cross-cutting training

In 2024, in order to "take care" of the overall development of its professionals in terms of specialist skills, safety, and soft skills, the Hospital renewed its commitment to the actions set out in *the Gender Equity Plan* through awareness-raising and training initiatives. The training courses, launched in 2023, continued also in 2024, involving the Managers of the Complex Operating Units in a reflection on gender bias, as well as all professionals interested in a course focused on communication and leadership "beyond gender boundaries". The two courses provided are:

- **Bias Lab**, dedicated to Department Managers, online, aimed at initiating reflection on the influence of gender bias on employee development, while improving the knowledge of the unconscious dynamics that animate the Hospital culture.
- **Gender Reflections**, with voluntary participation in virtual meetings, giving everyone the opportunity to contribute their perspective and enhance different points of view and approaches, generating value in their work through authentic relationships. The initiative attracted considerable interest, and three additional editions have been organized to give everyone who is interested the opportunity to participate in the course.

In line with 2023, the pathway "Mi prendo cura di te" (I take care of you) has been confirmed, dedicated to pregnant women and their partners, and focused on infant nutrition. The series of meetings was designed by the Hospital specialists to answer the most common questions and concerns of parents on the first months of life of their child, providing useful and practical information to deal with the delicate and sensitive stages of breastfeeding and the first feeding of the newborn, offering a space for listening and discussion. 2024 also saw the launch of courses dedicated to the development of three cross-cutting skills of strate-

gic value for the Hospital: project-based work, effective communication and promotion of teamwork, and working groups management.

Three courses were organized divided into several training modules to ensure optimal time management and greater flexibility in learning, with an interactive teaching method to promote a progressive and experiential learning path, also facilitated by in-person delivery.

- **Project-based work**, a 1.5-day program, was designed to foster a culture of project-based work. This approach, through work planning and organizing, monitoring, analysis, and risk mitigation, allows people to perform at their best in teams, replacing "working on a urgent basis" with accurate action planning
- **Effective communication and teamwork**, a two-day program, aimed primarily at supporting participants in increasing awareness of their communication style, providing practical tools to foster the development of personal skills and acquire assertive communication methods, effectively manage conflicts, misunderstandings, and aggressive behavior among colleagues and, in the case of healthcare personnel, also with patients and their families
- **Working group management**, also a two-day program, dedicated to organizational unit managers, to provide participants with a "toolbox" to guide their collaborators in working by processes and objectives, fostering their accountability.

Continuing Medical Education

Bambino Gesù Children's Hospital was accredited according to the requirements and standards of the Accreditation Model (Resolution of the Regional Council of December 23rd, 2011, No. 52/9) as a Standard Provider on December 19th, 2013, with the designation OPBG_IRCCS 784. On February 4th, 2021, the *Standard Provider* accreditation was renewed for the first time.

The Hospital's initiative to set up its own CME course provider in 2013 demonstrates its focus on investing in the clinical, technical, and managerial skills and abilities of all healthcare professionals, as well as on protecting safety in the workplace.

The training provided is based on the assessment of needs and represents an easily accessible resource for OPBG professionals who are ethically required to undertake continuous learning considering the rapid changes occurring in technology, knowledge, and the organizations in which they operate. The 2024 CME Training Plan, included in the Hospital training catalog, provided 87 of the 96 events proposed (for a total of 205 editions), covering various topics, mainly related to:

- pediatrics and the territory with family associations
- laboratory and technology
- neuroscience and neurorehabilitation

- clinical practice and emergency care
- genetic diseases
- research, technology transfer, and therapy.

The Plan also includes events focusing on safety in the workplace and communication in its various relational and organizational aspects. The types of training provided are RES (residential training) and FSC ("formazione sul campo", i.e. on-the-job training).

In 2024, two distance learning courses were completed:

- "Batti il 5" (High-five) - Good hand hygiene practices; with 38,605 participants who earned CME credits;
- "Safety in the hospital setting: risk management, prevention, and protection"; with 34,560 participants who earned CME credits.

Three distance learning courses were launched:

- "Understanding and treating chronic pain in pediatrics";
- "Safety in the hospital setting: risk management, prevention, and protection";
- "The Safety Manager in the healthcare sector" (Art. 37, paragraph 7 of L. D. 81/2008 - State-Regions Agreement 12/21/2011 - State-Regions Agreement 07/07/2016).

The quality of the CME events provided is monitored through event evaluation based on a satisfaction questionnaire and on the UNI EN ISO 9001:2015 quality system, which guarantees adequate organizational management based on ISO policies and related procedures, as well as a focus on continuous improvement of the quality of training. The Provider 784 OPBG-IRCCS is also ISO 9001:2015 certified.

The CME Scientific Committee

The CME Scientific Committee of Bambino Gesù Children's Hospital:

- examines and evaluates proposals regarding topics and events to be included in the annual CME Training Plan;
- assesses the clinical, technical, and scientific skills and the andragogical skills of the training events included in the annual CME Training Plan;
- is responsible for the scientific validation of the annual CME Training Plan and of individual projects not included in the Plan;
- monitors the scientific quality of events.

Residential Event (RES)

This is the most common type of CME training event. It includes conferences, congresses, seminars, workshops, symposiums, round tables, and plenary sessions. Only public and private CME providers, universities, CNR, IRCCSs, scientific foundations, professional associations, scientific societies, private companies and agencies can deliver CME events. The provider

must have a Scientific Committee with expertise in the topics that will be covered in the events.

On-the-job training (FCS)

On-the-job training (FCS) is a training activity characterized by the environment where it takes place and the type of learning. FCS is characterized by the fact that:

- the setting in which the training is provided corresponds to the participant's work environment
- this type of training simulates activities and behaviors to be implemented in the performance of work/professional activities
- it must create a close collaboration between the learner and the teacher/tutor.

Distance Learning (DL)

Distance Learning (DL) is a type of CME training in which activities are carried out by learners located in places other than those where the teacher/trainer operates, allowing the learner to be reached wherever they are. It uses web technologies to improve learning and educational exchange.

Training of healthcare professionals

In the clinical and healthcare training program, particular attention is paid to newly hired staff, in order to support their integration according to the Hospital's quality standards and to provide training in cardiopulmonary resuscitation.

In 2024, the orientation and induction program for new healthcare professionals has been enhanced, as required by *Joint Commission International* quality standards, with two new training courses dedicated to Social Health Workers and new staff from third-party companies. Furthermore, the implementation of the MOODLE platform has made it possible to certify the training of new medical, nursing, and healthcare professionals who participate in mandatory asynchronous online training courses.

In 2024, as required by the indicators of the plan for the improvement of the quality of care and by the indicators of the Pain Management Committee, on-the-job training was provided in the inpatient Operating Units and Emergency Department, as well as in synchronous online mode, focused on the correct approach to pain therapy. On-the-job training on pain reassessment after the administration of pain therapy will begin in 2025.

This training led to the improvement of the indicators assigned to the Operating Units. In addition, as required by JCI standards, five new asynchronous online courses have been launched on the MOODLE platform to verify the training and skills acquired by nursing staff in the use of POCT (Point of Care Testing) equipment in the Operating Units. All nurses involved took part in the training and obtained the certification.

In 2024, cardiopulmonary resuscitation training was provided to 1,424 healthcare professionals through 125 courses, 101 of which were held at facility of Viale di Villa Pamphili and 24 at Palidoro facility (Seminar Room), with 89% participation rate of those registered. The two new simulation classrooms of Viale di Villa Pamphili are equipped with the necessary technological and IT tools and simulation materials, which are available to teachers and participants.

Training for the prevention of occupational risks

Throughout the year, the Hospital continued to pursue its commitment to a robust, participatory, and future-oriented culture of safety, investing in human capital as a key factor for a safer and more efficient workplace. A structured training program was developed, ensuring that employees have the necessary skills to prevent and manage risk factors in the workplace. This commitment translates into learning paths that integrate updated regulations, roles of responsibility, prevention and protection strategies, behavioral best practices, and advanced use of personal and collective safety equipment.

Health and safety training is divided into mandatory courses as indicated below:

- **for the Occupational Safety Area:**
 - general training on risk and prevention, dedicated to all workers, delivered as a distance learning course (DL), ensuring accessibility and flexibility
 - in-person training on specific risks, both basic and refresher courses, for a theoretical yet practical and interactive approach
 - training for Safety Managers and Supervisors, who play key roles in the occupational safety chain (Article 2 of L. D. 81/08).

One of the most significant innovations of 2024 was the introduction of a course for Safety Managers designed entirely in-house and customized for the healthcare setting. This program, which is also open to external personnel, replaced the previous e-learning course provided by external suppliers, leveraging the Hospital's internal expertise to offer a tailored and effective training experience, always in compliance with the current regulations.

On-the-job training courses were also organized focusing on specific needs, including procedures for the management of hospital emergencies; the safe use of electrosurgical knives; behavioral rules and emergency management in the operating room; safety in the workplace and contractors; emergency response team procedures; prevention and protection in the use of lasers.

- **For the Fire Safety and Emergency Management Area,** a significant number of courses were organized for fire-fighting staff, including basic courses, which are preparatory to the appointment of Emer-

gency Management Officers, as well as refresher courses, in compliance with timelines established by the law. As usual, the courses were taught by the Fire Department, with which the Hospital has been working for years to ensure the highest level of professionalism.

Furthermore, in 2024, as in the previous year, the following questionnaires were prepared:

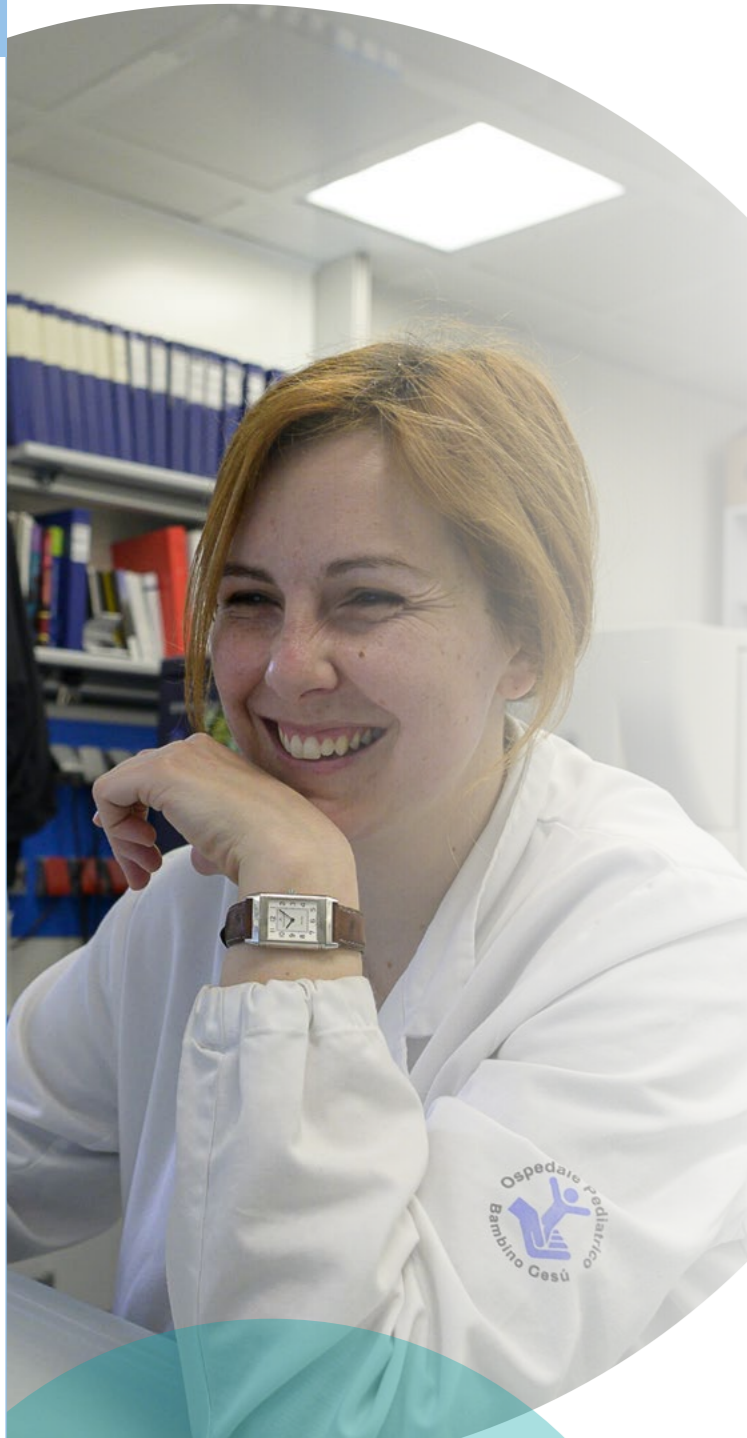
- the Fire Safety Questionnaire (available on the platform between June and September) to assess knowledge of safety measures in the event of fire
- the Aggression Risk Questionnaire (active from the

last two months of the previous year until March 2024), aimed at raising awareness among staff on the procedures to be adopted in the event of aggression, as described in the dedicated protocol.

Teaching materials and interactive tutorials were provided for both questionnaires. Overall, the safety training program generated a significant volume of activity during the year, through classroom events, on-the-job training, and distance learning courses. nell'anno il programma di formazione sulla sicurezza ha generato un volume di attività significativo, attraverso eventi in aula, formazione *on-the-job* e percorsi *e-learning*.



Health and safety in the workplace



Safety and risk management

The safety and health of people are one of the values of the Hospital's Code of Ethics and are strategic for the actions taken to manage related risks, to protect not only workers but patients and third parties as well.

In this context, a health and safety system has been established which - considering the size and complex structure of OPBG - is centered on the Delegate of Functions and the Delegates of Specific Functions, who support the Employer in ensuring adequate technical supervision of all areas requiring attention, and on other relevant professionals, namely:

- the Prevention and Protection Service Manager and the Radiation Protection Expert, who coordinate, in collaboration with the Delegate of Functions and Delegates of Specific Functions, all activities necessary to the assessment of the Employer's risks, also proposing improvement actions and related information and training programs and, more generally, providing specialist advice for the correct implementation of the structure defined by the management
- the Competent Doctor and Authorized Coordinating Doctor who, with the collaboration of the Competent Doctors and Authorized Doctors and with the involvement of the Delegate of Functions, support the Employer in the risk assessment process and carry out health surveillance in compliance with applicable regulations, based on health protocols defined according to specific risks.

At the operational level, the President, in his role as the Employer, the Delegate of Functions, and the Del-

egates of Specific Functions rely on the technical support of Managers and Supervisors who are in charge of implementing the specific actions identified, including monitoring, in accordance with the risk assessment and related directives issued by the Employer and aforementioned Delegates. The Emergency Management Officers and First Aid Officers also play key operational roles. The contribution of the Workers' Representatives and the direct and proactive involvement of all staff are also essential to the overall effectiveness of the Health and Safety System.

With regard to risk assessment in particular, the Company Risk Assessment Documents, drawn up in compliance with L. D. 81/08, as well as the specific risk assessments developed pursuant to L. D. 101/2020, play a significant role for all hospital and non-hospital facilities, as they outline the results of the analysis and the improvement actions to be planned and implemented in the Hospital.

Risk analysis is carried out with specific methodological tools and complex activities, including:

- periodic inspections by the FMS_JCI (Facility Management and Safety) group, which is the multidisciplinary Hospital team set up in accordance with the facility safety standards required by Joint Commission International accreditation
- periodic inspections carried out independently by the PPS (Prevention and Protection Service) team in all work environments
- reports on various health and safety issues submitted by workers and/or their representatives
- preparation of technical advisory opinions on issues falling within its competence, requested ad hoc by the Hospital Departments (on the safety of environments and substances, fire prevention, the choice of PPE and/or CPE, etc.)
- in-depth analysis by multidisciplinary teams of accidents, near misses, and aggressions, which allow to orient effectively the health and safety improvement process.

All this is carried out by collecting information through structured checklists, measurement campaigns, and the application of risk-specific assessment standards based on technical regulations and guidelines that define best practice in the field.

In addition to these activities, information and training are provided not only in the classroom and in distance mode, but also on-the-job, enabling workers to play an active role in the safety protection process through awareness of the risks associated with their activities and work environments, but also through direct reporting of any dangerous situations. Furthermore, emergency management includes the development of Emergency and Evacuation Plans and related tests for specific procedures, as well as subsequent debriefings.

In recent years, Emergency and Evacuation Plans have been progressively integrated with increasingly spe-

cific procedures on the management of risks arising from human factors (handling suspicious mail, terrorist phone calls, parcel bombs) and fire management on patients in the operating wards, in NORA procedures and wherever equipment with potential to start a fire (such as lasers, electrosurgical knives, etc.) is used. In order to test the effectiveness of these specific procedures, emergency and evacuation drills have been enhanced with ad hoc simulations that have made it possible to check the clinical times required to secure patients and evacuate them. Staff involvement in emergency management is also ensured through the annual administration of a fire safety questionnaire with notes to assist in its completion. In 2024, the questionnaire was completed by 3,349 users with OPBG credentials (including 2,609 OPBG employees).

Great attention to safety, to protect all those who access the Hospital, is also given in the contracts and agreements entered into by the Hospital through the development of Single Interference Risk Assessment Documents and the promotion of safety coordination activities with third parties. Furthermore, particular attention has also been paid to research, by defining ad hoc clauses to be mentioned in specific agreements, by increasing the number of Supervisors (appropriately designated and trained) to better ensure the correct implementation of the safety measures identified, and by training new researchers by means of a dedicated video that, thanks to the way it is produced and used, will allow to reach out to new staff quickly and promptly upon onboarding.

The activities of the multidisciplinary Working Group for the Management of Aggression Risk, established in the last four months of 2022, also continued. The group meets quarterly with the aim of integrating what has already been implemented concerning the psychological support for staff who are victims of acts of violence.

The Working Group, which includes Worker Safety Representatives to ensure worker representation, also updates the Violence Prevention Program (VPP), which brings together the measures (technical, organizational, procedural, and educational) identified for the deterrence, prevention, and containment of potential damage.

These measures have been identified thanks to the in-depth analysis of the reports submitted by a dedicated subgroup (Operational Team) which examines each event reported according to the assessment methodology adopted. The measures provided for in VPP are monitored on a quarterly basis by the Working Group and may be supplemented based on further investigations into new cases.

Of note for 2024, is the thorough analysis carried out by dedicated sub-groups, leading to the identification of a series of measures (which will be implemented in 2025) aimed at tackling the phenomenon of aggression, including the prompt activation of surveillance

via dedicated buttons, the implementation of a tool to alert healthcare staff in the event of the admission of users who have already been involved in acts of aggression against staff, and the assessment of measures to be implemented to enhance active and passive access control systems.

Also, specific studies have been launched on gender differences and harassment in the workplace. To ensure the involvement of all staff in the management of the risk of aggression, a dedicated questionnaire and explanatory notes have been made available on the Hospital Intranet since 2024, building on the experience in fire prevention. The questionnaire allows for the involvement of all staff and, more generally, of all those who, even if not employed, are in possession of OPBG credentials (e.g., freelancers, researchers, residents, etc.) on a specific topic.

Finally, the questionnaires are also sent in paper format to the main suppliers and voluntary associations through internal contact persons for contracts/agreements. The availability of specific detailed material provides respondents with dedicated tools to update their knowledge on the subject. During 2024, the aggression questionnaire was completed by 2,220 users.

Regarding assaults recorded at OPBG, in 2024 there were 75 reports of verbal and physical aggression, none of which resulted in injury. The number increased slightly compared to the previous year (70 in 2023). Among the reports submitted in 2024, two cases of harassment were also reported, while physical aggression decreased (11 in 2024 compared to 18 in 2023), while verbal aggression increased (52 in 2023 and 62 in 2024).

Particularly significant events requiring further investigation (due to their extent and potential damage) remained constant in the period 2023-2024 (16 cases in 2023 and 16 cases in 2024, plus the 2 cases of harassment). Consequently, it can be said that the severity of the events recorded remained substantially constant in 2024 compared to the previous year.

As to the victims of aggression, the category most affected was nurses (56%, same as in 2023), followed by doctors (21%, with a 10% decrease compared to 2023). Women are more exposed to the phenomenon than men (83% in 2024 compared to 75% in 2023). As regards the distribution of reports by shift, in the two-year period 2023-2024, there was a constant trend in aggressive incidents occurring during the morning shift, while there was an increase in incidents reported during the afternoon shift (from 24% in 2023 to 31% in 2024), with a consequent reduction in evening incidents (from 19% in 2023 to 12% in 2024).

Concerning the reporting of dangerous situations (near misses/adverse events) encountered by workers (including reports of verbal and physical aggression), it is worth mentioning the structured procedure implemented by the Clinical Risk Committee, in which the

PPS is involved in the analysis of adverse events that could have an impact on the safety of workers and, in general, of those who access OPBG facilities. Another channel is represented by direct reports from workers. All events/reports are analyzed in the same way as accidents, according to a methodology compliant with the provisions of ISO 45001.

The overall state of the art is illustrated and examined on an annual basis during the periodic safety meeting, pursuant to Article 35 of L. D. 81/08, which is attended by the Employer, Delegates, Managers, Worker Safety Representatives (WSR), Prevention and Protection Service Manager (PPSM) and Prevention and Protection Service Officer (PPSO), Competent and Authorized Doctors, Radiation Protection Expert, and Expert in Charge.

Health prevention in the workplace

Disease prevention is guaranteed through primary, secondary, and tertiary prevention measures implemented by the Occupational Medicine Department.

In 2024, over 22,000 services were provided, including medical examinations, instrumental and laboratory tests, vaccinations, discussions, specialist consultations, work-capacity assessments, information counseling, contact tracing, and epidemiological investigations. This regulatory obligation is monitored through effectiveness indicators, such as the number of occupational diseases in the last five years (0.97/1,000 workers) and accidents involving biological risk (34 in total), the percentage of work-capacity limitations (4.03%) and days of sick leaves (8.03/worker/year).

The Hospital figures were better than the benchmarks, in particular: the number of occupational diseases was 50% lower than the national INAIL data; work capacity limitations were 82% lower than the national figure and stable compared to the Hospital figures for 2023; the days of sick leave were significantly lower than the national figures (-36.3%).

The main preventive health activities of the Occupational Medicine Department were:

- 1,100 personalized risk assessments, carried out through visits, interviews, and inspections in the workplace with the implementation of effective preventive measures
- 583 coordination, discussion, and sharing meetings on activities, cases, and actions in working groups such as the Disability Management and Help Point Management groups, for the assessment of work-related stress risk, as well as the risk identified in the climate survey
- 21 in-depth analyses in the Operating Units based on reports of aggression against staff
- identification and organization of the Hospital first aid measures (Art. 45 of L. D. 81/08, M. D. 388/03)
- counseling activities (via company email address

and 24-hour telephone availability) and 165 hours of teaching in training courses on health, safety, and medical radiation protection (Art. 25 of L. D. 81/08, Art. 162 of L. D. 101/20)

- participation in the Healthcare-Associated Infections Committee (CICA), the Perceived Quality Committee, the Clinical Risk Committee (CRC) and the *FMS_JCI* group
- coordination, planning, and implementation of vaccination plans for workers pursuant to Art. 279 of L. D. 81/08 (1,551 COVID-19, flu, measles-rubella-mumps-chickenpox, and HBV vaccinations)
- health follow-up following 34 accidents involving biological risk
- contact tracing and monitoring of cases of contagious infectious diseases (96 tracings);
- 88 in-depth assessments of reports of verbal and physical aggression, with psychological support and analysis of possible improvement measures.

As part of the activities of coordination and consultation of the Hospital Departments and of communication on occupational health and safety, the following actions have been taken: *FMS tours* in the workplace, classroom training, on-the-job training, publication of Occupational Medicine content, procedures, instructions and tips on the Intranet, confidential and secure access to health and laboratory data relating to the worker personal state of health, coordination meetings with Managers, participation in the periodic meeting, participation in the Hospital group for aggression management and in the Working Group for the assessment and management of work-related stress.

Workplace accidents

In 2024, the accident rate for employees remained unchanged compared to 2023 (67 in 2024 and 67 in 2023), excluding accidents due to Covid-19 infection and those occurring while commuting. Compared to 2023, accidents with a prognosis of ≤ 3 days decreased slightly, with the main cause being biological (36 in 2024 and 38 in 2023), while the number of accidents with a prognosis of > 3 days, with the main cause being mechanical, increased very slightly (31 in 2024 compared to 29 in 2023). In 2024, 3 accidents had an overall prognosis of more than 60 days, although in both cases the initial prognosis was < 30 days. Furthermore, 10 accidents had a prognosis between 30 and 59 days, all with an initial prognosis < 30 days.

The distribution of injuries by cause shows that 51% of cases involved biological hazards (splashes of biological fluids, needlestick, etc.) and the remaining 49% were due to an accident (accidental falls, tripping or slipping, contact with chemicals, lifting/moving heavy loads, collisions and crushing, contact with sharp objects without biological fluids, falling objects).



Environmental protection

115,275 GJ
PURCHASED ELECTRICITY
(-4% COMPARED TO 2023)

~ 500
LED LIGHTS
REPLACED IN 2024

-20%
FUEL CONSUMPTION
FOR TRANSPORT COMPARED
TO 2023

+10%
INCREASE IN SCOPE 1 AND SCOPE
2 EMISSION INTENSITY COMPARED
TO 2023

226 ML
WATER CONSUMPTION
(-3% COMPARED TO 2023)

1,195 t
WASTE PRODUCTION
(+7% COMPARED TO 2023)

-1%
GASOLINE CONSUMPTION
COMPARED TO 2023

3,880,000 kWh
OF SELF-PRODUCED
ELECTRICITY
(+24% COMPARED TO 2023)



Ensure availability and sustainable management of water and sanitation for all



Ensure access to affordable, reliable, sustainable and modern energy for all

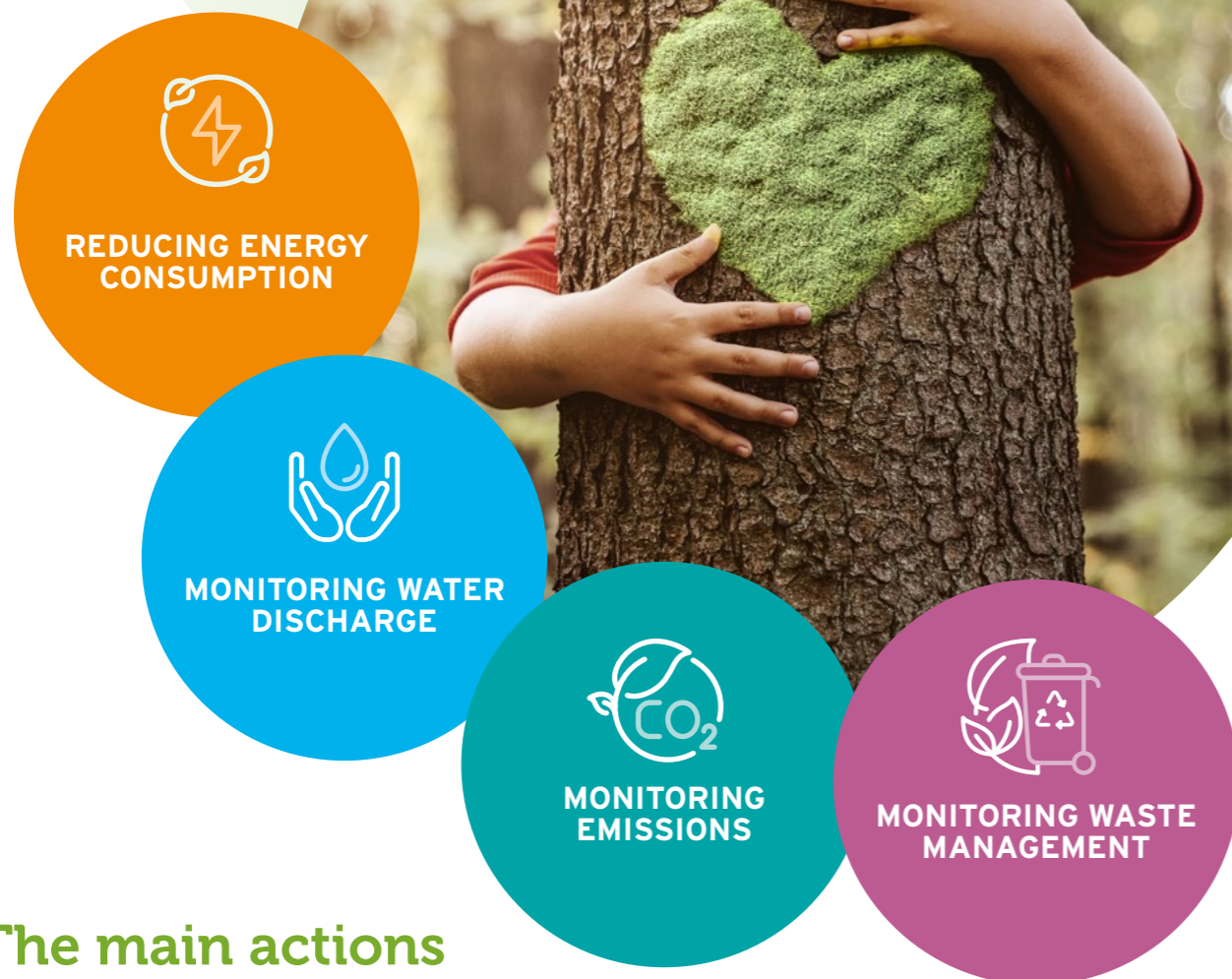


Ensure sustainable consumption and production patterns



Environmental impact management and energy efficiency

Bambino Gesù Children's Hospital considers environmental protection to be a fundamental value, and the relevant Departments are committed to consolidating actions aimed at environmental compatibility and sustainability.



The main actions implemented in 2024

Energy consumption

In 2024, the Hospital total energy consumption was 269,346 gigajoules (GJ), with an increase by 2.63% compared to 2023 (262,963 GJ) and by 8.34% compared to 2022 (249,090 GJ). This gradual increase is mainly due to the new facilities becoming fully operational, in particular the Microbiology Laboratories in Viale F. Baldelli facility, the opening of the offices on the 4th floor of the same building, and the full operation of the Pediatric Palliative Care Center in Passoscuro.

Methane gas consumption, used mainly for heating, increased by 7.44% in 2024 compared to 2023, from 3,225,435 m³ to 3,465,275 m³. This increase, which follows that already recorded in 2023 (+12.80% compared to 2022), reflects the increase in electricity/thermal and cooling energy self-produced with cogenerators and the trigeneration system at the facility of San Paolo Fuori Le Mura, where consumption growth is concentrated. As regards gasoline used for heating, there was a steady decrease in consumption: -1.34% in 2024 compared to 2023, and -4.03% in 2023 compared to 2022.

Regarding purchased electricity, there was a 4% decrease in 2024 compared to 2023, from 33,184,034 kWh to 32,020,766 kWh. This is particularly significant considering the expansion of activities, and it demonstrates the effectiveness of the energy efficiency policies implemented, in particular the replacement of light fixtures with LED technology, as well as the optimization of air conditioning systems (replacement of refrigeration units at Piazza Sant'Onofrio, Palidoro, and Santa Marinella facilities with newer and more efficient units).

As already mentioned, an extremely positive figure is the 23.69% increase in self-produced electricity, which rose from 3,136,770 kWh in 2023 to 3,880,000 kWh in 2024. In the global economic context, characterized by a partial stabilization of energy prices compared to the peaks of 2022-2023, the Hospital could benefit from relatively lower energy costs in 2024, despite the increase in consumption in absolute terms. Furthermore, in 2024, Scope 1 emissions were 8,563 tons of CO_{2eq} (+6% compared to 2023), while Scope 2 (location-based) emissions were 11,030 tons of CO_{2eq} (+11% compared to 2023). This rise is related to the increase in energy consumption due to the new Hospital facilities becoming fully operational.

Energy system efficiency

During 2024, light fixtures using traditional technology (fluorescent, halogen, or incandescent) were gradually replaced with LED technology for the lighting systems at the facility of Piazza Sant'Onofrio, where approximately 500 LED elements, both light fixtures and individual lamps, were installed in common areas and wards. The total installed power with LED technology was approximately 11 kW, corresponding to 33 kW in the classic version. Thus, the actual installed power

was reduced by 66%. Furthermore, the Hospital has completed the Energy Diagnosis Report for the facilities of Piazza Sant'Onofrio, San Paolo Fuori Le Mura, Viale F. Baldelli, Viale di Villa Pamphili, the Pediatric Palliative Care Center in Passoscuro, and Santa Marinella. The Energy Diagnosis Report is mandatory for energy-intensive companies (L. D. No. 102/2014), but it is an innovative analysis for a Hospital like OPBG, which comprises several facilities that are very different from each other, both in terms of structure and geographical location.

