Clinical and Translational Oncology

# Oncological Translational Research in the Spanish National Health System: The INTRO Study.

--Manuscript Draft--

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| **Manuscript Number:** | |
| **Full Title:** | Oncological Translational Research in the Spanish National Health System: The INTRO Study. |
| **Article Type:** | Special Articles |
| **Keywords:** | Clinical ant translational research; Oncology services; Spanish Hospitals |
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| **Abstract:** | Under the auspices of the Foundation for Excellence and Quality in Oncology (ECO), the Translational Research in Oncology Medical Services Study (INTRO) was conducted with the aim of describing the current state of, and future expectations for translational cancer research in Spanish medical centres. The first step in the investigation was intended to analyse the current condition of the national Medical Oncology Services network by examining different aspects of the oncology research field.<br>Methods: A descriptive and observational multicenter study was performed at a statewide level; information was collected by surveying a cross-section of all those responsible for Medical Oncology Services in Spain.<br>Results: The survey was completed by key-informants, who were selected independently by each service, between September 2010 and April 2011. We were able to gather comprehensive data from a total of 27 Spanish hospitals. These data |

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| **Additional Information:** | |
| **Question** | **Response** |
| Article text word count: | 5.444 |
| No. of references: | 16 |
| No. of figures: | 7 |
| No. of tables: | 3 |

# Oncological Translational Research in the Spanish National Health System: The INTRO Study.

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**Short running tittle:** INTRO study

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Under the auspices of the Foundation for Excellence and Quality in Oncology (ECO), the Translational Research in Oncology Medical Services Study (INTRO) was conducted with the aim of describing the current state of, and future expectations for translational cancer research in Spanish medical centres. The first step in the investigation was intended to analyse the current condition of the national Medical Oncology Services network by examining different aspects of the oncology research field.

Methods: A descriptive and observational multicenter study was performed at a statewide level; information was collected by surveying a cross-section of all those responsible for Medical Oncology Services in Spain.

Results: The survey was completed by key-informants, who were selected independently by each service, between September 2010 and April 2011. We were able to gather comprehensive data from a total of 27 Spanish hospitals. These data enabled us to describe the allocation of human and material resources devoted to clinical and translational research across the Medical Oncology Services and to describe the organisational and functional components of these services and units. These data included information pertaining to the activities developed, their funding sources, and their functional dependence on other internal or external bodies. Finally we explored the degree of dissemination and use of some specific techniques used for the genetic diagnosis of cancer, which have recently been introduced in Medical Oncology within the Spanish health care system.

Conclusions: A wide range of variability exists between different oncology services in Spanish hospitals. Time should be spent reflecting on the need and opportunities for improvement in the development of translational research within the field of oncology.

**Key words**: Clinical ant translational research, Oncology services, Spanish Hospitals

## INTRODUCTION:

The growth of knowledge in the field of oncology that has occurred in recent years is truly impressive. However in most cases, such progress has not resulted in changes in the treatment, prevention, or diagnosis of cancer, and has therefore produced a significant discrepancy between achievements in the laboratory and successful patient treatment. This discrepancy is determined

primarily by a distancing between basic research and clinical practice, which must be refocused more towards moving studies at the molecular or cellular level (*bench*) to patient treatments (*bedside*). This approach, called '*bench to bedside*' is permeating all areas of medicine and especially so in the field of oncology. In scientific fields, and increasingly in the press, this is also referred to as '*translational research*', and aims to accelerate the pace of the transfer of scientific discoveries made by basic research into clinical application. Translational research aims to go beyond the clinical trial to transfer concepts, ideas, and knowledge in a preliminary way, and may even include the use of animal models [1-4].

However, in Spain, the development of these initiatives remains, even today, largely symbolic. The report ordered and published by the Spanish government in April 2002, regarding the call for assistance in the development of research networks, states: "*With regard to these groups of diseases (neoplastic, cardiovascular, neurodegenerative, and infectious, among others), the critical mass of researchers in our country is small and of low quality, they are fragmented and there are weak links between basic and clinical researchers, and between the research structures of the various institutions of the National Health System, universities, and public research organisations* " [5].

Some years have passed since this pessimistic prognosis, and the genuine status of the involvement of Medical Oncology Services in Spanish translational research is now unknown. This study analyses the issue, and provides points for reflection and professional debate on one of the undoubtedly most important lines of future development within the specialty.

In this context it can be assumed that a possible variability factor between different centres and services may be the simple heterogeneity of physical and human resources, and the provision and availability of instrumentation within each unit, as key determinants of their research capabilities.

Under the auspices of ECO Foundation, the INTRO study was conducted with the aim of describing the current experiences and future expectations for translational oncology research in Spanish health care facilities. It is a starting point in a course of action aimed at the analysis of the current condition of the statewide network of services and medical oncology units in Spain.

## MATERIALS AND METHODS:

Study Design:

The study was a multicentre (statewide) descriptive and observational study, which collected information via a cross-sectional survey of those responsible for each of the Spanish Medical Oncology Services. The study was performed between September 2010 and April 2011, and consisted of survey completion by a key-informant, as determined at the discretion of each individual service surveyed. Each centre participated only once.

Despite having previously established a process and procedures for the selection of medical oncology units to be surveyed, in order to develop a fully comprehensive study we decided to send surveys to every Medical Oncology Service we could identify in Spain. A total of 62 surveys were sent, bringing together a large sample that was geographically dispersed throughout the country, which collected information from 27 oncology services (43.7%), and broadly represented the different characteristics of the largest centres in the various Autonomous Communities.

No particular form of sample selection was carried out; instead units at all levels of healthcare were considered eligible for the study as long as they met the following criteria:

- Medical Oncology services/units that were functionally active at the time of study, according to official health centre records in each autonomous region, within any type of health care organisation (public or private affiliation, or any other legal form of existing healthcare administration within the Spanish National Health System).
- There was at least one physician specialising in Medical Oncology on their staff.
- The manager (head of department or another equivalent senior position) expressly agreed with and consented to collaboration.
- Centres agreed to provide all the information requested in the study questionnaire, and to authorise the use of such data, once collated, for the research purposes stated in the project outline, and at the discretion of the INTRO study investigators.

The directors of all the eligible services identified were contacted directly with the aim of fulfilling our objective of 100% selected target recruitment. As an additional quality control criterion for recruitment, we reiterated to these healthcare providers that we were aiming to achieve a participation rate of not less than 80% of the oncology units/services contacted.

Study objectives:

The specific objectives of the study were:

1. To describe the allocation of human and material resources devoted to clinical and translational research in Spanish Medical Oncology Services.

2. To describe the organisation and basic operating of these services and units, including the activities undertaken, their sources of funding, and their functional dependence on other units/services, either located internally or externally.

3. To explore the degree of dissemination and use of some specific diagnostic techniques for the genetic diagnosis for cancer, which have recently been introduced into the Spanish health care setting within Medical Oncological Services.

Study Material:

In this project, the key-informants were deemed as those responsible for the services/units surveyed, or another reliable professional who was specifically delegated this representative task. In this case, a procedure was established where the formal unit supervisor had to check and confirm the information provided.

