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ORIGINAL RESEARCH

COVID-19 epidemic strongly affected cancer research in Italy: a survey of the Italian Cancer Society (SIC)

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Background: Italy was among the first countries hit by the pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The application of strict lockdown measures disproportionately affected both cancer patient care as well as basic and translational cancer research.

Materials and methods: The Italian Cancer Society (SIC) conducted a survey on the effect of lockdown on laboratories involved in cancer research in Italy. The survey was completed by 570 researchers at different stages of their career, working in cancer centers, research institutes and universities from 19 Italian regions.

Results: During the lockdown period, the impact of the COVID-19 pandemic emergency on face-to-face research activities was high, with a complete (47.7%) or partial (36.1%) shutdown of the laboratories. In the post-lockdown period, research activities were resumed in most of the respondents' institutions (80.4%), though with some restrictions (77.2%). COVID-19 testing was offered to research personnel only in ~50% of research institutions. Overall, the response to the pandemic was fragmented as in many cases institutions adopted different strategies often aimed at limiting possible infections without a clearly defined contingency plan. Nevertheless, research was able to provide the first answers and possible ways out of the pandemic, also with the contribution of many cancer researchers that sacrificed their research programs to help overcome the pandemic by offering their knowledge and technologies.

Conclusions: Given the current persistence of an emergency situation in many European countries, a more adequate organization of research centers will be urgent and necessary to ensure the continuity of laboratory activities in a safe environment.

Key words: SARS-CoV-2, COVID-19, cancer research

INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has resulted in an ongoing pandemic that affected >115 million people and caused >2.5 million deaths worldwide (https://coronavirus.jhu.edu/map.html).

Italy was among the first countries hit by this pandemic and its rapid evolution in Northern Italy led to the application of strict lockdown measures that profoundly affected all activities and disproportionately affected both cancer patient care as well as cancer research. This effect became then evident not only in Italy but worldwide, as recently reviewed by Painter and colleagues.[1] Cancer patients experienced a particularly adverse outcome upon SARS-CoV-2 infection.[1-3] The pandemic also negatively impacted cancer care with ~90% of cancer centers experiencing a reduction in their ability to provide services worldwide[4] and in the possibility to carry out cancer screening programs, especially for racial and ethnic minorities.[5,6]

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Furthermore, the COVID-19 pandemic had a relevant impact on clinical research in oncology, with a reduction of 74% of patients enrolled in clinical trials in May 2020 compared with the same period in 2019.[7] This drop in patient recruitment has been related to the decreased ability of clinical, support and preclinical units in providing nonessential activities and to the reallocation of resources to more critical services and trials.[7] For instance, between January and June 2020, >1200 SARS-CoV-2-related clinical trials have been registered in only nine countries.[7]

Basic and translational cancer research was also profoundly affected by the COVID-19 pandemic at different levels. A cut in cancer research funding due to the pandemic has been anticipated worldwide,[1,8,9] and many researchers reported a reduction or complete shutdown in their laboratory activities with possibly profound consequences on years of previous activities in building models, collecting samples and supporting clinical activities not only in Italy but also worldwide.[10-12]

Yet, although there is the clear perception that preclinical cancer research has been strongly affected by the current pandemic, we still do not have any systematic report on how the pandemic impacted at the national and/or international level on the activities of cancer research laboratories and how the cancer research community lived during the months of more severe lockdown.

To fill this gap, here we show the results of a survey conducted by the Italian Cancer Society (SIC) on the effect of lockdown on laboratories involved in cancer research in Italy during the first wave of the COVID-19 pandemic. The survey was completed by 570 researchers at different stages of their career, working in cancer centers, research institutes and universities from 19 Italian regions. We discuss what the Italian cancer community has learned from this experience and what we think should be the next steps to face the new challenges raised by the SARS-CoV-2 pandemic.

MATERIALS AND METHODS

In May 2020, the Italian Cancer Society (Società Italiana di Cancerologia, SIC; https://www.cancerologia.it) launched a survey to assess the impact of the COVID-19 pandemic on cancer research conducted in Italy. To deploy the questionnaire rapidly and for very fast data collection, a web-based modality was chosen. The Google Forms platform was the choice to implement the survey, and responses were automatically stored in a database built with Excel (Microsoft Office).

