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Intangible benefits of clinical trials: a survey on a hospital research community

Emanuele Calvario

IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy

Abstract

The ongoing pandemic is highlighting the strategic role of clinical trials as an essential step of biomedical research, with a potential life-saving impact on public health. Several studies have focused on the assessment of clinical trials' economic impact. Robust methods allow a reliable assessment of the impact of trials on population health in terms of new drugs development. This study shows the results of a survey administered to the research community of the IRCCS Ospedale Pediatrico Bambino Gesù. The goal of the survey was to assess how researchers' participation in clinical trials impacts on research capacity development, career improvement, health benefits, knowledge production. The study results suggest that clinical trials promote a significant improvement of research capacity by the development of scientific know-how, the creation of new research networks, the improvement of diagnosis and clinical decision-making skills, the openness to new therapeutic approaches, and the patient recruitment and data management capabilities. These results actually suggest that clinical trials lead to better care also because they contribute to create better physicians, and not only because they provide new drugs or devices. Economic benefits, patient recruitment and researchers' internal reputation have been highlighted as critical issues.

Key words

- clinical trials
- assessment
- impact
- survey

INTRODUCTION

There is a general global consensus on the importance of measuring the economic impact of biomedical research [1]. This has led to an extensive literature on the development and study of research impact models [2, 3]. However, there is no unique model for research impact analysis officially adopted in the EU [4]. Furthermore, an assessment model specifically dedicated to the impact of clinical trials on biomedical research centres conducting them, has not yet been developed [5, 6].

In Italy, universities and hospitals (but not yet regulatory authorities and policy makers) show a growing interest in the development of cost-benefit analysis models for clinical trials [7, 8]. However, there are no integrated models of analysis and evaluation that include the "intangible" benefits (i.e. not expressly economic or financial) of clinical research, *i.e.* how researchers' participation in a trial may impact on their professional and scientific growth [9, 10]. There are actually studies in the literature that have examined the impact of biomedical research on the research capacity of the scientific community. These studies are based on the so-called "Payback" [11, 12] impact assessment framework, which has been integrated with other variables to make it more robust and adaptable to different assessment scenarios [13]. One of these studies focuses on the socio- cultural impact of biomedical research on the scientific community itself [14].

A recent Italian study, focusing on the factors capable of improving the attractiveness of a biomedical research centre, has analyzed how different professionals of healthcare companies involved in drug trials perceived the advantages and disadvantages of such trials [15]. Following this study (which also includes "intangible" variables), the main advantage of experimental activity is its capacity to attract new trials. The authors attribute this effect to the "signaling" value of scientific trials in terms of scientific excellence and quality of the investigators.

The study carries out a perception analysis on the responses of a sample of clinicians involved in clinical trials and belonging to the same research community. It has been carried within the IRCCS Ospedale Pediatrico Bambino Gesù (OPBG), specifically focusing on clinical trials, and it aims at measuring the benefits that clinical trial participation produces on a community of researchers in terms of research capacity development, scientific knowledge production, researchers reputation and career development.

The investigation was conducted in an Italian context, as there is still relatively limited evidence on the organization and management of clinical trials in Italy and there is the need of building awareness on the impact of

Address for correspondence: Emanuele Calvario, IRCCS Ospedale Pediatrico Bambino Gesù, piazza Sant'Onofrio 4, 00165 Rome, Italy. E-mail: emanuele.calvario@opbg.net.

clinical research in a broader sense, not only economic, also considering the missed opportunities related to the lack of localization of the trials by companies.

METHOD

An *ad hoc* questionnaire was prepared to conduct the survey. Before starting the survey, the questionnaire was:

- presented informally to the OPBG principal investigators (PIs) to have their feedback and comments;
- tested with a group of volunteer young researchers to verify understandability, response times, effectiveness to research purposes.