It is a technical document that provides an in-depth analysis of the energy consumption profile of the facilities involved, highlighting possible saving opportunities, emission reduction, and technical and economic feasibility. The Energy Diagnosis Report, completed in 2024, identified the energy model of the buildings examined and identified numerous efficiency measures with the relevant payback period aimed at reducing energy expenditure and CO₂ and greenhouse gas emissions, thus establishing guidelines for future energy and environmental investments. The main opportunities for improvement identified include the optimization of gas consumption, the replacement of light fixtures with LEDs and of refrigeration units, and a new HVAC control system.

The analysis showed that OPBG has high electricity and heat consumption throughout the year, with electricity accounting for 71% of primary energy consumption. The adoption of the proposed measures could significantly reduce energy costs. The Hospital is currently reviewing the proposals suggested in the Energy Diagnosis Report, identifying priorities for action based on technical and economic feasibility, return on investment, and the significant energy and economic saving that can be achieved in the long term. In addition to the study, a report was also produced analyzing greenhouse gas (GHG) emissions from activities carried out at the Hospital facilities. The report was drawn up in compliance with the UNI EN ISO 14064 standard for direct emissions (Scope 1) and indirect emissions from imported energy (Scope 2).

An Energy Diagnosis study has also started for Palidoro facility, which is expected to be completed by the end of 2025, aimed at a major energy efficiency improvement program through the decommissioning of old gasoline-fueled plants and their replacement with more efficient and less polluting systems, such as the conversion of thermal power plants to methane, the construction of a trigeneration plant and the installation of photovoltaic systems.

Water consumption

Water is drawn from the public water supply system and is used for human consumption, washing (sanitary facilities, toilets), dishwashing, technological processes (filling technical, thermal, and refrigeration systems, steam production), and hospital processes (softening, demineralization, reverse osmosis, etc.).

2) For details on greenhouse gas emissions, please refer to the section "Tables of Indicators".

In 2024, the water consumption of the Hospital was 226 megaliters, with a decrease by 3.42% compared to 2023 (234 megaliters), but still 12.44% higher than in 2022 (201 megaliters). The reduction compared to 2023 is very significant considering the full operation of the new facilities, which demonstrates the effectiveness of awareness-raising policies on the responsible use of water.

Although higher than in 2022, 2024 data must be contextualized, considering the expansion of Hospital activities, in particular the opening of the Microbiology Laboratories at Viale F. Baldelli facility, and the full operation of the Pediatric Palliative Care Center in Passoscuro. All water used is taken from public water supply system, in areas of water stress. There is no wastewater treatment system, and wastewater is discharged directly into the public sewer system. The only exceptions are wastewater from Nuclear Medicine and wastewater coming from Laboratories processes, which are treated and disposed of by specialized third companies.

Waste management

Waste from the healthcare sector is an extremely complex element of environmental sustainability. An efficient collection system not only protects health, safety, and the environment, but also reduces costs, as the procedures for disposing of specific categories of waste are expensive: the smaller the quantities subjected to complex disposal operations, the lower the management costs. In this context, the Hospital places great emphasis on adequate training of staff for the correct disposal of all waste produced, in particular healthcare waste associated with biological, chemical, and radioactive risks. The waste produced in 2024 amounted to approximately 1,195 tons, increasing by 7% compared to 2023.

As to the distinction between hazardous and non-hazardous waste, the former accounts for 92.5% of the total, in line with the specific characteristics of the healthcare sector. Compared to 2023, data for the reporting period show a slight increase in hazardous waste (+7.4%) and a decrease in non-hazardous waste (-1.4%). Finally, 405 tons of special waste were sent for recycling or recovery during the year; 79% of them were hazardous waste and the remaining 21% non-hazardous waste.

Radioactive waste management

The Hospital has a system for storing all radioactive waste produced by patients undergoing treatment or diagnostic tests in the Nuclear Medicine (NM) Department. Radioactive waste produced by patients undergoing nuclear medicine examinations or treatments is collected in dedicated tanks (3 tanks for therapy with a total capacity of 15,000 liters and 2 tanks for diagnostics with a total capacity of 14,000 liters). The plant is equipped with a spectrometric measurement system with scintillation detector technology using Lanthanum Bromide ($\text{LaBr}_3:\text{Ce}$) crystals to ensure that the

patient excreta are released into the sewage system in full compliance with current regulations. The system operates continuously to prevent uncontrolled contamination within the Hospital and in the surrounding environment.

To this end, the Health Physics Department measures the concentration of activity when the stored waste is discharged into the municipal sewage system, in compliance with the limits established by current legislation. The correct functioning of the system is ensured by periodic routine maintenance, weekly monitoring of tank levels by Health Physics Department staff, and remote technical support. An automatic system calling the Hospital staff (active 24 hours a day, 7 days a week), that can promptly intervene both remotely and, if necessary, on-site, ensures more accurate monitoring and rapid response to any risk situations that may arise due to malfunctioning of the storage system for radioactive waste produced by patients in the Nuclear Medicine Department.

The Hospital implements specific procedures for the environmental impact of radioactive waste produced in order to separate the most contaminated waste from the weakly contaminated waste. The former is sent to a third company that collects and stores it safely in dedicated areas. In 2024, 175 barrels of radioactive waste were delivered, for a total of 4.3 tons of waste. For the rest, removal as treated hospital waste or as waste comparable to municipal waste is subject to verification by medical physicists of the absence of residual radioactivity. During 2024, 243 units of treated hospital waste from patients undergoing nuclear medical investigations or treatments, as well as 267 units of municipal waste were disposed of.

High-level solid and liquid radioactive waste produced by diagnostic and therapeutic activities is confined in special containers and delivered to a company authorized to transport and dispose of it. This waste is temporarily stored in the Operating Units and then handled by dedicated personnel. Waste collection is carried out by professionals who are adequately trained in correct waste management and rationalization, also to reduce the volume of waste produced as much as possible.

Containers of infectious hospital waste and solid waste comparable to municipal waste (from Operating Units where patients who have undergone nuclear medicine diagnostic tests or treatments are hospitalized) that may contain traces of residual radioactivity (low-level waste) are identified and recorded individually. Removal is subject to radiometric verification by the Health Physics staff.

Waste management requires to take all necessary measures to prevent any contamination of the environment. To this end, the Hospital is equipped with three fixed radiometric portals allowing to identify any contaminated waste before it leaves the Hospital. The portals are installed at the facilities of Piazza Sant'Onofrio and Palidoro.



Environmental protection initiatives

Implementation of eco-friendly technological solutions

When acquiring new equipment and upgrading existing technology, particular attention is paid during the evaluation phase to their environmental impact, i.e. reducing electricity and cryogenic gas consumption, minimizing the use of gases and fluids, reducing waste and wastewater, using low-GWP refrigerant gases, etc.).

This objective is pursued through structural initiatives, as well as individual targeted measures. The following actions have been implemented:

- where appropriate, compliance with specific environmental sustainability standards has been introduced in the technical requirements for selection procedures for the acquisition of biomedical technologies
- regarding the ecological effects of waste disposal, in the preliminary technical evaluation for purchase, preference is given to equipment that complies with the EU RoHS (Restriction of Hazardous Substances) Directive restricting the use of certain hazardous substances in electrical and electronic equipment
- when defining the configurations of biomedical technology systems involving local printing, preference is given to the possibility of connecting to existing network printers in order to reduce energy and toner consumption, as well as paper consumption
- in the technological renewal process, where possible, a virtuous process is initiated to verify the possibility of recovering decommissioned equipment, to avoid scrapping, either reusing it in other healthcare facilities or sending it to maintenance companies for the recovery of spare parts
- the renewal of the washer disinfectors installed at OPBG has started, with the purchase of equipment designed for greater energy saving without compromising cycle performance, ensuring respect for the environment with various solutions for thermal and acoustic protection, drainage, and ventilation.

Regarding cold chain technologies (biological refrigerators, blood bank refrigerators, laboratory freezers), two actions have been taken: on the one hand, during the evaluation phase, preference is given to systems that not only use refrigerant gases compliant with current regulations but also reduce heat dissipation into the environment, thus further reducing overall costs; on the other hand, attention has been paid to knowing the details of the equipment already installed and an inspection has been planned to verify, in particular, the type and quantity of refrigerant gas used and any requirements arising from current legislation. Ioni derivanti dalla normativa vigente in materia.

Dematerialization of paper documents

In 2024, the Hospital continued its activities for paper document dematerialization, extending the process to the radiation protection documentation of exposed workers (dosimetry records, radiation protection registers, training certificates, certificates of suitability issued by an authorized physician, risk assessment forms). The migration from paper to digital format also involved the exchange of documents between the units of the Hospital, to track the movements of professionals exposed to ionizing radiation in all phases, from their first access to the Hospital to the end of their work activity. All information concerning the movements of workers of interest to the Radiation Protection Expert is currently available through the Hospital SAP management system, thus achieving the additional objective of ensuring that the data can be consulted by all the units concerned.

Another area in which the complete dematerialization of documentation continued concerns safety standards at the Hospital magnetic resonance imaging sites, as indicated by the Ministry of Health in Ministerial Decree of 01/14/2021. This documentation includes the technical attachments to the installation notification, the outcomes of periodic safety checks, safety regulations, the list of authorized personnel, and the quality controls of MRI scanners.

Sustainable Mobility

Building on the work carried out in recent years and in line with the objectives set out in the *Decreto Rilancio* (Legislative Decree 34/2020), thanks to the synergy between the Hospital Mobility Manager and the Area Mobility Manager, the Hospital has been promoting sustainable mobility focusing on reducing the impact of its employees' commute on the environment.

Attention to the environment, by supporting sustainable mobility, is a fundamental contribution to reducing greenhouse gas emissions and ensuring a more sustainable future.

As to the operational, managerial, and cultural measures aimed at protecting the environment that the Hospital is implementing, the third edition of the Com-

mute Plan has been developed, based on the experience of the previous editions and focused on a series of new measures to be adopted, including:

- the development of an application for carpooling among colleagues
- seeking agreements with railway companies
- gradual replacement of the Hospital vehicles with vehicles with a lower environmental impact, depending on their use
- promoting transition to electric mobility
- an information and awareness-raising campaign aimed at all staff and focused on sustainable mobility
- direct link between the Hospital platform and platforms for travel monitoring and planning
- request to the competent authorities for additional local public transport.

Eco-Clean – Ecolabel Project

In 2024, an agreement was reached with the Municipality of Fiumicino to install two electromechanical composters at the Palidoro facility, for the management of solid urban waste and cellulose packaging. The new machines will make waste disposal more efficient, improving management of the area currently used for sorting waste.

09

Economic sustainability and financial independence

220

GRANTS ACTIVE IN 2024

Funded with 82.5 €/M

6.7 €/M

COLLECTED BY THE HOSPITAL THROUGH FONDAZIONE BAMBINO GESÙ PHILANTHROPIC INSTITUTION



Promote sustained, inclusive and sustainable economic growth, full and productive employment and decent work for all



Ensure sustainable consumption and production patterns



Promote peaceful and inclusive societies for sustainable development, provide access to justice for all and build effective, accountable and inclusive institutions at all levels

Value creation and economic and financial sustainability

Funding sources

The Hospital receives funding related to healthcare services provided in accordance with Law No. 187 of May 18th, 1995, which regulates its relations with the National Health Service and to which all the proceedings of the Permanent Conference for Relations between the State, the Regions and the Autonomous Provinces of Trento and Bolzano, as well as the Decrees of the Commissioners ad Acta are related, defining the current tariff system.

The Hospital also receives an annual contribution from the Italian State based on the unique nature of the facility within the national and international healthcare system and the recognized specific and innovative characteristics of the care provided, as provided for by Law No. 102 of August 3rd, 2009.

Funding sources for research activities

As a result of its research activities related to its recognition as a Scientific Institute for Hospitalization and Care, Bambino Gesù Children's Hospital receives:

- funding from the Ministry of Health for Current Research, allocated annually based on the assessment of three-year programs carried out from a scientific and financial point of view, also taking into account the annual verification of the quality of scientific production, the care provided, and the degree of translation of research activities to care activities
- funding for research provided by the Ministry of Health, other Ministries, the European Commission, national and international public bodies, and private entities based on calls for proposals or specific projects (Targeted Research)
- funding related to the allocation of the "five per thousand" of the Italian taxpayers' income tax to health research
- funding from private donations, including fundraising activities, as well as bequests
- funding from pharmaceutical companies for the sponsorship of clinical studies, in particular on new drugs and innovative therapies.

Breakdown of research funding

In 2024, the total value of new funding obtained to support research amounted to € 25.9 million, of which € 16.3 million came from external sources and € 9.6 million from 5x1000 funds and Current Research funds. (Figure 8 - Research funding - Historical data 2017-2024). These funds supported the launch of 188 new projects.

Most of this new funding comes from competitive grants awarded to the Hospital researchers for their participation in specific calls for proposals issued by public and private, national and international bodies; accounting for over € 11.6 million, including PNRR and PNC funds and IRCCS networks, this represents 45% of total research funding. In addition, donations were received by the Hospital from Fondazione Bambino Gesù Philanthropic Institution, sponsored clinical trials, and direct funding for which procurement activities were carried out by the researchers (Figure 9 - Breakdown by type of funding in 2024).

The competitive grants support a total of 42 research projects and come mainly from the Ministry of Health, Fondazione AIRC for Cancer Research, the European Commission, and other national and international bodies, associations, and foundations, including Fondazione Umberto Veronesi, Fondazione Telethon, Fondazione Fibrosi Cistica, and Cystinosis Research Foundation (Figure 10 - Breakdown of competitive grants by institution. Year 2024).

Competitive grants are the main source of funding for research, even when considering all projects active in 2024, including those launched previously. 220 grants were activated, supported by a total funding of € 82.5 million, of which € 38.8 million came from PNRR and PNC funds. The main funding bodies are the Ministry of Health and the Ministry of University and Research, the European Commission, Fondazione AIRC, Fondazione Veronesi and other national and international public and private bodies (Figure 11 - Active funding. Year 2024).

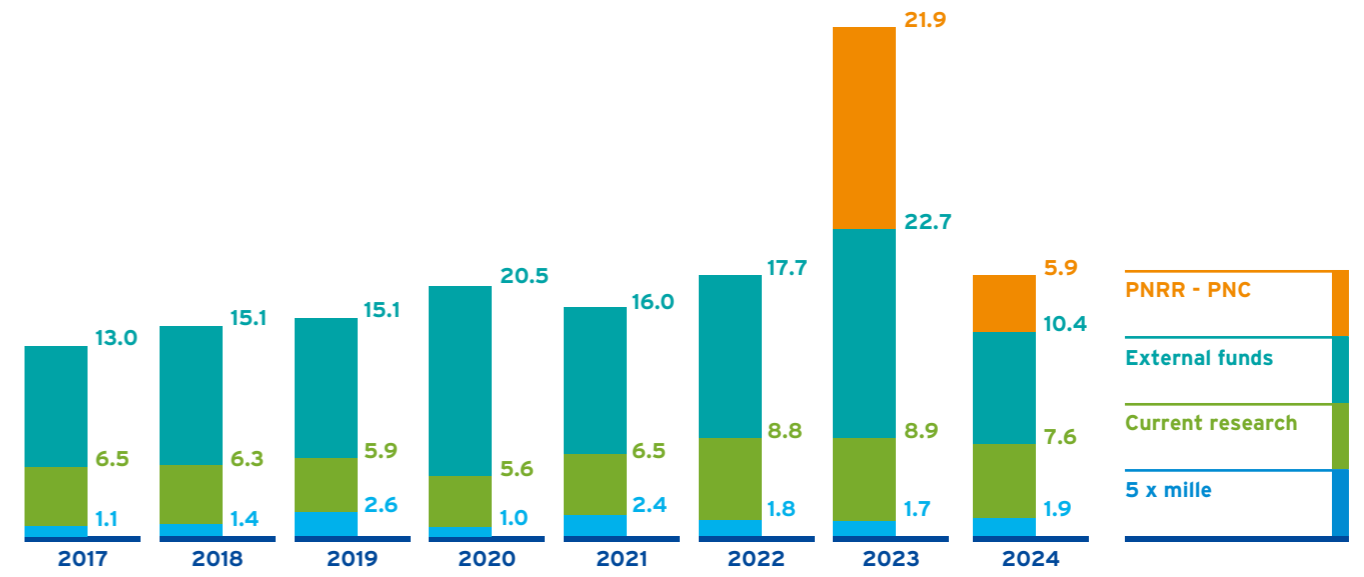


Figure 8. Research funding - Historical data 2017-2024.

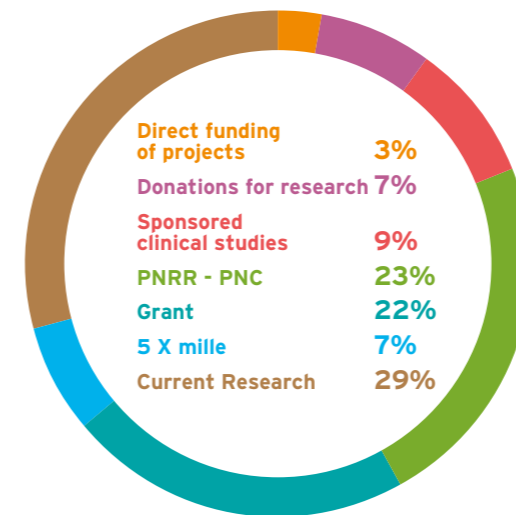


Figure 9. Breakdown by type of funding. Year 2024.

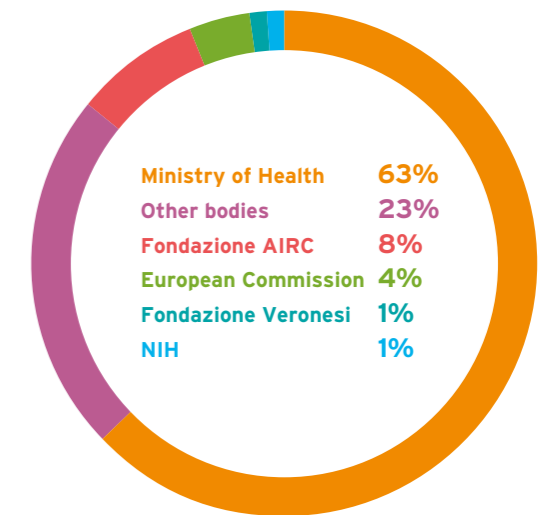


Figure 10. Breakdown of competitive grants by institution. Year 2024

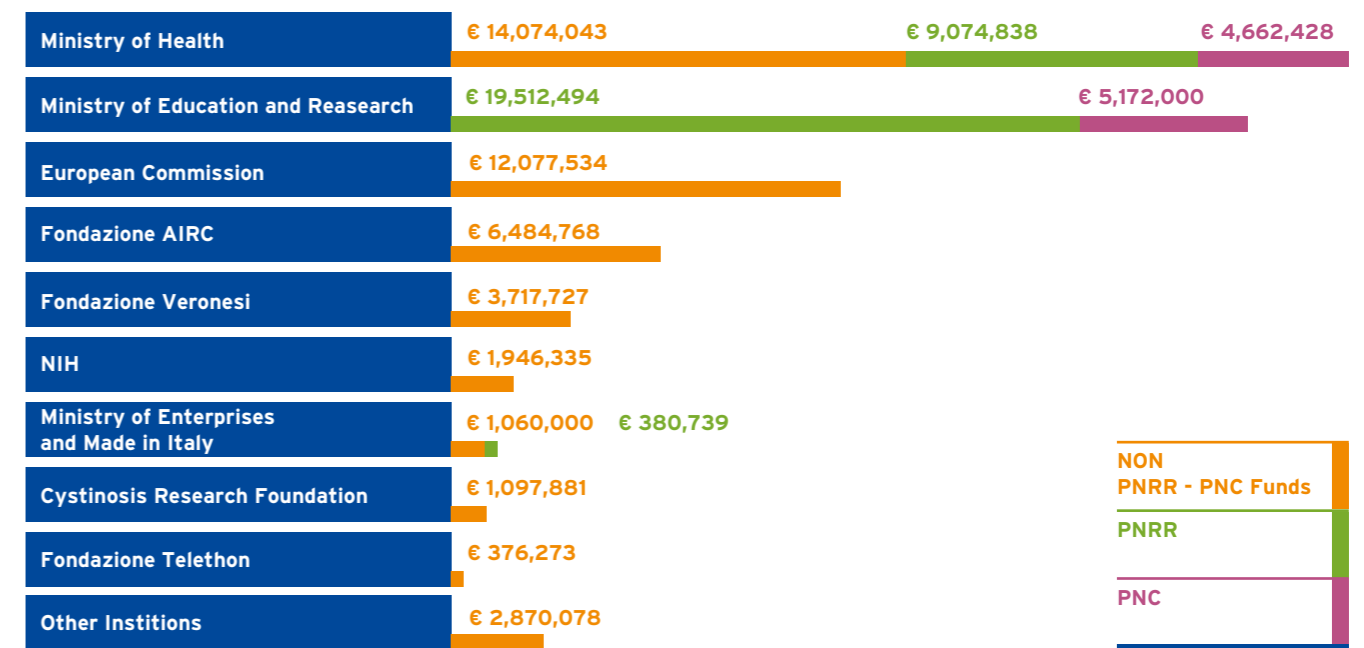


Figure 11. Active funding. Year 2024.

Fundraising for Bambino Gesù Children's Hospital

During 2024, the Hospital's healthcare and scientific activities continued to be supported by donations received through fundraising initiatives promoted mainly by Fondazione Bambino Gesù Philanthropic Institution. In accordance with the accrual principle, donations received from Fondazione Bambino Gesù Philanthropic Institution, totaling € 6.7 million, were

recorded under revenues, of which: (i) € 1.0 million for the Hospital clinical and research activities; (ii) € 1.8 million for healthcare provided to foreign patients who are disadvantaged due to their physical, mental, economic, and social conditions; (iii) € 2.9 million for the Pediatric Palliative Care Center in Passoscuro; (iv) € 0.2 million for humanitarian care; (v) € 0.8 million for other purposes (special projects, purchase of equipment, support to international activities, etc.).

Sustainable supply chain management

Suppliers are one of the Hospital's main stakeholders, as they provide medical resources, technologies, and services necessary to ensure the quality and continuity of care and research activities.

The selection and evaluation process for suppliers, contractors, and consultants is supported by the establishment of a register of suppliers and is carried out in accordance with the applicable procedures in the Vatican context, according to criteria that guarantee the cost-effectiveness of the goods and services purchased, sustainability, quality of service, safety and environmental protection, legal compliance, fairness, and transparency, as well as monitoring.

As part of supply chain management, the Hospital has initiated a process aimed at reorganizing the supply chain and logistics model for consumables, medicines, and medical devices. The new model, named *One Logistic*, allows, through the aggregation of purchasing processes and the pursuit of a balance between cost-effectiveness, efficiency, and effectiveness, to rationalize the levels of products stored in the central warehouse and in the ward warehouses, leading to an optimization of the use of resources (economic, human, and material), throughout the logistics chain in terms of efficiency and effectiveness, with a subsequent reduction in waste. The model implemented is based on the principle of outsourcing, where the management and handling of medicines has been entrusted to an external provider with proven experience in the sector and adequate technological/structural equipment.

Specifically, the new model will allow for potential saving in terms of effectiveness and efficiency of the entire logistics chain, leading to:

- optimization of stock levels in the central warehouse and ward warehouses
- improved traceability and tracking of the products managed
- enhanced synergies between different logistic activities
- optimization of space and resources
- reduced involvement of clinical staff in logistic activities
- rationalization of transport and internal and external handling costs
- optimization of product delivery times to the Operating Units.

Promotion of corporate social responsibility: verification and qualification of economic operators in the supply chain

As part of an increasingly structured commitment to sustainability, Bambino Gesù Children's Hospital has expanded the scope of its assessment activities to include a growing number of economic operators. This initiative is part of an ongoing process aimed at strengthening a procurement model based on principles of ethics and sustainability, promoting collaboration with partners who share and promote values of fairness, transparency, and responsibility. Through this activity, the Hospital aims to promote a health-care ecosystem based on solid values and sustainable development strategies, thus contributing to generate a positive impact throughout the supply chain.

10

Technology and digital transition

14,672

ELECTROMEDICAL EQUIPMENT AND ACCESSORIES

365

TECHNICAL EXPERT OPINIONS FOR THE PURCHASE OF ELECTROMEDICAL EQUIPMENT

5 PB

STORAGE MANAGED

116

IT SECURITY ASSESSMENTS

530

SERVERS MANAGED

35

NEW DEVELOPMENT PROJECTS COMPLETED

250

NETWORK DEVICES



Build resilient infrastructure, promote inclusive and sustainable industrialization and foster innovation

Technological innovations and digitalization

Biomedical technologies

Biomedical technologies are an essential resource for the provision of appropriate high-quality healthcare services and for research excellence. Over the last decade, the Hospital biomedical technology assets have more than doubled (in terms of number and value), reaching over 14,672 items at the end of 2024, including equipment and accessories installed at the different OPBG facilities.

The biomedical technology procurement process is supported by technical assessment, aimed at identifying the best solutions resulting from technological innovation, combined with clinical and economic assessment carried out by other Hospital functions. During 2024, 365 Technical Expert Opinions were issued for the purchase of biomedical technologies, to expand the healthcare services provided, as well as to replace existing equipment that was obsolete and could no longer be maintained.

The main projects developed by the Hospital during 2024 include:

- the evaluation of technological solutions for the setting up of new PNRR laboratories for the creation of a National Center for RNA Therapy and Gene Therapy
- the technological renewal and expansion of the *CoreLab* automation used by the Analysis Laboratory in Piazza Sant'Onofrio and the implementation of new analysis lines at the facility of Viale F. Baldelli, following the winning of the tender
- the technological renewal, reorganization, and rationalization of the equipment used at the *Lactarium* at Piazza Sant'Onofrio facility
- the computerization of the processes of the Ophthalmology COU at the facilities of Palidoro and Santa Marinella, integrated with the Hospital IT system, document repository, and radiology PACS
- the integration of the Digestive Endoscopy IT system with the traceability system for heat-sensitive endoscopes
- the replacement of heart-lung pumps in the Cardiac Surgery Unit
- replacement of all dental units installed at the Odontostomatology Department in Viale Baldelli with the introduction of innovative solutions to improve hygiene in dental procedures (elimination of the

water unit/basin) and multimedia systems to reduce stress in young patients and encourage their cooperation

- the technological renewal, reorganization, and rationalization of operating tables in all operating wards of OPBG facilities.

During the year, a preliminary analysis of needs was also carried out for the most significant development projects planned, including the expansion of the Pediatric Palliative Care Center in Passoscuro, the expansion of the Emergency Department, and the activation of the new Heart Failure, Transplant, and Cardio-Respiratory Mechanical Assistance Unit. In addition, project management activities were carried out for the renovation of the Dialysis and Nuclear Medicine Units, aimed at the improvement of the overall care processes provided by the two units, also with the installation of a PET/CT scanner.

The digitalization process

The quality of care and scientific research offered by Bambino Gesù Children's Hospital is also ensured by a constant commitment to improving and updating the IT technology available. Every year, new initiatives are launched to:

- upgrade or replace the software
- renew and upgrade the hardware, from data centers to communication infrastructure and PCs
- digitalize new workflows.

In particular, since the Hospital's high level of specialization in the healthcare and scientific fields benefits greatly from the availability of customized data and software, OPBG develops some of its own applications in-house. Among the digitalization initiatives for 2024 are:

- introduction of electronic informed consent in the first Complex Operating Units, thanks to the technology developed partly in-house, which will be rolled out to the rest of the Hospital in the coming years
- integration of a new order entry system for Transfusion Medicine compliant with ISBT 128 identification standard
- monitoring of service levels provided by IT technology suppliers.

As part of the renewal of the software already in use, the following projects were completed in 2024:

- in-house development and implementation of a new application for managing the activities of the Microbiomics SOU
- in-house development and release of new software for reporting rehabilitation services
- adaptation of the OPBG IT system to meet the new outpatient nomenclature of Lazio Region
- integration of outpatient schedules into the regional CUP (Central Appointment Service).

Several other internal software development initiatives were carried out in 2024, which will be completed in 2025, including:

- an application to manage the admission of international patients
- setting up of a new Intranet
- new software for setting objectives and evaluating staff
- digitalization of accident reports.

Our partners have also expressed interest in other projects that will continue in 2025:

- update of the electronic medical records for hospital stays and intensive care stays, for future integration with the Electronic Health Record 2.0
- digitization of milk preparation and enteral nutrition processes for the Neonatal Nutrition Education and BLUD SOU
- new software for the Odontostomatology COU.

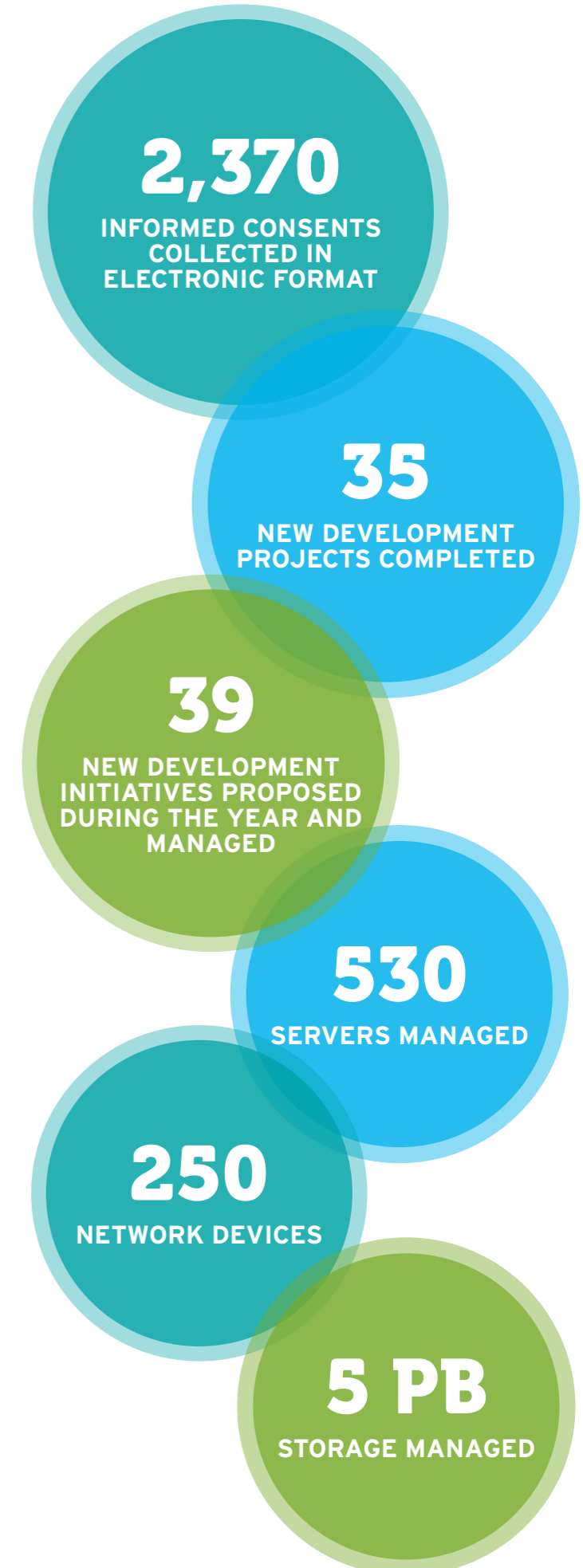
Since 2024, OPBG IT infrastructure has:

- new data storage resources
- more modern and high-performance Wi-Fi connection
- enhanced server resources based on container technology.

The next challenges

OPBG will update the network connectivity between different facilities and within the facilities themselves, releasing new software for the operating room activities and the new outpatient medical record. The process of renewing applications developed some time ago in-house and insourcing some software currently provided by third parties will also continue.

Main results



Privacy and Data Security

The right to personal data protection: continuous improvement process

During 2024, the Hospital continued to invest in training on the processing of personal data, ensuring that healthcare and administrative staff are constantly trained, in compliance with current legislation. Specific training activities were provided to resources involved in scientific research. This ongoing commitment shows the Hospital commitment to promoting responsible and compliant data management, reducing risks and ensuring transparency, also through the continuous updating and monitoring of information notices (pursuant to Articles 13 and 14 of EU Regulation 2016/679) and consent forms provided to data subjects.

At the same time, the internal audit program has been expanded to assess the effectiveness of the control measures in place, identifying possible areas of concern and opportunities for improvement. The audits, according to the principle of combined assurance, were carried out in an integrated manner with the Internal Audit Service. This approach made it possible to optimize the activities of the teams involved, while respecting their areas of expertise and independence. This method also improved the efficiency of operations, both for the structures subject to audit and for the auditors, thus ensuring optimal use of time and resources.