The survey study was sent in an electronic format which could be filled out by each key-informant through the ECO Foundation website (www.fundacioneco.es), or alternatively, the study surveys were also made available in a paper format (a printable PDF file). In this case the paper questionnaires were handled by staff specifically trained in questionnaire preparation, and were automatically scanned to ensure the accuracy of information capture, and to prevent errors in data collection.

The variables and the survey measurements are shown in Table 1.

## RESULTS:

The INTRO project collected comprehensive data from a total of 27 of the 62 Spanish hospitals surveyed (43.7%). Based on the average size of the responding hospitals (809 beds) and the average number of doctors working in them (11 physicians) most of the data were obtained from large hospitals. Median size of the hospital, defined by the average number of beds per hospital, was 800 beds with a wide range from 95 to 1500 beds. Almost half of the hospitals studied had between 500-1000 beds (Fig 1).

Identification and General Characteristics of the Centres and Medical Oncology Services Surveyed

The characteristics of each participating oncology service are described by their provision of human resources, physical space, the availability of communications and information technology equipment, the technical facilities in the day clinic (outpatient area), and the number of nursing consultations provided. Regarding human resources, there were an average of 11 physicians, 21 nursing staff, 15 auxiliary assistants, and 3 administrative assistants in the departments surveyed (Table 2).

When describing the physical space available, the approximate area destinated to the day clinic in oncology services averaged 410 $m^2$, with a median of 300 $m^2$ and a wide range of between 35 and 1500 $m^2$. Outpatient clinics surface was 392 $m^2$ on average, with a median of 200 $m^2$, and a range of between 50 to 2000 $m^2$. The vast majority of services (96.3%) had their own hospitalisation area (inpatient area). In addition, a further 42.3% could have inpatients hospitalised within other services. The median number of beds assigned for Medical Oncology was 24 [8-41].

The services had an average number of 8 consulting rooms that belonged exclusively to Medical Oncology [range: 6-23] and one-tenth of the departments surveyed (11%) shared consulting rooms/space with other services. Only 15 of the 27 participants in the survey were equipped with their own day clinic (Fig 2 and Fig 3).

With regard to the availability of communications and information technology equipment, more than 90% of the clinics in different Medical Oncology units were provided with both a connection to the computer network and with internet access. However, only two thirds of the departments

surveyed stated that they belonged to hospitals that kept electronic medical records, and only half of those said that they had already computerised their histories.

Electronic prescribing systems were present in 70% of day clinics in Medical Oncology, and 78% had a patient/medication/dose identification system.

Nursing consultations were available in 70% of the departments surveyed, and in most cases these were located in the day clinic (Fig 4a), in 50% of these cases the nurses' primary tasks were mixed, and included both clinical and research assistance (Fig 4b).

Infrastructure, Resources, and Research Activity in Medical Oncology Services

Of the responding departments 75% (20 sites) had their own clinical research units, and 52% of these also possessed their own Translational Research (TR) Laboratories.

The major source of funding for clinical research in Medical Oncology came from clinical trials, although in the majority of cases this was also supplemented with funds from public and private sources (Table 3). Referring solely to clinical trials, 23 of the 27 departments surveyed (85%) started a study of this type annually. Each year an average of 33 clinical trials were launched per service, with a median of 30, ranged from 4 to 130 trials. Phase III clinical trials were the most commonly performed (45%), with Phase I trials accounting for only 9.9% of the total (Fig 5).

Regarding the human resources data provided by the surveyed units, there was an average of one trainee and five clinical assistants per service linked to clinical and translational research. Together with clinical oncologists, other specialists dedicated to research in these units were biologists and chemists.

Where a dedicated TR laboratory was not available, 95% of the services participated in TR activities in collaboration with other departments or units, either within the same hospital (such as within Pathology, Clinical Biochemistry, Pharmacology, Genetics, Immunology, Molecular Biology, Pulmonary-Thoracic and Gastrointestinal Surgery, and Haematology), or in other institutions (such as universities, cooperative groups, or alliances with other hospitals or research institutions). There was only one Oncology Service, from all of the respondents, which had specialist medical oncology physicians exclusively dedicated to TR. Most commonly there was an average of three or four physicians with a stable relationship with the laboratory, dedicated to TR part time. Other types of laboratory

research personnel were biologists, biochemists, biotechnologists, nursing and pharmacy graduates, and laboratory technicians. Half of the TR laboratories had between one and two of these professionals working full time. Other contributors described by survey participants were students, senior technicians, healthcare assistants, laboratory technicians, and project managers. Three-quarters of the departments surveyed, with their own TR laboratories, had one or two dedicated technicians working there full time. Only three of the TR laboratories possessed administrative support staff, either full or part time, stably dedicated to TR. Half of the Medical Oncology Services that participated in this study had their own TR laboratory had a full-time TR data manager on staff, and the other 50% had one working part time.

The approximate area occupied by TR laboratories in those services equipped with them, was 140 $m^2$ on average: 46.2% of them were located in a general research area and 30.8% of them in a specific dedicated area. All of the laboratories surveyed were equipped to perform cell culture techniques, genomics, and protein analysis, 90.9% of them had spectrophotometry and microarray equipment available, and 70% had gene cloning technology available to them. Within the genomics techniques available, all laboratories performed standard PCR and real-time PCR, and 85% of these also used sequencing techniques; in the latter 61.5 and 73% respectively shared this equipment with other laboratories. With regard to technical protein analysis: immunohistochemistry, Western blotting, and 1D and 2D gel techniques were performed in almost all the departments surveyed (92.3%, 92.3% and 84.6% respectively). In terms of physical and human resources provided, 43% of Medical Oncology Services had their own TR lab with access to the computerised clinical history records, and 46% of them also had quality certifications, both general and for specific techniques.

In terms of scientific output, these laboratories had an average of 69 publications in the last five years (median 35), ranging between 5 and 326 publications. Of these publications, 54% were in the first impact factor quartile and 24% of them were in the second quartile. Focussing on hospital size and relating this to the number of clinical trials carried out, the existence of a molecular biology laboratory, or the number of annual publications: 13 of the 23 large hospitals (> 500 beds) reported having their own TR laboratory (56.5%) and 21 of them performed clinical trials (91.3%), with a mean of 34 trials per year.

Funding Translational Research Activities and Resources

In 58% of cases, the major source of funding for the facilities and staffing of TR laboratories came from the public sector, and in 42% of these funding also came from the private sector. The sources of public funding were through state and local European funding agencies, and from the university; state agencies most often funded TR laboratories (83.3% of them received public funding). Regarding private funding sources, mainly this was shared by the pharmaceutical industry and by non-profit organizations and/ or foundations (Fig 6 and 7).

The funding allocated to the employment of TR research staff came mainly from the private sector (55%), and within this, research foundations played a major role in providing funds for dedicated TR researchers in oncology. State funding agencies, which originate in the public sector (45%), were the main sources of funding for human resources in TR (70%), ahead of foundations and hospital research institutes.

As for research project funding, 61% of funding came from the public sector, within which, most of it was obtained through national funding agencies, such as Instituto de Salud Carlos III and the autonomic/ regional health or research agencies were the primary fund providers. Private funding for cancer translational research was split between foundations and philanthropic funders (55.8%) and the pharmaceutical industry (39.1%).

Relationship with the Hospital Administration and Translational Research Partnerships

Almost 70% of Medical Oncology Service respondents claimed to have support for their investigation, on the part of the hospital management.

