

Translational Research: the performance of the National Institutes of Science and Technology in the field of health

Pesquisa Translacional: o desempenho dos Institutos Nacionais de Ciência e Tecnologia na área da saúde

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ABSTRACT The National Institutes of Science and Technology Program was created to promote excellence in science and technology activities and their internationalization, foster their interaction with the business system, improve scientific education and the homogeneous participation of the regions of the Country in the production of knowledge. Translational medicine comprises accelerating the transmission of knowledge from basic research to clinical application, deepening clinical observations and applying this knowledge to the general population. This article aimed to identify and analyze the contributions of the National Science and Technology Institute for Translational Medicine (INCT-Health) in meeting the demands of Brazilian health, based on the concept of Translational Research. A qualitative, exploratory and descriptive research of the activities developed by INCT-Health was carried out. The 39 INCT-Health have contributed to the improvement of Brazilian health through the transfer of direct knowledge and the formulation/implementation of Public Health Policies. The INCT-Health has potential to meet the demand of the Brazilian population, in the health area, and have stood out in the interaction with companies and in the creation of startups. However, it is necessary to disseminate the results achieved by INCT-Health, as well as the elaboration and application of a methodology for monitoring and evaluation of Science, Technology and Innovation in Brazil.

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RESUMO O Programa Institutos Nacionais de Ciência e Tecnologia foi criado para promover a excelência nas atividades de ciência e tecnologia e sua internacionalização, fomentar a interação destas com o sistema empresarial, melhorar a educação científica e a participação homogênea das regiões do País na produção do conhecimento. Medicina translacional compreende a aceleração de transmissão de conhecimentos da pesquisa básica à aplicação clínica, o aprofundamento de observações clínicas e a aplicação desses conhecimentos à população geral. Este artigo buscou identificar e analisar as contribuições dos Institutos Nacionais de Ciência e Tecnologia em Saúde (INCT-Saúde) no atendimento às demandas da saúde brasileira, baseado no conceito de Pesquisa Translacional. Foi realizada uma pesquisa quali-quantitativa, exploratório-descritiva das atividades



desenvolvidas pelos INCT-Saúde. Os 39 INCT-Saúde têm contribuído para melhoria da saúde brasileira por meio da transferência de conhecimentos diretos e para a formulação/implantação de Políticas Públicas de Saúde. Os INCT-Saúde têm potencial para o atendimento da demanda da população brasileira, na área da saúde, e têm-se destacado na interação com empresas e na criação de startups. Contudo, é necessária a divulgação dos resultados alcançados pelos INCT-Saúde, bem como a elaboração e a aplicação de uma metodologia de monitoramento e avaliação da Ciência, Tecnologia e Inovação no Brasil.

PALAVRAS-CHAVE *Pesquisa médica translacional. Políticas e cooperação em Ciência Tecnologia e Inovação. Transferência de tecnologia.*

Introduction

The development of new technologies applied to health is complex, and few countries dominate the knowledge required for advances in this area. With this, governments, companies and academia have made efforts to accelerate basic research and make a new product available to the population. The dynamics of technological development depend on intense interaction between academia, government and companies. In this context, countries invest in Translational Research (PTrans) in order to improve human health from results of laboratory benches to patient beds. In a broad sense, this form of research builds the link between discovery, development, regulation and their effective use¹.

In Brazil, it is discussed how the PTrans model should be applied to the Brazilian reality as an instrument to catalyze the development of endogenous technologies capable of solving health problems with regional specificities. For at least two decades, the Brazilian State has sought to stimulate technological development and innovation through policies, programs and instruments that emphasized the installation of infrastructure and the formation of Human Resources (HR). From 2004 to the present, the State has regulated the incorporation of

technologies in the Unified Health System (SUS), and has been the main driver of innovation, guiding and financing Research and Development (R&D) activities².

However, some authors state that there is a gap between the provision of public technological services and the social demands for health services and products³. Part of this distancing can be explained by the adoption of the Linear Model by Vannevar Bush. This model, proposed in 1944, understands basic research as a dynamo for progress, and directs the public sector to invest in basic research (knowledge); and the private sector, in development and production (utilization), with separation of science and technology to avoid tension between them⁴. In Brazil, even if basic research has received adequate investment, it may be necessary to encourage other segments involved in the innovation chain. As a consequence of this model, there is an evident and detrimental separation between academia and the productive sector in Brazil³.