Furthermore, support continued to be provided to all organizational units in the review of contracts and agreements relating to the processing of personal data, as well as for the activities carried out by Fondazione Bambino Gesù Philanthropic Institution, also in terms of privacy by design and by default.

Data Security measures

In 2022, the Hospital launched a program to review its IT security measures, which is currently implementing the activities planned after an initial assessment. In this context, the results for 2024 include the implementation of a new system to manage the digital identities of OPBG staff, based on new software and new methods of collaboration between the IT Services and the Human Resources Functions. Also in 2024, a contract was signed for the supply of a software system for system administrator access control, with release scheduled for 2025. A process was also launched to assess the security, reliability, and sustainability of migration to the cloud of specific areas of the Hospital IT system. A total of 116 IT security assessments were carried out for the introduction of new services and technologies in the Hospital. The use of digital signature among OPBG doctors increased as well.



11

Attachments



Tables of indicators

TOTAL NUMBER OF EMPLOYEES BY CONTRACT TYPE, GENDER AND REGION										
Location	Contract type	2024			2023			2022		
		Men	Women	Total	Men	Women	Total	Men	Women	Total
Italy	Permanent	859	2,175	3,034	845	2,143	2,988	831	2,067	2,898
	Fixed-term	8	31	39	10	13	23	5	10	15
Total		867	2,206	3,073	855	2,156	3,011	836	2,077	2,913

Table 8. Total number of employees by contract type, gender, and region.

TOTAL NUMBER OF EMPLOYEES BY CONTRACT TYPE, GENDER AND REGION										
Location	Contract type	2024			2023			2022		
		Men	Women	Total	Men	Women	Total	Men	Women	Total
Italy	Full-time	864	2,170	3,034	853	2,116	2,969	831	2,067	2,898
	Part-time	3	36	39	2	40	42	5	10	15
Total		867	2,206	3,073	855	2,156	3,011	836	2,077	2,913

Table 9. Total number of employees by contract type, gender, and region.

NUMBER OF WORKERS WHO ARE NOT EMPLOYEES BY PROFESSIONAL CATEGORY AND GENDER										
Professional category	2024			2023			2022			
	Men	Women	Total	Men	Women	Total	Men	Women	Total	
Medical and non-medical Health Managers (University)	11	6	17	13	6	19	11	6	17	
Contracted religious personnel	4	9	13	4	10	14	5	9	14	
Collaborators	76	136	212	76	149	225	85	147	232	
Other (eg. coordinated continuous collaboration)	36	1	37	45	1	46	63	2	65	
Total	127	152	279	138	166	304	164	164	328	

Table 10. Number of workers who are not employees by professional category and gender.

EMPLOYEES COVERED BY COLLECTIVE BARGAINING AGREEMENTS			
Number of employees	2024	2023	2022
Number of employees with collective bargaining agreements	3,042	2,977	2,880
Total number of employees	3,073	3,011	2,913
Total percentage	99%	99%	99%

Table 11. Employees covered by collective bargaining agreements.

ENERGY CONSUMPTION WITHIN THE ORGANIZATION IN GJ ¹			
Energy consumption	2024	2023	2022
Natural gas (methane)	118,807	110,594	98,051
Gasoline	18,492	18,744	19,527
Electricity (purchased)	115,275	119,463	118,049
Electricity (self-generated)	13,968	11,292	10,456
<i>of which from renewable sources²</i>	29	28	30
Gasoline for generators	119	94	276
LPG Kitchen Consumption	864	921	879
Fuel (motor vehicles)	32	40	44
Diesel (motor vehicles)	1,790	1,816	1,809
Total	269,346	262,963	249,090

Table 12. Energy consumption within the organization in GJ. Years 2022-2024.

1) The source of the conversion factors in GJ is the "National Standard Parameters Table 2024 - Ministry of the Environment".

2) Following a malfunction in the energy measurement system of the Palidoro photovoltaic plant, only for 2024, the energy produced from renewable sources was obtained by estimating the average value for the years 2021, 2022, and 2023.

ENERGY INTENSITY			
	2024	2023	2022
Total energy consumption	269,346	262,963	249,090
Total services (length of stay, number of DH and DH rehabilitation visits, number of Emergency Room visits and number of outpatient services net of laboratories and genetics)	993,194	994,734	999,956
Total energy intensity	0.271	0.264	0.249

Table 13. Energy intensity. Years 2022-2024

WATER WITHDRAWAL IN MEGALITERS ¹						
Water withdrawal	2024		2023		2022	
	All areas	Water stressed areas	All areas	Water stressed areas	All areas	Water stressed areas
Third-party water (total)	226	226	234	234	201	201
Fresh water (≤ 1000 mg/L total dissolved solids)	226	226	234	234	201	201

Table 14. Water withdrawal in megaliters. Years 2022-2024.

1) All the Hospital facilities are classified by the Aqueduct Tool, developed by the World Resources Institute to identify potentially at-risk areas, in the category of very high water stress, i.e. "extreme scarcity".

EMISSIONS INTO THE ATMOSPHERE			
	2024	2023	2022
SCOPE 1 - CO₂ EMISSIONS [t CO₂]¹			
Natural gas	6,996	6,464	5,693
LPG	57.99	60.76	103.64
Gasoline	1,375.70	1,392	1,743
Fule - motor vehicles	2	3	4
Diesel - motor vehicles	132	134	158
Total	8,563	8,053	7,703
SCOPE 2 MARKET BASED - CO₂ EMISSIONS [t CO₂]²			
Purchased electricity - Italy	17,946	16,595	16,309
SCOPE 2 LOCATION BASED - CO₂ EMISSIONS [t CO₂]²			
Purchased electricity - Italy	11,030	9,730	9,274

Table 15. Emissions. Years 2022-2024

1) The source of the emission factors used to calculate Scope 1 emissions is the "National Parameters Standard Table 2024 - Ministry of the Environment".

2) The "Location-based" approach involves the use of average emission factors for specific national electricity generation mixes. The emission factor used for the Location calculation is sourced from ISPRA - Atmospheric Greenhouse Gas Emission Factors in the National Electricity Sector and in the Main European Countries. The "Market-based" approach involves the use of emission factors defined on a contractual basis with the electricity supplier. The emission factor used for the Market-based calculation is sourced from AIB - European Residual Mixes 2024.

GHG EMISSIONS INTENSITY (SCOPE 1 + SCOPE 2 LOCATION BASED)			
U.o.m. t CO ₂ eq	2024	2023	2022
GHG emissions (Scope 1 + Scope 2 Location based)	19,593	17,784	16,976
Total services (length of stay, number of DH and DH rehabilitation visits, number of emergency room visits and number of outpatient services net of laboratories and genetics)	993,194	994,734	999,956
GHG emissions intensity	0.0197	0.0179	0.0170

Table 16. GHG emissions intensity (Scope 1 + Scope 2 Location based). Years 2022-2024.

TOTAL WEIGHT OF WASTE GENERATED IN TONS			
Waste type	2024	2023	2022
Hazardous special waste	1,110.55	1,029.90	1,004.07
<i>of which radioactive waste</i>	4.38	1.87	1.10
<i>of which sent for recycling/recovery</i>	311.14	83.11	134.14
<i>of which directed to disposal</i>	795.04	944.92	868.83
Non-hazardous special waste	88.95	90.22	91.47
<i>of which sent for recycling/recovery</i>	56.89	36.79	25.63
<i>of which toner and/or printer cartridges sent for recycling</i>	3.08	1.93	1.67
<i>of which sent for paper recycling</i>	28.72	51.20	60.87
<i>of which directed to disposal</i>	0.26	0.30	3.30
Total	1,199.50	1,120.12	1,095.54

Table 17. Total weight of waste generated in tons. Years 2022-2024.

NEW SUPPLIERS THAT WERE SCREENED USING ENVIRONMENTAL CRITERIA			
	2024	2023	2022
New suppliers assessed based on environmental criteria	1	1	0
Total new suppliers	143	239	204
Total Percentage	0.7%	0.4%	0.0%

Table 18. New suppliers that were screened using environmental criteria.

NEW EMPLOYEES HIRES AND EMPLOYEE TURNOVER								
2024								
Entries	<30 years		30-50 years		>50 years		Total	
	Number	%	Number	%	Number	%	Number	%
Men	9	36%	29	5%	6	2%	44	5%
Women	28	25%	104	8%	3	0%	135	6%
Total	37	27%	133	7%	9	1%	179	6%
Exits	Number	%	Number	%	Number	%	Number	%
Men	0	0%	9	2%	24	8%	33	4%
Women	3	3%	15	1%	66	8%	84	4%
Total	3	2%	24	1%	90	8%	117	4%
2023								
Entries	<30 years		30-50 years		>50 years		Total	
	Number	%	Number	%	Number	%	Number	%
Men	7	29%	43	8%	3	1%	53	6%
Women	56	44%	83	7%	3	0%	142	7%
Total	63	41%	126	7%	6	1%	195	6%
Exits	Number	%	Number	%	Number	%	Number	%
Men	0	0%	4	1%	29	10%	33	4%
Women	0	0%	9	1%	55	7%	64	3%
Total	0	0%	13	1%	84	8%	97	3%
2022								
Entries	<30 years		30-50 years		>50 years		Total	
	Number	%	Number	%	Number	%	Number	%
Men	18	67%	55	11%	8	3%	81	10%
Women	62	61%	108	9%	4	1%	174	8%
Total	80	63%	163	10%	12	1%	255	9%
Exits	Number	%	Number	%	Number	%	Number	%
Men	1	4%	9	2%	27	9%	37	4%
Women	0	0%	14	1%	56	7%	70	3%
Total	1	4%	23	1%	83	8%	107	4%

Table 19. New employee hires and employee turnover. Years 2022-2024.

PARENTAL LEAVE ¹					
2024				Trend	
Number of people	Men	Women	Total	% M	% W
Total number of employees entitled to parental leave	52	293	345	15%	85%
Total number of employees who took parental leave	21	225	246	9%	91%
<i>of whom on 31 December 2024</i>					
Number of employees still on leave	3	20	23	14%	9%
Total number of employees who returned to work during the reporting period after taking parental leave	18	205	223	86%	91%
<i>of whom still employed by the organization in the 12 months following their return</i>	20	220	240	95%	98%
<i>of whom no longer employed by the organization</i>	1	5	6	5%	2%
Employee retention rate	N.D	N.D	N.D		
Return to work rate	100%	100%	100%		

Table 20. Parental leave.

1) Information relating to parental leave are reported for the first time, therefore data relating to the two-year period 2023/2022 are not available.

WORK-RELATED INJURIES						
Number of injuries	2024		2023		2022	
	Emp.	Collab.	Emp.	Collab.	Emp.	Collab.
Total number of deaths due to recordable work-related injuries	0	0	0	0	0	0
Total number of serious work-related injuries (excluding fatalities) among employees ¹	3	0	6	0	1	0
Number of recordable work-related injuries among employed workers ²	67	26	67	15	48	5
Rate of deaths due to work-related accidents	0%	-	0%	-	0%	-
Recordable work-related injury rate³	11.78%	-	12.28%	-	9.10%	-
Rate of serious work-related injuries (excluding fatalities)	0.53%	-	1.10%	-	0.19%	-

Table 21. Work-related injuries. Years 2022-2024.

1) Work-related accidents that resulted in injury from which the worker cannot recover, does not recover, or cannot realistically expect a full recovery and return to their pre-accident state of health within 6 months. In accordance with Italian law, injuries with a prognosis of more than 60 days are considered serious.

2) Commuting accidents are included only when transportation was organized by the Hospital.

3) The injury rate was calculated as the ratio between the total number of injuries and the total hours worked by employees (5,688,336 hours), using a multiplication factor of 1,000,000. It was not possible to calculate the accident rate for collaborators because OPBG has not implemented a monitoring system for the hours worked by external collaborators.

WORK-RELATED ILL HEALTH						
Number of injuries	2024		2023		2022	
	Emp.	Collab.	Emp.	Collab.	Emp.	Collab.
Total number of recordable cases of occupational disease	3	0	3	1	0	0
<i>including cases of death caused by occupational diseases</i>	0	0	0	0	0	0

Table 22. Work-related ill health. Years 2022-2024.

AVERAGE HOURS OF TRAINING PER YEAR PER EMPLOYEE									
Professional category	2024			2023			2022		
	Men	Women	Total	Men	Women	Total	Men	Women	Total
Medical and non-medical Health Managers	17.8	36.8	30.8	30.3	23.0	25.4	22.4	23.4	23.0
Administrative Managers	2.3	4.8	3.0	22.5	27.6	23.8	32.8	44.0	35.2
Healthcare Area	23.0	20.6	21.1	17.4	15.7	16.0	18.5	17.5	17.7
Non-healthcare Area	7.0	5.6	6.2	9.1	6.1	7.3	12.2	10.5	11.2
Total	16.7	23.0	21.2	19.7	16.3	17.2	18.6	18.1	18.2

Table 23. Average hours of training per year per employee.

DIVERSITY OF GOVERNANCE BODIES AND EMPLOYEES. BOARD OF DIRECTORS													
2024													
Professional Category	<30				30-50				>50				Total
	Men	% M	Women	% W	Men	% M	Women	% W	Men	% M	Women	% W	
Board of Directors	0	0%	0	0%	0	0%	0	0%	6	67%	3	33%	9
2023													
Professional Category	<30				30-50				>50				Total
	Men	% M	Women	% W	Men	% M	Women	% W	Men	% M	Women	% W	
Board of Directors	0	0%	0	0%	0	0%	0	0%	4	44%	5	56%	9
2022													
Professional Category	<30				30-50				>50				Total
	Men	% M	Women	% W	Men	% M	Women	% W	Men	% M	Women	% W	
Board of Directors	0	0%	0	0%	0	0%	0	0%	4	44%	5	56%	9
DIVERSITÀ NEGLI ORGANI DI GOVERNO E DEI DIPENDENTI													
2024													
Professional Category	<30				30-50				>50				Total
	Men	% M	Women	% W	Men	% M	Women	% W	Men	% M	Women	% W	
Medical and non-medical Health Managers	3	0%	2	0%	173	19%	441	49%	112	12%	177	19%	908
Administrative Managers	0	0%	0	0%	2	6%	1	3%	20	65%	8	26%	31
Healthcare Area	14	1%	106	7%	259	16%	715	44%	68	4%	451	28%	1,613
Non-healthcare Area	8	2%	5	1%	108	21%	149	29%	100	19%	151	29%	521
Total employees	25	1%	113	4%	542	18%	1,306	42%	300	10%	787	26%	3,073
2023													
Professional Category	<30				30-50				>50				Total
	Men	% M	Women	% W	Men	% M	Women	% W	Men	% M	Women	% W	
Medical and non-medical Health Managers	1	0%	1	0%	167	20%	402	47%	114	13%	168	20%	853
Administrative Managers	0	0%	0	0%	6	18%	2	6%	19	56%	7	21%	34
Healthcare Area	16	1%	123	8%	249	16%	675	42%	64	4%	470	29%	1,597
Non-healthcare Area	7	1%	4	1%	118	22%	149	28%	94	18%	155	29%	527
Total employees	24	1%	128	4%	540	18%	1,228	41%	291	10%	800	27%	3,011
2022													
Categoria Professionale	<30				30-50				>50				Totale
	Uomini	% U	Donne	% D	Uomini	% U	Donne	% D	Uomini	% U	Donne	% D	
Medical and non-medical Health Managers	0	0%	0	0%	153	19%	377	46%	124	15%	165	20%	819
Administrative Managers	0	0%	0	0%	6	18%	1	3%	20	61%	6	18%	33
Healthcare Area	22	1%	97	6%	235	15%	652	42%	63	4%	471	31%	1,540
Non-healthcare Area	5	1%	4	1%	120	23%	157	30%	88	17%	147	28%	521
Total employees	27	1%	101	3%	514	18%	1,187	41%	295	10%	789	27%	2,913

Table 24. Diversity of governance bodies and employees. Years 2022-2023.

SUBSTANTIATED COMPLAINTS CONCERNING BREACHES OF CUSTOMER PRIVACY AND LOSSES OF CUSTOMER DATA			
	2024	2023	2022
Total number of substantiated complaints submitted regarding breaches of customer privacy	0	0	3
of which received from external parties and confirmed by the organization	0	0	1
of which received from regulatory bodies	0	0	0
Total number of customer data leaks, theft, or loss	0	0	3

Table 25. Substantiated complaints concerning breaches of customer privacy and losses of customer data. Years 2022-2024.



**Scientific
research
and
clinical care
activities
2024**



01

Research Areas

The Research Areas are areas of the organizational structure that report directly to the Scientific Director for the scientific coordination of research units or complex groups of research projects with homogeneous content, with a view to consolidating research paths aimed at integration with healthcare and training activities.

The objectives and main results achieved by the four Research Areas, Functions and Research Units reporting directly to the Scientific Director on December 31, 2024, are listed below.

Molecular Genetics and Functional Genomics Research Function

Coordinator

Marco Tartaglia

Activities

The Function aims to improve knowledge of simple heritable diseases, identify new clinical conditions, understand their molecular basis, pathogenic mechanisms, and natural history, and to develop new diagnostic tools and disease models with the goal of achieving results for immediate clinical translation. The activity focuses primarily on rare and orphan diseases and uses new “omics” technologies to identify new disease genes, in silico analytical approaches, as well as *in vitro* and *in vivo* model systems to understand pathogenic mechanisms and identify new therapeutic targets

Results achieved

In the reference year, the Function achieved the following results:

- the projects coordinated by the Function have identified new diagnostic tools for rare and orphan diseases, showing the value of applying new omics technologies to healthcare and research. Of particular importance is the use of genome methylation profiling to improve the interpretation of variants of uncertain clinical significance
- the activity allowed for the identification of seven new disease genes, the clinical characterization of new nosological entities, the understanding of the molecular mechanisms implicated in the pathogenesis of several pediatric-onset neurodevelopmental and neurodegenerative diseases, and the generation of new disease models
- the results achieved by the working group have been the subject of 48 scientific publications.

Objectives

The Function aims to:

- understand the molecular basis of rare and orphan diseases
- characterize the pathogenic mechanisms and the natural history of the disease
- generate new model systems for the study of rare diseases
- Implement bioinformatics pipelines for the analysis of genomic data
- develop new analytical tools based on machine learning
- develop experimental *in vitro* and *in vivo* approaches for the classification of genomic variants of uncertain significance that can be applied on a large scale.

Rare Disease Research Function

Coordinator

Bruno Dallapiccola

Activities

The Function creates and implements a national network for undiagnosed patients. Worldwide, 300 million people live with a rare disease. Of these, 6% are undiagnosed, a rate that can reach 60% among pediatric patients with intellectual disabilities or complex syndromes. In Italy, there are approximately 2 million rare disease patients, over 100,000 of whom are undiagnosed. In 2016, OPBG set up an Outpatient Clinic dedicated to undiagnosed rare disease patients, the first of its kind in Italy, that integrates clinical experience and scientific research through collaboration with an extensive network of national and international expert clinical centers.

Results achieved

Bambino Gesù Children’s Hospital participates in the Lazio Regional Network for Rare Diseases and in the European Reference Networks (ERNs). The Lazio Regional Network includes 21 institutions, whose centers are dedicated to rare diseases included in the essential levels of care (LEAs; 921 disease groups/rare diseases). Currently, over 62,000 patients with rare diseases are registered in the Regional Network, 26% of whom are children. In 2024, the OPBG Rare Diseases and Medical Genetics Operating Unit treated 18,326 patients registered in the Network. Between 2014 and 2024, the Translational Cytogenomics and the Molecular Genetics and Functional Genomics Research Units identified approximately 100 new disease genes.

Objectives

The main goal of the Function is to combine the commitment to resolving the etiological diagnosis, which follows well-defined pathways, with a shared commitment and methodology in the management of these patients. It is well known that, in the absence of an etiological diagnosis or in parallel with it, it is always possible to reach a functional clinical diagnosis for each patient, to identify the areas of greatest fragility, as well as the clinical areas requiring specialized attention and/or rehabilitation. This allows for comprehensive assessments and multidisciplinary treatments that are essential to ensuring the best quality of life, regardless of whether an etiological diagnosis has been reached. In this context, it is crucial to integrate the care plan into the context of the family’s social life and the experiences of its members, with particular attention to identifying feasible and concrete social and healthcare interventions.

Cancer Immunology Research Unit

Coordinator	Lorenzo Moretta
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Activities

The Research Unit studies innate immune cells, with a focus on NK cells and helper ILCs in the tumor microenvironment. It also defines new NK cell subpopulations through single-cell analysis, and studies the regulatory mechanisms underlying the interactions between NK and T cells with tumor cells.

Results achieved

In the reference year, the Function achieved the following results:

- Study of NK cell heterogeneity through the integration of functional data with marker expression and single-cell analysis. Demonstration of distinct differentiation trajectories and study of CD34+D-NAM-1brightCXCR4+ precursors and their progeny in healthy donors and in patients with cancer
- Anti-tumor activity of NK cells and their soluble factors, including exosomes, on primary or metastatic tumor cells
- Study of the composition of T cell subpopulations, with particular reference to neuroblastoma, in the tumor infiltrate
- Study of the mechanisms regulating the production and function of soluble PD-1 in NK cells and implications for anti-tumor effects
- Demonstration that IL-1R8 functions as a molecular brake in human NK cells. Increased anti-tumor activity of NK cells following gene silencing. Action of IL-37 (of the IL-1 superfamily) on NK cells, enhancing their effector activity thanks to its ability to degrade the IL-1R8 "brake"
- TLR in NK-mediated anti-tumor therapy: strong increase in NK cell cytolytic activity induced by a TLR8-specific agonist.

Objectives

The Unit aims to:

- Analyze the effect of soluble factors and exosomes released by different ILC cell subpopulations on tumor cells cultured in 2D or 3D systems
- Identify and study different eosinophil subpopulations in allergic and neoplastic diseases
- Continue studies focused on the tumor microenvironment and the inhibitory effect on effector cells (T and NK cells), with particular attention to their ability to "corrupt" adjacent cells (endothelial cells, fibroblasts, macrophages, granulocytes, and T cells), resulting in the induction of pro-tumor activity
- Further study of soluble PD-1 and other tumor-induced inhibitory molecules on NK cells
- Expand studies on the phenotype and functions of PMN-MDSC myeloid suppressor cells in pediatric and adult tumors, with a particular focus on their diagnostic and therapeutic use
- Expand studies on interactions between IL-37 and IL-1R8, given the potential therapeutic role linked to the strong enhancement of NK cell antitumor activity.

Translational Pediatrics and Clinical Genetics Research Area

Coordinator	Francesco Emma
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 PUBLICATIONS: 483
 CORRECTED IF: 2,039

The research area is committed to improving knowledge of genetic diseases, identifying new clinical conditions, and understanding their molecular basis and pathogenic mechanisms.

Genetics of Complex Traits Research Unit

Coordinator: **Anna Alisi**

Activities

The Research Unit studies the pathophysiological mechanisms of non-alcoholic fatty liver disease (NAFLD) and other multifactorial liver diseases in children, with the aim of identifying new therapeutic targets with results that can be implemented in clinical decision support systems. It identifies and validates genetic, epigenetic, and circulating diagnostic markers of clinical impact and studies new therapeutic strategies for NAFLD in order to improve the clinical picture and liver parameters of patients. It also investigates the genetic, epigenetic, and inflammatory mechanisms that lead to certain chronic non-communicable liver diseases and their associated comorbidities.

Results achieved

In the reference year, the Unit:

- has contributed, in cooperation with the leading international hepatology societies, to the new nomenclature for fatty liver disease, now renamed MASLD (Metabolic Dysfunction-Associated Steatotic Liver Disease), to the identification of new criteria for diagnosis in children, and to the definition of the associated metabolic risk
- has identified new early risk factors and new genetic, circulating, or more generally non-invasive markers functionally and phenotypically related to liver damage in children diagnosed with MASLD
- participated, in the framework of *Associazione Italiana Studi del Fegato* (Italian Liver Study Association), in the national and international survey of artificial intelligence applications in liver diseases
- has identified new potential prognostic markers and applied artificial intelligence algorithms to pediatric and non-pediatric liver tumors to identify histological parameters for diagnostic purposes.

Objectives

The Unit aims to:

- enhance studies in the field of epigenetic biomarkers in liquid biopsy and their interactions with the microbiome and host genetics
- develop, with the help of artificial intelligence, one or more diagnostic tools capable of combining different genetic factors, circulating markers, and radiological imaging for non-invasive diagnosis of the disease
- improve knowledge of changes in energy metabolism associated with the disease
- consolidate collaborations with Biomedical Engineering to contribute to the development of a digital diagnostic system.

Bone Tissue Pathophysiology Research Unit

Coordinator: **Andrea Del Fattore**

Activities

The Research Unit aims to identify the molecular and cellular mechanisms responsible for rare bone diseases. It contributes to the characterization of new phenotypes and to the understanding of disease mechanisms, as well as to the development of new diagnostic and prognostic tools for diseases associated with bone mass changes. The Unit team defines bone and immunological changes in diseases associated with bone mass reduction and studies the mechanisms responsible for the onset of osteosarcoma, a primary bone tumor, developing new therapeutic approaches and analyzing the endocrine aspects of bone tissue.

Results achieved

In 2024, the Unit focused on:

- identifying a new therapeutic approach for diseases characterized by reduced bone mass (patent application filed)
- characterizing changes in circulating bone cell precursors in patients with Gorham-Stout disease
- evaluating the effects of coagulation factors on bone cells, identifying changes in circulating bone precursors in patients with hemophilia A
- generating new experimental models to study the effects of mechanical load on bone cells
- developing a system for measuring the mechanical properties of osteosarcoma cells.

Objectives

The Unit aims to:

- enhance studies in the field of liquid biopsy and circulating biomarkers
- improve knowledge of the endocrine role of bone tissue
- study the involvement of the mechano-environment in bone diseases, identifying new therapies for bone diseases that are currently incurable.

Innovations in Abdominal Organ Transplantation Research Unit

Coordinator: **Marco Spada**

Activities

The Research Unit carries out translational research to offer children with liver and gastrointestinal diseases new personalized diagnostic and therapeutic options.

The main research activities are:

- use of extracorporeal organ perfusion
- study of the pathophysiology of liver and gastrointestinal diseases
- application of cell, pharmacological, and gene translational medicine
- use of telemedicine and artificial intelligence.

The Unit participates in numerous national and international disease registries, in the drafting of national and international guidelines, and in the European Reference Networks (ERNS) TRANSPLANT-CHILD and RARE-LIVER.

Results achieved

The main results achieved in 2024 are:

- production of liver organoids from stem and progenitor cells
- study of the gut microbiota and microbiota transplantation in the treatment of chronic inflammatory disease
- drafting of international guidelines for liver transplantation in organic acidemias and urea cycle disorders
- identification of new fields of application for liver transplantation using the split liver technique
- study of methods for diagnosis, treatment, and prevention of vascular and biliary complications in liver transplantation
- development of an integrated platform for prolonged organ perfusion with the integration of semi-automatic systems for controlling perfusion flows, acid-base balance, and glucose concentration, and of a dialysis circuit, aimed at testing new gene and translational therapies
- prolonged perfusion, up to 72 hours, of livers explanted from patients undergoing transplantation for metabolic diseases, used for the characterization of compartmentalized liver metabolism and disease phenotype
- development of a mobile application (PopòApp) for the colorimetric recognition of alcoholic stools in newborns and rapid management of cholestatic infants
- drafting of Italian guidelines for the diagnosis and treatment of eosinophilic esophagitis
- study of the role of retrograde cholangiopancreatography and video endoscopy in cystic and neoplastic diseases of the biliary tract and inflammatory bowel diseases
- use of new diagnostic approaches and new therapies in hepatic steatosis and cholestasis, and in acute and autoimmune hepatitis
- study of the presentation of celiac disease.

Objectives

- Use the perfusion platform to test new therapeutic approaches such as gene and mRNA therapy or hepatic stem cell infusion
- measure the impact on diagnosis and treatment of biliary atresia
- expand the use of perfusion machines in abdominal organ transplantation, particularly in split liver procedures, by experimenting with new methods of measuring mitochondrial metabolism
- study the effectiveness of hemofiltration and plasma exchange in the treatment of acute liver failure to define standardized treatment protocols
- develop artificial intelligence algorithms for use in endoscopic diagnostics da utilizzare nella diagnostica endoscopica.

Innovative Therapies for Endocrinopathies Research Unit

Coordinator: **Marco Cappa**

Activities

The Research Unit promotes clinical research through drug trials based on the study of the genetic causes of endocrine disorders. The Unit identifies new therapeutic strategies for complex clinical presentations based on experimental therapies. Seven clinical trials are currently underway with innovative drugs: long-acting GH for GH deficiency, SGA, Turner syndrome, Noonan syndrome, incretins in pediatric obesity, Osilodrostat (a drug that blocks adrenal hyperproduction in Cushing syndrome), and the use of TRIAC in Herndon-Dudley syndrome.

Results achieved

In 2024, the Unit has:

- described a new method for puberty induction (prolonged priming with testosterone gel), a diagnostic method used to differentiate hypogonadotropic hypogonadism from constitutional delay of growth and puberty and GH deficiency, presenting data on final height of treated subjects compared to untreated subjects
- described a Delphi study of GH therapy in cancer survivors and produced a review of recGH treatment in patients with surgically treated pituitary neoplasms and radiotherapy
- described a Mediterranean diet adapted for nutritional therapy for X-linked adrenoleukodystrophy, with the aim of normalizing plasma VLCFAs
- published cross-sectional and longitudinal growth curves for Noonan syndrome, which will serve as a national and international reference for the management of patients with growth hormone therapy
- presented for the first time a treatment with an aromatase inhibitor (anastrozole) as an innovative therapy for patients with ACAN syndrome, to improve height outcomes by blocking rapid bone age maturation
- participated in the drafting of the World Anti-Doping Agency (WADA) guidelines for GH treatment in athletes with growth disorders
- published a review on the diagnosis of Cushing's disease
- published a review on growth and treatment of children with chronic renal failure
- participated in the drafting of international guidelines for the rapid and correct diagnosis and treatment of lipodystrophy
- produced an article aimed at calculating the real cost of GH therapy and its effectiveness.

Objectives

The Unit aims to use drugs, hormones, and administration techniques with less impact on the patient's quality of life but with greater efficacy.

Growth Pathophysiology Research Unit

Coordinator: **Stefano Cianfarani**

Activities

The Research Unit studies the pathogenic mechanisms of growth disorders. The main fields of research on which the working group focuses are:

- biochemical, endocrine, and molecular characterization of growth delay
- evaluation of the effect of exposure to environmental endocrine disruptors on the endocrine system of children
- molecular characterization and personalized treatment in children with early-onset severe obesity
- genetics, new medicines, technology, and artificial intelligence in children with diabetes.

Results achieved

During the reference year, the Unit achieved the following scientific results:

- the application of next-generation sequencing (NGS) and functional studies allowed for the identification of new genetic variants associated with idiopathic short stature and poor intrauterine and postnatal growth, thereby enabling precision therapy
- the application of artificial intelligence and machine learning has made it possible to identify predictive criteria for a good response to growth hormone therapy
- the use of the most advanced technologies for monitoring blood glucose levels in children with type 1 diabetes has demonstrated the efficacy of Advanced Hybrid Closed-Loop (AHCL) in controlling the disease
- identification of a new variant in the HNF1B gene as a cause of neonatal diabetes mellitus
- development, within an international group of experts, of new guidelines for diagnosis and management of male children with early puberty.

Objectives

The objectives of the Research Unit studies are:

- identify new personalized therapies for children with severe growth disorders or obesity
- apply transcriptomics in the assessment of individual sensitivity to corticosteroid therapy
- identify the molecular mechanisms associated with the risk of developing Klinefelter syndrome
- improve the metabolic status of children with diabetes through the appropriate use of new technologies and the application of artificial intelligence
- screening for type 1 diabetes in siblings of patients but also in the healthy pediatric population for early identification of individuals at risk, thus delaying the onset of full-blown disease with specific immunomodulatory therapy and reducing the risk of ketoacidosis.

Metabolic Diseases Research Unit

Coordinator: **Carlo Dionisi Vici**

Activities

The Unit carries out translational research on metabolic diseases, such as organic acidurias, urea cycle disorders, genetic and metabolic hypoglycemia, lysosomal and mitochondrial diseases. Specific areas of focus include the clinical field (emergency treatment, liver transplantation, innovative therapies, clinical trials), metabolomics for the search for new biomarkers, neonatal screening, and the drafting of guidelines. Another research area, in collaboration with the Laboratory of Drug Biology, focuses on the development of precision medicine pathways in pediatrics (TDM, pharmacokinetics, pharmacogenetics) in relation to oncological, antimicrobial, and antiepileptic therapies, participating in Phase I, II, and III clinical trials.