The questionnaire is divided into two parts. The first part is on personal information and aims at segmenting responders on the basis of age and expertise. The second part explores the main benefits of trial participation for researchers and includes four blocks of variables:

1. research capacity, *i.e.* the impact in terms of research ability and skills of the researchers and his/her team;
2. career improvement, *i.e.* the benefits for career and reputation;
3. healthcare benefits, *i.e.* the impact in terms of improvement in diagnosis and treatment skills;
4. knowledge production, *i.e.* the capacity of generating scientific knowledge also considering patenting (including entrepreneurial possibilities) and impact on policy making.

All the variables are described in detail in the Supplementary Material available online. They were chosen based on the available literature on research and biomedical research impact assessment [2, 9], and on studies on economic impact assessment of clinical research organizations and clinical trials [8,16].

The variables concerning the capability of improving health (healthcare benefits) and scientific knowledge (knowledge production) originate from the biomedical research assessment model called "Payback" and on its derivations of "social payback" [3] and "payback to society" [14], which underlined the importance of assessing the impact in terms of "research capability improvement" (Research capacity), considered also as the development of cooperation networks, research technologies and equipment acquisition, training of a new generation of researchers.

The questionnaire was presented informally to OPBG PIs asking their feedback and comments. They strongly suggested to include the improvement of methodological know-how in the variables concerning research capacity. They also suggested to consider career improvement (in terms of remuneration, reputation, networking with other hospitals and biotech companies) as an important variable to be assessed. This suggestion found confirmation in recent literature [15].

The aspect of patenting and entrepreneurial capacity has been inserted in order to open up a subsequent search possibility. In fact, it is assumed that these aspects are evaluated with very low scores, despite the fact that conducting clinical trials is an activity with a high content of industrial innovation. This could be an aspect of further investigation and study, promoting analysis of models capable of stimulating forms of participation by researchers in industrial development projects. The assessment point concerning policy making responds to one of the most highlighted aspects of scientific research impact analysis. Indeed, many studies note that research produces impact as much as its outcomes are taken into account in terms of public health policy [17].

The questionnaire includes multiple choice questions and ranking questions. No open questions are included. The questionnaire was submitted to the researchers involved in clinical trials at Ospedale Pediatrico Bambino Gesù. Anonymity of respondents was maintained. The list of respondents was provided by the Hospital Research Direction. The total number of respondents is 265.

The questionnaire was administered on-line through the web-based platform Monkey Survey, during March - April 2020. Respondents were reached through an e-mail message containing the rationale of the survey, bibliographic references and a link to the on-line questionnaire. Two reminders were sent by email 15 and 30 days after the first email. To stimulate participation, a number of researchers (one for each research department) were engaged ono to one.

Due to the descriptive nature of data, statistical analysis techniques were not used.

RESULTS

As indicated in *Table 1*, the survey target population is made of 265 persons, *i.e.* the healthcare personnel of the IRCCS Ospedale Pediatrico Bambino Gesù who have been involved in at least one clinical trial. Of this target population, 205 subjects took part in the survey. The respondent population is predominantly female (about 60%), and 77% of them are clinicians. The average age is of about 50 years. 43% of respondents have an over 10-year-experience in clinical trials. If we decrease the length of experience to a minimum of 5 years, the percentage rises to 80%. The average age and the length of experience in clinical trials suggest that the trial population can be defined as an "expert group" in clinical trials.

By crossing the clinical trial experience with the professional area of origin, it results that 90% of the population with an over 10-year experience in clinical trials is made of clinicians. Furthermore, 92 % of the surveyed population have been involved in clinical trials outside of Italy for less than 5 years. It is therefore legitimate to consider that the respondent's group has gained its experience mainly in Italy. Finally, 89% of the population confirmed their involvement in clinical networks. Based on the above results, we may define the respondent population as "a group of clinicians with a consolidated experience in the experimental studies, gained mainly in Italy and with a widespread participation in research networks".