The survey was proposed to scientists involved in cancer research in universities, cancer centers and research institutes. Responses were collected between 5 and 27 May, with 93% of responses registered in the first 10 days (Figure 1).

Twenty-nine questions were asked, including rating scale (from 0 to 10), multiple-choice, closed- and open-ended questions (Supplementary Table S1, available at https://doi.org/10.1016/j.esmoop.2021.100165). Questions covered the characteristics of responders, as well as the modality of research activity during the first two phases (phase 1 and 2) of the COVID-19 pandemic that in Italy were distinguished by over 2 months of total lockdown all around Italy (phase 1 from 9 March) and a gradual easing of lockdown from 4 to 18 May (phase 2). Rating scale responses (from 0 to 10) were recoded into three-level variables, combining the bottom three boxes (from 0 to 2) as low, the middle rates (from 3 to 7) as neutral, and the top three boxes (from 8 to 10) as high. Manual content analysis was carried out on multiple-choice and open-ended questions, and responses were categorized into three levels (no/partially/yes or increased/unchanged/decreased, as appropriate). Eleven questions related to the lockdown phase were further summarized by means of a 'lockdown score', representing the sum over the 11 responses, after having assigned the lowest (bottom three boxes/no/increased), middle (neutral/partially/unchanged) and the highest (top three boxes/yes/decreased) categories to 0, 0.5 and 1 values, respectively. The sum was then divided by 11 to normalize the lockdown score into range 0-1. High score represents a high impact on research activities during the lockdown phase.

Responses were described as frequencies and percentages, or median and first/third quartiles for categorical and continuous variables, respectively. Chi-square test was used to assess the association between variables. Kruskal–Wallis test was used to compare continuous distributions. P values <0.05 were considered statistically significant.

RESULTS

Italian cancer researchers were invited to respond to an online questionnaire aimed at verifying the impact of the COVID-19 pandemic and the consequent lockdown on their activity (see Materials and Methods). The response rate to this survey was high with a total of 570 researchers participating (Figure 1). Participants were 44 years old on average, 68.4% female and 28.8% male (Table 1). Over 200 survey respondents were group leaders, professors or directors of research institutions (Table 1). Cancer centers and universities were the prominent affiliations among survey respondents (81%; Table 1). Overall, research institutions were located in Northern (58.4%), Central (18.9%) and Southern (20.7%) Italy (Table 1). During the lockdown period, namely, phase 1 from 9 March to 4 May 2020, the impact of the COVID-19 pandemic emergency on face-to-face research activities was high (70.7%; high top three boxes; Tables 2 and 3), with a complete (47.7%) or partial (36.1%) shutdown of the laboratories (Tables 2 and 3). Geographical distribution of work area was significantly associated with research activity interruption ($P < 0.01$; chi-square test), with a prevalence in North Italy (60%-75%; Figure 2 and Table 3). This result could be interpreted in light of a higher number of COVID-19 infections in Northern Italy as well as of more severe restrictions to both access to research centers and individual mobility.