The perception that it is necessary to bring academia and the productive sector closer to the advancement of Science, Technology and Innovation (ST&I) was one of the motivations for the development of the National Institutes of Science and Technology Program (PINCT). The program was created through Ordinance

nº 429/2008 by the former Ministry of Science and Technology (MCT), now the Ministry of Science, Technology Innovations and Communications (MCTIC)⁵. The objectives of the program include the mobilization, articulation and creation of research groups on frontier and/or strategic themes for the sustainable development of the Country, as well as HR training, knowledge transfer to companies and society, education and training dissemination of science. PINCT also aims to boost basic scientific research and competitive fundamentals internationally, in addition to stimulating the development of scientific-technological research and innovation, cooperating with innovative companies⁵.

The PINCT is the result of the partnership established between the Coordination for the Improvement of Higher Education Personnel (Capes/Ministry of Education – MEC) and the Research Support Foundations (FAP) of several States, the Ministry of Health (MH) and the National Bank for Economic and Social Development (BNDES). The program is coordinated by MCTIC, which allocates resources from the National Foundation for Scientific and Technological Development (FNDCT) to the National Council for Scientific and Technological Development (CNPq), through the Financier of Studies and Projects (Finep). Operational management is carried out by CNPq, together with other partners who provide financial resources⁵.

Given the importance of the relationship between companies and the National Institutes for Science and Technology (INCT) so that technologies are disseminated in society, this article seeks to identify and analyze the contributions of INCT-Health in meeting the demands of Brazilian health, considering the burden of major diseases, based on the PTrans concept.

Material and methods

A qualitative and quantitative research was carried out, with an exploratory and descriptive purpose of the activities developed by INCT-Health. Quantitative research uses statistics to seek explanation of the data. Qualitative research can be defined as that based mainly on qualitative analysis, characterized in principle by the non-use of statistical instruments in the data analysis. Therefore, considering the distinct and varied results of the INCT-Health productions, and the difficulty of using a single approach, it was sought the complementarity of both forms of research⁶.

The variables used for quantitative analysis of INCT, as they are common to all Institutes, were the Federative Unit of the head office, the number of main researchers, the number of published articles, the number of patents produced and the formation of HR (masters, doctors and post-doctors). The reports did not describe how the data provided were constructed. For data analysis, medians and interquartile ranges were calculated, as well as presented in absolute and relative values.

For the qualitative study of the activities of the INCT, an exploratory study of the conceptual basis of PTrans was conducted, after a literature review of scientific articles available in the PubMed database, using the term 'Translational Research and definition'. The exploratory study brings elements for the detailing of questions and for the more precise formulation of concepts related to the studied theme⁷.

It was decided to consider the site of INCT/CNPq, as it makes available the results and activity reports of INCT declared by its coordinators⁸. Data collection took place in the period 7 to 9 August 2019, among the various work areas of the INCT, also relevant to the PTrans. *Chart 1* presents the relation of 39 INCT in the health area, in alphabetical order, analyzed in this study.

Chart 1. List of the 39 National Institutes of Science and Technology (INCT) in the health area, according to alphabetical order

1. INCT for Integrated Environmental Risk Analysis
2. INCT for Health Technology Assessment
3. INCT in Biofabrication
4. INCT of Science and Technology for Structural Biology and Bioimaging
5. INCT in Biomedicine of the Brazilian Semi-arid
6. INCT of Structural Biotechnology and Medicinal Chemistry in Infectious Diseases
7. INCT of Stem Cell in Human Genetic Diseases
8. INCT in Stem Cells and Cell Therapy
9. INCT for Cancer Control
10. INCT in Dengue
11. INCT for Diagnosis in Public Health
12. INCT of Papillomavirus Diseases
13. INCT in Tropical Diseases
14. INCT in Excitotoxicity and Neuroprotection
15. INCT of Drugs and Medicines
16. INCT for Viral Hemorrhagic Fevers
17. INCT in Photonics Applied to Cell Biology
18. INCT of Population Medical Genetics
19. INCT of Innovation Management in Neglected Diseases
20. INCT of Hormones and Women's Health
21. INCT for Pharmaceutical Innovation
22. INCT Brain-Machine Interface
23. INCT of Immunology Research
24. INCT in Medicine Assisted by Scientific Computing
25. INCT of Molecular Medicine
26. INCT of Radiation Metrology in Medicine
27. INCT of Translational Neuroscience
28. INCT of Obesity and Diabetes
29. INCT in Oncogenomics
30. INCT in Translational Research on Health and Environment in the Amazon Region
31. INCT for Alcohol and Other Drug Policies
32. INCT of Redox Processes in Biomedicine
33. INCT of Developmental Psychiatry for Children and Adolescents
34. INCT of Blood
35. INCT in Health
36. INCT in Toxins
37. INCT Translational in Medicine
38. INCT in Tuberculosis
39. INCT of Vaccines