All Medical Oncology services with their own TR laboratories had established alliances, both for clinical and translational investigation, with other service units, in particular with research centres, as well as with other hospitals. International external centres were used as strategic research alliances by only 40% of the services with their own TR laboratories. Specifically, they described partnerships with the DFCI, Harvard University, Oslo University, the Oncology Services in Aveiro (Portugal), Foggia University (Italy), and in other hospitals, universities, and research centres in Italy.

Addendum on specific techniques

Among the Specific techniques for genetic diagnosis of that have been recently transferred to the health care setting in Spain is the determination of ***KRAS*** gene, in the diagnosis of metastatic colorectal cancer. Of all the Medical Oncology Service respondents, 96.2% of them referred to performing this test, of which 80% performed it at their own centre. When samples were sent to other centres, it usually took them between 1 and 5 days to be sent, and the results were received with a delay of 7 to 10 days. In the centres performing the determination of the *KRAS* gene *in situ*, 47.6% performed it in the Pathology Department, and they had between one and two people dedicated to performing this technique. It took between 4 and 21 days (with a median of 7 days) to receive the test results when it was conducted at the centre. Most of the services (94%) determined *KRAS* mutational status by real time PCR, although 12% of the centres also performed direct sequencing techniques.

The main sources of funding for this diagnostic test were the pharmaceutical industry and the hospital itself. All of the Oncology Services respondents reported that the technique should be 100% financed by the Spanish National Health Service (NHS) because it is a basic diagnostic technique that increases drug spending efficiency, as it is a predictive biomarker of drug response.

The determination of the mutational status of ***EGFR*** gene in lung cancer was performed in 92.6% of responding Oncology Services. Of these, the test was performed at the centre itself 60% of the time. Where it was carried out at a reference centre (40%) it took the sample between 1 and 5 days to be sent and between 3 and 15 days for the results obtained. When *EGFR* mutations were determined at the centre itself, it was most frequently performed in the Pathology Service, and to do so they dedicated between one and three people, usually one or two technicians and a qualified molecular biologist. The median time in which the results were received was 10 days (2-15 days).

*EGFR* mutational status was determined by real time PCR in 81.3% of the services, with 25% also eventually performing sequencing techniques. At present, funding for the implementation of this technique mainly comes from the pharmaceutical industry (62.5%). With the same motivation as with the determination of mutations in *KRAS* gene, 96.2% of Oncology Services surveyed believed that the determination of *EGFR* mutations should be 100% subsidised by the NHS.

The determination of amplification or over-expression of the ***ERBB2*** gene in breast cancer is a molecular test that was carried out at the centre itself in all the Medical Oncology Services surveyed. In

addition to immunohistochemistry, 72% of the responding centers used FISH (fluorescent *in situ* hybridisation) and 46% CISH (chromogenic *in situ* hybridisation) techniques to determine its amplification or over-expression.

## DISCUSSION:

Scientific progress often correlates with the economic and cultural development of a country. Over the past 25 years, biomedical research in Spain has significantly improved due to several factors. These include Spanish integration into the European Union and the consolidation of scientific policy at a national and European level, which have both contributed to a significant increase in research activity. However, the fraction of Gross Domestic Product (GDP) that is dedicated to research, development and innovation in Spain, which acts as a measure of a country's intellectual development, continues to be disappointingly low. Currently, Spain devotes the 0.89% of its GDP to research and innovation, whereas the average in the European Union is around 1.9%. [6]

Whilst the relative number of researchers in Spain has doubled over the last decade, the current ratio of 3.7 researchers per 1000 inhabitants of the economically active population is still considerably lower than the ratios of the European Union (5.1) and the United States (7.4) However, according to bibliometric indicators, which determine the quality and quantity of scientific production, Spain is currently ranked eleventh on an international level, representing 2.8% of the world scientific production. A more detailed analysis of these figures shows that Spanish research groups linked to Universities are the main contributors to these scientific indicators (51%), followed by those attached to health institutions and hospitals (23%) and the Spanish National Research Council (13%), even though, the precise percentages varying somewhat with geographical location. Thus, the contributions of health institutions have an important impact on Spanish scientific production, and undoubtedly, one of the most significant areas of their contribution is in cancer research. [6]

Cancer represents a major disease burden in developed countries, with 16.7% of total healthy years lost in the EU-25. It is one of the most prevalent diseases in Spain and is, in fact, the leading cause of death. In the year 2000, 91,623 people (57,382 men and 34,241 women) died of cancer in Spain,

accounting for 25.6% of all deaths and the annual incidence of new cases in Spain is about the 155,000. In terms of individual risk, one in three Spanish men and one in five Spanish women will be diagnosed with cancer at some point in their lifetime [7].

In recent years, new techniques in molecular biology, genomics, proteomics, and other disciplines have offered a continuous stream of discoveries. For this new knowledge to be translated into increased and improved prevention, diagnoses, and disease treatments, it is not enough to solely rely on the proper functioning of traditional channels that link the world of basic research and the clinical world. The purpose of so-called *translational research* (otherwise known as *research transfer*) is to encourage and facilitate this relationship, accelerating the process of knowledge transfer and making it more productive.

Understandably, patients are in a hurry, and research aimed at solving their problems is often slow and, to a large extent, has its own intrinsic rhythms which cannot be accelerated, both in basic and in clinical phases. However, there are more stages in the journey from the laboratory to the patient than just basic experimentation and clinical trials. For example, the ease with which a basic researcher can make an observation and recognise that it may be useful in the clinic; the speed at which information can be accessed from human patients, or how fast a basic or clinical research group can overcome bureaucracy to reach a development agreement with a company. Lenfant summarised this in a paper published in the *New England Journal of Medicine* in 2003: "The transfer of knowledge from the shelves into practice, making it accessible to doctors and patients, and the achievement of an authentic marriage of knowledge with intuition and good judgment ... all that requires transfer" [8]. The editors of the *Journal of Translational Research* also clearly explained the problem: "[...] when new therapies find their way through preclinical testing, clinical trials, and the Phase III studies, they have often ceased to be 'state of the art'. They may even be scientifically obsolete." [9]. In response to these problems, some hospital and university research and development (R&D) departments in Canada, the home of *translational research*, have made the integration of drug discovery and development a priority [10, 11]. From there, the so-called "*bench to bedside*" approach has spread throughout the scientific world, in a growing number of disciplines, most notably with a clear predominance in cancer research [2].

Over the past few decades, basic science researchers have worked in isolation to unravel the cellular and molecular mechanisms involved in cancer development, while clinical researchers have studied the effects of new drugs and other treatments in cancer patients. Nevertheless, in recent years major efforts have been made to align these two tasks, and to translate laboratory findings so as to develop increasingly more effective anti-tumoral treatments. However, the development of new cancer treatments requires a previously unseen level of integration in all aspects of basic and clinical research, requiring the obsolete and artificial barriers that divide different groups of scientists to be abandoned [12, 13].