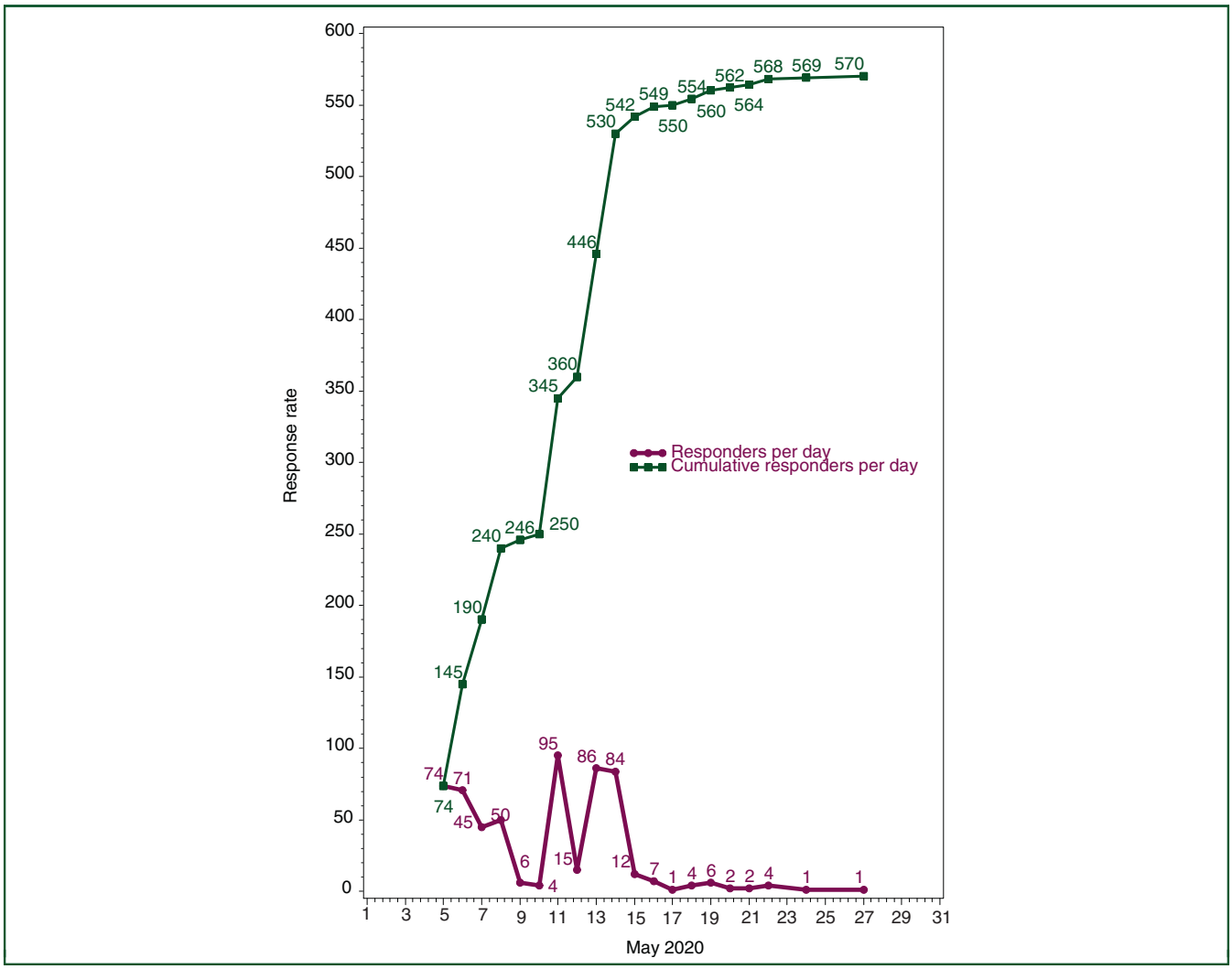

Figure 1. Survey response rate between 5 and 27 May.
Dots represent the number of responders per day. Squares represent the cumulative number of responders per day.

The use of smart-working modality was the choice to continue research activities (85.3%; neutral and high top three boxes; Figures 2 and 3 and Tables 2 and 3). This helped maintain regular communication among laboratory members (97.2% of agreement, Table 2) and maintaining research collaboration with other research facilities (52.6% of agreement; Table 2). Remarkably, survey respondents positively evaluated smart-working modality used in combination with face-to-face meetings in a future post-pandemic situation (Supplementary Table S2, available at https://doi.org/10.1016/j.esmoop.2021.100165). On the other hand, the COVID-19 emergency had a negative impact on the interaction between researchers and clinicians as expected, with 69.1% of activities ceased in phase 1 (Table 2).

Importantly, a sizable fraction of researchers was involved in COVID-19 research activities/diagnostics (31.9%; Figure 2 and Table 2) with, as expected, a high percentage of group leaders/professors/directors (41.9%, $P = 0.0031$; Figure 3 and Table 3) contributing to drafting COVID-19 research protocols and reorganization of research infrastructures. Lastly, salary remains overall unchanged (94.6% of agreement; Figure 2 and Tables 2 and 3).