Results achieved

In 2024, research activities focused on:

- liver and liver-kidney transplantation in metabolic diseases, which showed, through targeted metabolomics studies combined with neuroimaging investigations and clinical evaluations, the positive impact of transplantation on patients' neurodevelopment and quality of life
- OPBG is now a key player in the field of liver transplantation for metabolic diseases, with a leading role in ERN Networks (MetabERN, RARE-LIVER, TRANSPLANT-CHILD), international consortia (E-IMD, CERTAIN), and in national and international collaborations (TIGEM, University of Zurich)
- development and validation of an innovative normothermic perfusion system for the ex vivo study of livers explanted from metabolic patients undergoing transplantation.

An untargeted metabolomics study has been published identifying new biomarkers and new pathophysiological mechanisms in propionic acidemia, methylmalonic acidemia, and cblC deficiency. Clinical research has clarified and improved understanding of pathophysiological and therapeutic aspects in mitochondrial diseases and genetic hypoglycemia. The drug biology area has conducted studies on the use of antibiotics, antifungals, and sedatives, and on drug interactions in critically ill pediatric patients admitted to high-complexity intensive care units.

Objectives

The Unit focuses on:

- translational studies for the development and application of innovative therapies (e.g., mRNA), using the ex vivo model of normothermic perfusion of liver explanted from metabolic patients undergoing transplantation, as well as cellular models
- using a combination of omics and machine learning techniques to create predictive models of the natural history of metabolic diseases

- identifying precision medicine models applied to specific areas of pediatrics.

Clinical Genetics and Dysmorphology Research Unit

Coordinator: **Maria Cristina Digilio**

Activities

The Unit studies genetic syndromes, with the aim of characterizing clinical signs, natural history, and clinically relevant phenotype-genotype correlations.

Among the genetic disorders historically studied are:

- Noonan syndrome and other RASopathies
- 22q11.2 deletion syndrome
- overgrowth syndromes, cohesinopathies/chromatinopathies (Kabuki syndromes, KBG syndrome and other conditions)
- skeletal dysplasia
- hypercholesterolemia.

Thanks to advances in molecular genetic laboratory techniques, research has expanded to include the clinical characterization and the definition of care protocols for new genetic syndromes caused by variants in newly identified genes.

Results achieved

During the reference year, the Unit focused on:

- expanding the phenotype of rare syndromes (related to the ERF, KMT2E, LZTR1, and NALCN genes)
- characterization of specific clinical signs in rare and ultra-rare genetic syndromes (congenital heart disease in Sotos syndrome)
- diagnosis, clinical signs, and follow-up of neonatal genetic phenotypes (22q11.2 deletion, Marfan syndrome, atrioventricular canal defect with aortic coarctation).

Objectives

The Unit aims to:

- characterize clinical presentations related to multiple genetic defects
- establish care guidelines for new genetic syndromes and phenotype-genotype correlations in the field of anatomical variants of congenital malformations and subtypes of intellectual disability, in collaboration with the Hospital genetics laboratories and other clinical specialists.

Neuromuscular Diseases Research Unit

Coordinator: **Enrico Silvio Bertini**

Activities

The Unit studies rare genetic progressive neurological diseases, in particular:

- muscle diseases

- peripheral nerve diseases
- leukodystrophy, spastic paraplegia
- ataxia
- mitochondrial diseases.

These are neurogenetic heterogeneous diseases, largely lacking effective treatment, that require multi-center natural history studies for the development of therapies. In particular:

- diagnosis in symptomatic patients and predictive neonatal diagnosis of spinal muscular atrophy
- genotype-phenotype correlation
- natural history profile of diseases and development of biomarkers
- identification of disease mechanisms for the development of therapies on cell or multicell models
- monitoring of post-treatment efficacy.

Results achieved

In 2024, research activities focused on:

- characterization of a new gene, TRiC, responsible for a developmental disorder with brain malformations
- characterization of a new gene, KCND1, causing the developmental disorder
- characterization of a new phenotype of myoclonic epilepsy syndrome related to dominant variants in the POLR3B gene
- analysis of cerebrospinal fluid proteomic signatures in patients with spinal muscular atrophy
- characterization of the neurocognitive profile of patients with Becker muscular dystrophy
- demonstration through an international multicenter clinical trial that Givinostat is effective in slowing disease progression in DMD
- definition of an inflammatory signature in fibroblasts from patients with Friedreich ataxia.

Objectives

The Unit aims to:

- develop translational medicine in the field of neuromuscular and neurodegenerative diseases, including through the study of cell models
- contribute to defining new phenotypes and identifying new disease genes for neurogenetic diseases
- innovate functional assessment protocols for progressive diseases
- develop algorithms to integrate clinical, neuroradiological, myopathological, enzymatic, and genetic diagnosis
- define the natural history of rare diseases of interest
- identify diagnostic and prognostic biomarkers for spinal muscular atrophy, Friedrich's ataxia, and mitochondrial disorders
- develop redox biomarkers in Paelizeus Merzbacher disease, X-linked leukodystrophy, and SPG20 ataxia
- use in vitro combination therapies to study the crosstalk between oxidative stress and inflammation in neurodegenerative diseases.

Nephrology Laboratory Research Unit

Coordinator: **Marina Vivarelli**

Activities

The Research Unit develops new therapeutic approaches to rare genetic diseases, like nephropathic cystinosis, immune-mediated kidney diseases, such as idiopathic nephrotic syndrome, and complement-mediated diseases, through pre-clinical studies on cell cultures and animal models, observational clinical studies, and clinical trials. It participates in several disease registries and in the drafting of national and international guidelines on kidney diseases. It supports the activities of various patient associations and takes part in numerous national and international collaborations promoting the setting up of networks, which are fundamental in the field of rare diseases.

Results achieved

In the reference year, the Unit achieved the following results:

- identification, through high-content drug screening, of a group of molecules that correct the disrupted differentiation in C2C12 Ctns^{-/-} myoblasts
- positive impact of methionine-enriched diets in a cystinosis animal model
- efficacy and safety profile of the phytoestrogen genistein in a cystinosis rat model, with a focus on the reproductive system
- identification of genetic variants on cell transcripts of patients with renal tubulopathies and impact on cell phenotype through in vitro studies
- identification of biomarkers predictive of recurrence from disease onset through the development of a standardized method for the characterization of the lymphocyte repertoire in children with idiopathic nephrotic syndrome
- identification of anti-nephrin autoantibodies associated with disease activity in children with idiopathic nephrotic syndrome with the coordination of an international multicenter study.

Objectives

The Unit aims at applying the knowledge acquired and the therapeutic candidates identified in clinical trials involving:

- patients with nephropathic cystinosis (ketogenic diet)
- patients with corticosteroid-dependent nephrotic syndrome in whom a personalized treatment approach with anti-CD20 will be evaluated (MEMORINEPH study).

It identifies and characterizes antigen-specific memory cells in patients with idiopathic nephrotic syndrome. The results achieved in nephropathic cystinosis will be consolidated by extending the studies to extrarenal compartments and generating a new Ctns^{-/-} mouse model suitable for this purpose. Finally, the mechanisms of action underlying the effect of the ketogenic diet on cystinosis will be studied in vitro.

Perinatal Medicine Research Unit

Coordinator: **Andrea Dotta**

Activities

The work of the Research Unit is mainly based on clinical research studies focusing on the most crucial period of life: the first 1,000 days, from conception to the end of the second year of life. Much of a person's future health is determined during these first 1,000 days. The Research Unit activities are closely integrated with clinical care and focus specifically on:

- prenatal areas, with diagnostic and interventional fetal assessments in cases of particularly severe congenital malformations or functional disorders
- perinatal and neonatal areas, with a particular focus on a multi-specialist and multi-omic approach at birth
- perinatal distress due to severe difficulties in cardio-respiratory, cerebral, and gastrointestinal adaptation at birth
- complications mainly related to prematurity, congenital or acquired infectious conditions
- congenital metabolic disorders diagnosed through extended neonatal screening or subsequent multi-disciplinary assessments.

Results

The Unit works closely with other Research Units in this and other research areas of the Hospital, as well as with other national and international research groups, focusing mainly on clinical research. The areas of research can be summarized as follows:

- neurology
- Point of Care Ultrasound (POCUS) and high-fidelity simulation
- neonatal infectious diseases
- echocardiography, hemodynamic monitoring, and respiratory function assessment
- neonatal nutrition
- clinical research on congenital diaphragmatic hernia
- research on rare diseases, biobanking, and bioethics.

In 2024, the Unit was involved in several research projects, including projects funded by 5x1000 ("Role of miRNAs in defining cardiac phenotype in patients with congenital diaphragmatic hernia and in newborns with late-onset sepsis" and "Role of neurobiomarkers as prognostic parameters of brain damage in newborns with congenital heart disease") and in the project funded by *Ricerca Corrente* (Current Research; annual funding from the Ministry of Health) developed jointly with the Perinatal Surgery and Preventive and Predictive Medicine Research Units entitled "Exploring potential predictors of neurological outcome in congenital malformations through artificial intelligence".

Objectives

Several research projects are underway, both with 5x1000 and Current Research funding. In particular, the project "New diagnostic and therapeutic ap-

proaches in neonatal, pediatric, and adolescent diseases" and the Current Research project entitled "Use of biomarkers in newborns with congenital malformations or infections: a prospective study" have been approved. More clinical trials and research collaborations will be carried out, integrated with clinical practice and neonatal care.

Neurological and Neurosurgical Diseases Research Unit

Coordinator: **Nicola Specchio**

Activities

The Research Unit carries out translational research in the field of neurology and neurosurgery. Areas of excellence include epilepsy, movement disorders, comorbidities in epilepsy, genetic studies, advanced and experimental treatments, complex neurosurgical diseases, and brain tumors. In the preclinical area, the Unit collaborates with the EBRI Foundation (European Brain Research Institute Rita Levi Montalcini) on the neurophysiological characterization of focal cortical dysplasia through the analysis of brain tissue from patients who have undergone surgery for drug-resistant epilepsy (epilepsy and brain connectivity). Part of the Unit's research focuses on the application of new technologies such as robotics, telemedicine, and artificial intelligence.

Results achieved

The following results were achieved by the Unit in 2024.

Epilepsy:

- in the field of imaging, the usefulness of magnetic resonance post-processing techniques was examined, using brain machine learning algorithms to improve the ability to recognize focal cortical dysplasia
- impact of epilepsy surgery in the long term in adolescents with follow-up of more than 3 years. The results showed that mood and anxiety disorders persist despite the resolution of seizures
- impact of epilepsy on the quality of life of families, examination of clinical factors related to stress in parents and children
- In 2024, 21 pharmacological clinical trials were carried out involving patients with drug-resistant epilepsy and rare neurological disorders, with a focus on innovative therapeutic strategies
- genetic epileptic and developmental encephalopathies and characterization of the electro-clinical phenotype and precision therapy
- use of fluoxetine in epilepsy of infancy with migrating focal seizures and of cenobamate in epileptic and developmental encephalopathy caused by SCN2A and SCN8A gene mutations
- use of artificial intelligence techniques leading to accurate predictions (60-70%), promoting a new project to study wake-sleep staging and evoked responses in patients monitored with SEEG.

Neurosurgery:

- the surgical experience of craniopagus and the development of specific prosthetic systems were presented for the treatment of the malformation
- augmented reality-supported surgical techniques were developed
- anatomical and functional networks in the pediatric field were analyzed and intraoperative cortico-cortical evoked potentials (CCEPs) were applied to the study of cortical and subcortical-cortical connectivity
- structural and neurocognitive aspects of intrinsic and diffuse brain stem tumors (DIPG) were analyzed.

Objectives

The Unit has the following objectives:

- implementation of precision medicine derived from research on developmental encephalopathies and genetic epilepsies
- understanding the decision-making process in children through the administration of cognitive behavioral tasks and the analysis of evoked responses in collaboration with University La Sapienza (Rome)
- study of sleep cycles and EEG signal prediction in collaboration with ISS (Italian Institute of Health). Modulation of the different phases of sleep and development of predictive tools for the management of patients with SEEG implants
- prediction of epileptic seizures through digital twin models, personalized virtual representations of the patient's brain
- early-onset epilepsy and electro-clinical prognostic factors in epilepsy with onset in the first year of life
- effectiveness of antisense oligonucleotides (ASOs) administered intrathecally, opening the way to new therapeutic perspectives for refractory epilepsy
- translational research on iPSC cells in specific epilepsy syndromes, such as those caused by mutations in the CAMK2A-2B and PCDH19 genes, with the aim of developing cellular models to test new therapeutic strategies
- neurophysiological study of human brain tissue in organotypic cultures
- development of neural networks used for machine learning to be applied in neurosurgery
- development of haptic modalities in the field of robotics.

Neuropsychiatry Research Unit

Coordinator: **Stefano Vicari**

Activities

The Unit defines the neurocognitive and psychopathological profile of children and adolescents with psychiatric and neurodevelopmental disorders, in order to identify developmental trajectories and optimize diagnostic pathways. It defines innovative evidence-based intervention procedures (pharmacological and non-pharmacological).

The Unit studies in particular:

- intellectual disability and genetic syndromes
- autism spectrum disorder
- attention deficit/hyperactivity disorder
- specific learning disorders, communication disorders, psychopathological disorders related to abuse and mistreatment, psychotic disorders
- anorexia and eating disorders
- mood and anxiety disorders, obsessive-compulsive disorders.

Results

During the reference year, the Unit:

- applied and is carrying out studies with non-invasive brain stimulation (tDCS) for the treatment of clinical symptoms in numerous neurodevelopmental and psychiatric disorders in the developmental age, such as dyslexia and dyscalculia, anorexia nervosa, and autism
- developed a double-blind, placebo-controlled study protocol to compare the effects of direct current transcranial stimulation and transcranial random noise stimulation on reading in children and adolescents with dyslexia. The results will contribute to the development of new forms of intervention for dyslexia
- carried out a study to examine the clinical characteristics of treatment-naïve children with ADHD, evaluating their response to methylphenidate (MPH). The results indicate that the presence of oppositional defiant disorder may negatively affect the effectiveness of MPH treatment, with important implications for the personalization of interventions
- evaluated the effectiveness of group neuropsychological and cognitive-behavioral therapy in young adults with fragile X syndrome, who showed improvements in emotion management, communication, and adaptive functioning, with a reduction in anxiety and depression and an improvement in family quality of life
- studied the adaptive and behavioral functioning profile of children with Down syndrome (DS) and co-occurring autism spectrum disorder (ASD). Comparison with a group of children with DS without ASD showed lower adaptive abilities in the first group, despite similar IQs. Greater social withdrawal, stereotypical behaviors, and restricted interests were observed, highlighting the importance of early diagnosis and targeted interventions
- analyzed the vulnerability of people with intellectual disabilities (ID) to traumatic events, highlighting that young people with ID show more severe post-traumatic symptoms and adaptive difficulties
- studied the cognitive factors associated with the severity of depression in children, reporting that children with suicidal ideation have higher Verbal Comprehension Index scores. This suggests the importance of monitoring cognitive functioning in young people with depression
- studied irritability in mood disorders in 289 ado-

lescents, finding that irritability as assessed by parents was more strongly associated with bipolar disorder, while self-reported irritability was related to depressive symptoms and mood lability

- studied the relationship between sleep disorders and ADHD in children, highlighting poorer adaptive functioning, lower school performance, greater inattention, and difficulties in emotional regulation in participants with sleep disorders.



Objectives

The Unit will focus on:

- characterizing complex clinical pictures associated with psychiatric and neurodevelopmental disorders, studying their biomarkers, developmental trajectories, risk factors, and protective factors
- expanding the areas of application of non-invasive brain stimulation as a treatment option for genetic and psychiatric disorders.



Immunology, Rheumatology, and Infectious Diseases Research Area

Coordinator	Fabrizio De Benedetti
	PUBLICATIONS: 235
	CORRECTED IF: 1,221

The Research Area focuses on the immunological aspects of autoimmune and infectious diseases. Its research areas include studies of cellular mechanisms in rheumatic diseases and their treatment, immunodeficiencies, vaccines, and the diagnosis and treatment of food allergies.

Immunorheumatology Research Unit

Coordinator: **Fabrizio De Benedetti**

Activities

The Unit carries out translational research projects aimed at identifying pathogenic mechanisms and mediators involved in numerous pediatric rheumatological diseases, including juvenile idiopathic arthritis, macrophage activation syndrome, autoinflammatory diseases, and systemic autoimmune diseases. The results obtained through preclinical studies on primary cells or tissues from patients and/or animal models are then applied to clinical management as new biomarkers for diagnosis and disease severity or as new therapeutic targets. The Unit conducts numerous observational clinical studies and clinical trials and participates in the drafting of international guidelines and disease registries. In addition, new guidelines on the diagnosis and management of Still disease, coordinated by the Unit, have been published.

Results achieved

In the reference year, the Unit:

- applied, for the first time in the world, CAR-T cell therapy (anti-CD19) in the treatment of pediatric patients with autoimmune diseases (SLE and juvenile dermatomyositis) with extraordinary efficacy (in collaboration with the Oncohematology Research Area)
- continued studies on the activation of the interferon pathway and its role in the activation of B lymphocytes in patients with systemic lupus erythematosus (SLE), demonstrating the efficacy of anifrolumab in the treatment of monogenic SLE
- studied the proinflammatory role of nlrp2 in cystinosis, demonstrating its value as a potential therapeutic target.

Objectives

The Unit aims to:

- identify the molecular and cellular pathogenic mechanisms of rheumatic diseases in children
- identify new biomarkers predictive of diagnosis, disease severity, and response to innovative biological therapies through a better understanding of pathogenic mechanisms
- identify new targets and new therapeutic strategies.

Innate Immunity Lymphoid Cell Research Unit

Coordinator: **Paola Vacca**

Activities

The Unit studies the immune system focusing on innate immune cells in pediatric oncological, autoimmune, and inflammatory diseases, assessing their frequency, functions, and diagnostic and prognostic impact. It investigates new strategies to enhance natural killer (NK) cell activity in immunotherapy and stud-

ies the interactions of innate lymphoid cells with cells present in the microenvironment, particularly myeloid-derived suppressor cells (MDSCs). It also analyzes the reconstitution of innate immune cells in patients with hematological tumors who underwent allogeneic hematopoietic stem cell transplantation.

Results achieved

In 2024, the Unit achieved the following results:

- filing of a patent for the generation of genetically modified NK cells with powerful antitumor activity for the development of new therapeutic approaches
- identification of the most effective therapeutic approach for patients with Vernal keratoconjunctivitis
- characterization of circulating ILCs in patients with systemic juvenile idiopathic arthritis in the inactive phase
- identification of interactions between ILCs and macrophages in the tumor microenvironment
- characterization of the molecular mechanisms regulating the differentiation of hematopoietic stem cells in ILC subsets
- identification of myeloid suppressor cells in the peripheral blood of patients with autoimmune diseases and cancer and characterization by single-cell RNA sequencing
- validation of the patent that allows for the specific identification of PMN-MDSC cells enhancing immunotherapy.

Objectives

The Unit aims to:

- develop new innovative therapeutic approaches to exploit the immune system for patient-specific treatments
- develop therapeutic strategies aimed at modulating the functions of innate immune cells and immunosuppressive cells
- implement clinical and diagnostic pathways including the analysis of innate lymphoid cells and MDSCs in allergic and autoimmune diseases
- identify cellular and molecular mechanisms that have a strong impact on the regulation of NK cell antitumor activity through multi-omic approaches.

Primary Immunodeficiencies Research Unit

Coordinator: **Caterina Cancrini**

Activities

The focuses on the clinical, immunological, and molecular characterization of groups of patients with primary immunodeficiencies (PIDs), recently defined as inborn errors of immunity (IEIs). The main aim of the Unit is to translate immunological and genetic data derived from the application of advanced next-generation sequencing technologies (NGS) into new clinical tools designed to accelerate diagnosis and improve the management of these patients, but also to identify

new therapeutic strategies. Through the integration of multiomic data, the Unit investigates predictive markers in different groups of IEIs, including:

- combined immunodeficiencies (CID) and common variable immunodeficiencies (CVIDs)
- congenital neutropenia
- del22 syndrome
- chronic granulomatous disease (CGD)
- monogenic inflammatory bowel diseases (IBDs)
- ataxia-telangiectasia (AT) and cytoskeletal defects.

Other projects include:

- study of the pathogenesis of immunoregulatory manifestations in primary immunodeficiencies
- study of inflammatory manifestations in chronic granulomatous disease
- study of cellular components involved in the immune response to specific infections
- study of the etiopathogenesis of type I diabetes and autoimmune polyendocrinopathies.

Results achieved

In 2024, the Unit:

- identified new variants in genes - both new and already known - that encode factors involved in the immune response and responsible for specific clinical and immunological entities, including STAT6. The Unit successfully treated a patient with a mutation in STAT6 with Dupilumab (paper currently being drafted)
- as part of the study on the pathogenic mechanisms of immune dysregulation in IEI patients, it identified diagnostic and prognostic markers for defining specific categories of patients who may benefit from similar treatments
- characterized the molecular interactions between components of innate immunity (cytotoxic cells, natural killer cells) involved in the immune response to specific infections, including EBV in patients with IEIs
- studied the molecular mechanisms involved in the etiopathogenesis of type I diabetes and autoimmune polyendocrinopathies, focusing on APECED syndrome, to develop specific immunotherapies
- as part of the study on patients with APDS, the Unit collaborates with the Italian and European registries to collect data on APDS patients. It is also working on the development of a method for diagnosis and validation of variants of uncertain significance (VUS), and on the monitoring of treatment in APDS and APDS-like patients.

Objectives

The Unit aims to:

- optimize next-generation sequencing (NGS) protocols and their interpretation in IEIs to accelerate molecular diagnosis
- correlate clinical, immunological, and genetic data with targeted functional studies

- identify new pathogenic mechanisms to clarify the role of the different cellular components involved in defense mechanisms against pathogens and in the maintenance of tolerance, underlying the phenomena of immune dysregulation and/or autoimmunity in IEIs
- identify predictive markers to improve increasingly personalized therapeutic strategies, in particular in immunodeficiencies associated with severe chronic cytopenia and/or lymphoproliferation
- identify the molecular mechanisms involved in the etiopathogenesis of type 1 diabetes and autoimmune polyendocrinopathies, with particular reference to APECED syndrome, to develop specific immunotherapies
- evaluate genetic and environmental susceptibility factors and immunological response factors in severe tuberculous and non-tuberculous mycobacterial infections in the pediatric population with and without immunodeficiency; evaluate the cytotoxic response of NK cells in patients with IEIs and chronic EBV infection and/or associated with an increased risk of lymphoproliferation.

Allergology and Cystic Fibrosis Research Unit

Coordinator: **Alberto Giovanni Fiocchi**

Cystic Fibrosis Activity

In recent decades, the natural history and treatment of cystic fibrosis (CF) have changed significantly. The cystic fibrosis research group focuses on the pathogenesis of the disease, with particular attention to extending access to personalized therapy to as many patients as possible. For the first topic, the expression of IL-17 in respiratory epithelial cells has been evaluated, documenting its importance. For the second aspect, various strategies are being implemented:

- assessment of functional damage and evaluation of the therapeutic response to modulators already available in respiratory epithelial cells of children and patients with unknown or uncharacterized mutations
- evaluation of the introduction of new drugs in younger patient groups. In particular:
 - growth in children with cystic fibrosis aged 6-11
 - changes in the quality of life of the child and their family after the introduction of the drug
 - evolution of respiratory function in the same children using the nitrogen washout technique
- prospective evaluation of the effects of introducing triple therapy, ETI
- optimization of the prediction of clinical responses to CFTR modulators.

Particular attention is paid to the evaluation of the response to ETI in patients who are not eligible for triple therapy. The response of intestinal organoids harboring genotypes currently unsuitable for ETI therapy suggests that a large portion of patients with rare CFTR variants without access to ETI may benefit from this treatment.

Allergology activity

Allergic diseases and asthma have a significant social impact because they affect large segments of the population. The Research Unit is active in several areas:

- understanding molecular pathogenesis
- using this knowledge to develop specific molecules for proactive use
- identifying biomarkers that predict and monitor the therapeutic efficacy of the drug
- conducting definitive randomized studies in all age groups, especially in pediatrics
- identifying objective tests that can ensure early and specific diagnosis.

The Research Group is involved in a series of projects with the European Academy of Allergy and Clinical Immunology (EAACI) and the World Allergy Organization to develop guidelines and recommendations that require preliminary meta-analyses or consensus-building processes using the e-Delphi method.

Results achieved by the Cystic Fibrosis group

- the expression of the IL-17 family in respiratory epithelial cells may play a role as an autocrine inflammatory amplification loop in the airways of CF
- many patients who are not eligible for therapy because they do not carry the Delta-F-508 variant respond to it in vitro and can be treated with hope for clinical benefit
- the production of reference tables for variables related to OGTT in the Italian population with cystic fibrosis has been completed
- the course of COVID-19 in CF has been described and found to be mild, probably due to factors intrinsic to this population.

Results achieved by the Allergology group

- efficacy and safety of IL-4 and IL-13 inhibitors in the long-term treatment of severe asthma in children - quality of life aspects, efficacy biomarkers
- reactivity of children with severe food allergies to products with precautionary labeling for allergens - new reactivity thresholds described for children allergic to baked forms of egg and milk versus those tolerant to these forms
- effect of IgE inhibitors in children with severe food allergies
- quality of life of children treated with IL-4 and IL-13 inhibitors for the long-term treatment of severe asthma
- description of nasal polyposis in children
- generation of the first score for assessing the severity of food allergy, within the World Allergy Organization, its implementation and development
- description of hypersensitivity reactions to foods triggered by non-steroidal anti-inflammatory drugs (NSAIDs).

Objectives of the Cystic Fibrosis Group

The introduction of new therapies has changed the natural history of the disease, which is now more treatable but not yet curable. The immediate challeng-

es concern the treatment of patients for whom therapies are not yet available. In particular:

- exploring the possibilities for conducting functional studies on organoids and cell biology in general
- the study of the pathophysiological and psychological aspects of patients with cystic fibrosis
- further clinical research into new perspectives opened up by therapy.

Objectives of the Allergology Group

The working group aims to develop its areas of research. For food allergies, research activity mainly focuses on:

- internal and external validation of the DEFASE severity score
- advancing studies on the use of biologics in food allergies
- implementation of studies on oral immunotherapy for food allergies
- implementation of studies on epicutaneous immunotherapy for food allergies
- evaluation of the response thresholds of children with food allergies.

Respiratory Diseases Research Unit

Coordinator: **Renato Cutrera**

Activities

The Unit carries out clinical research on diseases involving the respiratory system.

Primary diseases specific to the respiratory system:

- bronchiolitis and asthma
- rare respiratory diseases, including primary ciliary dyskinesia, pulmonary interstitial diseases, and surfactant protein deficiencies
- malformations of the respiratory system
- congenital central hypoventilation syndrome or Ondine syndrome.

Secondary diseases, i.e., diseases of other organs and systems that evolve into chronic respiratory failure:

- genetic diseases
- metabolic diseases
- neurological diseases
- neuromuscular diseases
- outcomes of neonatal and cardiac conditions and rare diseases in general.

Results achieved

During 2024, the Unit achieved numerous clinical results leading to various research activities with related publications in international scientific journals:

- in the field of rare respiratory diseases, the Research Unit team coordinates the SIMRI Research Group on primary ciliary dyskinesia and non-CF bronchiectasis and promotes several multicenter studies

- it participates in European research projects within the ERN-LUNG network on primary ciliary dyskinesia, lung malformations, cystic fibrosis, and Ondine Syndrome
- publications on the respiratory support needs of patients with neurological and neuromuscular diseases
- results on the efficacy of nusinersen on neurocognitive outcomes and sleep quality of patients with SMA; in addition, innovative therapies had an impact on the need for ventilation during sleep in patients with SMA
- provision of telemedicine services for fragile patients on home ventilation in Lazio region and other regions, with both clinical and research results
- contributions on the epidemiology and costs to the National Health System of respiratory syncytial virus, early respiratory infections, and recurrent bronchospasm.

Objectives

The Unit aims to:

- consolidate new telemedicine care models, especially for the most complex or severe patients and for the treatment of rare diseases
- increase knowledge and improve the management of patients with rare diseases by cooperating with leading European centers that are part of the ERN-LUNG network
- develop control and intervention strategies established by reference clinicians in agreement with local professionals.

Pathogenesis and Innovative Therapies in Infectiology Research Unit

Coordinator: **Alberto Villani**

Activities

In 2024, the Unit's activities focused mainly on three macro areas. In the field of antimicrobial resistance, two prospective multicenter studies are underway on the treatment of severe gram-negative bacterial infections: the ESCAPE study on the efficacy and safety of ceftazidime/avibactam in pediatric patients and the PACCOF study on the pharmacokinetics and pharmacodynamics of ceftazidime/avibactam and cefiderocol, in regimens with and without fosfomycin.

The SEPTI-CAFE' project investigates the correlation between the genomic characterization of isolated bacterial strains and the clinical phenotype of patients with gram-negative sepsis in intensive care. In the context of HIV infection, the Unit is carrying out a study in collaboration with the Microbiology and Immunology Diagnostics COU to investigate the role of viral DNA mutations in a cohort of patients with long-term HIV infection and prolonged virologic suppression. Two clinical trials on antiretroviral medicines are also underway. Regarding congenital infections, the Unit is participating, together with the Fetal and Perinatal Medicine and Surgery COU, in an Italian mul-

ticenter study on the effects of valaciclovir therapy in preventing vertical transmission of cytomegalovirus during pregnancy. Concerning bronchiolitis, the Unit has completed a study on the evaluation of the efficacy and predictive factors of response to standard oxygen therapy versus high flow oxygen therapy. The multicenter RESPIRAMO study has been launched to assess the economic impact of the management of this disease. Finally, following the introduction in Italy of universal prophylaxis with nirsevimab, the NEVIR monocentric study was launched to describe epidemiological changes and trends in hospitalizations for RSV-related bronchiolitis and other viruses over the next three seasons.

Results achieved

The Unit is currently involved in the following observational studies and clinical trials:

- RESPIRAMO - Italian Hospital Surveillance for lower respiratory tract infections
- NEVIR - New epidemiology of respiratory viruses. Study duration: three bronchiolitis epidemic seasons (2024-2027)
- *Role of HIV-DNA mutations in a pediatric patient cohort with a long history of infection*
- training and information for adolescents and young adults with and without HIV infection
- training of peer supporters and methodology for transition to adult centers
- Italian multicenter study MEGAL-ITALI (4-year extension of the study)
- use of RNA biomarkers to differentiate infection from inflammation
- identification of markers of intestinal dysbiosis in patients with tuberculosis infection and disease
- evaluation of the efficacy and safety of ceftazidime/avibactam in children: a prospective multicenter observational study
- *Pharmacokinetic/pharmacodynamic analysis of ceftazidime/avibactam or cefiderocol with or without fosfomycin for the treatment of difficult-to-treat Gram-negative infections* (PACCOF study). The study is being conducted as part of the PNRR Inf-Act WP 3.5 project
- SEPTI - CAFE' (sepsis in pediatric intensive care): genomic characterization of isolated strains and correlation with the clinical phenotype of patients.

Clinical Trials:

- *A Phase 2/3, Open-Label Study to Evaluate the Pharmacokinetics, Safety, and Antiviral Activity of Bictegravir/Lenacapavir in Children and Adolescents With HIV-1*
- open-label rollover study on rilpivirine in combination with a background regimen containing other antiretrovirals (ARVs) in subjects with human immunodeficiency virus type 1 (HIV-1) who participated in pediatric studies on rilpivirine. Study TM-C2781FD3004.

In 2024, collaboration continued with various national and international scientific societies, with active par-

ticipation in the drafting of guidelines:

- guidelines for antiretroviral treatment in pediatric patients with HIV infection (EACS and National AIDS Commission)
- italian infectious disease recommendations for sexual abuse in children (SITIP)
- national guidelines on the diagnosis and treatment of tuberculosis in children.

41 scientific articles were published in national and international journals.

Objectives

The Unit has the following objectives:

- analyze and present data from the RESPIRAMO study
- describe the trend in hospitalizations for RSV-related bronchiolitis in the next three epidemic seasons following the introduction of nirsevimab prophylaxis
- identify useful tools to control the phenomenon of antimicrobial resistance and strengthen antimicrobial stewardship programs in hospitals and outside hospitals
- implement pharmacokinetic and pharmacodynamic assessments in children for new anti-infective therapies.