In Spain, the development of basic and translational cancer research has undergone significant structural changes over the past two decades. Initially, research was carried out in isolation, by specific groups in certain centres, the number of which was steadily increasing. These groups were principally found in hospitals, universities and in groups belonging to the Spanish National Research Council (known as CSIC). As an example of the little attention paid to cancer research in the past, it is remarkably that the first Congress of Cancer Research was not held until 1982, when a group of pioneers met in Madrid to highlight the urgent need for the implementation of a government scientific policy to facilitate the development of basic, applied, and clinical cancer research [14, 15]. Fortunately, in the late 80's and early 90's, the situation in clinical research started to change, among other factors, aided by the influence exerted by the introduction of the National Plan for R&D, which provided explicit support for oncological investigation [14]. However, even today the development of these initiatives seems to be symbolic in Spain, with few researchers, and inadequate links between basic and clinical investigation, the various institutions in the Spanish NHS organisations, and universities etc.

In 1995, the Spanish Association of Cancer Research (ASEICA) published its first directory of oncology research units, comprising a total of 63 groups. Between 1996 and 2001, the number of active groups was 73, revealing a growing trend. Furthermore, in the same period, 13 specialized centres were established in Spain, which were exclusively dedicated to cancer research.

The first initiative for the establishment of research activities in networks was settled in 2002, by the Spanish Ministry of Health, creating Networks of Centres and Networks of Groups of Biomedical

Research. Since then, there was an evolution in the experiences of cooperative cancer research networks in Spain until its present organization. The main objective of this kind of research networks is to improve the synergyzation and the enhancement of the quality of cancer research performed by individual groups at the national level. There was an initial Network of Cancer Research Centers (RTICCC) established during the years 2003-2006 that encompassed 23 research centers located on 12 autonomous regions of Spain. In 2006, the model was switched from the research centers to the individual groups and a new network was established, the RTICC which involved the cooperative work of 95 research groups distributed in institutions located in 13 different autonomous regions. The RTICC activities have been extended for a total of 6 years until the end of 2012. The current RTICC has a new organization and consistently with the significantly reduced budget, there are only 70 groups participating in this new collaborative structure (www.rticc.org).

Between 1998 and 2008, spending on I+D+i in Spain tripled, but the cuts of recent years (more than 40% since 2009) have pushed back to I+D+i at the levels of a decade ago. The health and social services budget was reduced by 13.65% in 2012, with disproportionately high cuts professional training (75%) and public health and quality programmes(45%). These budgetary changes were accompanied by a structural change that was introduced, unusually, not after parliamentary debate, but by a royal decree. The controversial Spanish Research strategy and development plan 2013-2020 and the state of I+D that implements it, pursue the one hand reduce public support for basic research and education and bring to applied research, market-oriented, encouraging private participation. In addition, today we have a very distorted view of how the I+D+i, since in any developed country is built applied research and innovation by competition with basic research.[16]

At present, the status of real involvement of Spanish Medical Oncology Services in translational research activity is unknown, therefore we aimed to analyse the issue with this study. We found that a great variability exists between different Spanish hospitals, as measured by the considerable heterogeneity in physical and human resources and instrumentation available in each unit, as major determinants of their research capabilities.

One noticeable feature that emerged from the data regarding unit characteristics was that only 55.5% of the oncology service respondents possessed their own day clinics, and of those 11% of them shared consulting space with other services. In terms of technology, we noted that 90% of oncology services had access to the computer network and internet access, and 70% of the day clinics worked with electronic prescribing. In terms of research, it stood out that 75% of the departments surveyed had their own clinical research units, but only 52% of them had their own translational research laboratories, and if we look only at Level 1 hospitals (with more than 500 beds) only half of them (56%) had their own TR laboratories. Most of the research staff funding came from clinical trials and 85% of respondents had clinical trials underway, although only 9.9% of those being conducted were Phase I trials. On average, 34 clinical trials start in large hospitals annually. As for specialists working in TR laboratories, there was a wide variation; only one of the services had a full-time clinical oncologist completely dedicated to investigation, in the remaining they worked part-time, and only 37% of services reported having at least one biologist on their staff. Only 11 of the 23 Level 1 hospitals (47.8%) reported having published in the last 5 years.

With these data, the INTRO study has helped us to take a snapshot of the current structural and organisational situation in TR in the various Spanish Medical Oncology Services. This has allowed us to realise that great variability exists among different Spanish hospitals, and helps us to reflect on the need and possibilities for improvement in translational research in the speciality. We cannot explore if a dichotomy exists between large and small hospitals nationally, since most of the hospitals that participated in the study (85.2%) were Level 1 (>500 beds). However, we can highlight the fact that only 56.5% of these hospitals possessed their own TR laboratories, and that we only have data on publications in the last 5 years in 11 of 23 of the participating units (47.8%).

Following our analysis of the current state of basic and translational research in Spain, in which we have taken into account the rapid rate of development over the past few years, several aspects have proven to be unsettling.

There is no doubt that the progress achieved in recent years has resulted from an increased financial investment in research, however, to consolidate this trend, it is necessary to continue to increase this investment. Regional governments, industry and (civil society?) should be highlighted as

important emerging sources of funding. Yet, today there are still financially neglected areas of research, such as clinical trials sponsored by collaborative research groups that, in the absence of financial support from state agencies, depend almost exclusively on the pharmaceutical industry.

Parallel to the requisite increase in funding, it is imperative to have a solid strategy that outlines comprehensive plans for the development, financing and promotion of cancer research. These plans should comprise an overview of the epidemiology, prevention and management of the diagnosis and treatment of the disease at all levels, and should also cover aspects of basic, translational and clinical research. Furthermore, within the NHS Hospital System, investment in research, facilitating the development of scientific programs, must be promoted, so as to create research jobs within hospital complexes and to engender the attitude that research provides an added value that brings prestige to institutions.

We believe that the 'handing over' of healthcare to the Autonomous Regions, albeit with clear advantages for the management of Health Services, is also causing a growing divergence in the local standards of each Autonomous Community, including within each individual health centre. These standards help determine the provision for, and operation of these health care units, and the resources dedicated to the research carried out in them. A problem that arises from such imbalances in provision is the influence on healthcare professionals and their involvement with the healthcare organisations on which they depend, including their degree of motivation to improve their practices within these organisations. Recent data from all types of medical specialties show a high prevalence of burnout among medical professionals, a fact associated with, among other factors, the perception of the limited career possibilities and deficiencies in the physical conditions and facilities available in the workplace. Among other possible motivation factors, participation in quality research activities is generally recognised as a powerful incentive for clinicians in the different specialties that have been analysed.

As the ECO Foundation, we strongly believe that investing in research is profitable in the short and long term. We need a reliable, internationally-compatible research strategy that takes advantage of all available resources, scientific or clinical, increasing investment in both staff and materials. The hospital environment is required for translational research, and such research confers

Within this setting, the ECO Foundation has several valuable reasons for promoting this project: firstly the need to encourage the participation of a growing critical mass of specialists in cancer

research, secondly the desire to promote positive competition among units to form *benchmark* processes (replication of best clinical, organisational, or scientific practices). Last, but not least, upholding the mandate of conduct which commits all health professionals to continually improve the services they provide, an impossible task without quality translational research.


## ACKNOWLEDGEMENT:

A los Doctores: Alberto Abad, Emilio Alba, Enrique Aranda, Manuel Benavides, Javer Casinello, Manuel Constela, Hernan Cortes-Funes, Juan Jesús Cruz, Francisco Javier Dorta, Pilar García, José Luís García, Carlos Jara, Ana Lluch, Guillermo López, Luis Paz Ares, Emilio Esteban, Joan Albanell, Jose María Tabernero, Agustí Barnadas, Antonio Lorenzo, Pedro Sánchez, Rosario García, Edelmira Vélez de Mendizabal, Antonio González, Juan Antonio Virizuela y Angel Artal.