Concerning the analysis of the four variables, it has been observed that:

a. Research capacity: the distribution of answers to the question on the economic benefit related to the participation in clinical trials is surprising: respondents do not consider as highly significant the economic benefits obtained through their participation in the trials. The most

Table 1
Analysis of the survey respondent population

	Number	Percentage
Category		
Target population	265	
Survey participants	205	
Male	86	42%
Female	119	58%
Job area		
Clinic	124	61%
Surgery	29	14%
Laboratory	17	8%
Research Department	13	6%
Other	23	11%
Job description		
Physicians	157	78%
Sanitary personnel	32	16%
other	13	6%
Years of experience in clinical trials		
1 - 3	43	22%
4 - 6	39	20%
6 - 10	31	15%
More than 10	85	43%
Years of experience abroad		
5 or less than 5	181	92%
6 - 10	14	7%
More than 10	2	1%
Involved in clinical network	178	89%
Experience as Expert Evaluator in international calls	55	28.6%

frequent response is "fairly significant"; more than half of the population (65%) considers the economic impact as not significant (score: 1,2,3. Weighted average: 2.9). Similarly, the additional aspect concerning the benefit in terms of research infrastructure or technologies obtained as a result of the trial, has been considered as not particularly significant *(Figure 1)*.

The distribution of answers to the questions concerning the intangible impact of the trials (*i.e.* the impact in terms of increased clinical and methodological know-how and in terms of relational connection in research networks – *Figure 1*) suggest, on the contrary, a highly significant impact (score 4 and 5 for 85% of respondents). As regards the questions on organizational benefits, the majority of respondents considered that their participation in clinical trials significantly improved their involvement in the organizational and information processes of their research organization. Such impact can also be considered as "intangible" since it is a functional benefit consisting in a stronger connection of the researchers and their teams to the organizational flows of the Hospital.

b. Career improvement: as regards the analysis of responses regarding the impact on professional improvement, almost 70% (68%) of the population surveyed considers their participation in trials as significantly important for their professional growth. Among them, one out of four respondents (25%) considers it as extremely relevant to their professional development. These answers need to be interpreted and it seems legitimate to wonder why the population surveyed think that the trials have helped or are helping them in their professional growth. The answer to this question is not related to an increase in reputation or professional prestige within the research organization where the researchers belong, as this aspect is considered as as not highly significant by respondents, and certainly less significant than the reputation acquired outside the research organization they belong in. The population surveyed, in fact, seems to believe that participation in the trials has first of all improved the following professional skills *(Figure 1)*:

- clinical decision: 32% of respondents believe that participation in clinical trials has significantly increased (rating: 4 out of 5) their diagnose ability and clinical decision- making. This percentage increases to 45% if we consider those who gave the maximum rating (4 and 5) to this question;
- openness towards new therapeutic approaches: 34% of respondents consider that their participation in clinical trials contributed very significantly (rating: 4 out of 5) to the increase of their openness to new therapeutic approaches. This percentage increases to 50% if we consider those who gave the maximum rating (4 and 5) to this question;
- data management: one out of three respondents (33%) considered that participation in clinical trials contributed significantly (rating: 4 out of 5) to the improvement of their abilities in data collection & management. This percentage increases to over 50% if we consider those who gave the maximum rating (4 and 5) to this question;
- data analysis: more than 50% of respondents consider that participation in clinical trials contributed in a significant way (rating: 4 and 5 out of 5) to the improvement of their abilities in data analysis. The ability to analyze, interpret and understand data is the skill, which has received the best rating (highest weighted average rating).

Among the benefits in the professional field, the positive impact on external reputation has been considered as much greater than that on internal reputation. Almost 70% (69%) of respondents rated external reputation 4 and 5 out of 5, thus considering that participation in clinical trials had increased their external visibility, which also resulted in an attractiveness for potential partners and investors. It is the writer's opinion that this external visibility and professional attractiveness may translate into an improvement of scientific reputation, an increase in professional connections and opportunities and consequently also in the improvement of job opportunities and remuneration.