Source: Own elaboration based on the information on the INCT-Health page. Available at: <http://inct.cnpq.br/>. Access on: 04/12/2019.

Despite the publication of three Notices concerning INCT, only the activities related to Notice nº 15/2008⁹ were analyzed. Notice nº 71/2010¹⁰ was directed to the Exploration of Marine Resources, and Notice nº 16/2014¹¹ did not present for analysis of activities in data sources, therefore, were not the object of this study.

Results and discussions

PTrans is a recent term in the process of consolidation. Possibly, it appeared in the 1990s, but there are few published references on the subject in that period. The term originates from the National Cancer Institute (NCI) of the United States, incorporated by the National Institutes of Health (NIH) in 2003, and later (2012), the National Centers for the Advancement of Translational Science (NCATS) was created, dedicated to PTrans¹². This institute seeks to accelerate the generation of innovative methods and technologies that can improve the Research, Development and Innovation (RD&I) of diagnoses and therapies, for various diseases¹³.

Cooksey¹⁴ understands that PTrans refers to the dynamics of taking the findings from basic research or clinical research, and making use of them to drive innovations in healthcare environments. According to this author, there are two key moments in the translation of health research, considered by him as 'gaps'. The first moment is the translation of the ideas of basic research and clinical research into the development of new disease products and treatments and, subsequently, the use of these new products and treatments in clinical practice.

On the other hand, Guimarães¹² questions the theoretical and conceptual solidity of PTrans. It considers the existence of many gaps between basic research and clinical research that are not addressed in this concept, and innovation is much more complex than the linear model proposed (from bench to bed).

The author believes that, in some approaches, practical issues such as funding difficulties, lack of communication channels, and scientists' perception of social demands are not discussed. In the author's view, 'is only about stimuli for a shake on the tree, so that its fruits ripen and can then fall'.

PTrans is concerned with identifying ways to overcome existing barriers throughout the process from applying basic research results to disseminating new therapies, prevention models and diagnostics. The main barriers are observed between Phase T1 (involves the process between ideas and initial human testing) and T2 (involves conducting clinical research and developing guides)¹⁵. The accomplishments of phases T1, T2, and T3 have complexities that can take up to 13 years at a cost of approximately US\$ 1 billion with a 95% risk of failure. This interval is also called Death Valley¹⁶.

Other bottlenecks are also observed between T3 (related to research implementation and dissemination) and T4 (involving results and effectiveness in populations)¹⁵. This is because, throughout the process, companies can identify insecurity (serious adverse effects) and ineffectiveness in proposing a new product. Therefore, this process must be robust enough for companies to demonstrate to regulatory agencies that the proposed new product is safe, effective and of adequate quality for human consumption. In addition, the incorporation of new products into health systems depends on a good cost/benefit ratio, evidenced by economic studies.

In order to have radical innovation in the area of health, it is necessary to transfer or incorporate the knowledge generated in each of these phases. At the same time, epidemiology allows the interpretation of the results generated in these phases and applies throughout the PTrans cycle, from the design of the studies to the interpretation of the outcomes, and in the decision-making of public health policies¹⁷.

Thus, it is observed that even though there

is a consolidation process of the PTrans concept, there is still a diversity of interpretations about the term. In order to verify the adherence of the Ptrans concept in the INCT-Health, searches of documents were carried out that presented the concepts used by them, as well as activities developed and results achieved by INCT-Translational Medicine (INCT-TM), INCT-Translational Research in Health and Environment at the Amazon Region (INCT-INPeTAm) and the INCT-Translational Neuroscience (INCT-INNT). These INCT were the object of concept analysis, as they identify with the activity of Translational Research.