## CONFLICT OF INTEREST:

The authors declare that they have no conflict of interest relating to the publication of this manuscript.

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**TABLES**

## TABLE 1: Variables and Measurements

| | |
|---|---|
| **1. Identification and general characteristics of the Medical Oncology Services surveyed.** | • Human resources<br>• Physical space<br>• Approximate area<br>• Provision of information, communications, and other technologies<br>• Structure of clinical and/or translational investigation |
| **2. Infrastructure, resources provided and research activity.** | |
| 2.1 For Clinical Research | (personnel, funding, activity) |
| 2.2. For Translational Research (TR): | • Availability of the clinical research unit in the Medical Oncology Service.<br>• Availability of IT in the laboratory.<br>• Dedicated physical space.<br>• Quality Certifications.<br>• Resources provided/techniques available:<br>a. Cell culture.<br>b. Genomics: PCR and sequencing.<br>c. Protein analysis.<br>d. Spectrophotometry.<br>e. Others.<br>• Research staff: number and dedication to TR.<br>• Professional categories and academic training.<br>• Publications. |
| **3. Sources of TR funding in the unit: fiscal, EU programs, other public funds, private funding (pharmaceutical industry, foundations, etc.), other sources (university, etc.).** | • Self-financing of TR within the laboratory (facilities, staffing).<br>• Funding for the employment of TR researchers.<br>• Financing of TR projects. |
| **4. Relationship with the hospital administration, collaboration with other services and other agencies** | • Perception of TR and its support from the management (yes/no).<br>• Independence of the laboratory (shared/own).<br>• Partnerships internal/external to the hospital (yes/no). |
| **5. Addendum: availability, use and service financing of specific genetic diagnosis techniques recently transferred to the Spanish healthcare setting** | • The K-ras gene in metastatic colorectal cancer (MCRC).<br>• The EGFR gene in lung cancer.<br>• The oncogene ErbB2 in breast cancer. |

**TABLE 2: Human Resources in the Medical Oncology Service Departments Surveyed**

| **Human Resources** | Mean | Median | Std. Dev. | P25 | P75 | Range |
|---|---|---|---|---|---|---|
| Nº of Doctors | 11 | 11.0 | 5.20 | 10.0 | 13.0 | 29 |
| Nº of Nurses | 21 | 18.0 | 10.75 | 14.8 | 25.3 | 44 |
| Nº of Clinical Assistants | 15 | 15.0 | 7.59 | 10.0 | 19.0 | 29 |
| Nº of Other Healthcare Personnel | 1.5 | 1.0 | 0.80 | 1.0 | 2.0 | 4 |
| Nº of Administrative Assistants | 3 | 3.0 | 1.89 | 2.0 | 4.8 | 7 |
| Nº of Non-medical Personnel | 2 | 1.0 | 1.03 | 1.0 | 2.0 | 3 |

**TABLE 3: Sources of Personnel Funding (Percentage Distribution)**

| Sources | Mean | Median |
|---|---|---|
| Clinical Trials | 61.6 | 72.5 |
| Private Funds | 22.1 | 10 |
| Public Funds | 14.6 | 5 |

**FIGURES**

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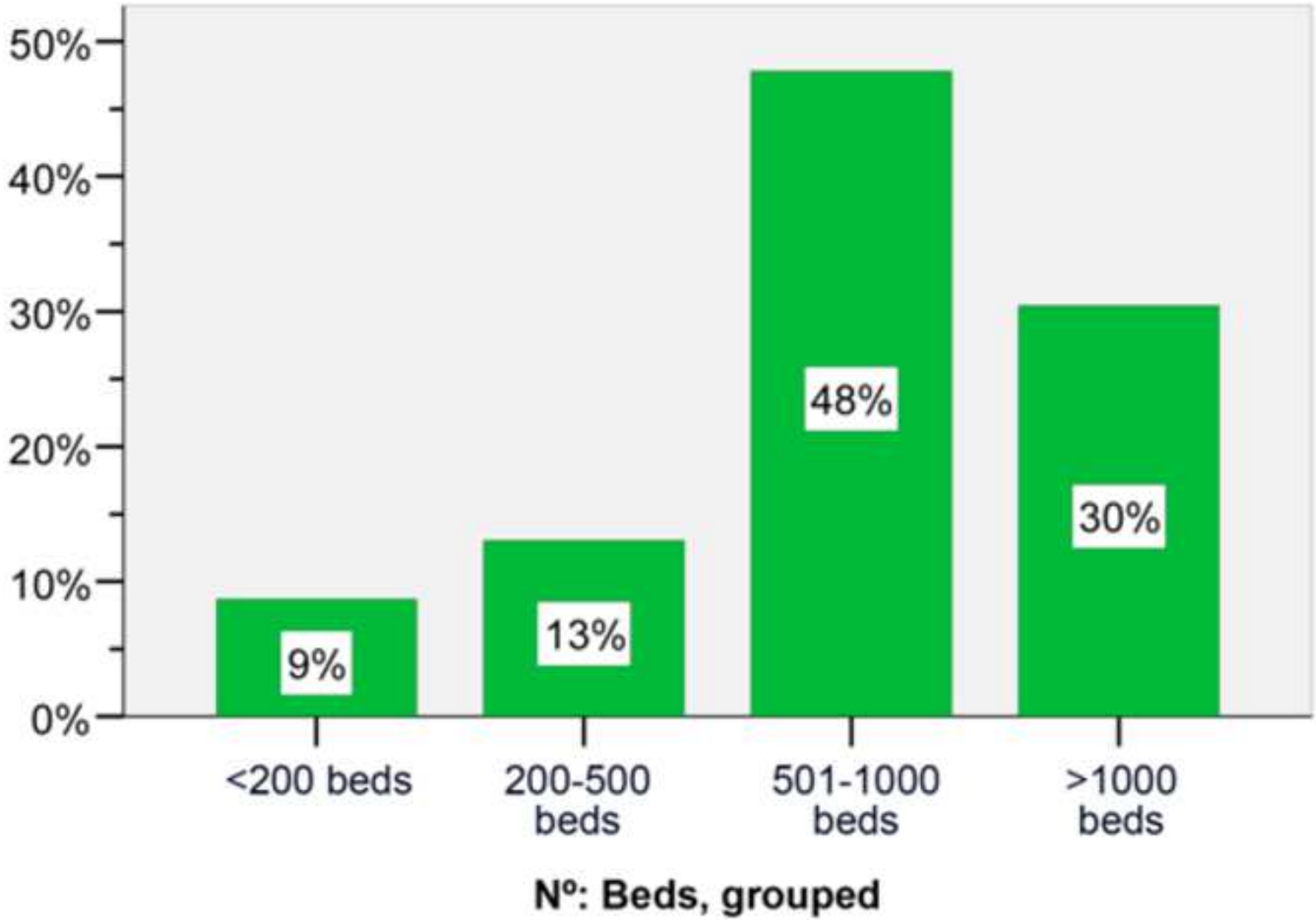