As regards part of the assessment of the impact of participation in clinical trials on careers, *Figure 1* de-

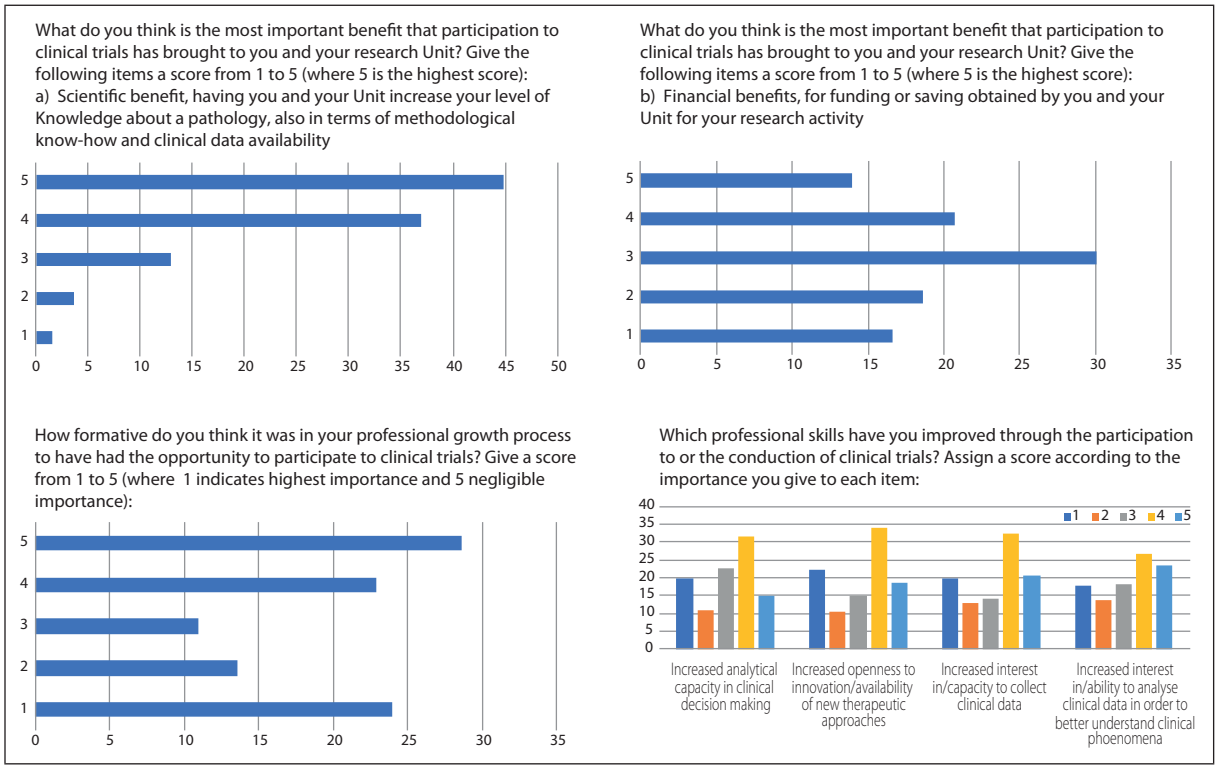

Figure 1
Impact of clinical trials participation on research capacity and professional skills.

serves particular attention, as it seems that the respondent population provided contradictory answers. The interpretation of these results required an analysis of the data in which respondents of different ages and professional experience were assumed to have given different answers. The above data were then cross-referenced with data on age and professional experience. *Table 2* is the resulting contingency table. It shows how, as professional experience increases, the importance given to participation in clinical trials in terms of "training impact" on professional career decreases. *Figure 2* shows the different distribution of answers based on the experience of respondents (junior: less than 6 years of experience; senior: more than 6 years of experience). These results show that respondents with less experience tend to attach a greater importance (scores 1 and 2) to participation in trials in terms of educational impact than respondents with more experience (scores 4 and 5). It may be concluded that, according to the interviewed population, the less professional experience the inter-