In the post-lockdown period, i.e. phase 2, research activities were resumed in most of the respondents' institutions (80.4%; Figure 2 and Tables 3 and 4) though with some restrictions for new internal guidelines (77.2%; Table 4) to primarily ensure safety in the workplace and productivity. Workplace space reorganization and work shift modification happened quite frequently in 60.5% and 82.5% of instances (Table 4). Furthermore, COVID-19 testing was offered to research personnel in ~50% of research institutions (Table 4). Group leaders, professors and directors of research departments/institutes were also frequently involved in drafting internal guidelines for resuming research activities ($P < 0.0001$; Figures 2 and 3 and Tables 3 and 4).

Finally, we developed a 'lockdown score' (see methods) to assess the overall impact of the COVID-19 emergency on research during phase 1, considering the geographical distribution of research centers as well as the career level of interviewed researchers. Cancer research in Southern Italy

Table 1. Characteristics of responders; *N* = 570

	N	%
Gender		
Male	164	28.8
Female	390	68.4
NA	16	2.8
Age (years)		
20-25	8	1.4
26-30	76	13.3
31-35	90	15.8
36-40	89	15.6
41-50	114	20.0
>50	185	32.5
NA	8	1.4
Educational level		
PhD	363	63.7
PhD Fellow	49	8.6
No PhD	142	24.9
NA	16	2.8
Main country of work		
Italy	562	98.6
Not Italy	4	0.7
NA	4	0.7
Italian geographical area of work		
Northern Italy	333	58.4
Central Italy	108	18.9
Southern Italy	118	20.7
NA	11	1.9
Role		
Director/Group leader/Professor	215	37.7
Junior group leader	15	2.6
Researcher	190	33.3
Student	58	10.2
Technician/Administrative/Consultant	41	7.2
NA	51	8.9
Time spent on computer activities		
Low	12	2.1
Neutral	327	57.4
High	229	40.2
NA	2	0.4
Research fields (multiple options)		
Basic research	301	39.3
Translational research	395	51.6
Preclinical/Clinical research	59	7.7
Public health	1	0.1
Bioinformatics	3	0.4
Epidemiology	2	0.3
Biomedical research	1	0.1
NA	3	0.4
Research institute		
University	195	34.2
Cancer center	267	46.8
University and cancer center	27	4.7
Other	77	13.5
NA	4	0.7

Percentages do not add up to 100% due to rounding.
NA, not applicable.

seemed to be slightly less impacted by COVID-19 ($P = 0.0566$; Figure 2 and Supplementary Table S3, available at https://doi.org/10.1016/j.esmoop.2021.100165), while the impact on 'junior group leaders' appeared to be significantly high ($P = 0.0419$; Figure 3 and Supplementary Table S3, available at https://doi.org/10.1016/j.esmoop.2021.100165).

DISCUSSION

This survey, for the first time, provides a quantitative estimation of the impact of COVID-19 on cancer research in Italy during and immediately after the lockdown in 2020. The results of this survey are very impressive as they clearly demonstrate that the emergency linked to COVID-19 has severely interrupted the activities of numerous laboratories engaged in the fight against cancer for many months. Although this survey refers to the first wave of the pandemic, its results are very current given the persistence of the emergency and the slowness of the vaccination campaign in many countries.

The impact on research activities was most evident in the Northern Italian regions, but this should not be surprising given the greater spread of the epidemic in this part of the country in the first quarter of 2020. The consequences of this limitation are difficult to estimate, but we can safely say that the reduction in the activities of laboratories involved in cancer research will result in a delay in those fundamental discoveries for developing new technologies to fight cancer. In 2020, precision oncology reached several important milestones. A number of highly active new targeted therapies become available for diseases that are extremely difficult to treat.[13] The pandemic likely jeopardized the development of new drugs as well as the identification and validation of innovative biomarkers for diagnosis anticipation and prognosis prediction. This will negatively impact cancer patients' prognosis in the short term.