Regarding the activity report of the INCT, based on the PTrans conceptualization, the analysis of those who emphasize this type of research in its objectives is emphasized. In the activity report of the INCT-TM¹⁸, studies related to synthesis, characterization of molecules, preclinical studies (including the development of an animal model for bipolar disorder) and clinical studies were observed. Therefore, this center has the capacity to perform activities of the initial stages (T1, T2, T3). However, in the evaluated report, it was not possible to verify how the knowledge generated in each stage is being integrated to the next phase; the methods that INCT-TM uses to accelerate technology generation have not even been identified. On the other hand, several themes are perceived as objects of the institute's research. One wonders how these projects are integrated into one another. However, it was found that activities were carried out to train researchers on translational medicine. In addition, the INCT-TM has developed a Biomarker Quantification kit for Non-Small Cell Lung Cancer. In this INCT report, partnerships with companies were mentioned. However, it was not possible to establish a relationship with the production of this diagnostic kit and its diffusion in the health system¹⁸.

INCT-INPeTAm has developed HR in

the region on topics related to biotechnology, bioengineering, technological development and innovation, as well as doing work focused on health education. In the report of this institute¹⁹, it is not explicit which definition or concept of PTrans is used. However, it is observed that it has been monitoring the population for possible poisoning caused by mercury and other agents resulting from environmental degradation, as well as training doctors and teachers on malaria prevention, endocrine dysfunctions and metabolic syndrome that arrives with the economic progress of the region. INCT-INPeTAm also reported the performance of various activities of T1, T2 and T3, starting from the identification of the burden of diseases of the Amazon Region reaching the prevention of injuries, through community health education, of doctors and teachers. However, it is not clear how knowledge is incorporated into the report consulted. In the activity report of the center, it was possible to identify the negotiation according to cooperation of an INCT-INPeAm group with the company Extracta Moléculas Natural SA. Some members of the research group focused on the development of new drugs and bioactive molecules belong to the said company. The group was looking for new compounds that could be used to treat malaria and leishmaniasis.

In the case of INCT-INNT²⁰, the concept of PTrans is explained in the activity report as

the integration of advances in basic science with clinical studies in order to conduct bench-to-bed research and clinical observation of patients to the bench.

However, it is not clear how PTrans is doing in the midst of the many projects carried out by the institute and there are no reports on the methods used to integrate the generated knowledge or to accelerate technological development. In the report, it is evident the importance given to basic research and the translation of the knowledge generated by

it, in the advances needed to identify new diagnoses, prevention techniques, and treatment of diseases, seeking to improve the health of the population.

On the other hand, in the available reports of these three INCT, self-denominated translational, there was an effort to produce knowledge. It was observed that INCT-TM¹⁸ sought to train researchers in PTrans, as well as developed a proposal for a diagnostic kit. INCT-INPeTAm¹⁹ sought to identify the burden of disease in riverside communities; characterize, through genomics, the common etiological agents in the region; research ways of treatment and diagnosis for the prevalent diseases in the region; empower the community with ways to prevent disease; sought cooperation with the company Extracta to find molecules that could treat prevalent diseases in that population. Furthermore, it conducted research on environmental variables and their interference with the health of the local population. The INCT-INNT²⁰ made a major contribution to article production and HR training, but it was not clear what forms of technology transfer were performed or even which products were generated by this institute.

The interaction between INCT and companies can be a path to sustainability of these institutes, as the gains from licensing and technology transfer may outweigh their spending. In addition, through large-scale production and sale of medicines, vaccines and diagnostic kits, the population will be able to access disease prevention and treatment. Given the importance of this interaction, in 2019, the Center for Management and Strategic Studies (CGEE)²¹ conducted a Survey that assessed the interaction between INCT and companies. In this Survey, questionnaires were sent to the 122 INCT of the PINCT. From these, 74 (60%) questionnaires answers were obtained and 62 INCT responses were validated. Of the 62 INCT, 17 (49% of validated INCT)

belonged to the health area. To analyze the amount of interactions with the business sector, the following question was asked: 'Was there any interaction between this INCT and the business sector?'. Among the respondent coordinators, over 85% stated that there is interaction between the INCT and the business sector²¹.

The INCT that have the most interactions with the business sector are in the areas of nanotechnology, exact and natural, agrarian sciences and agribusiness, energy and engineering and information technology. However, this value should be relativized, since in some cases companies require a confidentiality agreement to be signed (Non-Disclosure Agreement – NDA), in order to protect information on projects during the negotiation and execution period provided for in the contract. In some cases, the relationship with the contracting company²¹ is not mentioned.