B Lymphocyte Research Unit

Coordinator: **Rita Carsetti**

Activities

The Unit studies the development and function of B cells, i.e., the cells that produce antibodies to protect us from infections and represent immunological memory, in healthy individuals and in patients with primary or secondary immunodeficiencies as well. The Unit identifies the mechanisms that induce not only systemic but also local immune protection in the respiratory tract, through which many viruses and bacteria penetrate. It also studies changes in immunological memory at different ages to identify the best defense strategies for all ages and individuals. The Unit also investigates the response to vaccines to find new biomarkers of efficacy.

Results achieved

The results achieved in 2024 by the Unit include:

- identification of B cells that migrate from the blood to the respiratory mucosa. Immunity induced by vaccines and/or infections protects against severe disease, but not against infection. This is why SARS-CoV-2 continues to circulate and generate variants. The Unit has demonstrated that the inability to prevent infection depends on the mechanism that regulates the migration of memory cells to the mucosa
- persistence of immunological memory in asplenic patients. A study investigated immunological

memory in asplenic patients, comparing adults and children without spleen with healthy controls, eighteen months after COVID-19 vaccination. Antibody levels were normal, but spike protein-specific memory B cells were significantly reduced or absent. Post-2020 spleen analyses showed that these cells localized to the spleen after vaccination, confirming their key role in the preservation of immune memory. These results highlight the need for personalized vaccination protocols, with more frequent boosters, for asplenic patients

- Impact of spleen absence on NK and gamma delta cells. The study of peripheral blood from splenectomized individuals also highlighted a previously unrecognized role of the spleen in the homeostasis of two types of lymphocytes with innate functions: NK cells and Vδ2 T cells. In the absence of spleen, these populations have an altered phenotype and impaired function in adults but not in children, suggesting that other tissues may support the development of innate cells in early life. Reduced innate lymphocyte function represents an additional immune compromise and a risk factor in splenectomized individuals.

These findings highlight the irreplaceable role of the spleen in maintaining immunological memory at all ages and suggest that its absence also causes innate immune dysfunction in adults.

Objectives

Ongoing projects continue to investigate the defense mechanisms of immunological memory and B cell compartment reconstitution after transplantation. In particular:

- study of B cell compartment reconstitution after stem cell transplantation (isolated from different sources: bone marrow, peripheral or cord blood) in patients with neoplasia or immunodeficiency or after treatment with CAR-T cells in patients with autoimmune diseases and hyperacute kidney rejection
- identification of early biomarkers of vaccine response
- identification of the role of activated B cells in autoimmune diseases
- investigation of the presence of a lymphoid stem/progenitor cell located in the human spleen capable of generating B and T cells with innate functions, in addition to NK cells, after birth
- description of the mechanisms of immunological memory in children and the elderly, the two age groups most susceptible to infection.

Nutritional Therapy for Complex Diseases Research Unit

Coordinator: **Antonella Diamanti**

Activities

The Nutritional Therapies for Complex Diseases Research Unit focuses on the evaluation and investigation of the nutritional management of patients with

complex diseases, for whom advanced nutritional strategies are required. The Unit mainly carries out clinical research aimed at optimizing nutritional strategies based on retrospective experience, to identify innovative approaches based on prospective studies.

The main areas of activity of the Unit for 2025 will be:

- reassessment of the usefulness and indication of gastrostomy in patients undergoing neonatal intestinal resection
- use of pyridostigmine to improve gastrointestinal tolerance in patients with intestinal pseudo-obstruction
- clinical relevance of mRNA dosage in the diagnosis of celiac disease
- gastrointestinal tolerance to enteral nutrition and the enteroendocrine environment.

Objectives

The research activities planned for the coming years will focus on the following areas:

- standardized anti-inflammatory diet for patients with gastroenterological, rheumatological, dermatological, and hepatological inflammatory diseases
- estimation of the prevalence of complicated and uncomplicated obesity in children
- safety and efficacy of blended diets in the nutritional management of patients with complex diseases on home enteral nutrition
- clinical relevance of mRNA dosage in the diagnosis of liver disease associated with intestinal failure.

Genodermatosis Research Unit

Coordinator: **May El Hachem**

Activities

The Unit carries out clinical and translational research on genodermatoses, in particular:

- hereditary epidermolysis bullosa and ichthyosis
- rare vascular malformations
- autoimmune bullous diseases
- atopic dermatitis and pediatric psoriasis.

Experimental activity focuses on the analysis of pathogenic mechanisms, molecular determinants, and genotype-phenotype correlations to improve knowledge of etiopathogenesis and identify new diagnostic markers and therapeutic targets. Clinical research focuses on studies on clinical manifestations and natural history of rare genetic skin diseases, quality of life, development and updating of diagnostic and therapeutic guidelines, and participation in clinical trials.

Results achieved

The main scientific results achieved by the Unit in 2024 include:

- development of a multidisciplinary consensus based on the Delphi method for the management

of patients with recessive dystrophic epidermolysis bullosa (RDEB) from birth to adulthood (El Hachem et al. *Orphanet Journal of Rare Diseases*, accepted for publication)

- participation in the development of a multidisciplinary consensus for the management of patients with Sturge-Weber syndrome (El Hachem et al. *Orphanet Journal of Rare Diseases*, 2025)
- participation in a collaborative study describing the therapeutic effects of dupilumab, a monoclonal antibody inhibiting the activity of interleukin IL-4 and IL-13, in patients with innate immune errors and early-onset atopic dermatitis unresponsive to conventional therapies (Zangari et al. *Pediatric Allergy and Immunology*, 2024)
- translation into Italian of two questionnaires for assessing the disease burden of epidermolysis bullosa (EB) for patients and their families. Pilot administration of the questionnaires to a group of patients and caregivers representing all types of EB (El Hachem et al. *Italian Journal of Pediatrics*, 2024)
- identification of miR-129 as a new molecular determinant in pro-fibrotic processes active in the dermis of patients with RDEB
- launch of a study to test the therapeutic potential

of nirogacestat, a NOTCH pathway inhibitor, in a mouse model of RDEB. Definition of the treatment regimen, assessment of safety and tolerability, analysis of the presence of the drug in the skin and bloodstream through biochemical and molecular analyses

- other ongoing studies: "Preclinical Development of Gene Therapy for Dystrophic Epidermolysis Bullosa" and "Validating the fibrosis-limiting activity of PF-03084014 (nirogacestat) and valproic acid in skin fibrotic disorders: towards novel therapeutic strategies to counteract fibrosis onset and progression in adult and pediatric patients".

Objectives

The Unit will study pro-fibrotic and pro-inflammatory processes in patients with dystrophic EB to identify/validate new therapeutic targets. Regarding rare skin diseases, the Unit will:

- study the pathogenic role of non-coding RNAs
- develop or update guidelines for diagnosis and treatment
- study the quality of life and the socio-economic impact.

Oncohematology Research Area

Coordinator **Franco Locatelli**



PUBLICATIONS: 186



CORRECT IF: 1,111

The Research Area develops new molecular diagnostic approaches aimed at optimizing the characterization and risk stratification of pediatric patients with cancer.

It also investigates the innate and T-cell-mediated immune response and develops innovative cell and gene therapy protocols, from the laboratory to the bedside.

Cell and Gene Therapy for Hematological Diseases Research Unit

Coordinator: **Franco Locatelli**

Activities

The Research Unit studies hematopoietic stem cells obtained from various sources, including bone marrow, peripheral blood after mobilization with growth factors, and cord blood. It studies in vitro the immunoregulatory characteristics of mesenchymal stromal cells and their action on cells involved in the inflammatory response. The Unit also characterizes the efficacy of mesenchymal stromal cells obtained from donors in different clinical contexts and uses mesenchymal stromal cells in regenerative medicine. The primary objective of the Unit's work is to develop gene therapy and genome editing clinical approaches to hemoglobinopathies and to validate innovative approaches to hematopoietic transplantation in pediatric hematological diseases. Particular attention is also paid to new therapies aimed at accelerating immune reconstitution in pediatric patients undergoing hematopoietic stem cell transplantation.

Results achieved

In 2024, the Unit focused on:

- clinical translation of a gene-addition therapy in patients with thalassemia
- studying the role of mesenchymal cells in the hematopoietic niche of patients undergoing CAR-T cell therapy
- development of a mouse model to study the role of MAIT cells in allogeneic transplantation.

Gene Therapy for Cancer Research Unit

Coordinator: **Concetta Quintarelli**

Activities

The Unit develops innovative cell and gene therapies in the field of pediatric oncology. In particular, the Unit develops adoptive immunotherapy approaches, which are based on cells from the immune system of patients or genetically modified cells from healthy donors using viral vectors to induce the expression of chimeric receptors (CAR) against antigens expressed on the membrane of neoplastic cells. It also performs immunoprofiling of patients undergoing CAR-T cell treatment with constant monitoring to verify the pharmacokinetics/dynamics of the infused cells and the onset of specific toxicities.

Results achieved

In 2024, the Unit achieved the following results:

- development of a CAR-T therapy based on GD2 antigen recognition for the treatment of medulloblastoma
- development of autologous CAR-T cell therapy targeting the CD19 antigen in patients with refractory juvenile dermatomyositis

- induction, by tumor-derived G-CSF, of an immunosuppressive microenvironment in osteosarcoma, resulting in reduced response of anti-GD2-CAR-T cells
- immunomonitoring of adoptive therapy with anti-GD2-CAR-T cells from allogeneic donors for patients with recurrent or refractory neuroblastoma
- development of a new suicide gene system to be integrated into adoptive immunotherapy regimens for patients with hematological malignancies and solid tumors (manuscript under review in *Haematologica*)
- completion of a European survey, carried out within the *T2Evolve* consortium, to identify the analytical methods used in CAR-T cell therapies, from cell collection by apheresis to post-infusion immunomonitoring (manuscript under review in *Frontiers Immunology*)
- evaluation of humoral and cellular immune response after SARS-CoV-2 mRNA vaccine in children undergoing cancer treatment: an observational pilot study (study in collaboration with other Units)
- genetic or pharmacological inhibition of HDAC3 as a promising new therapeutic strategy to overcome radioresistance in PAX3-FOXO1 translocation-positive rhabdomyosarcoma (study in collaboration with other Units).

Objectives

In 2025, the Unit will focus on:

- development of a CAR-T therapy to target the tumor microenvironment (CAF) in solid tumors
- consolidation of activities related to the National Center for RNA Therapy and Gene Therapy PNRR project, as leaders of *Spoke 10* (Pre-clinical development, GMP production, and clinical trials for gene therapy products), and to the National Complementary Plan *Hub Life Science* Advanced Therapies project as leaders of the national consortium
- development of a CAR-T therapy based on B7-H3 antigen recognition for the treatment of medulloblastoma
- development of an NK-based therapy and virotherapy: a combinatorial approach for the treatment of osteosarcoma
- GMP development of an off-the-shelf allogeneic therapy with NK cells modified with anti-CD123 CAR for the treatment of acute myeloid leukemia.

Pathogen-specific Immunity Research Unit

Coordinator: **Chiara Agrati**

Activities

The Unit characterizes the immune response to infectious agents in immunocompromised pediatric hosts. Hematological and oncological diseases are often associated with immune dysfunction, and the therapies used contribute significantly to immunosuppression. The Unit's activities focus on the study of protective antiviral immune profiles, with particular attention to immunocompromised patients and the impact of

different immunological fragilities. It also identifies crosstalk mechanisms between different immune populations to improve the specific antiviral response. Finally, the Unit evaluates the immune response to vaccinations, with a particular focus on its generation and persistence in fragile pediatric populations.

Results achieved

In 2024, the Unit achieved the following results:

- analysis of the kinetics of the cell-mediated immune response to SARS-CoV2 vaccination in pediatric patients with different types of immunodeficiency
- initiation of qualitative/quantitative analysis of virus-specific T lymphocytes in pediatric patients undergoing different types of hematopoietic transplantation
- identification of a protective antiviral profile of $\gamma\delta$ T lymphocytes in pediatric patients undergoing hematopoietic transplantation
- identification of the role of human suppressor cells (MDSC) in reducing the efficacy of GD2-CAR-T cells in an osteosarcoma model
- activities related to WP4.5 of the National Complementary Plan *Hub Life Science* Advanced Therapies project
- activities of the clinical trial "Impact of postbiotic administration on the clinical outcome of allogeneic bone marrow transplantation: a double-blind randomized interventional study".

Objectives

The main objectives of the Unit include:

- analysis of antiviral immune profiles in immunocompromised pediatric patients that can support the identification of patients particularly at risk
- identification of new targets for immunotherapies aimed at enhancing antiviral immune response
- characterization of crosstalk between immune cells and evaluation of the impact of microbiota on immune reconstitution processes
- characterization of the response to vaccinations and of the impact of different immunological fragilities

Pediatric Cancer Genetics and Epigenetics Research Unit

Coordinator: **Franco Locatelli**

Activities

The Research Unit characterizes genetic and epigenetic molecular changes involved in the pathogenesis of hematological and solid tumors in children. The Unit's priority objectives are to identify molecular targets susceptible to targeted and specific drug treatment and to characterize the changes involved in glioblastoma. The Unit also identifies new molecular targets (microRNAs and proto-oncogenes) that are important for the treatment of glioblastoma through studies in cell systems and in vivo. Finally, it studies

and characterizes the immune component in the tumor microenvironment of pediatric patients with high-risk neoplasms to develop new prognostic and immunotherapeutic strategies.



Results achieved

In 2024, the Unit focused on:

- defining RNA molecules capable of reducing the growth of high-grade glioblastoma cells
- defining the molecular mechanisms that regulate tumorigenicity in rhabdomyosarcomas characterized by the absence of PAX3/7-FOXO1 fusion
- developing tumor-derived organoids as a new approach to improve research in the field of pediatric oncology
- modulation of innate immunity in patients with neuroblastoma to improve response to chemo-immunotherapy
- updating the national dataset for the methylation profile of patients with brain tumors.



Management, Diagnostic, and Clinical Pathway Innovations Research Area

Coordinator	Massimiliano Raponi
	PUBLICATIONS: 612
	CORRECT IF: 2,176

The Research Area promotes and carries out studies aimed at assessing the impact of organizational innovations on the quality of care, measured based on effectiveness, appropriateness, equity, and patient and operator satisfaction, in order to promote the dissemination of good clinical practices and improve efficiency standards. It also studies and promotes innovative approaches to surgery, advanced diagnostic imaging, as well as diagnostic and laboratory medicine.

Outcomes and Clinical Pathways Research Unit

Coordinator: **Marta Luisa Ciofi degli Atti**

Activities

The Unit carries out clinical studies to evaluate the outcomes of pediatric clinical and care pathways and the impact of interventions to improve the quality of care.

It focuses on:

- prevention and control of healthcare-associated infections, one of the most important areas for ensuring safe care
- outcomes of surgical procedures and intensive care, which are highly complex and specialized areas
- emergency hospital admissions, to assess access to the Emergency Department and urgent admissions
- appropriate use of antibiotics in the hospital to limit the risk of antibiotic resistance, one of the most significant global health threats.

All studies have an immediate translational impact with benefits for patients and families.

Results achieved

In the reference year, the Unit carried out:

- a study on emergency hospital admissions for acute respiratory infections (ARI) and their association with respiratory viruses' circulation from January 2018 to June 2023. Urgent hospitalizations were closely aligned with predictions made by multivariate regression models, and seasonal peaks reflected the circulation of respiratory syncytial virus (RSV), highlighting how RSV prevention is fundamental to limiting the risk of urgent ARI-related hospitalizations
- a study of RSV in children with ARI seen by family pediatricians during the 2019/2020 season in two Italian regions. Out of 293 children with ARI, 41% tested positive for RSV. The average duration of the illness was 7 days; 6% were hospitalized. In 95% of cases, medication was prescribed and in 31% antibiotics. The determinants of greater use of healthcare services were RSV subtype B infection and region of residence
- a study to monitor the trend of RSV between 2018 and 2022 and predict seasonal peaks using a SARIMA model. After the 2020 pandemic season, when RSV circulation was almost absent, RSV infections peaked earlier and higher than in pre-pandemic seasons, with a proportional increase in children over one year of age. The SARIMA model predicted the 2023 RSV peak and documented how it is reached 4-5 weeks after cases double.

Objectives

The Unit has the following objectives:

- study outcomes and clinical pathways to improve quality of care
- provide accurate and up-to-date data on the qual-

ity of care that contributes to the growth of the scientific community, to the health education for families, and to public information.

Health Professions Research Unit

Coordinator: **Emanuela Tiozzo**

Activities

The Unit proposes studies that have an impact on clinical practice and on meeting the care needs of children and their families, by implementing scientific evidence, effective interventions and organizational processes to improve the quality of care in the Hospital and in the community. It pays particular attention to patients with chronic and complex conditions (CMC) or under palliative care, regarding continuity of care, promotion of self-care, innovation and professional integration, and safe care pathways. Finally, it contributes to translating research results into care practice.

Results achieved

- The study on specialist skills in pediatric oncology described and identified the role, training, policies, and advanced skills in nursing care in pediatric oncology in Europe, highlighting regulatory and training differences between countries and suggesting the need for change to improve care
- *Global Intensive Feeding Therapy* (GIFT) has been used in pediatric diseases that cause feeding and swallowing disorders. It has been applied to patients with Down syndrome to assess its effectiveness and the anatomical abnormalities that contribute to feeding and swallowing disorders
- prevention of *Post Intensive Care Syndrome* and humanization in critical neonatal areas. Evaluation of the effectiveness and safety of the systematic implementation of educational and involvement interventions proposed to parents in critical and sub-intensive neonatal areas. The type of educational interventions documented in the medical records and the actions that parents implement for their children are also described
- *Trigger Tool* for parents of children with CMC at home: the experiences of use, acceptability, and usability of the tool are being explored, with follow-up questionnaires every 3 months administered to parents, for early detection of deterioration. The educational material developed promotes better understanding of critical signs
- PedRES-Q on cardiac arrest. Monitoring of in-hospital cardiac arrests with 35 cold debriefings. The high level of satisfaction among professionals led to the launch of training and organizational interventions to improve prevention and emergency response.

Objectives

The Unit has the following objectives:

- promote access to the PhD program for nurses and healthcare professionals, as well as for post-docs, to promote research continuation. Encourage col-

laboration with universities and the sharing of research areas

- establish new national (e.g., professional associations, pediatric centers) and international collaborations
- develop networks to participate in grants for research funding in the nursing and healthcare professions
- enhance the development of assessment tools and promote their implementation in clinical practice in order to improve the quality of care.

Technological Innovations in Plastic and Maxillofacial Surgery Research Unit

Coordinator: **Mario Zama**

Activities

The Unit focuses on research and development of technological innovations for malformations and post-traumatic conditions in the field of plastic and maxillofacial surgery.

The two main areas of research are:

- the evaluation of photobiomodulation in the treatment of chronic lesions in children
- the study of mucoperiosteum gene reprogramming methods for the development of bioengineered tissue that can promote palate regeneration in children with cleft palate.

Results achieved

During 2024, the Unit has:

- redefined therapeutic protocols
- improved patient care pathways
- implemented research on regenerative medicine and tissue engineering.

Perinatal Surgery Research Unit

Coordinator: **Paolo De Coppi**

Activities

The Research Unit focuses on maternal-fetal medicine, prenatal diagnosis and counseling, and therapies for complex fetal and neonatal diseases, with a strong emphasis on continuity of care. It focuses in particular on congenital anomalies that can be corrected surgically, with a process that begins in the first weeks of gestation and continues in stages until the age of two, and even beyond in some cases. Given the delicate nature of the clinical/scientific field and the fragility of the patients involved, the Unit activity goes beyond the technical and surgical aspects to embrace basic research and regenerative medicine, psychological approaches, pre/perinatal counseling and reception, and clinical ethics.

Results achieved

During 2024, the Unit focused on:

- using regenerative medicine techniques to obtain

laboratory-engineered segments of the esophagus and trachea that can be used in clinical practice

- further characterizing lung organoids for new strategies for the management and treatment of congenital surgical conditions such as hypoplasia and persistent pulmonary hypertension, still causing mortality in 30% of patients with CDH, as well as severe morbidity
- studying perinatal fluids (amniotic, tracheal, and bronchoalveolar lavage) to understand and predict more accurately and earlier organ damage in the fetus and newborn, thanks to the study and better understanding of the phenotype of the fetal and neonatal lung epithelium
- developing tissue-specific organoids, derived during gestation or immediately after birth, to test drug response in a patient-specific manner
- in-depth study of the glycoprotein LRG1 and its role in pediatric diseases, including tumors, heart diseases, inflammatory and immunological neurological conditions, as well as other areas in which the protein appears to be involved in terms of pathogenesis. LRG1 could play a potentially significant therapeutic role in the future
- studying the role of LRG1 in fetal vascular malperfusion in congenital conditions characterized by hemodynamic defects (e.g. CDH or Galen vein aneurysm), through the analysis of placental tissues
- defining of the role of the placenta on the neurological outcome in fetuses/newborns with CDH. Increase in the number of cases and indications for fetal surgery, including in the cardiological and neurological areas
- maintenance and updating of the international registries of rare diseases of the ERNICA and eUROGEN ERNs
- maintenance and extension, until transition, of remote follow-up of complex surgical anomalies
- retrospective analysis of available data lakes and prospective study of neurodevelopmental outcomes using artificial intelligence technologies and algorithms.

Multimodal Imaging Research Unit

Coordinator: **Aurelio Secinaro**

Activities

The Unit focuses on enhancing and strengthening diagnostic imaging for precision medicine, by improving diagnostic performance: 3D modeling, AI applied to imaging, radiomics applied to neuro-oncology, risk prediction in the cardio-thoracic-vascular area, and neurological and neurodevelopmental disorders. It also explores new therapeutic options: engineering design of new medical technologies, 3D printing and bioprinting, radiopharmaceuticals.

Results achieved

During 2024, the Unit:

- carried out approximately 20 projects, still ongoing, in the cardio-thoracic-vascular area, in oncolo-

gy and neuroscience

- used approximately 12 prototype MRI sequences currently undergoing clinical trials
- produced over 172 3D models for therapeutic planning and analyzed over 3,000 subjects using different AI and radiomics methods
- acquired cutting-edge 3D equipment for the production of anatomical models and medical devices. In particular, a high-volume filament 3D printer, a stereolithographic resin 3D printer, and a high-tech powder-based 3D printer
- collaborated with over 20 national and international organizations.

Objectives

The Unit will focus on:

- providing increasingly accurate, simple, and less invasive diagnostic tools to support care pathways in the pediatric and transition age
- enhancing the Hospital's diagnostic resources and introducing new imaging biomarkers, medical technologies, and radiopharmaceuticals into clinical practice
- establishing a Multimodal Imaging Research Center with spaces and equipment dedicated to translational research.

Translational Cytogenomics Research Unit

Coordinator: **Antonio Novelli**

Activities

The Unit develops an integrated omics approach to the analysis of the genome in its three-dimensional complexity. The objective is twofold: to diagnose rare genetic syndromes that have not yet been classified and to investigate the role of regulatory elements in phenotypic expression, identifying new pathogenic factors.

Results

In 2024, the Unit:

- identified 16 new disease genes (6 published, 10 being published)
- launched the S4C (*ScreenforCare*) project for neonatal genomic screening, with the sequencing of the first DNA samples from dried blood spots (DBS), on a cohort of 21,000 newborns in Italy (Ferrara, Modena, Rome, Siena) and other European countries (Germany, France, Greece)
- introduced the BIONANO Optical Genome Mapping (OGM) technology platform into the translational research-diagnosis pathway to identify structural genomic variants with high sensitivity (>99%) and without the biases of NGS. OGM has diagnostic applications in somatic tumor rearrangements and in the monitoring of genomic stability, improving the identification of alterations that are not detectable with traditional methods
- validated a quantitative colorimetric micromethod for the analysis of respiratory chain enzyme activi-

ties on a small number of fibroblasts collected from a large biobank belonging to the Medical Genetics Laboratory COU, for the validation of Variants of Uncertain Significance (VUS) in mitochondrial diseases

- launched a prospective pilot study to evaluate the workflow, feasibility, and diagnostic and clinical value of whole genome sequencing (WGS) in critical newborns and children admitted to the Neonatal Intensive Care Unit (NICU) and Pediatric Intensive Care Unit (PICU).

Objectives

The Unit aims at transferring advanced genomic technologies currently used in research, including whole genome sequencing, transcriptome and methylome analysis, supported by new bioinformatics tools, into clinical practice. The analysis of large amounts of data will enable the discovery of new disease genes, the assessment of genetic risk, and the development of personalized therapies.

Predictive Molecular Pathology Research Unit

Coordinator: **Rita Alaggio**

Activities

The translational research carried out by the Unit focuses on the use of whole RNA sequencing methods to define the gene expression profile of pediatric solid tumors. On the one hand, this allows for the immediate translation of data into the clinical setting (identification of new molecular alterations for the classification of neoplasms with primitive or unusual morphological characteristics and identification of potential therapeutic targets); on the other hand, it is a powerful analytical tool that identifies the characteristics of the neoplasm in terms of activated molecular pathways and their role in prognosis and response to therapy. The analysis of over 500 pediatric solid tumors has expanded current knowledge of certain types of tumors by identifying new morphological features associated with specific known molecular alterations. Furthermore, additional molecular alterations predictive of greater lesion aggressiveness have been identified. In particular, a large profiling study of myofibroblastic neoplasms was conducted, defining emerging molecular categories, including those with potentially targetable EGFR alterations (e.g., EGFR-KDD). New molecular changes have been identified as drivers of sarcomas and other pediatric malignancies. A molecular panel for the study of epilepsy has recently been developed to define associated molecular changes.

Results achieved

During 2024, the Unit achieved the following results:

- PI for the PNNR SAPERE project: for the setting up of a platform for the collection of histology (digital slides), molecular raw data (RNAseq and WES), imaging, and clinical data from patients with sarcomas (including intracranial) enrolled in AIEOP studies
- scientific collaborations on pediatric sarcomas with

study groups from the Princess Maxima Center (Utrecht), UPMC (Pittsburgh), Children's Hospital (Cincinnati), CHOP (Philadelphia), and St Jude (Memphis)

- collaboration and promotion of projects on liver tumors within the European and international liver tumor groups SIOPEL and CHIC. Within the EPSSG (European Pediatric Sarcoma Study Group), it takes part in projects on rhabdomyosarcomas and non-rhabdomyosarcoma sarcomas in children
- participation in the European study on pediatric melanomas MELCAYA.

Objectives

The Unit will carry out following activities:

- SAPERE project for the setting up of an IT platform that integrates RNAseq data in sarcomas with morphological aspects. Completion of the "molecular" classifier
- spatial transcriptomics analysis as a tool for identifying relationships between neoplasm and microenvironment and its role in cell differentiation and response to therapy in embryonal tumors.

Multimodal Laboratory Medicine Research Unit

Coordinator: **Carlo Federico Perno**

Activities

The Unit focuses on development and optimization of new tools and advanced methods to support diagnostics, with the aim of improving patient management and care pathways. It pursues the following strategic objectives:

- studying the genetics and replication of pathogenic microorganisms, especially emerging or re-emerging ones, identifying their disease-causing elements
- developing new tools for early diagnosis and personalized therapy
- analyzing clinical practice data using innovative methods to correlate the presence of pathogens with specific pediatric diseases.

Results achieved

During 2024, the following were implemented:

- use of sequencing for the analysis of common and rare pathogens in pediatrics, characterizing:
 - invasive bacterial and fungal strains
 - Human Adenovirus (HAdV) species with potential impact on pediatric disease progression to inform HAdV-specific T cell therapies
- use of FTIR spectroscopy to detect hospital outbreaks and persistent longitudinal isolates in patients undergoing antibiotic treatment.

In addition, the following have been developed:

- a study on the circulation and co-circulation of respiratory viruses, with a focus on respiratory syncytial virus and its clinical impact in pediatric patients

- a non-invasive diagnostic pathway for early detection of invasive fungal infections in oncohematological patients, to guide therapeutic choices
- Droplet-Digital PCR (ddPCR) protocols to reduce the time to diagnosis of invasive bacterial or fungal infections, achieving accurate quantification of microbiological targets in biological samples that are difficult to analyze.

In addition, longitudinal sequencing of *Pseudomonas aeruginosa* from patients with cystic fibrosis allowed for the identification of a new epidemic clone, highlighting the importance of constant genomic surveillance.

Objectives

The Unit will focus on:

- investigating the role of pathogenic bacteria in pediatric infections
- researching new microorganisms in so-called orphan diseases through the application of metagenomics
- identifying and implementing new, rapid, and innovative diagnostic methods to optimize therapy.

Innovative Models in Neurorehabilitation Research Unit

Coordinator: **Enrico Castelli**

Activities

The Unit studies rehabilitation strategies in children with neurological, genetic, metabolic, and malformative conditions causing multiple disabilities. Specific areas of analysis include neurodevelopmental disorders, muscle spasticity, movement disorders, hereditary ataxia, nonverbal communication, dysphagia, low vision, and hand prosthetics. The Movement Analysis and Robotics Laboratory, which is essential to the research activities, is equipped for robotic rehabilitation, movement and balance analysis, and study of fatigue.

Results achieved

In 2024, the Unit:

- was recognized as Center of Excellence for Ataxia (the only one in Italy) by the *National Ataxia Foundation* (USA) for the quality of its assessment, rehabilitation, and research activities in hereditary ataxias
- participated as pediatric expert in the *European Friedreich's Ataxia Consortium for Translational Studies* (EFACTS)
- developed a pediatric prototype knee exoskeleton to improve walking in children with disabilities
- organized the SIMFER-SINPIA National Inter-Society Congress "New Strategies in Pediatric Rehabilitation: Future Challenges", Rome, June 20-22, 2024
- organized the "Advanced course in movement analysis in rehabilitation clinics", Rome, April 10-12, 2024
- launched the only level I Master's Degree in Italy

on "Assessment and rehabilitation of pediatric neuro-visual disorders", in collaboration with LUMSA University (Rome)

- managed the following Master's programs:
 - the Level II Master's Degree in "Pediatric Neurorehabilitation", in collaboration with Rome University Campus Biomedico
 - the Level I Master's degrees "Neurorehabilitation and Neuroscience in Childhood" "Neuropsychology in Childhood", and "Language and Learning Disorders", in collaboration with Humanitas University Consortium (Rome).

Objectives

The Unit aims to:

- improve the personal independence and quality of life of children with disabilities by developing new rehabilitation strategies and using robotics and virtual reality
- identify strategies to limit neurological damage in the acute phase with a focus on functional recovery, leveraging the principles of neural plasticity activation
- continue to promote rehabilitation knowledge, also through scientific courses and conferences.

Preventive and Predictive Medicine Research Unit

Coordinator: **Alberto Eugenio Tozzi**

Activities

The Unit focuses on artificial intelligence techniques for the development of clinical tools for disease classification, prognosis prediction, and patient pathway optimization. The Unit supports the development of telemedicine models and hybrid pathways for complex patients. In this context, it experiments with cybersecurity applications for medical devices. It also studies the prevention of vaccine-preventable diseases and nutrition in the first 1,000 days of a child's life. The working group studies the factors that cause early-onset obesity and its metabolic, cardiovascular, and cognitive consequences. Finally, it studies new disease markers based on miRNA.

Results achieved

During the reference year, the Unit:

- applied a Common Data Model to data from the care pathway of patients with central nervous system neoplasms and made it available on the European Medicines Agency website for the development of multicenter studies
- developed an AI model to predict the time between admission and neurosurgery in patients with central nervous system tumors
- examined the effects of cybersecurity incidents in the pediatric population
- contributed to the development of national and international guidelines for a more accurate definition of obesity and for the treatment of the disease and its comorbidities

- completed a European project (EuroNanoMed-TEN-TACLES) on the regeneration of deep skin wounds, which led to the identification of a combination of microRNAs accelerating the healing process in both *in vitro* and *ex vivo* models
- in the field of pediatric disease characterization/diagnosis, it studied the key role of microRNAs contained in exosomes in communication among high-grade pediatric glioma clones, suggesting that modulation of exosome biogenesis may represent a strategy to inhibit cell motility and dissemination in this type of tumor
- initiated a study for the development of an electrochemical sensor detecting circulating microRNAs for the diagnosis of celiac disease and adherence to a gluten-free diet to develop a portable and user-friendly Point-Of-Care (POC) device.

Objectives

The working group aims to:

- act as a cross-disciplinary resource for clinical and research groups planning to develop artificial intelligence solutions
- identify new disease biomarkers based on microRNAs
- develop an electrochemical sensor for the analysis of circulating microRNAs
- increase the use of liquid biopsies for disease diagnosis
- facilitate the introduction of lab-on-chip and nanomedicine approaches in research and diagnostics
- use advanced classification and risk prediction systems for metabolic and cardiovascular diseases in obese patients that can provide information for the diagnosis of obesity in pediatric patients.