Table 2
Clinical trial "training impact" on professional career

			How formative do you think it was in your professional career to have had the opportunity to participate to clinical trials? Give a score from 1 to 5 (where 1 indicates maximum importance and 5 negligible importance):					
			1	**2**	**3**	**4**	**5**	**Total**
Years of working experience	**<7**	number of answers	26	13	9	18	13	79
		% years of working experience	32.9%	16.5%	11.4%	22.8%	16.5%	100%
		% score given	56.5%	52%	42.9%	40.9%	23.6%	41.4%
	>6	number of answers	20	12	12	26	42	112
		% years of working experience	17.9%	10.7%	10.7%	23.2%	37.5%	100%
		% score given	43.5%	48%	57.1%	59.1%	76.4%	58.6%
Total		number of answers	46	25	21	44	55	191
		% years of working experience	24.1%	13.1%	11%	23,00%	28.8%	100%
		% score given	100%	100%	100%	100%	100%	100%

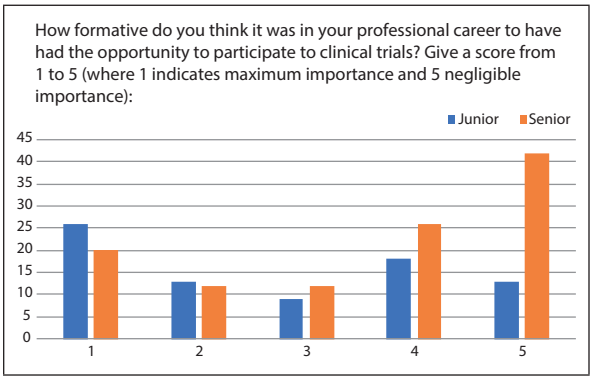

Figure 2
Impact of clinical trial participation on professional career (answers distribution related to years of working experience. Junior: working experience less than 6 years; Senior: more than 6 years).

viewees have, the greater the importance they attach to clinical trials in terms of educational impact. This may be because younger respondents consider the participation in clinical trials as particularly formative.

c. Healthcare benefits: respondents consider the impact of participation in clinical trials on their ability to care and generate health ("Healthcare benefits - health improvements") as very significant. Understandably and quite predictably, in numerical terms, the variable considered as the most significant was treatment capacity; because trials allow using and administering innovative devices and drugs (score 4 and 5 given by 71% of respondents). However, when comparing the weighted average values (3.88 *vs* 3.93), ability to diagnose and clinical decision-making seem to be considered as the most significant, as the trial allows acquisition of a higher level of knowledge on the specific condition involved in the trial itself. On the other hand, it should be noted that the scores given to "recruitment capacity" have had the lowest weighted average compared to the other variables of the block "health benefits" (3.64 *vs* 3.88 and 3.93). The respondents probably consider that participation in clinical trials has a less significant impact (although patient recruitment is inherent in the very nature of clinical trials) on the ability to attract new patients in relation to the condition involved in the clinical trial itself.

d. Knowledge production: impact assessment of participation in clinical trials on the ability to generate scientific knowledge has had different results depending on the areas analyzed. The most significant weight has been found in the scientific production capacity. 70% of respondents gave the highest scores (4 and 5) to this area. There is no doubt, therefore, that participation in trials had an impact on the publication of new scientific papers and on scientific and cultural production in general within the scientific community. Equally, a very important weight was unanimously given to the capacity of innovation: 69% of respondents gave the highest scores (weighted average: 3.84) to "capability in developing new drugs or devices", which represents the core activity of clinical trials.

A completely different weight was given to the ability to contribute to patenting, which almost 40% of respondents considered as insignificant: almost 60% of the survey population gave a score of 1 and 2 out of 5 to this area. The same applies to the "entrepreneurial" impact: 57% of the survey population seems to believe that participation in clinical trials did not open entrepreneurial opportunities in terms of spin-offs or start-ups.