The INCT-Health stand out from the others for presenting the largest number of NDAs signed, with a total of 7 (11% of validated respondents). Even so, of the health respondents, 9 (53%) assumed that they had interactions with the business sector. The INCT-Health also stand out regarding the technology transfer with the business sector, and 25% said they perform this type of activity surpassing even the agrarian and agribusiness INCT (17.1%). In this Survey²¹, 232 technology transfers were accounted for. Of this total, the health area made 27, behind only the INCT-Nanotechnology that made 147 transfers. It is important to highlight that there are other INCT that also serve the healthcare area, such as Engineering and IT, that claimed to have interacted with companies in the sectors of production of materials for medicine and dentistry. Moreover, some of the interactions of INCT-Health occurred with companies from different sectors, not necessarily with drugs, medicines and medical devices.

As for the creation of companies

(startups), 18 INCT reported having created 20 companies. INCT-Health contributed the most for the creation of companies, with a total of 5 among the validated respondents, surpassing INCT-Nanotechnology, Agrarian Science (4) and Agribusiness (3). INCT startups founders include INCT-TM, INCT-Dengue and the National Institute of Science and Pharmaceuticals and Medicines Technology (INCT-Inofar)²¹.

Still regarding interaction with society and companies, it is important to emphasize that not all INCT-Health were created to perform this direct interaction. Some intervene in partnership with a government agency, such as the National Health Surveillance Agency (Anvisa) or the MH, and, even then, the population will

indirectly benefit through programs or public policies. In this case, it should be noted that the National Institute of Science and Technology for Policies on Alcohol and Drugs (INCT-Inpad)²² was created to support Public Policies to Combat Chemical Addiction, by conducting epidemiological studies and training personnel on the theme. Another emphasis is the Institute for Health Technology Assessment (HTA), which is not expected to intervene directly in society, as its results support the MH in Health Technology Assessment. INCT-Iats conducts economic impact analysis regarding the use of new technologies/products/practices to be incorporated into the SUS protocols. See in *chart 2* below some of the results identified of the INCT-Health.

Chart 2. Highlights of some of the INCT-Health results between 2009 and 2013

INCT-HSM

- Development of ethical and regulatory standards for assisted reproduction and installation of SRHA.
- Project of Guidelines of the Brazilian Medical Association and the Council of Medicine.
- Reproduction endocrinology training program for clinicians and embryologists of Latin America.
- Preparation of Clinical Protocols for Marital Infertility.
- Contraception courses applied to public health.

INCT-INOD

- Course of translational medicine for the general practitioner demonstrating the physiopathological basis of DM2 and obesity, as well as the mechanism of action of the medicines used in the treatment of these diseases.
- Course on insulinization.

INCT-INP and Tam

- Training of multipliers in Health Education with visits to groups responsible for malaria control programs and field work in riverside communities.
- Prevention of endocrine disruptors and the diagnosis of metabolic syndrome that may arise with the progress of the region, by visiting physicians and teachers of physical education.

INCT-CD

- Kit for immunodiagnosis of canine visceral leishmaniasis.
- Phase III essay to verify the efficacy of the combination of pentoxifylline and pentavalent antimonial for the treatment of cutaneous leishmaniasis

INCT-MACC

- HeMoLab; ImageLab; AToMH; GeoHealth Web and the CyberMed. 5.
- Development and construction of a manikin for simulation of cardiac and pulmonary auscultation and training for medical teaching.

INCT-FHV

- It is in use in the IEC and in several laboratories of the national network of public health laboratories of the Ministry of Health (MH) for the diagnosis of dengue in up to 4 hours.
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Chart 2. (cont.)

INCT Blood

- Studies of bone marrow stem cells for treatment of chronic arterial obstruction and its application in suture wires to reduce the complications of intestinal surgeries.

INCT-Tuberculosis

- A molecular test for tuberculosis was developed and registered. This test is being produced as a diagnostic kit (Detect TB) by the Brazilian Labtest industry.
- The antimicrobial agent, called IQG-607, was also developed.

INCT INPD

- Epidemiological study addressing the mental health of children and adolescents, several Brazilian regions, identifying the correlation of local cultural and social factors with expression of psychopathology.

INCT Vaccines

- Commercialization of recombinant vaccine against canine visceral leishmaniasis, released by the Ministry of Agriculture. The vaccine was developed in cooperation with a Brazilian company.