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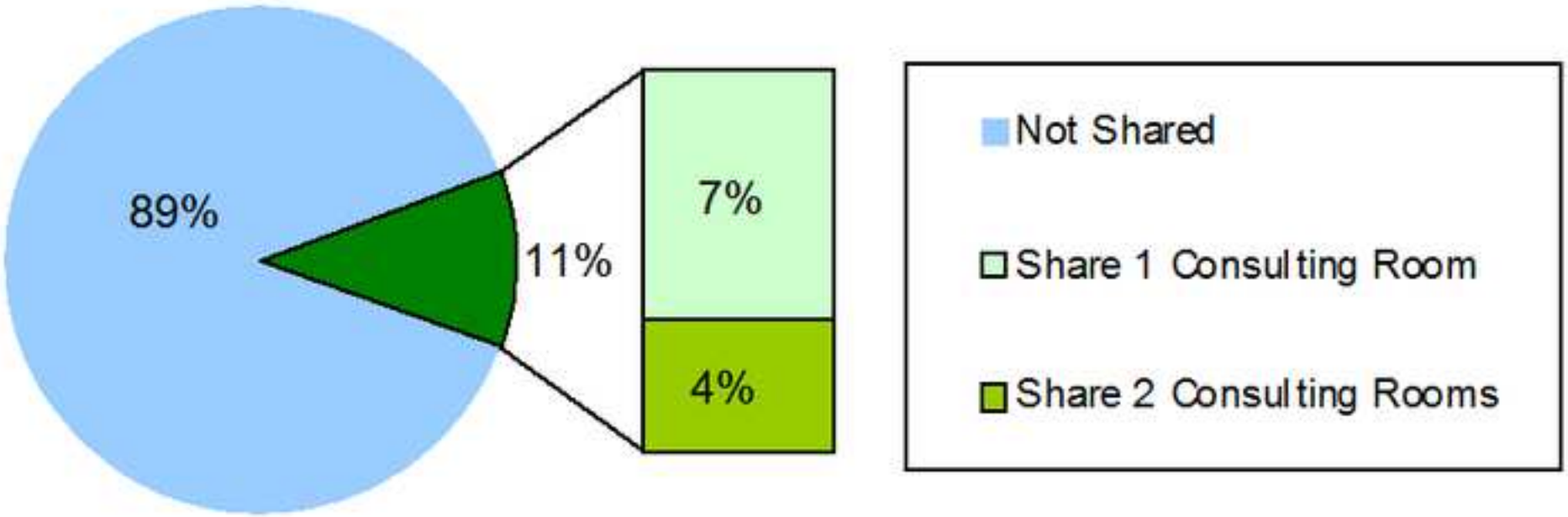

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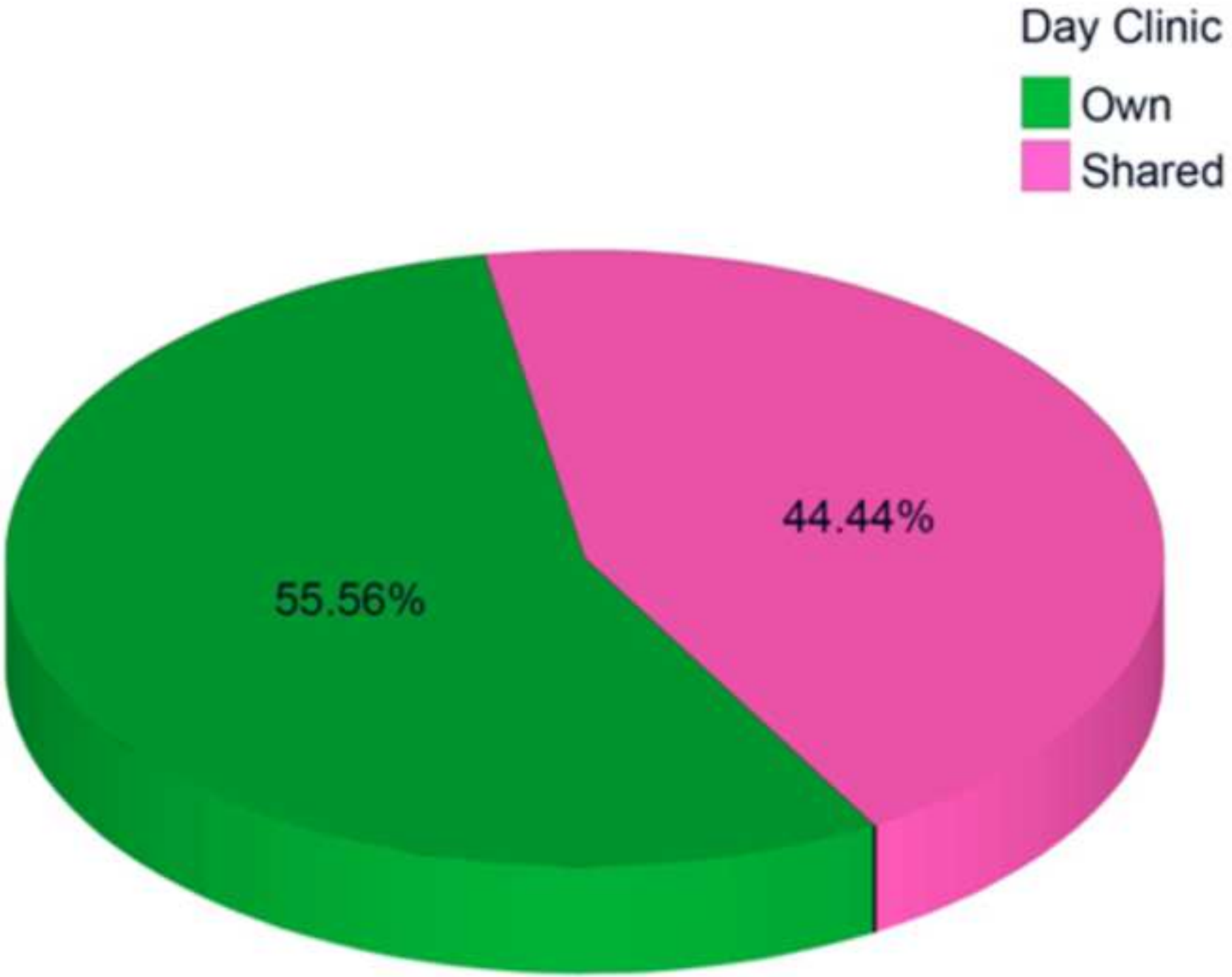