On average, the impact on involvement in policymaking processes through the production of documents with a regulatory impact or on participation in study commissions or public initiatives at an institutional level has been evaluated as not very significant. One out of four respondents (24.6%) believed that their participation in clinical trials did not give them any role in policymaking processes related to the field of the trial itself.

DISCUSSION

Based on the above data, the following conclusions, summarized in synthetic statements, may be proposed (see below).

Clinical trials mean "better researchers" rather than "higher budget": the main finding of this survey is that participation in clinical trials increases research capacity. There is almost unanimous agreement that participation in clinical trials produces a significant improvement in the researcher's level of knowledge about a specific condition, in terms of methodological know-how and available clinical data. Participating in trials also means more connections with research networks and therefore exchange of information and know-how related to a specific condition. The innovative aspect, which would deserve further research, is that this positive impact is considered as greater in an intangible sense than in a tangible one. In other words, the interviewed population believes that clinical trials increased their research capabilities in terms of improved scientific know-how and research connections, more than in terms of available economic resources and infrastructure.

Clinical trials mean "better physicians": questions on career improvement were asked to analyze the impact of participation in trials in terms of career opportunities. All respondents agree that participation in clinical trials had a positive impact on their careers and improved their professional skills, thanks to a significant development of their diagnosis and clinical decision-making skills, an increased openness towards new therapeutic approaches, and an improved competence in the collection, management and interpretation of clinical data. Considering that the survey population is a "group of experienced physicians", as previously established, it could be concluded that participation in clinical trials helped them become better doctors. If we also consider the results related to the reputation, we can conclude that participation in trials made them become "better doctors" both in terms of clinical competence and effectiveness and in terms of external reputation and professional prestige.

Clinical trials mean learning opportunities for young researchers: the younger respondents are, the more they feel participating in trials had a strong educational im-

pact. This finding confirms that participation in clinical trials increases clinical and methodological know-how and this is particularly felt by younger researchers.

Reputation and professional prestige emerge as a rather controversial aspect: in fact, the interviewed population considers the improvement of their reputation as researchers more in relation to the external scientific community (and related funding opportunities) than within the professional community of their own institution. This finding may suggest a certain frustration among the surveyed population and it may have implications both for HR Management and Internal Communication policies.

Clinical trials mean "Better care more than better drugs": this conclusion derives from a critical reading of the results on "Health improvement". Clinical research leads to better treatments, not only because it makes available new and potentially more effective drugs, but above all because, according to the interviewed population, they improve clinical decision-making skills. We may therefore conclude that clinical trials lead to better treatment because they help train better doctors, and not only because they provide access to potentially better drugs and devices;

"Patient recruitment as a critical issue": the survey does not explicitly address the issue of patient recruitment, but this aspect emerged quite critically in the context of "Health improvement" questions. The interviewed population believes that participation in clinical trials improved their ability to administer better drugs or use biomedical devices, and that it improved their diagnosis and clinical decision-making skills, but did not as much improve their ability to attract new patients. This is rather surprising, as patient recruiting is a fundamental aspect of clinical trials and one of its success factors. The topic of patient recruitment seems to be a critical issue, which emerged from this survey, even though it is not its focus.

Clinical trials mean scientific knowledge and system: the survey population does not question the fundamentals of "Knowledge production": clinical trials produce new knowledge and new biomedical technologies. The respondent population unanimously agreed on this. This new knowledge is made available to the scientific and health community and strengthen the fundamentals of research. Participating in clinical trials establishes or strengthens professional links and connections with new research groups. Clinical trials, therefore, help develop a "scientific research system".

Clinical trials mean researchers but not entrepreneurs: the low scores given to the impact on patenting or entrepreneurial capabilities need to be further examined also in relation to the so-called third mission of research institutions and universities. In fact, it is now universally recognized that research and academia need to have an important role in technology transfer for the development and promotion of technologies resulting from the research projects they conduct, and more generally, in the management of intellectual property. This survey results are not enough to conduct a comprehensive critical analysis of these aspects, however, our findings suggest a negative perception of the possibility of being involved in patenting or other business activities. The interviewed population seems to be almost unanimous on the belief that clinical trials today do not open business opportunities to researchers.