INCT Immunology

- Studies for the development of rheumatic fever vaccines and HIV vaccine have been initiated. Patents have been requested for both.

Source: Own elaboration based on the information on the INCT-Health page. Available at: <http://inct.cnpq.br/>. Access on: 04/12/2019.

As established in Notice nº 15/2008⁹, the strategic areas of activity were defined according to Brazilian demands, including biotechnology; nanotechnology; information and communication technologies; the health; biofuels; electricity, hydrogen and renewable sources of energy; oil, gas and coal; agribusiness; biodiversity and natural resources; the Amazon; the semiarid; climate change; the space program; the nuclear program; national defense; public safety; the education; the sea and Antarctica; and social inclusion.

In this study, it was observed that the distribution of INCT-Health between those dedicated to Chronic Noncommunicable Diseases (NCDs) and Communicable Diseases (CD) is balanced, and several are conducting research on both types of diseases. Some INCT-Health are dedicated to researches that may result in new ways to prevent, diagnose diseases typical of the burden of Brazilian diseases, such as yellow fever, tuberculosis, dengue, cancer, diabetes and obesity. Therefore, INCT-Health has the potential to meet the demands for health solutions, considering

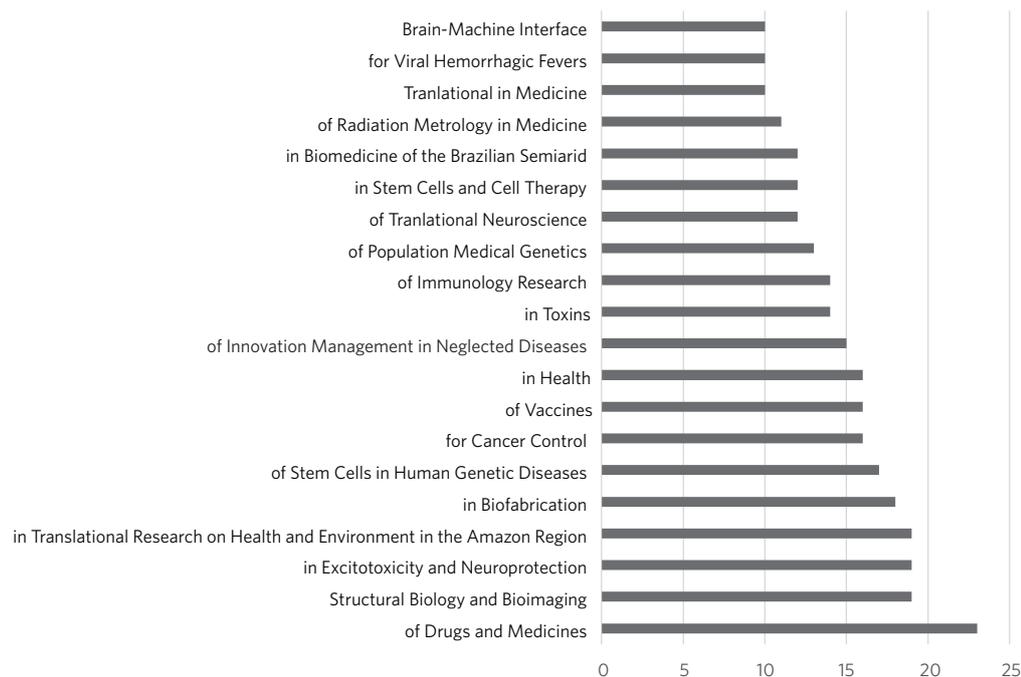
the burden of existing diseases in Brazil. The Core Indicators: Health Situation in Americas²³ reveals that the mortality rate of Noncommunicable Diseases (NCDs) exceeds CD rates, ranging from 427,6 and 59,9 in the Americas to 446,0 and 89,4 in Brazil, respectively. According to the National Health Survey/Brazilian Institute of Geography and Statistics (IBGE)²⁴, NCD represent 70% of the causes of death in Brazil. Cases of diseases such as malaria (129,250 cases in 2016), dengue (252,041 cases in 2017), yellow fever (779 in 2017), tuberculosis (incidence rate of 35.2/100.000 inhab in 2015) still occur in Brazil. Thus, INCT-Health directly relates to all themes recognized as necessary for the development of Science & Technology (S&T) to meet the demands of the population (*chart 1*).