Heart Failure and Transplantation Research Unit

Coordinator: **Antonio Amodio**

Activities

The Heart Failure and Transplantation Research Unit is dedicated to the study and testing of new innovative therapies for the treatment of heart failure and pulmonary hypertension in children and adolescents. The Unit carries out studies ranging from artificial heart implantation to heart transplantation, with the aim of improving the treatment options available to young patients. The main research activities include the study of patients awaiting heart and lung transplantation and those who have undergone transplantation, to monitor and optimize post-operative treatment pathways. In addition, important clinical studies are underway on both primary and secondary pulmonary hypertension, involving a multidisciplinary network of hospital experts. From a pharmacological point of view, the Research Unit conducts innovative clinical studies, also taking part in international trials testing drugs currently available only for adults, with the aim of transferring them to a pediatric setting. Great effort is being devoted to research into the *Infant Jarvik*, an artificial heart for low-birth-weight infants, in the

framework of a European clinical study to evaluate its efficacy and safety.

Objectives

The Unit will take part in research projects on:

- advanced cardiovascular therapies for heart failure and pulmonary hypertension, with a focus on therapeutic innovation
- artificial heart implantation, studying both its use as a temporary solution while awaiting transplantation and as a permanent alternative, with a special focus on safety and efficacy in very young children
- ECMO (Extracorporeal Membrane Oxygenation), exploring the use of this extracorporeal circulation technique in the most critical contexts to improve patient stabilization and ensure safe transport to specialized centers.

Innovations in Interventional Cardiology in Pediatric and Congenital Adult Conditions Research Unit

Coordinator: **Gianfranco Butera**

Activities

The Research Unit for Innovations in Interventional, Perinatal, Pediatric, and Congenital Adult Cardiology aims to develop and coordinate research on interventional cardiology areas from the fetal period to birth, as well as long-term follow-up of adult patients with congenital conditions. This goal is achieved through multidisciplinary and integrated collaboration with other groups within the Hospital, as well as at the national and international level.

In the two-year period 2023/2024, internal activities and international collaborations led to:

- leadership in the creation and management of the Italian registry on percutaneous implantation of self-expanding pulmonary valves
- development, in collaboration with a group of engineers from Politecnico University of Turin, of a project investigating 4D flow MRI and fluid dynamics in patients with Tetralogy of Fallot; also, in the field of cardiac resonance imaging, research was oriented towards the development of an MRI-guided catheterization program
- collaboration, in the field of Perinatal Cardiology, with CHOC Hospital (California), which led to the development of fetal-perinatal diagnostic models based on artificial intelligence, including an algorithm for the prenatal diagnosis of vascular rings; contribution to the European Horizon project for the creation of a Digital Twin for formula in newborns with complex heart diseases
- extension of research to the study of the heart-placenta-brain axis, to the definition of the birth pathway from a precision medicine perspective, to neurodevelopment in CHD, and to the role of the microbiota in relation to surgical and infectious outcomes in newborns with complex heart diseases.

Objectives

The Research Unit's objectives for 2025 are to advance and complete ongoing projects and to launch new projects, including:

- development of clinical research studies on the treatment of atrioventricular valve diseases in congenital heart conditions
- development of a multi-imaging platform for pre-procedural assessment in patients undergoing pulmonary valve implantation
- enhancement of perinatal precision medicine, analysis of new possible etiologies of congenital heart diseases related to placental development, and integration of artificial intelligence for increasingly accurate diagnosis
- GUCH patient education project and study of outcome improvement
- project on the transition from pediatric to adult units and analysis of improvements in therapeutic compliance
- study of follow-up in patients treated with advanced medications.

Heart Disease Research Unit

Coordinator: **Fabrizio Drago**

Activities

The Unit conducts research on the diagnosis and medical and surgical treatment of congenital heart diseases and cardiomyopathy. It also focuses on the diagnosis and medical and interventional treatment of pediatric onset primary and secondary arrhythmia.

Results

During 2024, the Unit focused on:

- CT (computed tomography)-guided irrigated catheter ablation of epicardial accessory pathways in the coronary sinus
- transjugular approach to cryoablation of para-Hisian and right anterior accessory pathways
- transvenous advancement of the electrode catheter in pediatric cardiac pacing to overcome problems related to electrode catheter stretching induced by growth
- impact of growth on electrophysiological properties of ventricular pre-excitation in pediatric athletes
- assessment of the risk of intermittent ventricular pre-excitation in children
- long-term incidence of arrhythmias in the extracardiac Fontan conduit and comparison between left and right systemic ventricles
- role of Nt-Pro-Bnp in predicting outcome in pediatric hypertrophic cardiomyopathy
- arrhythmias in left ventricular hypertrabeculation in children
- significance of T wave inversion in young athletes
- implantable cardioverter defibrillator (ICD) in pediatric patients with arrhythmogenic cardiomyopathy.

- multimodal immune dynamics of pre-COVID-19 Kawasaki disease after intravenous immunoglobulin
- ventricular arrhythmias and cardiac death in cardiac tumors
- additional value of cardiac magnetic resonance parametric mapping in tissue characterization in the most common pediatric benign cardiac tumors
- timing of mitral surgery in patients undergoing surgery for anomalous left coronary artery.

Objectives

The Unit aims to:

- develop artificial intelligence algorithms for pediatric ECG
- new pacing and ICD implantation methods in the absence of fluoroscopy
- evaluate the follow-up of pacemaker implants at the para-Hisian site
- new strategies for transcatheter ablation of arrhythmias
- adapted physical and sports activities (AMPA) for patients with univentricular physiology
- study ventricular arrhythmias to differentiate benign and non-benign forms
- study the follow-up of patients with CPVT and short QT syndrome
- biomarkers of life-threatening arrhythmias in patients with non-ischemic cardiomyopathy
- use of ibuprofen in patients with myocarditis.

Microbiome Research Unit

Coordinator: **Lorenza Putignani**

Activities

The Unit characterizes the gut microbiota and microbiotas of other areas (respiratory, oral, tissue), contributing to the establishment, through its translational research and related diagnostic and clinical activities, of the discipline of Microbiomics, i.e., the science of microbiota based on systems medicine methods and on omics disciplines. The Unit studies disease models associated with multifactorial, genetic, and infectious diseases, proposing the microbiota as an essential factor in the stratification of disease phenotypes, together with clinical-anamnestic and laboratory medicine variables. It develops omics methods for the agnostic characterization of bacterial, fungal, viral, and parasitic communities of the microbiota, developing "shotgun" methods for next generation sequencing (NGS) studies, as well as mass spectrometry methods for the metaproteomic study of their composition and functions and for the proteomic study of the microbiota-host interaction. It identifies metabolic, intestinal permeability, and inflammation markers responsible for host-microbiota interaction and designs protocols for qualitative and quantitative determinations for diagnostic applications.

Results achieved

The Microbiome Research Unit, in collaboration with the Microbiomics SOU:

- used the Unit's mass spectrometry platform for high-resolution and high-throughput investigations
- participated in the drafting of the following national guidelines and international consensus documents, including:
 - an international consensus, Porcari S, et al., Putignani L, et al., Gasbarrini A, Ianiro G. *International consensus statement on microbiome testing in clinical practice. Lancet Gastroenterol Hepatol.* 2025 Feb;10(2):154-167. Epub 2024 Dec 5; for the standardization of the production of intestinal microbiota reports
 - guidelines for the diagnostic pathway for intestinal microbiota and the implementation of fecal transplantation in pediatrics under the auspices of the Society of Microbiology and Clinical Microbiology (AMCLI)
 - an update requested by SIGENP, the Italian Society of Pediatric Gastroenterology, on fecal transplant activities at OPBG
 - an update of the procedures for the preparation of fecal emulsions from fresh and frozen samples, based on the experience gained in 41 procedures performed on 28 patients between 2017 and 2024. Each patient was given one or

more infusions, depending on their specific clinical needs. This work formed the basis for discussion with the CNT in 2024 and contributed to the definition of the current pilot studies: one single-center study (FMT and IBD) and two multicenter studies (MDR control in oncohematological patients; FMT transplantation in patients with GVHD).

Objectives

The Unit's objectives include:

- preparation of capsules for pediatric fecal transplantation
- setting up a stool bank for products to be infused from frozen emulsions
- starting to coordinate 10 pediatric IRCCSs, in collaboration with IDEA Network, for the evaluation of pediatric diseases through disease phenotype stratification based also on human microbiota characterization
- organizing the Digital Biobank of digital microbiota profiles to establish an Italian hub for the hub-spoke system of all IRCCSs in the IDEA Network in the field of pediatric microbiomics.



02

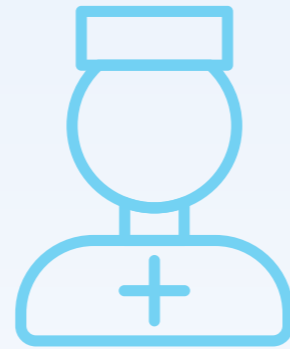
Clinical care activities

The clinical care activities of the Health Department are centered on the Complex Operating Units (to which the Simple Operating Units belong), which have clinical, managerial, and budgetary responsibility for their own areas of activity.

The following paragraphs provide details on the activities carried out, based on the organizational structure on December 31st, 2024.



Health Department



Medical Director: **Massimiliano Raponi**

Epidemiology, Clinical Pathways and Clinical Risk COU

Coordinator: **Marta Luisa Ciofi degli Atti**

The Epidemiology, Clinical Pathways and Clinical Risk COU carries out service and research activities to promote transfer of evidence into clinical practice, evaluate the effectiveness, efficiency and safety of care, conduct research on outcomes, and support epidemiological research at OPBG. The Unit coordinates the production of clinical protocols reporting recommendations derived from national and international guidelines, as well as evidence derived from scientific literature, with the aim of implementing innovation in clinical practice. It also ensures the selection, collection and monitoring of clinical indicators. In selecting indicators, priority is given to data that can be derived from electronic databases and with available benchmarks, which may be based on scientific literature, on results obtained by national or international networks, or on OPBG internal data.

The Unit coordinates the Clinical Risk Committee to promote a culture of safety, adopting a systematic and proactive approach based on learning from mistakes and multi-professional and multidisciplinary collaboration. It collaborates with all sectors of the Hospital, supports the Operating Units in the process of continuous improvement of the quality of care, and manages the accreditation process by Joint Commission International. As to methodology, it supports the design and conduct of epidemiological studies for scientific research, healthcare organization, and assessment of the quality of care. The Unit provides training on epidemiology and research methodology and is the point of reference for defining and implementing agreements relating to clinical and healthcare training (specialization and advanced training schools, Master's Degrees, internships, voluntary attendance).

Pharmacy COU

Coordinator: **Tiziana Corsetti**

The activity of the Pharmacy COU focuses on drugs, medical devices, diagnostic devices, and other healthcare materials, from purchasing to distribution to all sites and wards of the Hospital.

The activities of the Operating Unit include:

- programming, planning, purchasing, coordination of the drafting of technical specifications, participation in technical evaluation committees for procurement
- warehouse management with quantitative and qualitative control
- verifying the correct storage and distribution of medicines and devices
- distribution to inpatients, patients discharged after hospitalization, and outpatients
- management of drugs administered on an outpatient basis (File F) with centralized galenic preparation
- management of drugs in clinical trials
- participation in strategic Hospital committees: Therapeutic Formulary Committee, Healthcare-Associated Infections Committee, Equipment Planning and Monitoring Committee, Ethics Committee, Clinical Risk Committee, Committee for the Proper Use of Blood
- pharmacovigilance and EudraVigilance activities.

In particular, at the request of doctors and with the use of LOG80 software, the Pharmacy COU optimizes drug use through centralized and personalized therapies such as:

- chemotherapy
- parenteral and rehydration nutrition
- galenic preparations
- antibiotics
- narrow therapeutic index drugs
- high-cost drugs.

The process of dispensing medical devices and drugs is managed just-in-time through a micro-logistics system, which allows for the recording of all actions performed, of the identity of the person who performed them, the time they were entered into the system, and the batch processed, thus ensuring a significant reduction in costs and stocks in the Hospital and ensuring complete traceability of the entire process from the request for goods to their use and accounting.

Health Physics COU

Coordinator: **Vittorio Cannatà**

The Health Physics COU applies medical physics methodologies to diagnostic and therapeutic medicine, in particular to the use of ionizing and non-ionizing radiation. The team works to prevent risks and ensure the safety of patients and operators by measuring and assessing radiation exposure, optimizing medical exposure, and guaranteeing the quality of procedures. The Operating Unit aims to improve the care provided to children and teenagers in all activities involving the use of radiation or advanced technologies.

Legal Medicine and Appropriateness COU

Coordinator: **Caterina Offidani**

The Legal Medicine and Appropriateness Unit carries out specialist medical-legal activities within the strategic area of the Health Department. It also verifies the adequacy and appropriateness of healthcare services. Specifically, its activity focuses on:

- medical-legal disputes
- relations with judicial authorities
- opinions and proposals on health regulations
- verifying the management of waiting lists and, more generally, the adequacy and appropriateness of healthcare services within the Clinical Appropriateness Committee
- issues relating to the acquisition of informed consent.

The Unit, in collaboration with other units of the Health Department, participates in activities on the proper management of medical records, in committees for clinical risk prevention, and in the review of adverse events and sentinel events.

Third-Party Funded Patients COU

Coordinator: **Maria Osti**

The Third-Party Funded Patients COU - *Children's Global Health* - is responsible for the needs, clinical and care management upon admission, and organization of the individual care pathways of all children not covered by the National Health Service. It also receives requests for humanitarian admission and, in accordance with defined strategic guidelines, prepares them for internal authorization until their arrival at the Hospital, collaborating with Fondazione Bambino Gesù Philanthropic Institution for matters within its competence. In particular, it focuses on:

- coordinating the management, in accordance with the expected timelines and specificities, of requests for clinical care, including the completeness of the documentation available on the patient for clinical evaluation by the Hospital
- coordinating, involving administrative functions,

the process for the admission of the patient and of everything that is necessary to estimate the costs related to the clinical pathway proposed by the Hospital, as well as those related to the relevant measures to regulate the patient's relationship with the Hospital directly with the families and with any institutions contributing to the expenses

- coordinating the organization of activities, involving the relevant departments of the Hospital, including logistics, to ensure that the patient and their family receive adequate reception and care, taking care of the communication with the patient's family and with the aforementioned institutions at all stages of the treatment process.

The Unit collaborates with the International Activities Department in the study, development, and joint management of new institutional programs that meet the needs of both the non-profit sector and the private market. It collaborates with the functions of the Administration Department in defining, identifying, and implementing collaboration offers with insurance companies and health funds.

Trials COU

Coordinator: **Marina Vivarelli**

In 2024, the COU monitored 115 clinical trials, including 8 Phase I, 34 Phase II, 69 Phase III, and 4 Phase IV trials. A total of 78 new patients were enrolled, with 1,455 visits during the year. Following the studies, two drug regulatory approvals were granted by the FDA in 2024: Duvyzat (givinostat) for Duchenne muscular dystrophy (DMD) in pediatric patients aged ≥ 6 years and Limvarli (maralixibat) for the treatment of cholestatic pruritus in pediatric patients with Alagille syndrome.

The COU has continued the "forMaL" project, which involves the use of machine learning techniques in the implementation of clinical trials, supporting the production of the documents necessary for the initiation and conduct of non-profit clinical trials. The COU also organized training courses dedicated to the professional training of Clinical Research Coordinators (CRCs) and to education on Good Clinical Practice (GCP).

URP and Reception COU

Coordinator: **Lucia Celesti**

The COU is divided into the following sectors: Public Relations Office (URP), Reception Services, and Recreational Services. The purpose of the COU is to take care of families in the Hospital: reception is fundamental because a warm welcome is an important part of the care pathway for children and adolescents. In particular:

- the URP (Public Relations Office) simplifies relations between the Hospital and families, also by managing the experience of family members, complaints, and praises

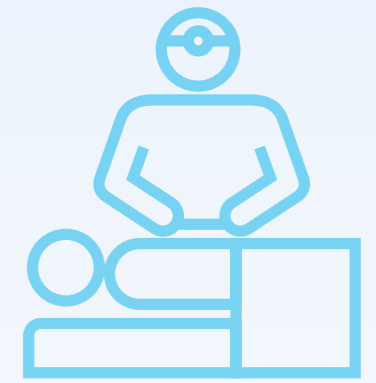
- the Reception Services act as a point of reference for families, providing support in accessing the different services offered by the Hospital and temporary homes
- the Recreational Services, run by professional educators, offer support and care to children and adolescents in the Hospital through expressive activities aimed at processing trauma.

Medical Genetics Laboratory COU

Coordinator: **A. Novelli**

In recent years, investments in equipment and human resources have enhanced genomic research and the genetic diagnosis laboratory, now the largest in Italy linked to the National Health Service, with over 38,000 tests performed in 2024. The implementation of advanced sequencing techniques and bioinformatic tools (dedicated pipelines) has expanded the possibilities to study human genetic diseases. To manage the analysis of large volumes of data, the JuliaOmix™ platform has been implemented, which digitizes the entire clinical-diagnostic process, ensuring high safety standards in compliance with EU Regulation 2016/679.

Surgery and Anesthesia Area



Functional Coordinator of the Clinical Area: **Daniela Perrotta**

Resuscitation and Operating Wards COU, Palidoro

Coordinator: **Daniela Perrotta**

- **Anesthesia and Operating Rooms SOU**
Coordinator: **Gianmichele di Cosimo**

The Palidoro Resuscitation and Operating Wards COU takes care of children and adolescents in serious and critical conditions who are hospitalized or arriving at the Emergency Room with a serious malfunction of one or more vital organs. The Resuscitation Unit is highly specialized in the care, both in the critical and chronic phases, of children and adolescents with severe respiratory failure related to diseases of the nervous and/or muscular systems. The Resuscitation service also provides mechanical ventilation for children and young people being treated in the neurorehabilitation wards of Palidoro facility.

An important activity carried out by the COU in 2024 was the anesthesiologic and perioperative management of patients undergoing surgery in the operating rooms, radiology, and hemodynamics departments in Palidoro, with the implementation of specific care protocols for fragile patients and local-regional anesthesia techniques that ensured a faster post-surgical recovery. Approximately 9,500 surgical procedures were performed, including inpatient and outpatient surgeries. Synergy with all the Operating Units and the Pediatric Palliative Care Center in Passoscuro for the management of more complex patients ensured an optimal response to the intensive care needs of the Resuscitation Unit.

Pain therapy programs were implemented at the Palidoro and Santa Marinella outpatient clinics for fragile patients, and at the San Paolo Fuori Le Mura outpatient clinic for patients undergoing complex procedures, with the application of pulsed radio frequencies, thus quickly responding to ever-increasing clinical needs.

The Unit held training courses on invasive and non-invasive ventilation techniques, PBLS (Pediatric Basic Life Support), PALS (Pediatric Advanced Life Support) and ALS (Advanced Life Support), and collaborated with the COUs of Neurorehabilitation, UDGEE (Rehabilitation Unit for Severe Developmental Age Disabilities), and Multispecialty Pediatrics to train local pediatricians. In addition, the Unit collaborated with Palidoro Level I Emergency Department to train pediatricians

in procedural sedation and pain management in the Emergency Room. Finally, it took part in European clinical trials on mechanical ventilation and transfusion monitoring.

Resuscitation, Red Zone, and Operating Wards COU

Coordinator: **Corrado Cecchetti**

- **Anesthesia and Perioperative Intensive Care SOU**
Coordinator: **Simone Reali**
- **Pediatric Neuro-resuscitation SOU**
Coordinator: **Francesca Stoppa**
- **Pediatric Poison Control Center SOU**
Coordinator: **Marco Marano**
- **E.C.M.O. SOU**
Coordinator: **Matteo Di Nardo**

The COU performs 13,500 anesthetic procedures for the same number of surgical procedures with integrated anesthetic, resuscitation, and nursing management with rapid turnover. The Unit is a national and international reference point for both acute liver failure and liver transplant patients. The use of machine learning, based on automated learning algorithms, supports the Red Area in the creation and evaluation of a predictive model of hospital mortality among critical patients with acute kidney injury undergoing continuous renal replacement therapy (CRRT). Purification techniques are used in the "cytokine storm," a potentially fatal immune reaction.

In addition, in hospitalizations lasting longer than 24 hours, delirium is assessed using the CAPD (Cornell Assessment of Pediatric Delirium) scale, and preventive measures are implemented to promote sleep-wake rhythms. An artificial intelligence program is used to optimize mechanical ventilation. Surgery is planned and performed on highly complex malformations, such as the one performed to separate conjoined twins.

The COU also provides multidisciplinary care for chronic post-surgical pain and, thanks to a nursing team with a Master's Degree in Wound Care, it also provides complex wound care, which is a fundamental tool in the PICU (Pediatric Intensive Care Unit). The Unit implements the CRM (Crisis Resource Management) methodology in daily practice and in simulated scenarios to prevent errors and to manage the emergency team correctly.

Audiology and Otolaryngology COU

Coordinator: **Pasquale Marsella**

Among the most significant clinical activities, the Audiology and Otolaryngology Unit is a regional reference center for neonatal deafness, treating approximately 200 deaf children from all over the country, performing 40 cochlear implants in 2024. It is also a center of excellence for cholesteatoma surgery (with approximately 200 major otological surgeries performed in 2024), as well as a reference center for the prosthetic and surgical treatment of malformations of the outer and middle ear.

In the field of clinical and healthcare innovations, it participates in the coordination of:

- the multidisciplinary “Neuro-ORL” working group, aimed at improving diagnostic imaging protocols for ear disorders and discussing clinical cases
- the multidisciplinary assessment group for children with otomandibular dysplasia
- the working group for the cross-cultural adaptation and validation of instrumental tests and questionnaires for assessing listening skills and quality of life in deaf children.

Continenence Surgery and Neuro-urology COU

Coordinator: **Giovanni Mosiello**

- **Andrology Surgery SOU**
Coordinator: **Massimiliano Silveri**

The Continenence and Neuro-urology Surgery COU focuses on the diagnosis and reconstructive surgical treatment of congenital and acquired urogenital disorders with repercussions on continence and urinary tract function, from the prenatal period to young adulthood. The Unit is a training center for pediatric urologists, gathering specialists from Italian schools, as well as European and non-European visitors; it is recognized by UEMS and other international urology societies (ESPU - European Society of Pediatric Urology; SIU - Italian Society of Urology; EAU - European Association of Urology). The Unit Coordinator is the President of the Italian Society of Pediatric Urology and Coordinator of the ERN eUROGEN (complex and rare urogenital malformations) and of the ERN ITHACA (spina bifida).

Andrology Surgery SOU

The Andrology Surgery SOU includes the highly specialized area of developmental gynecology. The Unit is dedicated to the diagnosis and treatment of congenital and acquired diseases of the inguinal canal, and of complex malformations of male genitalia (hypospadias, epispadias, recurvatum penis) and female genitalia, including laparoscopic/endoscopic treatment of congenital vaginal obstructions (OHVIRA), minimally invasive treatment of malformations of the genitourinary tract (Zinner syndrome/OSVIRA), and calibrated

and multistaging treatment of pelvic-perineal forms of hypospadias in 2 stages (STAG) versus 3 stages (STAC). In addition, the Unit’s team is an integral part of the Intersex Team, managing children and adolescents with disorders of sexual differentiation.

Hepato-Biliary-Pancreatic Surgery and Liver and Kidney Transplantation COU

Coordinator: **Marco Spada**

In 2024, the activities of the Hepato-Biliary-Pancreatic Surgery and Liver and Kidney Transplantation COU focused on three main areas:

- Hepato-biliary-pancreatic surgery; 75% of liver, bile duct, and pancreas procedures were performed with laparoscopy. The minimally invasive approach reduced length of stay and ensured low morbidity (<2%)
- Surgery for portal hypertension and hepatic-mesenteric vascular malformations. Thanks to collaboration with interventional radiologists and to the inclusion in international networks, alongside shunt surgery, the first percutaneous recanalization of the portal vein in cases of portal thrombosis was performed, a technique allowing for the treatment of patients who are not eligible for traditional surgery
- Liver and kidney transplantation. Transplantation is a highly complex activity with a low volume in absolute terms and is therefore subject to fluctuations depending on various factors. Nevertheless, in 2024 the Unit confirmed the positive trend in liver and kidney transplantation in terms of numbers and results, with survival rates above 90% and of 100% in living donor transplants, consolidating the center’s position as a center of excellence both at the national and international level. Extracorporeal perfusion technologies for organs to be transplanted are increasingly used; in this regard, the center is a national and international reference point in the pediatric field.

Pediatric Surgery COU, Palidoro

Coordinator: **Francesco De Peppo**

The Palidoro Pediatric Surgery Unit focuses on the diagnosis and surgical treatment of diseases affecting the organs of the abdominal cavity (bowel, colon, liver, stomach, esophagus, pancreas, gallbladder, liver, bile ducts, as well as breast and thyroid). The main conditions treated are hernias (hiatal and inguinal), ulcers, diverticulitis, cysts, polyposis, and gallstones. The examination that allows for the diagnosis of various conditions requiring surgery is a general surgery visit. In addition to routine pediatric surgery and to the management of all surgical and endoscopic emergencies performed at Palidoro facility, the Unit also performs specialized surgery focusing mainly on the following areas:

- Endoscopic and surgical treatment of obesity:
 - endoscopic treatment with an intragastric balloon is mainly intended for younger children

(<12 years) and/or those with grade I-II obesity (<40 BMI)

- surgical treatment is reserved for the most severe cases, which undergo laparoscopic adjustable gastric banding (BMI >35), while patients with a BMI >40 or severe comorbidities undergo sleeve gastrectomy (the only center in Italy)
- Treatment of palmar, axillary, and facial hyperhidrosis:
 - the procedure involves thoracoscopic clipping of the intrathoracic sympathetic nerve trunk at different levels depending on the area affected (the only center in Italy for adolescents)
- Minimally invasive treatment of pilonidal disease using EPSIT (Endoscopic Pilonidal Sinus Treatment).

The treatment drastically reduces healing times and post-operative pain, as well as secondary complications compared to traditional surgical techniques.

Plastic and Maxillofacial Surgery COU

Coordinator: **Mario Zama**

The Plastic and Maxillofacial Surgery Unit treats all malformations of the skull and face (cleft lip and cleft palate, syndromic and non-syndromic craniosynostosis, craniofacial microsomia, etc.) with a multidisciplinary team from within and across departments with different specializations: plastic surgeons, maxillofacial surgeons, craniofacial surgeons, microsurgeons, and experts in wound care. The COU is a reference center for craniofacial malformations. Every year, approximately 40 new cases of young patients with craniosynostosis are treated, in addition to over 200 new cases of cleft lip and cleft palate, accounting for more than 25% of all children born with this anomaly in Italy. Significant focus is placed on the treatment of vascular anomalies, in collaboration with dermatologists and interventional radiologists, and on bone and face soft tissue oncology. In recent years, microsurgical activity has been increasing both in emergencies (reimplantation of amputated fingers) and in elective surgery, also in collaboration with other Operating Units, in particular with the Orthopedics COU. In the area of ear malformations (otodysplasia), the collaboration with the ear surgery team has been growing, with an increasing focus on reconstruction with porous polyethylene prostheses.

Children with highly complex diseases who require periodic follow-up are managed on an outpatient basis (Day Hospital). These are often diseases that are treated by clinicians with different skills, not only surgical. The Day Hospital of the Plastic and Maxillofacial Surgery COU also carries out thorough examinations prior to surgery, visits for respiratory problems related to malformations, and meetings to help families use eating aids for children with malformative diseases. The Craniofacial Clinic, in particular, is dedicated to children with rare and complex craniofacial malformations, who are monitored from diagnosis to full development.

Finally, in the Day Hospital clinic, orthodontists visit their patients to plan orthognathic surgery to correct the maxillary and mandibular bones. The COU also focuses on research and development of technological innovations for malformative and post-traumatic conditions requiring plastic and maxillofacial surgery.

Ophthalmology COU

Coordinator: **Luca Buzzonetti**

- **Outpatient Eye Surgery SOU**
Coordinator: **Antonino Romano**

The Ophthalmology COU treats all congenital and childhood eye diseases through specific clinical pathways with dedicated specialists. Surgery is mainly performed on an outpatient and day surgery basis. In 2024, the Unit actively participated in the activities of the ERN-EYE (European Reference Network dedicated to rare eye diseases), the European network promoted and established by the European Commission based on a selection of facilities to develop common pathways for the diagnosis and treatment of rare eye diseases. The COU took part in the Working Group for the drafting of guidelines on retinitis pigmentosa and keratoconus in children, for which it is also responsible. The Unit also focuses on corneal transplantation, ocular oncology, and hereditary retinopathies, with the first treatments based on gene therapy.

Odontostomatology COU

Coordinator: **Angela Galeotti**

The Odontostomatology COU focuses on the prevention, diagnosis, and treatment of dental and oral diseases, from the most common to the most complex. The COU provides services for all dental conditions in the 0-18 age group based on specific skills. The team includes pediatric dentists (orthodontists, endodontists, oral surgeons), dental hygienists, and nurses who work in a multidisciplinary manner, collaborating with other specialists within the Hospital. In 2024, the Odontostomatology COU, in collaboration with the Advanced Cardiothoracic and Fetal Imaging COU, developed a process for the production of orthodontic devices using 3D printing: an in-house system allowing for the production of models for aligners with significant clinical advantages (e.g., speed of production/delivery) and of surgical templates for the placement of mini-screws (greater safety of the surgical procedure, accuracy of positioning, and reduction of intraoperative risks).

Orthopedics COU

Coordinator: **Pier Francesco Costici**

The Orthopedics COU treats congenital and secondary musculoskeletal deformities resulting from neuromuscular, genetic, metabolic, and post-traumatic conditions. In 2024, over 2,200 surgical procedures were

performed, and 22,000 outpatient visits were provided. The Unit specializes in neuro-orthopedics with a focus on deformities associated with cerebral palsy in children. The innovations implemented include percutaneous surgery with micro-scalpels and baclofen pump implantation. Vertebral surgery is another area of excellence, the Unit being one of the centers with the higher number of scoliosis cases in Europe. Reconstructive surgery of pelvic, hip, and lower limb deformities is another area of specialization, with corrective osteotomies and lower limb lengthening. Other areas of specialization include knee and shoulder arthroscopy, foot surgery, treatment of benign neoplasms in collaboration with interventional radiology, and hand surgery. In the scientific field, ten papers have been published in indexed journals and presentations have been made at national and international conferences.

Otorhinolaryngology COU

Coordinator: **Giovanni Cristalli**

- **Airway Surgery SOU**
Coordinator: **Marilena Trozzi**

The Otorhinolaryngology (ENT) COU focuses on the diagnosis and on the medical and surgical treatment of rare and common ENT disorders in children and adolescents. The professional training of the staff and the Unit's equipment allow for the treatment of these patients in compliance with national and international standards and guidelines identified by the relevant scientific societies. In 2024, a Level II OSAS (Obstructive Sleep Apnea Syndrome) clinic was established, allowing for the multidisciplinary assessment of complex snoring patients and their follow-up via telemedicine. A multidisciplinary pathway has been developed for thyroid neoplasms, with samples sent to the biobank for genetic analysis.

The Unit also conducts studies in the field of rhinology/allergology, to evaluate:

- the incidence of genetic mutations in patients with polyposis
- the association between the incidence and recurrence of polyposis and positive allergy tests/cytological grading of nasal inflammation
- the incidence of non-allergic rhinitis in children and its association with clinical and instrumental data.

Traumatology COU

Coordinator: **Francesco Falciglia**

The Traumatology COU manages children and adolescents with trauma or musculoskeletal disorders, including the surgical treatment of systemic and localized primary or secondary diseases, both congenital and acquired. In 2024, the protocol for requesting MRI scans for patients with vertebral fractures was modified and implemented to avoid prolonged or unnecessary hospitalizations.

Theoretical and practical training was provided to three orthopedic surgeons on innovative procedures for the treatment of capsuloligamentous lesions of the knee in children and adolescents using arthroscopic techniques. In order to improve individual knowledge and identify shared treatment protocols, on a monthly basis each doctor presents to the Unit an orthopedic traumatology topic, previously assigned to them, to highlight any new developments in the literature. Particular attention was devoted to cultural training and practice in the implementation of new external fixation techniques for the treatment of fractures, osteomyelitis, and complex limb deformities, as well as to the use of advanced techniques for the treatment of complex wounds.