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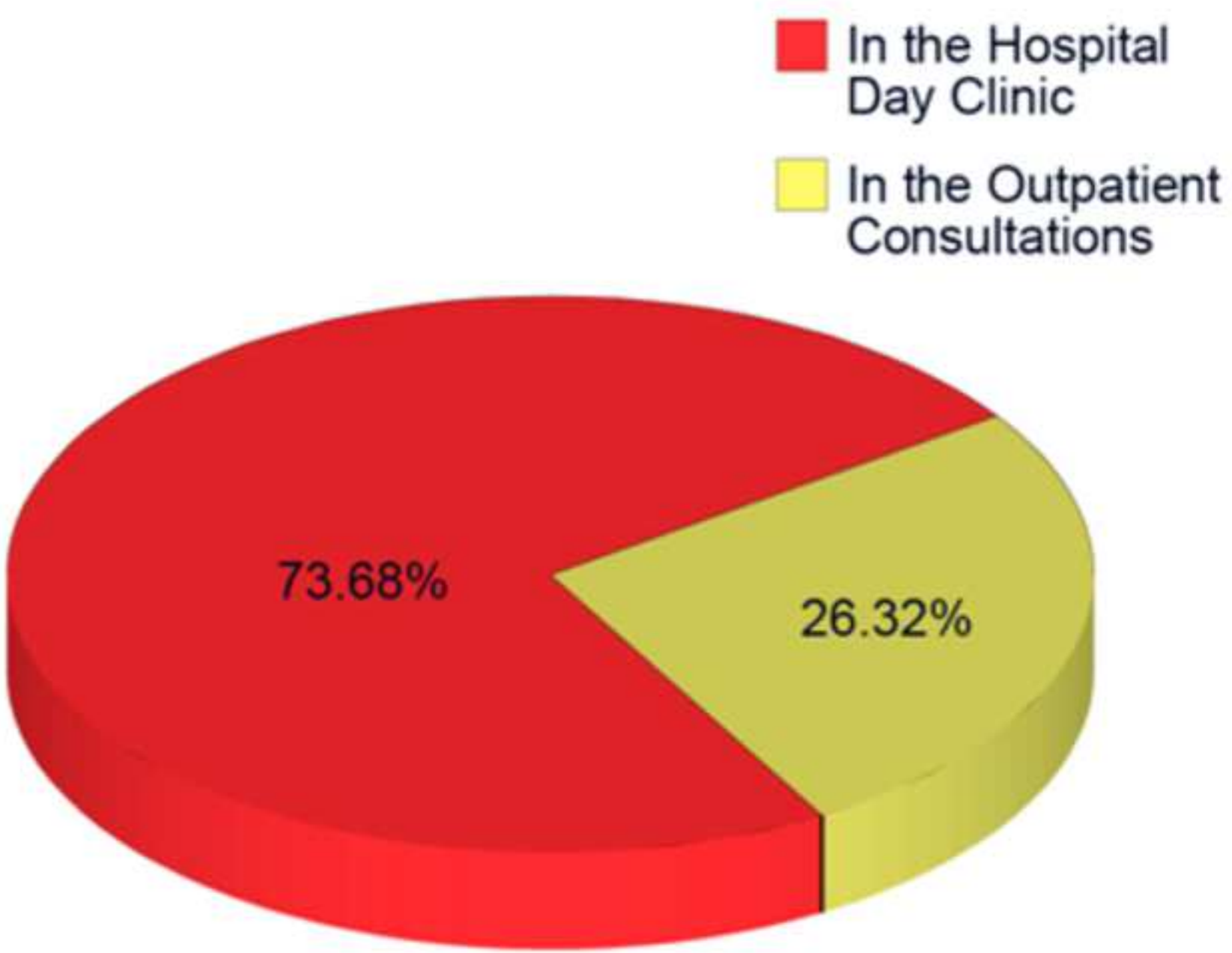

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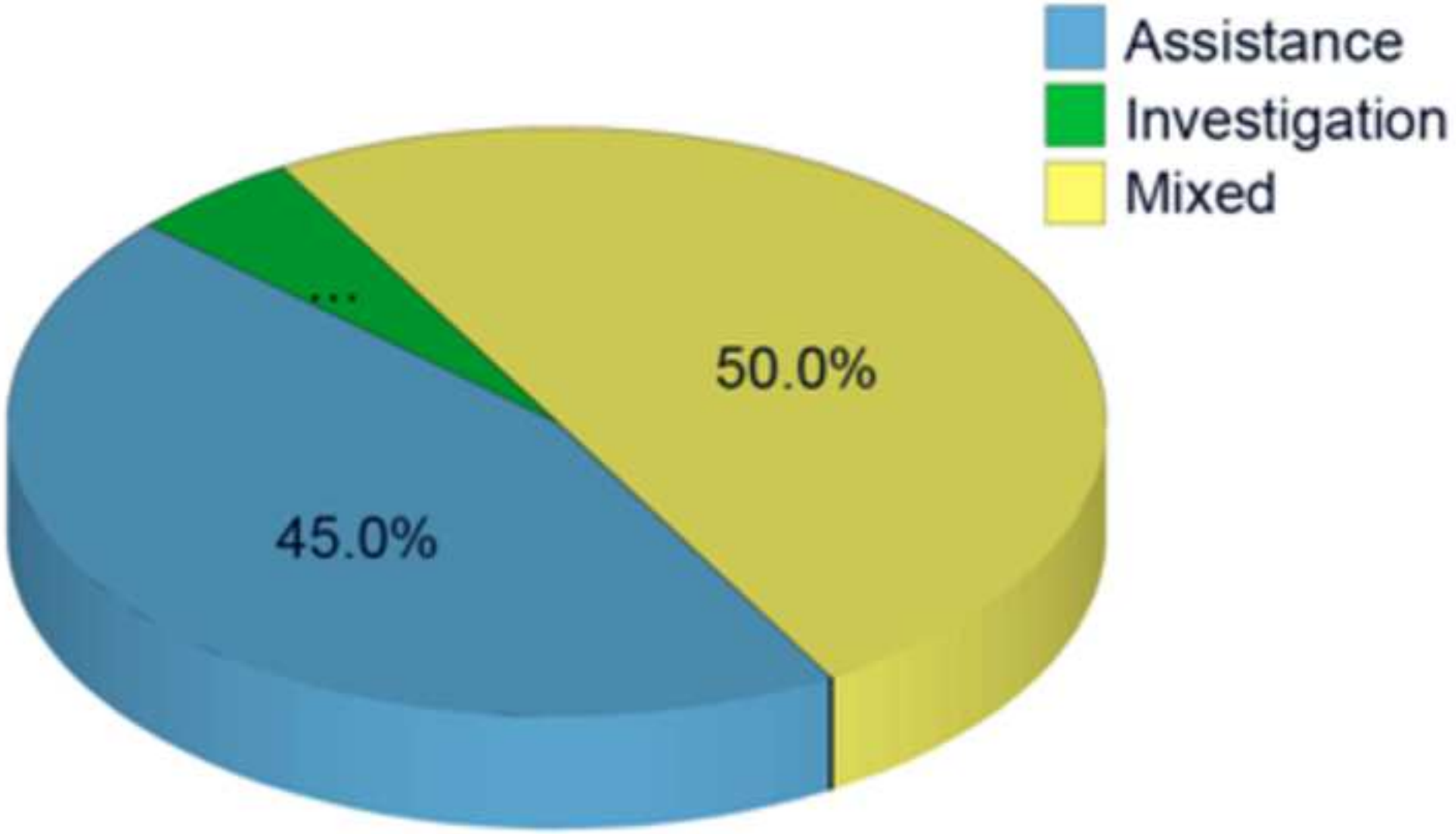