The INCT are formed by a Headquarters Institution (HI) with recognized competence in scientific production, as well as high qualification in HR training. Other laboratories or groups associate with HI forming scientific-technological networks. The median of

institutions participating in the INCT-Health was 10 (IQR 7-15), however, many of these institutions participate in several institutes

(figure 1). The INCT with the largest number of institutions involved was the Drug and Medicines INCT (n=23, 5.5%).

Figure 1. The 20 INCT-Health with the highest number of participating institutions



The high number of institutions participating in some INCT may be related to government incentive. In 2007, Law nº 11.487/2007²⁵ was sanctioned with a new incentive for technological innovation and modification of the rules regarding accelerated amortization for investments linked to research and development, in compliance with the Science and Technology and Innovation Action Plan 2007-2010²⁶. The Plan was developed recognizing a favorable scenario for the S&T area, allied to the period of stability and sustained growth of the economy. The law also establishes tax exemption for companies that invest in research, developed by Scientific and Technological Institutions (S&TI) with definition of criteria. In addition,

there was a strong link between S&TI Policies and Industrial and Health Policies. Priorities were set within the Executive Group for the Health Industrial Complex (Gecis), created in 2008, in order to develop actions that would result in health development under the coordination of the MH²⁷.

Another factor to consider is the location of the HI. The program recognized the extent of national territory, economic and social inequalities and the misallocation of S&TI assets as needs to be controlled. This reality was justified by the fact that qualified HR, R&D, laboratory infrastructure, research institutes and other components of the national S&TI system remain with the highest concentration in the Center-South of the Country.

However, the distribution of INCT-Health headquarters showed no change. The state of São Paulo concentrates 43.6% of the institutes, and with the other states of the Southeast and South they reach 84.6%. Notice nº 15/2008⁹ determined that the Research Support Foundation (FAP) of Minas Gerais, Rio de Janeiro and Sao Paulo (Fapemig, Faperj and Fapesp) would participate in the Program, with co-funding of proposals with HI in their respective states, and this may explain the higher concentration in these states.

Throughout these years, the study evaluated the differences in the composition of health regions between the Brazilian macroregions (North, Northeast, Central-West, Southeast and South) in 2000 and 2016²⁸. It was observed that the percentage of regions with low level of development socioeconomic status and low complexity of health services (predominantly in the Northeast) decreased from 76.4% to 40%, presenting a similar profile to the Southeast and South macroregions. The causes identified by the authors for this change were the increase of the Gross Domestic Product (GDP) *per capita*, of the household income per capita that increased, of the level of education, and the significant reduction of poverty²⁸. Although the triggering factors

of improvement are not directly related to INCT, it is evident the combination of strategies related to social, economic and regional policy for the promotion of development with generation of well-being more disseminated in the territory, object of the PINCT.

The INCT for Pharmaceutical Innovation stood out in the number of leading researchers (n=411, 18.9%). Considering that the development of S&T projects, patents, articles and HR training demand a large number of people, more professionals make it possible to reach the goals. Thus, it was observed that this institute also presented the highest percentage of published articles (19.5%) and patent applications (42.8%) among INCT-Health.

Among the 32,671 articles published in national and international journals, INCT-INNT, INCT-INPeTAm and INCT-TM¹⁸ published a total of 3,503, corresponding to 10.7% of INCT-Health. For future analysis, it is suggested to evaluate the impact of all INCT-Health publications. To obtain comparison parameters, for the next studies, it is proposed to verify the productivity regarding the publication of articles in the INCT of other sectors that have benefited from PINCT. In *chart 3*, the ranking of the 10 INCT-Health that published the most articles between 2009-2014.

Chart 3. Ranking of the 10 INCT-Health that published the most articles, between 2009-2014

Ranking	INCT	Abbreviation	Nº of publications
1º	Pharmaceutical Innovation	INCT-IF	6,376
2º	Translational in Medicine	INCT-TM	1,778
3º	Drugs and Medicines	INCT-INOFAR	1,534
4º	Excitotoxicity and Neuroprotection	INCT-EN	1,527
5º	Integrated Analysis of Environmental Risk	INCT-INAIRA	1,263
6º	Cancer Control	INCT-PCC	1,233
7º	Translational Neuroscience	INCT-INNT	1,121
8º	Structural Biology in Bioimaging	INCT-INBEB	1,085
9º	Stem Cells and Cell Therapy	INCT-C	1,049
10º	Medicine Assisted by Scientific Computing	INCT-MACC	861

Source: Own elaboration based on the information on the INCT-Health page. Available at: <http://inct.cnpq.br/>. Access on: 04/12/2019.