Pediatric Urology COU

Coordinator: **Marco Castagnetti**

The COU focuses on the diagnosis and treatment, usually through surgery, of congenital malformations and acquired diseases of the urinary tract and genitals from the neonatal period to adolescence. In 2024, the clinical activity of the Pediatric Urology COU focused primarily on strengthening its networking with other institutions for the management and follow-up of patients with genital abnormalities, in particular patients with virilization of female genitalia and patients with hypospadias and a history of multiple failed treatments. This led to the organization of a joint multidisciplinary conference with colleagues from the Endocrinology and Diabetology COU. The Unit has also promoted the international visibility of the center by participating in panels for the drafting of the pediatric urology guidelines of the European Association of Urology.

Neonatal and Pediatric Surgery COU

Coordinator: **Andrea Conforti**

- **Oncology Surgery SOU**
Coordinator: **Alessandro Crocoli**
- **Surgery and Rehabilitation of Intestinal Failure SOU**
Coordinator: **Fabio Fusaro**
- **Emergency General Surgery SOU**
Coordinator: **Ivan Pietro Aloï**

The Neonatal and Pediatric Surgery Unit provides cutting-edge treatments for a wide range of pediatric surgical conditions, from congenital malformations to thoracic surgery, from surgical emergencies to oncology, as well as rehabilitation for intestinal failure. The team actively collaborates with leading national and international study groups, including EUPSA, ESPES, IPSO, SICP, CDH Study Group, ERNs ERNICA and eUROGEN, contributing to research and innovation in the field. In neonatal and pediatric surgery, the implementation of minimally invasive techniques, such as laparoscopy and thoracoscopy, has revolutionized the surgical approach in newborns and infants, ensuring less

traumatic procedures and faster recovery times. The use of indocyanine green (ICG) has further improved surgical accuracy, while the adoption of ERAS protocols contributed to reduce significantly post-operative hospital stays.

Oncology Surgery SOU

In the Oncology Surgery SOU, the use of indocyanine green (ICG) represents a fundamental innovation, allowing for more accurate tumor resection and better preservation of healthy tissue. This technology improves intraoperative visualization and reduces the risk of post-surgical complications, optimizing outcomes for young patients.

Surgery and Rehabilitation of Intestinal Failure SOU

In the Intestinal Failure Surgery and Rehabilitation

SOU, transit scintigraphy, combined with CT scan, allows for the accurate localization of any obstructions, and to differentiate functional from mechanical causes. This advanced diagnostic approach contributes to the personalization of treatment, optimizing therapeutic strategies and improving clinical outcomes.

Emergency General Surgery SOU

In the Emergency General Surgery SOU, the management of pediatric pleural empyema is a multidisciplinary challenge involving pediatricians, surgeons, and anesthesiologists. The introduction of video-assisted thoracoscopy (VATS) for early treatment proved to be a safe and effective option, allowing for minimally invasive procedures with better clinical outcomes and shorter hospital stays.

Imaging Clinical Area



Functional Coordinator of the Clinical Area: **Aurelio Secinaro**

Nuclear Medicine COU

Coordinator: **Maria Carmen Garganese**

- **Oncological Neuroradiology and Advanced Diagnostics SOU**
Coordinator: **Giovanna Stefania Colafati**

The Nuclear Medicine CUO is a specialty area of diagnostic imaging using radioactive substances (radiopharmaceuticals) for both diagnostic and therapeutic purposes. It is the only Nuclear Medicine Unit in Italy performing scintigraphy studies exclusively on children, located in a pediatric hospital. In 2024, the Unit continued to grow in the field of hybrid diagnostics based on semi-quantitative data (image fusion) and theranostics (integration of a diagnostic method with a specific therapeutic intervention), in line with the development of international nuclear medicine. In particular, this approach allows for better study of specific characteristics of the disease in order to define increasingly accurate and personalized treatments, both within the field of nuclear medicine, with radiometabolic therapy, and in the patient's overall care pathway. It also collaborates with the Oncohematology Clinical Area providing diagnostic support in the review of exam findings, coming from external centers, of patients who are candidates for CAR-T treatment, through consultations on scintigraphy and PET-CT scans. Finally, collaboration continues with an external center for hybrid lymphoscintigraphy studies to locate sentinel lymph nodes in melanomas, thanks to the expertise of the Unit's medical staff and the quality of the technological equipment available.

Diagnostic and Interventional Neuroradiology and Vascular Anomalies COU

Coordinator: **Carlo Gandolfo**

The Diagnostic and Interventional Neuroradiology and Vascular Anomalies COU is an international reference center for the study of central nervous system (CNS) disorders. In 2024, the Unit increased its good clinical practices in MRI procedures under sedation, performed on an outpatient basis rather than during hospitalization, so as to cause less discomfort to the patient and reduce costs. Furthermore, clinical Diagnostic and Therapeutic Care Pathways (PDTA) were produced, including the *Stroke* protocol for out-of-hos-

pital care. The Unit has improved diagnostic protocols for cerebral cortical lesions (HARNESS) and for the study of the orbit (RB), and took part in the creation of a support prosthesis for MRI loop coils.

Diagnostic Radiology COU, Palidoro

Coordinator: **Andrea Magistrelli**

The recently established COU focuses on optimizing resources and improving accessibility for patients by setting up an ultrasound room at the Santa Marinella facility for inpatients and outpatients using available but unused equipment. It runs a Level II ultrasound clinic for neonatal hip dysplasia, thus improving the diagnostic and treatment pathway for patients. In addition, it optimized the clinical management of CT and MRI scans, planning investigations according to clinical needs, with an increase in diagnostic quality and productivity.

Diagnostic and Interventional Radiology COU

Coordinator: **Gian Luigi Natali**

- **Radiology SOU, S. Paolo**
Coordinator: **Marco Cirillo**
- **Digestive Imaging and Liver Transplantation SOU**
Coordinator: **Lidia Monti**

In the diagnostic radiology area, the group dedicated to neuroblastoma is very active, with specific examinations and sessions, as well as active participation in meetings within and outside the Hospital. A structured report is currently being defined, initially intended for the examination of patients with neuroblastoma and subsequently extended to other patients. In addition, the number of slots for whole body MRI scans under sedation and for whole body MRI scans at the San Paolo Fuori Le Mura facility has been increased. In interventional area, in 2024, several innovative percutaneous techniques in pediatric oncology have been adopted. They are used daily in the adult population and many of them are included in international guidelines as first-line therapies for the treatment of certain types of cancer (e.g., TACE in Early A and Intermediate B stages according to the BCLC staging system for the management of HCC). With the aim of evaluating their effectiveness in the pediatric population,

and based on the underlying technical and therapeutic rationale, as well as on extensive data available in the literature on adult population, a number of cases eligible for these approaches were selected during multidisciplinary meetings. The technique of electrochemotherapy/reversible electroporation was adopted for the treatment of solid tumors and vascular malformations. This technique is based on the percutaneous placement (ultrasound-guided, CT-guided, fluoroscopy-guided) of special electrodes capable of creating a voltage field inside or around the lesion to be treated, allowing the cell membranes to open temporarily to allow for the intracellular delivery of cytotoxic chemotherapy (usually bleomycin or cisplatin), and then close again, restoring the normal membrane potential (reversible electroporation). The technique of transarterial chemoembolization (TACE, deb-TACE) combined with infusion of molecularly loaded particles with doxorubicin was adopted in the bridge-to-transplant treatment of a primitive HCC nodule in a patient with liver cirrhosis of unknown etiology in a syndromic setting. The Unit has implemented the technical note on percutaneous cryoablation, used until now mainly for the treatment of lung secondary tumors or to control oligometastatic disease, for the treatment of aneurysmal bone cysts.

Advanced Cardio-thoracic-vascular and Fetal Imaging COU

Coordinator: **Aurelio Secinaro**

The Advanced Cardio-thoracic-vascular and Fetal Imaging COU plans and performs complex instrumental studies in cardiology, in particular cardiac magnetic resonance imaging (MRI) and cardiovascular computed tomography (CT). These examinations play a key role in the care of children with heart conditions and

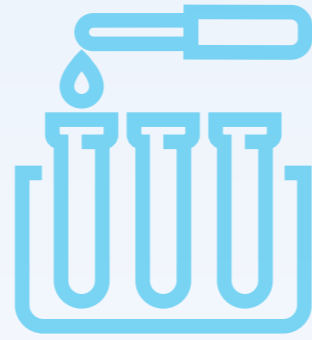
adults with congenital heart diseases. The COU has made significant progress in optimizing the efficiency and accessibility of treatments by increasing productivity in advanced studies, implementing innovative procedures, and training new generations of professionals.

The use of prototype sequences, three-dimensional technologies, and fetal diagnostics, with combined techniques including MRI-guided cardiac catheterization and dynamic MRI study of central lymphatics, has led to a significant improvement in clinical practice, with a strong focus on personalized diagnosis. The Unit's active participation in clinical trials shows its commitment to innovation. Continuous training of physicians is essential to ensure the sustainability of the sector and promote continuous development of skills. This integrated approach reflects a commitment to clinical and care sustainability, ensuring high standards of care and fostering professional development. The COU aims to enhance diagnostic imaging in a precision medicine context, improving diagnostic performance through technologies such as 3D modeling, artificial intelligence applied to imaging, radiomics in neuro-oncology, and risk prediction in the cardio-thoracic-vascular field, as well as in neurological and neurodevelopmental disorders. The Unit also actively investigates new therapeutic opportunities, including the engineering design of cutting-edge medical technologies, 3D printing, bioprinting, and the use of radiopharmaceuticals.

Great effort and careful management are devoted to expanding fetal MRI and fetal cardiac MRI.

- MT case series (28 patients, 41 procedures) in REDCap.

Laboratory Medicine Clinical Area



Functional Coordinator of the Clinical Area: **Carlo Federico Perno**

Anatomical Pathology COU

Coordinator: **Rita Alaggio**

The Anatomical Pathology COU examines tissues (biopsies, surgical resection specimens) and cytological material (from fine-needle aspiration or exfoliative sampling) to achieve the appropriate diagnostic categorization of a neoplasm or define the characteristics of non-neoplastic lesions, contributing to the final classification of the disease. The Anatomical Pathology laboratory is a reference center in Italy for the histological diagnosis of soft tissue and kidney tumors, retinoblastoma, and myelodysplasia. It is also an Italian and European reference center for pediatric liver tumors.

In 2024, the activity of the COU continued to increase in all areas, especially molecular diagnostics, which allows for the characterization of pediatric solid tumors (neuroblastoma, sarcoma, brain tumors, and rare cancers in general) and of rare tumors in adults using DNA-NGS and RNA-NGS panels, real-time PCR panels for rapid molecular diagnosis and for the identification of therapeutic targets, whole RNA sequencing, and molecular diagnosis on individual genes to identify somatic mutations of DICER1, beta-catenin, BRAF, and GNAS.

Clinical Analysis Laboratory COU

Coordinator: **Ottavia Porzio**

- **Analysis Laboratory SOU, Palidoro**
Coordinator: **Michaela Carletti**

2024 saw the strengthening of diagnostic activities of the Clinical Analysis Laboratory COU across all OPBG facilities. At the facility of Piazza Sant'Onofrio, the analytical productivity of the highly automated Corelab system for clinical biochemistry tests increased (+30% in clinical chemistry, drug, hormone, tumor marker, and cardiac tests). At the Viale Baldelli facility, a new laboratory was set up to respond more effectively to urgent clinical chemistry and hematology requests coming from the facility and from the facility San Paolo Fuori Le Mura as well.

At the same time, the Allergology and Autoimmunity Laboratories have been integrated into the Viale

Baldelli Laboratory. Furthermore, accesses to the Blood Collection Centers increased significantly, particularly at the facility of San Paolo Fuori Le Mura (69,991 visits; +10% compared to 2023). The project for the digitization of PoCT reports continued, and was extended to coagulometers and blood cell counters, allowing for self-validating reports that are available on all hospital applications. In 2024, 169,581 samples undergoing PoCT testing were reported in the Laboratory Information System (LIS).

Transfusion Medicine COU

Coordinator: **Ottavia Porzio**

- **Apheresis SOU**
Coordinator: **Giovanna Leone**

The Transfusion Medicine COU collects whole blood and performs multicomponent apheresis. It also produces, processes, and distributes blood components. Furthermore, it focuses on immunohematological diagnostics, therapeutic apheresis, and the collection of stem cells and effectors for cell therapy. Collection takes place at the Hospital and in the area through external collection units and mobile blood collection units. The Transfusion Medicine COU collects peripheral stem cells, both autologous and allogeneic, and lymphocytes, in accordance with OPBG protocols on transplantation, CAR-T cell therapy, and gene therapy. The COU is accredited by the National Transplantation Center and by JACIE (Joint Accreditation Committee of the International Society for Cellular Therapy & European Society for Blood and Marrow Transplantation). The Unit is involved in all clinical trials carried out at the Hospital on stem cell transplantation, CAR-T cell therapy, and gene therapy.

Pre-transfusion tests are performed in the Blood Component Allocation and Distribution area, while Level I and II diagnostic tests are performed in the Erythrocyte Typing area, both as an inpatient and outpatient service. In the Erythrocyte Immunohematology area, screening tests are performed for the diagnosis of immune hemolytic anemia and the subsequent identification of the antibodies involved, both as an inpatient and outpatient service (the same laboratory also performs platelet immunohematology tests).

Microbiology and Immunology Diagnostics COU

Coordinator: **Carlo Federico Perno**

- **Microbiology SOU**
Coordinator: **Paola Bernaschi**
- **Virology and Mycobacteria SOU**
Coordinator: **Cristina Russo**
- **Microbiomics SOU**
Coordinator: **Lorenza Putignani**

The COU focuses both on immune-cytofluorimetry and functional testing, supporting the identification and monitoring of immunodeficiencies related to susceptibility to infections. In some specific settings, the laboratory plays a strategic role in the therapeutic decision-making process in fragile patients (e.g., anti-rejection immune modulation in heart transplant patients treated with thymoglobulin). Furthermore, in line with its mission, the laboratory is at the forefront of the rapid identification of lymphoproliferative diseases. As part of its innovation process, the COU develops viral antigen response methods to identify the risk of developing serious infections in transplant and immunocompromised patients.

Microbiology SOU

In 2024, the Microbiology SOU introduced the rapid phenotypic antibiogram testing (4-6 hours) from positive blood culture samples, providing timely information on bacterial pathogens and their antimicrobial susceptibility for the management of patients with sepsis. FT-IR spectroscopy was also used both to determine microbial clusters in possible clinical outbreaks in 3-4 hours and to identify failed eradication/reinfection of *Pseudomonas aeruginosa* in CF patients, supporting clinicians in choosing the appropriate antibiotic therapy.

Virology and Mycobacteria SOU

In 2024, in order to better characterize the infectious profile of patients, the laboratory of the Virology and Mycobacteria SOU performed over 400 analyses re-

sponding to infectiology needs, ranging from antibody tests for the identification of immune response, to molecular biology investigations, both pathogen-specific and syndromic (tests for the multiple detection of respiratory viruses and of viruses responsible for gastroenteritis).

The range of activities also includes the use of new generation techniques (next generation sequencing) for the correct management of infections in fragile patients (study of drug resistance in Cytomegalovirus and HIV), as well as for virus characterization. The Virology and Mycobacteria SOU is an integral part of the national networks for integrated epidemiological surveillance (coroNet-INFLUNET, RespiVirNet, MoRoNET, EuPert). It also has a Level 3 Biosafety Laboratory for the proper handling of samples from patients with suspected tuberculosis and non-tuberculous mycobacterial infections, as well as pathogens causing severe and emerging diseases that can be life-threatening to humans. It is a regional reference center for hepatitis of unknown etiology.

Microbiomics SOU

In 2024, the main activities of the SOU included:

- the "Clinical Applications of Gut Microbiota Characterization" outpatient clinic for the clinical application of microbiota diagnostics
- collaboration with the National Transplant Center (CNT) in the drafting of quality documents and hospital protocol for fecal microbiota transplantation (FMT) and for the recognition of the SOU as a STOOL BANK for FMT
- automation of microbiota profile reporting using the *Dysbiotrack* platform
- participation in the AMCLI Working Group on the standardization of FMT procedures
- revision of the OPBG-Bologna-Padua Multicenter FMT Protocol
- archiving all pediatric FMT case series (28 patients, 41 procedures) in REDCap.

Oncohematology, Cell Therapy, Gene Therapy, and Hematopoietic Transplantation Clinical Area



Functional Coordinator of the Clinical Area: **Franco Locatelli**

- **Oncohematology, Hematopoietic Transplantation, Cell Therapies, and Trials COU**
Coordinator: **Franco Locatelli**
- **Neuro-Oncology SOU**
Coordinator: **Angela Mastronuzzi**
- **Oncohematological Therapies SOU**
Coordinator: **Stefania Gaspari**
- **DH Oncohematology SOU**
Coordinator: **Annalisa Serra**
- **Cell Manipulation SOU**
Coordinator: **Giuseppina Li Pira**
- **Transplant Immunogenetics SOU**
Coordinator: **Marco Andreani**

The Oncology, Cell Therapy, Gene Therapy, and Hematopoietic Transplantation Clinical Area is characterized by its extensive work in the development of innovative therapies for pediatric oncological and hematological diseases. In addition to transplants from partially HLA-compatible family donors, these treatments include therapies based on the use of CAR-T cells.

The term CAR-T is an acronym for Chimeric Antigen Receptor T-cell, indicating T cells expressing chimeric antigen receptors. The term refers to a type of immune system cell, T lymphocytes, taken from a person and genetically modified in the laboratory to enable them to selectively attack diseased cells (e.g., neoplastic cells) once they are reinfused into the same person from whom they were taken. The strategy aims to enhance a mechanism already present in the immune system: the ability of a particular type of cell, cytotoxic T lymphocytes, to attack cells in the body (for example, because they have become malignant).

Lymphocytes recognize abnormal cells because the latter have the target molecule on their surface. The lymphocytes recognize the antigen through a specific receptor on the surface of the lymphocyte itself. In the laboratory production of CAR-T cells, the lymphocyte is modified in such a way that it expresses on its surface the receptor capable of recognizing the antigens present on the target cells and of transmitting an activation signal to the lymphocyte to eliminate them. The design of the OPBG Pharmaceutical Workshop began in 2013; in 2017, AIFA authorized it to produce gene therapies.

Within the framework of the *CAR-T Italia* Project, the Pharmaceutical Workshop has been identified as a

center of excellence for the production of CAR-T cells.

OPBG is recognized as a center of excellence for the administration of CAR-T cells, based on the following four criteria defined by AIFA:

- certification issued by the National Transplant Center and the National Blood Center on the compliance of the Bone Marrow Transplant Center with the requirements of European Directives
- JACIE 7.0 accreditation for allogeneic transplantation
- availability of an intensive care and resuscitation unit
- availability of a qualified multidisciplinary team for the clinical management of patients and of any complications.

Treatments with CAR-T cells were performed on patients with acute lymphoblastic leukemia, both B cell and T cell (for the latter, OPBG is the only active center in Europe), neuroblastoma, central nervous system neoplasms, and autoimmune diseases mediated by auto-reactive B lymphocytes (systemic lupus erythematosus, dermatomyositis, progressive systemic sclerosis).

The efficacy in the treatment of neuroblastoma at OPBG was evaluated in patients up to 25 years of age; the overall response to treatment was 63%, while the overall 3-year survival rate was 60% (*The New England Journal of Medicine*, 2023;388:1284-95). OPBG has also pioneered the development of allogeneic CAR-T cells, i.e., obtained from a donor, showing both a good safety profile and significant efficacy (Del Bufalo, et al. *Blood*, 2023; Quintarelli et al. *Nature Medicine*, 2025).

In the future, there will be different types of CAR-T cells, which will differ from each other based on the single receptor they are induced to express and, consequently, the target they are able to attack.

In the short and medium term, OPBG will guarantee the production of CAR-T cells for patients suffering from the diseases treated to date and from different histotypes of tumors, such as Hodgkin's lymphoma, acute myeloid leukemia, osteosarcoma, and Ewing sarcoma.

Based on the above, the potential development of these innovative and personalized therapies in the

fields of research, clinical practice, and training is vast. From the perspective of the National Health System, they will not only save lives that would otherwise be at high risk, but will also allow for investments derived from saving on the extremely high costs associated with the long-term treatment of chronic diseases,

which often require life-long treatment. Of note, is also OPBG pioneering role in the validation and approval of gene therapy approaches in hemoglobinopathies (Locatelli et al. *The New England Journal of Medicine*, 2021; Locatelli et al. *The New England Journal of Medicine*, 2023).

University and Hospital Pediatrics Clinical Area



Functional Coordinator of the Clinical Area: **Alberto Villani**

Allergology COU

Coordinator: **Alessandro Giovanni Fiocchi**

Allergic diseases and asthma have a high social impact because they affect large segments of the population. In this regard, the COU focuses on many areas, including:

- understanding molecular pathogenesis
- using this knowledge to develop specific molecules for proactive use
- identifying biomarkers that predict and monitor the therapeutic efficacy of drugs
- conducting definitive randomized studies in all age groups, especially in pediatrics
- identifying objective tests that can ensure early and specific diagnosis.

The COU takes part in a series of projects within the *European Academy of Allergy and Clinical Immunology (EAACI)* and the *World Allergy Organization* to draft guidelines and recommendations that require preliminary meta-analyses or consensus-building processes using *e-Delphi*.

The main results achieved by the group include:

- long-term efficacy and safety of IL-4 and IL-13 inhibitors in the treatment of severe asthma in children, with a focus on quality of life and efficacy biomarkers
- reactivity of children with severe food allergies to products with precautionary labeling for the respective allergens: new reactivity thresholds have been described for children allergic to baked forms of egg and milk compared to those tolerant to these forms
- effect of IgE inhibitors in children with severe food allergies
- quality of life of children treated with IL-4 and IL-13 inhibitors for the long-term treatment of severe asthma
- description of nasal polyposis in children.

As part of its work on cystic fibrosis, the Unit focuses on the pathogenesis of the disease, with particular attention to extending access to personalized therapy to as many patients as possible. In this regard, the expression of IL-17 in respiratory epithelial cells was examined, documenting its importance. The response to ETI (Elexacaftor-Tezacaftor-Ivacaftor) has also been

evaluated in patients who are not eligible for triple therapy. The response of intestinal organoids harboring genotypes currently unsuitable for ETI therapy suggests that a large proportion of people with rare CFTR variants without access to ETI may benefit from this treatment.

Pediatric Palliative Care Center COU

Coordinator: **Michele Salata**

In 2024, the Pediatric Palliative Care Center implemented a home care model for children eligible for pediatric palliative care, activating the Multidimensional Assessment Unit with the home care services provided by the local health authorities. This model has allowed for greater integration between the Hospital and local communities, enabling more appropriate definition of individualized care plans. The model has been applied to both patients residing in the Lazio region and patients from other regions. The Pediatric Palliative Care Center has been identified as a school, making it possible to guarantee school attendance for all hospitalized children and their siblings. A multimedia room is available, providing innovative teaching tools and technologies, thus ensuring the continuity of programs with the schools of origin. Thanks to the support of the Health Department, the range of voluntary associations present daily at the Center has been expanded, thus ensuring support for families and implementing care interventions, such as animal-assisted interventions, music therapy, ceramics therapy, clown therapy, etc. Monthly meetings have been organized with the Neuro-Oncology SOU for the early referral of patients, allowing families and patients to learn about the Center, offering day hospital services and regular hospitalizations for the control of refractory symptoms, in particular for pain management and follow-up, respite care, terminal care, and end-of-life care.

Dermatology COU

Coordinator: **May El Hachem**

- **Center for Complex Chronic Dermatitis and Genodermatosis SOU**
Coordinator: **Andrea Diociaiuti**

In 2024, the activity of the Dermatology COU continued increasing in terms of outpatient dermatology

surgery under local and general anesthesia, with an excellent performance of multidisciplinary diagnostic and therapeutic approaches for patients with ichthyosis, incontinentia pigmenti, epidermolysis bullosa, and vascular anomalies. The Unit participated in the activities of two ERNs: ERN-Skin, as a member of the coordinating team, and VASCERN's VASCA Group, as the only Italian center.

In the field of healthcare innovation, it is launching:

- a pharmacological therapy based on biologics approved for pediatric use for inflammatory skin diseases, specifically: atopic dermatitis, psoriasis, alopecia areata, and vitiligo
- a joint dermatology-allergology clinic for the management of children with atopic dermatitis and food or other allergies
- a joint dermatology-plastic surgery clinic for the management of giant congenital nevi

As regards ongoing activities:

- research is being conducted on fibrosis in patients with epidermolysis bullosa
- a PNRR project is underway for a "Multicenter interventional study for the selection of patients with recessive dystrophic epidermolysis bullosa (EBDR) eligible for gene therapy and for the preclinical development of a GMP product for ex vivo gene therapy of EBDR" (EBDR/ PNRR-MR1-2022-12376725)
- clinical trials have been initiated on both inflammatory diseases and epidermolysis bullosa.

Endocrinology and Diabetology COU

Coordinator: **Stefano Cianfarani**

- **Endocrine Pathology of Chronic and Post-Tumor Diseases SOU**
Coordinator: **Armando Grossi**
- **Pediatric Endocrinology SOU**
Coordinator: **Carla Bizzarri**

The Unit focuses on the prevention, diagnosis and treatment of endocrine and glucidic metabolism disorders, as well as on clinical and translational research, carrying out innovative clinical trials, and improving the quality of life of patients and their families. In 2024, trials began on the use of artificial intelligence in the treatment of patients with type 1 diabetes. In children with monogenic diabetes mellitus, the large-scale implementation of next generation sequencing led to the identification of new genetic variants and to the personalization of therapy. In the field of genetic and hypothalamic obesity, trials have begun on new drugs capable of reducing body weight and improving the metabolic profile.

A new biochemical and endocrine approach has identified exposure to the environmental endocrine disruptor bisphenol A as a risk factor for obesity in girls. In the field of growth retardation, a diagnostic algorithm has been developed for the genetic characterization of children with severe forms of short stature,

and new causative genetic variants have been identified. In the field of precocious puberty, the clinical and endocrinological characteristics associated with the risk of brain damage in males with central precocious puberty have been identified. Finally, a service dedicated to the endocrinological follow-up of children with a history of neoplasms has been launched.

Gastroenterology and Nutrition COU

Coordinator: **Paola De Angelis**

- **Digestive Endoscopic Surgery SOU**
Coordinator: **Tamara Caldaro**
- **Nutritional Rehabilitation SOU**
Coordinator: **Antonella Diamanti**

Gastroenterology and Nutrition COU and Digestive Endoscopic Surgery SOU

The Gastroenterology and Nutrition COU and the Digestive Endoscopic Surgery SOU manage patients with complex digestive disorders, whether malformative, inflammatory, or post-traumatic, requiring medical, endoscopic, and/or surgical treatment, often in combination. Patients are frequently referred to the Operating Units from other Italian and European hospitals for the management and endoscopic/surgical treatment of complex diseases. In 2024, there were 955 hospital admissions and 996 day hospital and day surgery services; approximately 1,941 EGDSs, 603 colonoscopies, 95 ERCPs, and 150 major surgical procedures were performed. The activity also includes specialist clinics and pathophysiology services for the digestive system (esophageal/antroduodenal/colonic/anorectal manometry and pH impedance testing).

Innovative activities carried out in 2024 include:

- activation and consolidation of multidisciplinary clinics, including Gastroenterology-Rheumatology and Gastroenterology-Hepatology for chronic inflammatory bowel diseases with extraintestinal manifestations and the Microbiota Clinic with dysbiosis therapies, including in patients with autism spectrum disorders
- structured management of enterostomies by medical and nursing staff
- management of chronic inflammatory bowel diseases and complex autoimmune enteropathies with off-label drugs, clinical trials, and surgery
- endoscopic treatment of tracheoesophageal fistulas and esophageal perforation using autologous stem cells
- innovative endoscopic third space procedures (hot-Axios for gastro-entero anastomosis/drainage of pancreatic pseudocysts; POEM for achalasia; resorbable Ella stents for recurrent esophageal strictures and esophageal perforation).

Nutritional Rehabilitation SOU

The Nutritional Rehabilitation SOU specifically manages patients with intestinal failure and complex extra-intestinal diseases who are dependent on artificial

nutrition, on an inpatient (400 patients/year on average), outpatient (3,500 patients/year), and day hospital (150 patients/year) basis. For the Lazio Region, the Nutritional Rehabilitation SOU is a certifying center for:

- home artificial nutrition, managing a total of 1,450 patients on parenteral and/or enteral nutrition throughout Italy
- coeliac disease (3,500 patients managed) and rare gastrointestinal diseases (220 patients managed).

In the framework of artificial nutrition programs for complex diseases, in 2024 the Nutritional Rehabilitation SOU used:

- GLP2 analogues and systematic use of enteral nutrition to reduce dependence on parenteral nutrition
- enteral nutrition mixtures to optimize tolerance and promote growth.

Clinical Immunology and Vaccinology COU

Coordinator: **Paolo Palma**

- **Primary Immunodeficiencies SOU**
Coordinator: **Caterina Cancrini**
- **Immuno-infectiology SOU**
Coordinator: **Andrea Finocchi**

In 2024, the Clinical Immunology and Vaccinology COU strengthened its role as a reference center for the diagnosis, treatment, and vaccination of pediatric patients with primary and secondary immunodeficiencies, actively participating in the European Reference Network for Rare Immunodeficiency, Autoinflammatory and Autoimmune Diseases (ERN RITA). Clinical and care activities included multidisciplinary and personalized management of complex patients from all over the country and abroad, with treatment and vaccination plans tailored to each patient's clinical and immunological profile. The COU has contributed to the definition of internal protocols for the vaccination of vulnerable children (solid organ transplant), facilitating an integrated approach to prevention even in the most delicate hospital settings. The outpatient clinic for vaccinations during pregnancy has also been enhanced to promote maternal immunization and passive protection of newborns in the early stages of life. During the year, new vaccines have been introduced for vulnerable patients, including the dengue vaccine and nirsevimab, a monoclonal antibody for the prevention of respiratory syncytial virus (RSV) infection in newborns. To support clinical decision-making, the Unit has intensified its clinical and translational research activities, participating in international trials and developing predictive biomarkers to guide personalized precision therapies, including innovative treatments with dupilumab, abatacept, and lioesib. The Unit also developed advanced laboratory tests, such as proteomic analysis and RNA sequencing, with the aim of profiling patients and optimizing therapeutic and vaccine response. At the same time, efforts have continued to personalize vaccination for individuals

with allergies, chronic diseases, immunodeficiency, or previous adverse events from vaccines or drugs, ensuring efficacy and safety. The COU also provides continuous information and counseling on vaccines to families, both through direct consultations and through an email support service at infovacini@opbg.net, promoting a culture based on appropriateness, safety, and awareness.

Infectious Diseases COU

Coordinator: **Laura Lancella**

- **Complex and Perinatal Infections SOU**
Coordinator: **Stefania Bernardi**

The Infectious Diseases COU focuses on diagnosis, treatment and follow up of suspected or ascertained infectious diseases. In 2024, the doctors of the Infectious Diseases COU performed clinical, care, and research activities, always keeping the patient and their family at the center of their effort. Teleconsultation on infectious diseases for patients admitted to the Palidoro facility increased from 141 teleconsultations in 2023 to 373 in 2024 (+164.5%). There has been an increase in the number of patients with osteomyelitis and severe skin infections who have received long-acting antibiotic therapy (dalbavancin) on an outpatient basis, with weekly intravenous administrations, leading to a reduction in hospital stays and risk of hospital-acquired infections: 4 patients treated in 2023 compared to 13 in 2024 (+225%). A clinic dedicated to sexually transmitted diseases (STDs) was set up at the San Paolo Fuori le Mura facility, active on Saturday mornings, aimed at adolescents and chronic patients at risk of infectious diseases. As part of "Good Practices", some adolescents and young adults with HIV infection have been supported in the transition to adult care centers thanks to a training and information program based on the presence of peer supporters. Screening for cytomegalovirus infection in pregnant women in their first trimester has been implemented, and primary prevention measures have been disseminated. Research activities mainly focused on severe infections and antimicrobial stewardship. Thirty-six scientific articles were published in national and international journals.

Metabolic Diseases and Hepatology COU

Coordinator: **Carlo Dionisi Vici**

- **Hepatology and Transplantation Clinics SOU**
Coordinator: **Andrea Pietrobattista**
- **Metabolic Diseases Inpatient Ward SOU**
Coordinator: **Diego Martinelli**

The Metabolic Diseases and Hepatology COU focuses on diagnosis, treatment (pharmacological, diet, enzyme therapy, and liver and/or kidney transplantation) and follow-up of children and adolescents with hereditary metabolic diseases. It also takes care of newborns as part of the neonatal screening program and manages children and adolescents, both during hospitaliza-

tion and through dedicated outpatient clinics. The COU is recognized by Lazio and Abruzzo regions as a reference center for neonatal screening and participates in the Ministry of Health's Working Group. Together with the other Operating Units of the Hospital, it coordinates liver and liver-kidney transplantation programs and is a national and international reference center for transplantation in patients with metabolic diseases. It coordinates and is a member of several ERNs (Metab-ERN, ERN RARE-LIVER, ERN TRANSPLANT-CHILD). It participates in clinical trials on innovative therapies. The COU has a laboratory for translational research on metabolic diseases and pediatric precision medicine, specifically focusing on therapeutic drug monitoring.