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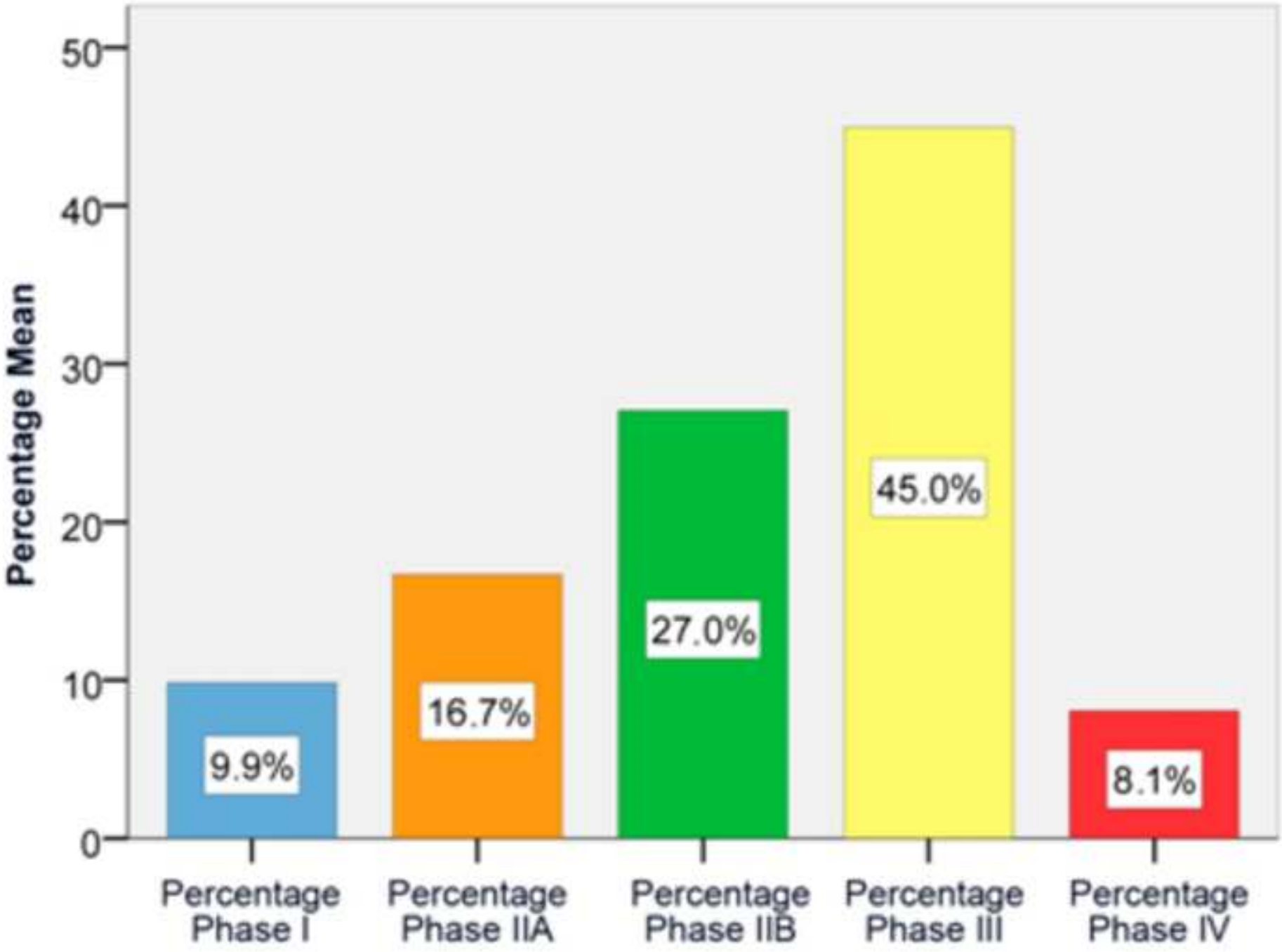

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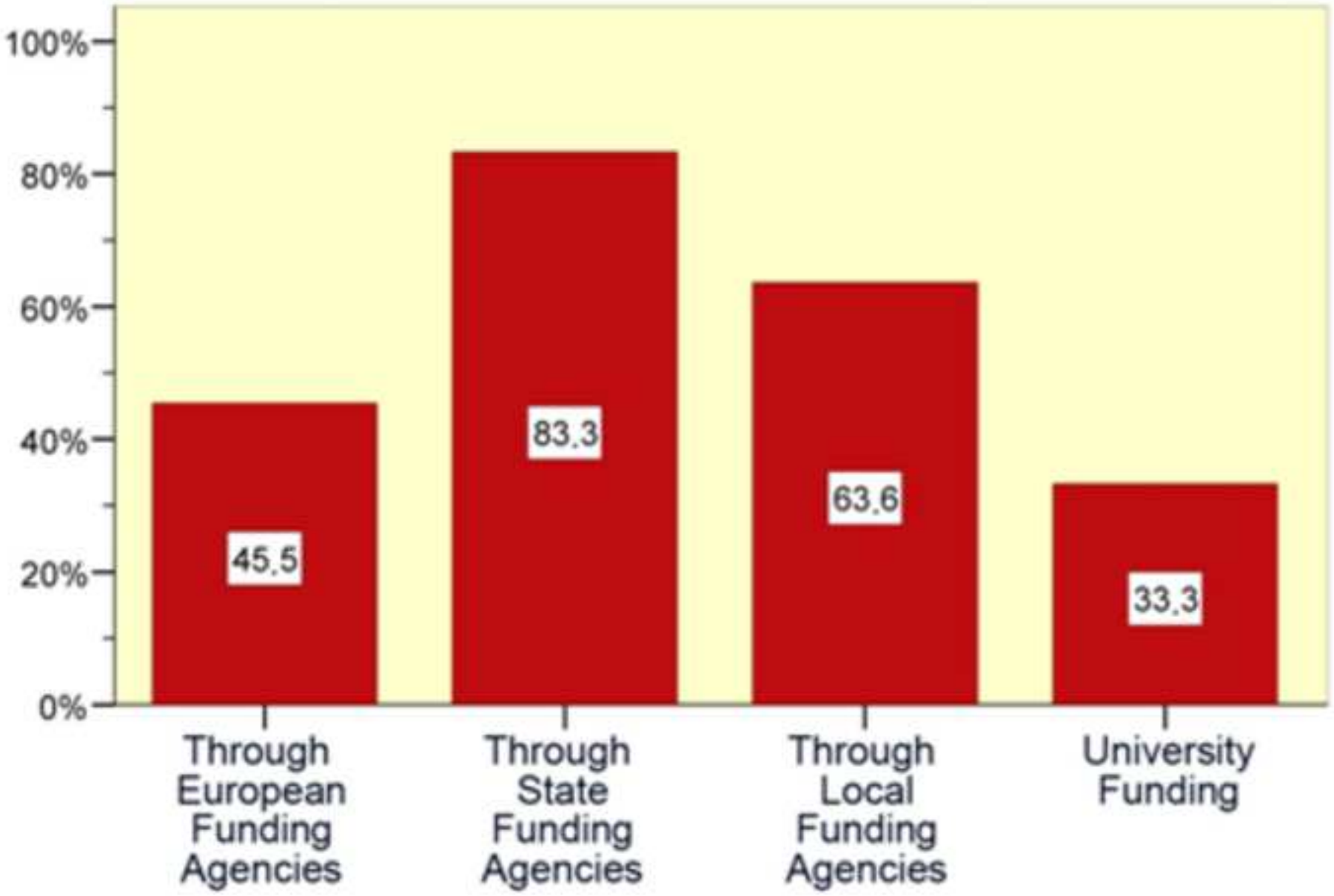

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