Regarding HR training, it is observed that the INCT-Health trained a total of 13,650 professionals, of which 8,005 masters (58.6%, median 144, IQR 92.5-206.5), 4,418 doctors (32.4%, median 89.0, IQR 55.5-127.5), and 1,227 postdocs (9.0%, median 24.5, IQR 11.5-42.8). It is noted that the drug Institutes, INCT-Pharmaceutical Innovation and INCT-Pharmaceuticals and Medicines, were the ones that developed the most postgraduate courses (22.3% and 6.0% respectively).

This effort in HR training is fundamental for technological innovation in health, both in order to renew the staff of professors and

researchers at universities and for the health industries. INCT-Inofar²⁸ considers in its report, that the dissemination of scientific results obtained with PINCT “has attracted business partners interested in internalizing part of the technologies developed”. Perhaps a strategy to be adopted by INCT-Health is the dissemination of the results obtained, in view of the need to have innovation as a result, as well as the very sustainability of the institutes.

In *chart 4*, it is possible to verify the ranking of the 10 INCT-Health that most trained professionals, between 2009 and 2013.

Chart 4. Ranking of the 10 INCT-Health that most trained professionals, between 2009 and 2013

Ranking	INCT	Total nº of professionals
1°	Pharmaceutical Innovation - INCT-IF	3,039
2°	Tuberculosis - INCT-TB	831
3°	Drugs and Medicines - INCT-INOFAR	820
4°	INCT-PCC	672
5°	Cancer Control - INCT-INBEB	667
6°	Excitotoxicity and Neuroprotection - INCT-EN	605
7°	Medicine Assisted by Scientific Computing - INCT-MACC	539
8°	Translational Neuroscience - INCT-INNT	478
9°	Translational in Medicine - INCT-TM	468
10°	Health Technology Assessment - INCT-IATS	348

Source: Own elaboration based on the information on the INCT-Health page. Available at: <http://inct.cnpq.br/>. Access on: 04/12/2019.

The main limitation of the study was the data source. Reports containing information on activities and results are very limited and insufficient for verifying the application of PTrans in INCT-Health. It would be interesting for publicly available data to be periodically updated to enable studies, strategies and incentives for companies to invest in the development of S&T.

It should also be considered that the transformation of bench knowledge into

improvements in population health is a process that can last more than ten years. Thus, further studies are needed to evaluate the results, making them available to the population, given their public policy character. This process is complex and can occur in different ways, considering the resources and reality that each institute has. Therefore, the relevance of an evaluation methodology and a previously established communication plan for monitoring results is highlighted.

Final considerations

INCT-Health has contributed to the improvement of the Brazilian population, either through the transfer of direct knowledge to society, or by contributing to the formulation/implementation of public health policies. Some INCT-Health have been successful in transforming the knowledge generated in basic research directly to the population without the need for intermediaries, especially those whose projects serve specific communities through the provision of innovative services. Even though there is no clarity on the methods of accelerating the generation of new technologies, used by the three INCT, declared as 'Translational', it is clear that their results have reached society, either with products or with training.

Efforts to publish articles, HR training and obtaining patents are noticeable. The INCT-Health have been highlighted in the interaction with companies before others, but there is still room for strengthening this relationship. It is important to emphasize the role of these INCT in the generation of new companies that can contribute to a new dynamic in the health innovation ecosystem.

Interactions with companies have potential, and perhaps this is the time to 'shake the tree' to reap the rewards. However, for this, it is essential to disseminate the results and to establish an evaluation methodology to highlight what INCT-Health have achieved in terms of results. It lacks clarity about the future of INCT-Health; in the reports evaluated, the next steps are not foreseen, not even how the activities have been completed to date.

Collaborators

Bosio CGP (0000-0003-2341-9421)* contributed to the elaboration of the methodology, consolidation, interpretation of data and revision of the final text. Fujimoto RHP (0000-0002-2521-0018)* contributed to the conception, approval of the final version and agreement on responsibility for the aspects of the work. Souza MBCP (0000-0002-4902-7592)* contributed to the conception and planning of the article. Bosio M (0000-0001-8031-7654)* contributed to the search for information, review and consolidation of data. ■

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