Rare Diseases and Medical Genetics COU

Coordinator: **Andrea Bartuli**

- **Medical Genetics SOU**
Coordinator: **Maria Cristina Digilio**

The COU provides diagnostic and care services to patients with rare and genetic conditions and to highly complex undiagnosed patients. Clinical activities are carried out on an outpatient basis, with day hospital or regular hospitalization depending on specific needs and in accordance with dedicated protocols and clinical pathways. For years, the COU has been participating in the drafting of national and international care protocols for the most common genetic syndromes, with structured care and research activities in the field of undiagnosed genetic and rare conditions, autism and genetic intellectual disability, overgrowth syndromes, bone dysplasia, neurofibromatosis, genetic dyslipidemia, Gorham Stout syndrome, PROS syndromes, Noonan syndrome and other rasopathies, 22q11.2 microdeletion syndrome (DiGeorge/VCF syndrome), Williams syndrome, Kabuki syndrome, and KBG syndrome. The COU is a regional, national, and European reference center for the drafting of guidelines for the main rare and genetic conditions and participates in the relevant care networks. Specifically, it is a reference center for three ERNs, the European networks dedicated to rare diseases: ERN BOND (for bone disorders), ERN GENTURIS (for hereditary tumor risk syndromes), ERN-ITHACA (for rare malformation syndromes and developmental disorders), and participates in international collaborations and experimental studies on specific rare and ultra-rare conditions. The staff takes part in scientific committees of patient and family associations, promoting the continuous improvement of care and research.

Nephrology COU

Coordinator: **Francesco Emma**

- **Pediatric Dialysis and Kidney Transplant Clinics SOU**
Coordinator: **Isabella Guzzo**

In 2024, the activities of the Nephrology COU included a very high number of kidney transplants for the

second consecutive year. Thirty-seven transplants were performed, including 10 from living donor and 2 combined liver-kidney transplants. Thanks to these numbers, the Hospital ranks first in Italy and among the top centers in Europe. Clinical trials have also been initiated on the use of new complement system inhibitors for the treatment of immune-mediated kidney diseases. As part of the NEPHNET project (PNRR), the collection of biological specimens from nephropathic patients at our biobank was completed on schedule.

As to the Unit's organization, a multidisciplinary team has been set up to treat abdominal vascular malformations, including nephrologists, interventional radiologists, hepatobiliary surgeons, sports medicine physicians, and geneticists. The team meets four times a year to discuss very rare cases of vascular malformations in an interdisciplinary manner in order to provide comprehensive and integrated care to patients.

General Pediatrics and Level II Emergency Department (DEA) COU

Coordinator: **Alberto Villani**

- **General Pediatrics Follow-up SOU**
Coordinator: **Diletta Valentini**
- **Highly Complex Care Pediatrics SOU**
Coordinator: **Maria Rosaria Marchili**
- **Emergency Pediatrics Inpatient Ward SOU**
Coordinator: **Anna Maria Caterina Musolino**
- **Level II Emergency Department**
Coordinator: **Sebastian Cristaldi**

The General Pediatrics COU and Level II Emergency Department (DEA) focus on the diagnosis and treatment of major pediatric diseases. As part of the care pathway that our Hospital guarantees to patients suffering from eating disorders (EDs), an Eating Disorders Clinic has been set up to identify nutritional disorders and diagnose pathological conditions at an early stage (150 patients) in collaboration with the Gastroenterology and Nutrition COU and the Child and Adolescent Neuropsychiatry COU. Care pathways have been activated to ensure a reduction in hospital admissions and/or days of hospitalization for patients with EDs. Over 500 televisits and over 750 outpatient chest ultrasound examinations have been performed. Close follow-up of Emergency Department patients is ensured with scheduled follow-up appointments upon discharge (reducing the number of early returns to the Emergency Department).

Multispecialty Pediatrics COU

Coordinator: **Andrea Campana**

Compared to previous years, in 2024 the activities of the Multispecialty Pediatrics COU focused more on the multidisciplinary management of patients with highly complex chronic disabling conditions by enhancing outpatient and day hospital care, as well as home care through teleconsultation, to reduce the number and

duration of ordinary hospitalizations. This joint effort, in collaboration with the Neurorehabilitation - UDGEE (Rehabilitation Unit for Severe Developmental Age Disabilities) COU and the Passoscuro Pediatric Palliative Care Center, combined with the implementation and improvement of pathways, aims to ensure the management for the many patients requiring multispecialty assessment. A Headache Clinic has been set up in collaboration with the Developmental Neurology COU. Particular attention is also being devoted to the creation of a care network with the surrounding area through the "Pediatric Refresher Days", a course that takes place throughout the year for the training of family pediatricians.

Level I Emergency Department (DEA), Palidoro

Coordinator: **Maria Antonietta Barbieri**

- **Emergency Pediatrics SOU**
Coordinator: **Andrea Campana**

The Level I Emergency Department (DEA) provides emergency care at the Palidoro facility, taking care of clinical emergencies in children (0-18 years of age). It plays an important role in the management of pediatric emergencies in the area, providing services according to a severity scale ranging from mild to severe. In 2024, 42,429 patients visited the ER, of whom approximately 2.38% left before being seen by a doctor, and 2,436 (5.7% of total visits) resulted in hospitalization. In November 2022, a "protected discharge" clinic was set up for all patients that were borderline for ordinary hospitalization, which was active twice a week and, since February 2023, three times a week.

In 2024, 565 follow-up visits were provided following protected discharge (compared to 492 in 2023). Six clinicians were trained on lung ultrasound at the DEA Department, which is performed after the physical examination in order to reduce the number of chest X-rays. Over 80% of DEA doctors have completed theoretical and practical training, in collaboration with the Resuscitation and Operating Wards COU (Palidoro), on procedural sedation, to reduce the number of anesthesiology consultations and improve pain management in the Emergency Room. The total number of sedations was approximately 20, with a reduction in patient stay times in the Emergency Room and improved clinical management. The remaining 20% of doctors will complete the training by the end of 2025.

The COU provides PALS and BLS training, training for pediatric residents at the Universities of Rome Tor Vergata and La Sapienza through monthly meetings, as well as one-to-one mentoring between specialists and residents with final assessment of the skills acquired. Furthermore, on-site simulations are implemented with the staff (doctors and nurses) on duty, using a high-fidelity manikin (Laerdal), in accordance with AHA guidelines.

Pulmonology and Cystic Fibrosis COU

Coordinator: **Renato Cutrera**

- **Respiratory Semi-Intensive Care SOU**
Coordinator: **Maria Giovanna Paglietti**
- **Sleep Medicine and Long-Term Ventilation SOU**
Coordinator: **Martino Pavone**

The Pulmonology and Cystic Fibrosis COU focuses on acute and chronic pediatric respiratory diseases and particularly on the differential diagnosis of children with chronic or recurrent cough and patients with difficult-to-treat and severe asthma. It is a regional and European reference center for rare respiratory diseases (ERN-LUNG). During 2024, the Pulmonology and Cystic Fibrosis COU continued its program of clinical and care innovation in the various areas in which it operates. In the field of rare diseases, the immunofluorescence diagnostic method was introduced in collaboration with the Anatomical Pathology COU, and multicenter national and international research projects were carried out.

As to respiratory pathophysiology, oscillometry was introduced for the follow-up of non-cooperative patients with cystic fibrosis (CF). Calorimetry has also been implemented to promote a targeted nutritional approach in both patients with neuromuscular diseases and patients with CF. During 2024, the Unit also provided access to a series of innovative therapies:

- off-label gene modulator for CF patients
- gene therapy with zolgenema for a patient with SMA 1 with prenatal diagnosis
- anti-IL4-IL13 for school age children with severe asthma
- anti-TSLP for adolescents with severe asthma.

Finally, in collaboration with colleagues from the Muscular and Neurodegenerative Diseases COU and the team of respiratory physiotherapists, specialist follow-up of neuromuscular patients has been implemented, specifically aimed at the management of respiratory physiotherapy techniques.

Rheumatology COU

Coordinator: **Fabrizio De Benedetti**

- **Rheumatology Inpatient Ward SOU**
Coordinator: **Antonella Insalaco**

The Rheumatology COU focuses on the diagnosis and treatment of acute and chronic rheumatic diseases through dedicated pathways that include ordinary hospitalizations, day hospital activities, and outpatient care. Over the years, there has been a steady increase in the number of visits and services provided. The outpatient clinic is dedicated to initial rheumatology consultations for children with suspected rheumatological diseases for an initial clinical assessment. Outpatient rheumatology check-ups are also provided for

patients with a diagnosis of ascertained or suspected rheumatological disease. In this context, biologics and other medications that can only be dispensed in hospitals are also provided. Outpatient joint surgery and ultrasounds for patients with juvenile idiopathic arthritis (JIA) are increasing. In addition to the different forms of JIA, the Unit manages children and adolescents with systemic lupus erythematosus, juvenile dermatomyositis, rare connective tissue diseases, vasculitis,

autoinflammatory diseases, and hyperinflammatory diseases. The COU also participates in the development of innovative drugs based on better knowledge of disease mechanisms obtained through translational research carried out in collaboration with the Immunorheumatology Laboratory. The Unit participates in, and in some cases coordinates, several international trials on new biotechnological medications.

Neuroscience Clinical Area



Functional Coordinator of the Clinical Area: **Stefano Vicari**

DH Neurorehabilitation and Adapted Sports COU

Coordinator: **Gessica Della Bella**

The COU focuses on the clinical assessment and rehabilitation of children and adolescents with oral motor disability while feeding (dysphagia) in the context of complex disabilities. It also focuses on the definition of personalized Adapted Physical Activity (APA) for children and adolescents with intellectual, motor, and sensory disabilities. Adapted sports are now considered an integral part of the Individual Rehabilitation Project, thanks to the physical, psychological, and social benefits of training and to the way they contribute to improving the child's quality of life in the family and social context, responding to the biopsychosocial model of the *International Classification of Functioning*.

We constantly verify what is reported in the scientific literature, also thanks to the projects "Lo sport per tutti" (Sport for All) by Fondazione Baroni and the RAGGIO project (5x1000), which made it possible to launch an assessment and initiation program for adapted sports. This program is provided on an outpatient basis by trained staff and researchers. This innovative idea stems from the synergy between clinical practice and research, with the common goal of producing scientific evidence in a rapidly growing and highly relevant field.

Neurosurgery COU

Coordinator: **Carlo Efsio Marras**

- **Functional Neurosurgery SOU**
Coordinator: **Alessandro De Benedictis**
- **Oncology Neurosurgery SOU**
Coordinator: **Andrea Carai**

The Neurosurgery COU provides surgical treatment for all congenital and acquired diseases of the central and peripheral nervous system, thanks to the development of technologies that support treatment pathways based on the principles of precision medicine. The development of neurophysiological monitoring techniques for numerous Operating Units significantly optimized surgery outcomes. The implementation of robot-assisted neuromodulation techniques led to the effective treatment of drug-resistant psychiatric disorders. Numerous surgical procedures have been

performed and patients with central nervous system neoplasms have been enrolled in innovative research protocols. The Unit has also enhanced and developed 3D reconstruction technologies integrated with virtual and augmented reality to support the performance of complex procedures. It has also actively contributed to the complex and successful separation of a pair of craniopagus twins (joined at the head), affected by one of the rarest and previously untreated forms of the condition.

Epilepsy Neurology and Movement Disorders COU

Coordinator: **Nicola Specchio**

The Epilepsy Neurology and Movement Disorders COU is composed of a team of neurologists, psychologists, neuropathophysiology technicians, and specialized nurses, focused on the diagnosis and treatment of all forms of childhood onset epilepsy. In particular, it treats rare and complex forms, including drug-resistant ones. In 2024, the COU implemented an integrated approach to the treatment of drug-resistant focal epilepsies, based on the use of advanced techniques and artificial intelligence (AI) systems. AI has improved the prediction of surgery outcomes and, through innovative tools such as the MELD (Multicentre Epilepsy Lesion Detection) algorithm, has accelerated the automated detection of epileptogenic lesions, also making it more accurate, through the analysis of neuroimaging data. High-density electroencephalogram (EEG) signal analysis has improved the localization of focal lesions. Finally, intracranial signal analysis using AI systems has supported sleep mapping and staging, as well as seizure prediction, ensuring more personalized and effective clinical management.

Developmental Neurology COU

Coordinator: **Massimiliano Valeriani**

- **Muscular and Neurodegenerative Diseases SOU**
Coordinator: **Adele D'Amico**

The Developmental Neurology COU focuses on the diagnosis, treatment, and follow-up of children and adolescents suffering from neurological diseases. It is the only pediatric center where children with multiple sclerosis are treated with level I and II disease-modifying therapies. The Unit has introduced new therapeutic

measures (botulinum toxin and nerve blocks) for headaches. Enrolment has begun for several clinical studies on muscular dystrophy, spinal amyotrophy, headaches, multiple sclerosis and neuromyelitis optica. The COU has initiated compassionate use of several drugs for mitochondrial diseases. Two important research projects, funded by the PNRR and Telethon, have been launched for patients with tuberous sclerosis. In addition, in collaboration with Vittore Buzzi Children's Hospital and Carlo Besta Neurological Institute (IRCCS Foundation) in Milan, the Leukodystrophies multicenter network has been established.

Child and Adolescent Neuropsychiatry COU

Coordinator: **Stefano Vicari**

- **Anorexia and Eating Disorders SOU**
Coordinator: **Valeria Zanna**
- **Autism Spectrum Disorders SOU**
Coordinator: **Giovanni Valeri**
- **Psychology SOU**
Coordinator: **Deny Menghini**

The Child and Adolescent Neuropsychiatry COU focuses on diagnosis, treatment, and care of patients with neurodevelopmental disorders or childhood/adolescence psychological conditions. The Unit is a national reference center for autism spectrum disorders and a regional reference center for psychiatric emergencies, anorexia, and attention deficit/hyperactivity disorder (ADHD). In 2024, the COU carried out several innovative activities to improve care for child and adolescent psychiatric disorders.

High-intensity protocols were created for the treatment of severe disorders such as social withdrawal, psychosis, self-harm, and suicide, which also led to intensive consulting activities at other Hospital units. In addition, group intervention protocols have been implemented for adolescents with genetic syndromes and social anxiety, and the use of non-invasive brain stimulation has been introduced for children with autism, learning disorders, and Down syndrome.

Finally, for patients with anorexia and eating disorders and their families, the high care program has been expanded with the introduction of a day hospital treatment group. The large number of cases, the wide range of care offered, and the intense research and dissemination activities through information channels

have made it possible to host medical and psychology residents from all over the country.

Neurorehabilitation UDGEE Inpatient Ward COU

Coordinator: **Donatella Lettori**

- **Pediatric Sub-Intensive Rehabilitation SOU**
Coordinator: **Susanna Staccioli**
- **Functional Rehabilitation SOU**
Coordinator: **Flaminia Frascarelli**

The Neurorehabilitation UDGEE (Rehabilitation Unit for Severe Disabilities in Childhood) Inpatient Ward COU treats children and young people aged 0 to 18 with severe disabilities due to:

- pre-, peri- and post-neonatal conditions
- genetic and metabolic syndromes
- acquired brain injuries (of traumatic, hypoxic, neoplastic, infectious, inflammatory, or vascular origin)
- drug-resistant epileptic syndromes
- neuromuscular and connective tissue diseases.

Over the last year, the study on surgical treatment of childhood cerebral palsy (CP) through selective dorsal rhizotomy (SDR) of the afferent nerve roots L1-S2 continued, with the aim of modulating the reflex arcs that feed spasticity in the lower limbs. The study, which began in 2019, is the result of a collaboration between the Neurorehabilitation and Neurosurgery professionals of our Hospital. To date, approximately 30 children aged between 5 and 10 years have been enrolled, with CP with a motor impairment level ≤ 3 on the *Gross Motor Function Classification System* (GMFCS) and an adequate cognitive profile. All enrolled children were assessed through a series of motor and neuropsychological tests in both the pre- and post-operative phase. Following the surgical procedure, children underwent intensive rehabilitation for 4 weeks, with repetition of the intensive rehabilitation cycle at 6, 12, 18, and 24 months with integration of the LOKOMAT or HIROB robotic device. So far, good results have been observed in enrolled patients, with evident functional improvements mainly in the lower limbs, but also in the upper ones, as well as progress in neurocognitive functions. This overall improvement, both motor and neuropsychological, supports the hypothesis that SDR has a plastic effect on the organization of the brain networks involved in motor and cognitive functions. However, further studies are needed to confirm these findings.

Fetal, Neonatal, and Cardiology Sciences Clinical Area

Functional Coordinator of the Clinical Area: **Lorenzo Galletti**



Interventional Cardiology COU

Coordinator: **Gianfranco Butera**

- **Perinatal Cardiology SOU**
Coordinator: **Alessandra Toscano**
- **Adult Congenital Cardiology SOU**
Coordinator: **Claudia Montanaro**

The Interventional Cardiology COU performs heart surgery on fetuses, newborns, children, and adolescents with congenital heart disease without opening the chest, using minimally invasive techniques. The clinic is dedicated to children and adolescents who are eligible for or have already undergone hemodynamic procedures.

The main activities of the Interventional Cardiology COU for 2024 include:

- interventional treatment of lymphatic anomalies in patients with congenital heart disease. This project has been carried out in collaboration with the Diagnostic and Interventional Radiology COU, the Advanced Cardio-thoraco-vascular and Fetal Imaging COU, and the Children's Hospital of Philadelphia (CHOP). There are currently no active centers in Italy or Europe
- implementation of the experience in the use of self-expanding valves has led to a significant improvement of knowledge, participation in multicenter scientific projects, and the activation of systematic follow-up using CT scan, which is useful for the early detection of any valve function abnormalities. The Unit is the leader of the Italian registry on self-expanding valves and actively participates in teaching projects, both on-site and off-site, at the national and European level
- further developments with the possibility of using Alterra and Harmony, increasing the number of patients who can avoid open-heart surgery. Thanks to its expertise, the Unit is currently able to treat up to 80% of patients with right ventricular outflow tract dysfunction using transcatheter techniques
- implementation of magnetic resonance imaging catheterization (MRI-Cath) was possible thanks to the participation in research projects and initiatives to improve the quality of care, with a particular focus on the correlation between MRI and catheterization in flow analysis and indirect assessment of

oxygen saturation. The team also participated as speakers in the World Congress on Cardiac Resonance Imaging held in Washington in 2025

- the second phase of the CARDIOMEMS project to monitor pulmonary pressure levels in patients with congenital heart disease. Participation in multicenter projects
- closure of atrial septal defects: OPBG is a teaching center at the national and European level, organizing dedicated workshops. It also leads the European survey on atrial septal defect closure, collecting data on complications from a cohort of approximately 15,000 patients from 46 participating centers
- setting up of the teaching center for fellows of the European Society of Pediatric Cardiology. Thirty-five fellows from across Europe gathered for three days to learn from an OPBG and European faculty
- the use of the Impella support system in children: OPBG is the only center in Italy and one of the few in Europe to offer this service 24 hours a day. It also leads a European study on the use of Impella
- further implementation of the procedure for Botallo duct closure in premature infants bringing the lower treatment limit to 700 g. OPBG is the Italian hospital with most experience in this field
- analysis of the quality of outcomes and treatments using clinical governance tools, which allow for an in-depth analysis of activities, results, organizational and technical issues, and the re-evaluation and implementation of initiatives aimed at improving quality on a quarterly basis
- interprofessional team support activities aimed at improving interaction, communication, and participation in joint work through scheduled meetings throughout the year
- launch of a project on atrioventricular valves in congenital heart disease, as the only center in Italy and one of the very few in Europe
- Italian single-topic conference on the treatment of right heart diseases.

The Perinatal Cardiology SOU treats patients with complex heart disease diagnosed in utero, including cardiac surgery and follow-up for the first year of life. The main activities for 2024 include:

- teaching at the Master's Degree in Fetal and Neonatal Cardiology (Policlinico Gemelli-OPBG) for the training of perinatal cardiologists and obstetricians

- with expertise in fetal cardiology
- collaboration with The Sharon Disney Lund Medical Intelligence and Innovation Institute, CHOC Hospital for innovation in cardiology
- development of fetal diagnostic models using artificial intelligence
- creation of an AI diagnostic algorithm for fetal diagnosis of vascular anomalies (vascular rings) presented at the World Congress on Artificial Intelligence in Healthcare in Orlando in November 2024 (AIMED)
- international multicenter study of the Fetal Heart Society on Fetal Aortic Stenosis
- study of the Heart-Placenta-Brain axis and maternal hemodynamics in fetal heart disease related to the study of brain neurodevelopment
- participation in the collection of placenta samples from fetuses with heart disease for the OPBG Biobank
- study of fetal cardiac severity parameters with selection for hospital birth pathway and fetal therapy (precision medicine)
- participation in the cardio-neurodevelopmental pathway of patients with congenital heart disease
- neonatology training on the use of functional cardiology in intensive care within the Neonatal Semi-Intensive Medical Care and Follow-up Unit (SIN)
- participation in the Horizon project on the creation of a Digital Twin of formula milk for newborns with complex conditions
- internal scientific research and training activities, including the submission of abstracts to national, international, and world conferences and participation in these events
- participation in the implementation of perinatal protocols for the care pathway of patients with complex heart disease from fetal life.

The Adult Congenital Cardiology SOU ensures continuity of care for patients with congenital heart disease after the age of 18, ensuring timely and correct treatment of heart diseases using innovative techniques. The main innovations include:

- analysis of the quality of outcomes and treatments using clinical governance tools which, on a quarterly basis, allow for an in-depth analysis of activities, results, organizational and technical issues, and the re-evaluation and implementation of initiatives aimed at improving quality
- increase in clinical activity by approximately 20% per year over the last two years
- constant presence in the Unit of a GUCH (Grown-up congenital heart disease) cardiologist, shared and officially assigned to the hemodynamics group
- implementation of a pregnancy program with direct contact with Agostino Gemelli IRCCS University Hospital and San Pietro-Fatebenefratelli Hospital.

Cardiology and Arrhythmology COU

Coordinator: **Fabrizio Drago**

- **Cardiology Inpatient Ward SOU, Palidoro**
Coordinator: **Massimo Stefano Silvetti**
- **Echocardiography SOU**
Coordinator: **Gabriele Rinelli**
- **Sports Medicine and Arterial Hypertension SOU**
Coordinator: **Ugo Giordano**

The Cardiology and Arrhythmology Unit treats children and adolescents with arrhythmias, cardiomyopathies, channelopathies, and heart diseases requiring invasive and non-invasive diagnostic and therapeutic treatments. Since 2017, the Unit has been member of the European Reference Network for Rare Heart Diseases (ERN GUARD-Heart) as a healthcare provider. The main activities carried out in 2024 include:

- pacemaker implantation with reduction or elimination of fluoroscopic radiation
- implantation of pacemaker electrodes in para-Hisian sites using 3D technology to optimize cardiac contraction synchrony during pacing
- radiofrequency transcatheter ablation of epicardial atrioventricular accessory pathways in the coronary sinus using 3D technology integrated with CT imaging
- transcatheter cryoablation of right anteroseptal atrioventricular accessory pathways using a transjugular venous approach
- recognition of ventricular arrhythmias associated with the onset of arrhythmogenic cardiomyopathy
- ACE inhibitor therapy in hypertrophic cardiomyopathy
- adapted preventive physical activity in patients who underwent kidney transplantation or with complex heart diseases
- risk stratification of ventricular repolarization abnormalities in athletes during childhood.

Fetal and Perinatal Medicine and Surgery COU

Coordinator: **Leonardo Caforio**

The Fetal and Perinatal Medicine and Surgery COU focuses on maternal-fetal medicine, prenatal diagnosis and counseling for complex fetal diseases, and fetal therapy. In cases of complex fetal conditions, the Unit manages mothers from the diagnosis of their child's disease to the perinatal period, i.e., the period immediately before and after birth (including cases of high-risk deliveries). The Fetal and Perinatal Medicine and Surgery COU focuses on:

- diagnosis (invasive and non-invasive) and multidisciplinary prenatal counseling
- fetal surgery
- pre-perinatal and delivery management in pregnancies with fetal conditions
- adolescent and transition gynecology.

In 2024, the Unit introduced important innovations concerning:

- fetoscopic fetal surgery (laser in monochorionic twin pregnancies, tracheal occlusion in diaphragmatic hernia) and ultrasound-guided surgery (correction of complex heart defects, shunts)
- collaboration with centers of excellence in obstetrics for childbirth at OPBG, EXIT procedure, and unconventional neonatal care
- pathways for comfort care and perinatal palliative care
- care for adolescents and young adults with malformations, chronic or neoplastic diseases and associated gynecological conditions
- national clinical and scientific collaborations (Policlinico Casilino, Policlinico Universitario Agostino Gemelli IRCCS, Ospedale San Pietro-Fatebenefratelli, Ospedale Santo Spirito in Sassia) and international collaborations (Cincinnati Children's Hospital, Great Ormond Street Hospital in London, University of Leuven, University of Glasgow, University of Giessen, Mater Dei Hospital in Malta).

Heart Failure, Transplantation, and Cardiocirculatory Mechanical Support COU

Coordinator: **Antonio Amodeo**

- **Advanced Cardiovascular Therapies SOU**
Coordinator: **Rachele Adorisio**

The Heart Failure, Transplantation, and Cardiocirculatory Mechanical Support COU treats children and adolescents with heart failure and pulmonary hypertension. The main activities carried out in 2024 include:

- multidisciplinary and multiparametric management of patients with heart failure and pulmonary hypertension, both in-hospital and out-of-hospital in patients admitted with dedicated beds
- development of therapeutic strategies for the prevention of heart failure exacerbation
- optimization of the patient pathway in myocarditis
- development of non-profit studies on cardiological therapies and on pathophysiological mechanisms of heart failure, leading to the definition of the first home telemonitoring program
- telemonitoring for patients with heart failure and pulmonary hypertension.

Anesthesia and Cardiac Surgery Resuscitation COU

Coordinator: **Luca Di Chiara**

The Anesthesia and Cardiac Surgery Resuscitation COU admits children and adolescents from all over the country on an emergency basis, at the request of other hospitals and for international missions. It also provides post-operative care to patients admitted for scheduled cardiac surgery or for interventional cardiologic procedures. As part of the Fetal, Neonatal, and

Cardiology Sciences Clinical Area, it provides anesthesia and intensive care services for patients with congenital or acquired heart disease, from newborns to adults. The service is carried out in collaboration with other clinical areas. Specifically, the service provides the intra- and perioperative care to cardiac patients: from preoperative stabilization to transfer to another ward. Particular attention is given to knowledge and pharmacological management of the pathophysiology of congenital heart diseases.

The Unit also focuses on heart failure: from conventional medical treatment to mechanical cardiovascular support. In this context, it manages the machine-patient interaction and related coagulation issues. It also operates in the peri- and intraoperative pathway of thoracic transplantation and of trachea and large bronchi surgery. Other areas of focus include antibiotic stewardship in intensive care, neuromonitoring in the operating room and intensive care unit, and hemodiafiltration techniques in cardiac patients. Particular attention is paid to aspects of clinical ethics, for which the Unit works closely with the relevant department.

Cardiac Surgery COU

Coordinator: **Lorenzo Galletti**

- **Arrhythmias Cardiac Surgery SOU**
Coordinator: **Sonia Albanese**
- **Cardiology Inpatient Ward SOU, Rome**
Coordinator: **Antonella Santilli**
- **Semi-Intensive Cardiology SOU**
Coordinator: **Roberta Iacobelli**

The COU focuses on the surgical treatment of all congenital and acquired heart diseases in newborns and children, including the transposition of the great arteries and hypoplastic left heart syndrome, with multidisciplinary care and treatment pathways starting from the fetal period. The Unit has launched a program for minimally invasive treatment of simple congenital heart diseases. Minimally invasive surgical treatment of simple heart defects has been consolidated through the introduction of the axillary approach. This innovative approach guarantees the same results as the classic sternotomy approach, while accelerating healing, with a significant aesthetic advantage due to the absence of scars on the chest. The introduction of this treatment was possible thanks to specific training and institutional collaborations. The Cardiac Surgery COU also provides outpatient services through the joint cardiology-cardiac surgery clinic, which assesses and manages patients diagnosed with congenital or acquired heart disease who are eligible for surgical treatment. In this clinic, the cardiologist and cardiac surgeon assess the case with a thorough cardiologic examination including an electrocardiogram and color Doppler echocardiography, followed by a joint cardiac surgery consultation and the development of a treatment plan, which may be supplemented with other second-level diagnostic tests to complete the preoperative process.

Complex Cardiac Surgery with Innovative Techniques COU

Coordinator: **Adriano Carotti**

The Complex Cardiac Surgery with Innovative Techniques COU operates in the field of cardiac and thoracic surgery, mainly in the following areas of specific expertise:

- repair and reconstructive heart valve surgery, particularly aortic and tricuspid valve surgery
- pulmonary vascular reconstructive surgery
- intrathoracic airway surgery (and treatment of any associated congenital heart disease)
- lung and heart-lung transplantation surgery.

The Unit provides services both independently and in collaboration with the Cardiac Surgery COU, the Airway Surgery SOU, and the Digestive Endoscopy Surgery SOU. With the latter two, it participates in the Hospital multidisciplinary aerodigestive team (Laryngo-Tracheal Team). The COU is an internationally recognized center for the treatment of an extreme and particularly complex form of tetralogy of Fallot, called "Pulmonary atresia with ventricular septal defect and major systemic-pulmonary collaterals".

It is also a national reference unit for aortic valve neocuspidation surgery (Ozaki procedures) in children, intrathoracic airway surgery in children, mixed cardiotoracic-digestive setting (e.g., for the treatment of recurrent intrathoracic tracheoesophageal fistulas), and pediatric lung transplantation.

Neonatal Intensive Care COU

Coordinator: **Andrea Dotta**

- **Neonatal Semi-Intensive Medical Care and Follow-up SOU**
Coordinator: **Annabella Braquaglia**
- **Neonatal Nutrition Education and BLUD SOU** -
Coordinator: **Guglielmo Salvatori**
- **Post-Surgical Intensive Area and STEN SOU** -
Coordinator: **Irma Capolupo**

The Neonatal Intensive Care COU manages infants less than 30 days old or weighing less than 5 kg. The Unit

has 22 beds, 11 of which are dedicated to the Post-Surgical Intensive Care Area and 11 to newborns who require intensive care for medical conditions or who need complex and advanced intensive care. The COU operates within the Regional Neonatal Intensive Care Network as a reference hub for all Level I and II birth centers with multispecialty skills for the admission of newborns with conditions requiring life support. It also collaborates with leading Italian and international centers in the same fields.

However, a cutting-edge hospital department not only offers the best medical care: it is also a place where medicine and humanization go hand in hand. For this reason, particular attention is paid to the psychological outcomes for the entire family in the event of hospitalization during the first weeks of a newborn's life. In terms of organization, collaboration has been implemented with the Anesthesia and Cardiac Surgery Resuscitation Unit to promote the sharing of diagnostic and care protocols for newborns with heart diseases and facilitate the flow of patients between the two Units.

In addition, to facilitate rapid clinical and therapeutic assessment of patients, the use of the POCUS (Point of Care Ultrasonography) approach has been implemented by neonatologists trained in performing multi-duct (cerebral, functional cardiac, thoraco-pulmonary) ultrasound scans at the patient's bedside.

Also, the care provided within the OPBG Birth Project and the Neuro-NICU activity with neurologists, neuro-radiologists, and neurosurgeons has been further developed. The COU manages and implements the activities of the Donor Human Milk Bank (BLUD), the only bank in Lazio region, which selects, collects, stores, and distributes breast milk for use, after pasteurization, for specific medical needs. The Neonatal Intensive Care COU also develops and coordinates research through a multidisciplinary Working Group composed of neonatologists dedicated to clinical practice and research, neonatologists dedicated entirely to research, psychologists, nursing staff, and other specialists, including surgeons, cardiologists, gynecologists, and radiologists. Numerous international collaborations with highly specialized centers (London, Glasgow, Rotterdam, Bonn, Brussels) are underway. The Neonatal Intensive Care COU is also involved in many clinical trials.



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