Lack of engagement in policymaking: a mode of interaction between the world of research and the society lies on the ability (of research) to improve the general well-being by increasing knowledge, cultural and educational contents and awareness. In this regard, the importance of being involved in policymaking is crucial. The interviewed population considers their contribution to policy making in the field of experimental research to be of little significance. Our survey seems therefore to confirm the lack of dialogue between researchers and policy makers. This aspect calls for a reflection on the opportunity to involve researchers engaged in clinical trials in institutional forums, as well as on the ability of research institutions to present the results achieved in political settings. The importance of the use of health research in policy-making, and of understanding the mechanisms involved, is increasingly recognized. Recent reports calling for more resources to improve health in developing countries, and global pressures for accountability, draw greater attention to research-informed policy-making [18]. The utilisation of health research in policy-making should contribute to policies that may eventually lead to desired outcomes, including health gains [19].

CONCLUSION

The aim of this study was to give a contribution to the debate on the economic and cultural impact of clinical trials on the society. The main variables and methods to assess the social impact of biomedical research have been used [20]. A survey was administered to a population of researchers to assess impact under a different perspective.

The choice of the IRCCS Ospedale Pediatrico Bambino Gesù is motivated by the specific experience of this Hospital, the largest children's hospital in Europe and one of the largest in the world, which makes it particularly adequate to the aims of this study [21]. OPBG is in fact one of the most attractive facilities in terms of paediatric clinical research, with a high number of researchers and of ongoing clinical trials [22].

The choice to administer the questionnaire to a limited population is a limit of this study, but it opens the possibility to replicate it to a more extensive population, e.g. the entire group of the so called IRCCS (Italian biomedical Research Hospitals), which have different legal natures, operate within different biomedical and clinical research areas, and have different geographical positions. Such an extension of the study would make it more comprehensive, robust and with a national perspective. Another limit is that the method of impact assessment does not consider the different research areas. In fact, researchers on different research areas may evaluate differently the impact of their participation in trials. A possible development of this study could therefore also consider the differences in the assessment following the different research ar-

eas. Recent literature has showed that hospital management has a low awareness of the benefits clinical trials provide to hospitals [7, 8, 23]. In this regard, another limit of this study is that managers have not been included in the survey.

The above discussion leads to new questions. For example, considering the benefits that researchers recognize in their participation in clinical trials, it is legitimate to wonder how much research institutions encourage and enhance researchers' participation in trials. From another point of view, the interviewed researchers consider the "cultural" benefits more important than the economic and infrastructural benefits. It would therefore be interesting to see which are the policies and instruments research centers activate to make participation in trials more economically meaningful. In addition, new policies would be needed to allow researchers' direct access to funds for entrepreneurial development related to their research. Our survey results also suggest that there are communication issues: internal communication within the research center, external communications towards patients (for recruiting purposes), communication between research groups and health policy makers (in order to bridge the gap between science and policymaking [24]).

The ongoing pandemic emergency has had consequence and induced accelerations on many aspects of the debate about research impact. There is no doubt that this pandemic has strongly focused the attention of policy makers as well as public opinion on the strategic importance of clinical research in protecting the health of the population. Even more, it highlighted the strategic importance of medical doctors having research experience and know-how. This survey confirms how clinical trials can strengthen this know-how and skills. The hope is that the experience of this pandemic emergency will have a positive legacy, improving the ability of policy makers and research facilities to govern clinical trial processes through increasingly effective models, and give doctors and researchers the role of active players in our national health system for the benefit of the population health.

Conflict of interest statement

The Author declares he has no financial or personal relationship with other people or organizations that could inappropriately bias conduct the study.

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