Importantly, our survey also revealed that the response to the pandemic was fragmented as in many cases institutions adopted different strategies often aimed at limiting possible infections without a clearly defined contingency plan. It is worth noting that such a disorganized response to the emergency was expected because our country, as likewise many others, was not at all prepared for this challenge, as evidenced by the high number of deaths that we continue to record. During the first phase of the pandemic, Italian health care workers did not have access to adequate personal protective equipment (PPE), such as face masks, that was difficult to find. Therefore, in order to avoid massive infection of health care workers, clinical center directors decided to shut down research laboratories rather than trying to develop contingency plans and protocols to allow them to work safely. This evidence is also confirmed by the fact that some research laboratories in Northern Italy had not resumed activities even after the lockdown. Even more surprisingly, no specific measures, such as swabbing research workers, were adopted when the laboratories reopened in some centers, thus underlying the absence in many instances of COVID-19 work safety protocols for resuming research activities.

The COVID-19 lockdown has affected all research laboratories, but the observation that junior group leaders have been affected by this difficult period more than others highlights how this situation of uncertainty can negatively impact particularly younger researchers at the beginning of their academic career.

A limitation of this study was our inability to assess the response rate of the survey since the invitation was intentionally left open to all researchers and not limited to members of the Italian Cancer Society. However, we think

Table 2. Research activities during lockdown (phase 1); $N = 570$

	N(%)			
	Low Bottom 3-boxes	Neutral	High Top 3-boxes	NA
Impact on research activities	37 (6.5)	210 (36.8)	323 (56.7)	0
Impact on face-to-face research activities	44 (7.7)	110 (19.3)	403 (70.7)	13 (2.3)
Use of smart working	82 (14.4)	171 (30.0)	315 (55.3)	2 (0.4)
	No	**Partially**	**Yes**	**NA**
Institute research activities shutdown	90 (15.8)	206 (36.1)	272 (47.7)	2 (0.4)
Research group internal communication ceased (no mail/no virtual meeting/no phone call)	554 (97.2)	—	13 (2.3)	3 (0.5)
Collaboration with other facilities ceased	300 (52.6)	—	78 (13.7)	192 (33.7)[a]
Collaboration with clinicians ceased	171 (30.0)	—	394 (69.1)	5 (0.9)
Involvement in COVID-19 research protocols	386 (67.7)	—	182 (31.9)	2 (0.4)
Involvement in COVID-19 research activities/ diagnosis	403 (70.7)	—	165 (28.9)	2 (0.4)
	Increased	**Unchanged**	**Decreased**	**NA**
Number of worked hours per week	153 (26.8)	205 (36.0)	207 (36.3)	5 (0.9)
Salary variation	9 (1.6)	539 (94.6)	12 (2.1)	10 (1.8)

Percentages do not add up to 100% due to rounding.
NA, not applicable.
[a] Including 189 responders not using facilities for their research.

Table 3. Distribution of research activities during lockdown phase 1 and phase 2, according to Italian geographical area of work and role of responders; distributions for significant association (chi-square test) are reported

	Italian geographical area of work			**Role**				
	Northern $n = 333$	Central $n = 108$	Southern $n = 118$	Director/GL/ Professor $n = 215$	JGL $n = 15$	Researcher $n = 190$	Student $n = 58$	TAC $n = 41$
Lockdown phase								
Institute research activities shutdown	$P = 0.0003$							
Low	6.9	4.6	6.8					
Neutral	33.3	30.6	54.2					
High	59.8	64.8	39.0					
Impact on face-to-face research activities	$P = 0.0029$			$P = 0.0434$				
Low	9.2	2.8	8.9	7.1	0.0	5.5	14.3	10.0
Neutral	15.6	23.4	30.1	24.5	13.3	20.8	5.4	20.0
High	75.2	73.8	61.1	68.4	86.7	73.8	80.4	70.0
Use of smart working	$P = 0.0121$			$P < 0.0001$				
Low	13.3	7.4	22.0	16.4	13.3	6.3	15.8	43.9
Neutral	27.8	36.1	30.5	32.2	26.7	30.0	26.3	19.5
High	58.9	56.5	47.5	51.4	60.0	63.7	57.9	36.6
Involvement in COVID-19 research protocols	$P = 0.0284$			$P = 0.0031$				
No	71.2	68.5	57.8	58.1	86.7	71.4	79.3	68.3
Yes	28.8	31.5	42.2	41.9	13.3	28.6	20.7	31.7
Involvement in COVID-19 research activities/diagnosis				$P < 0.0001$				
No				56.3	80.0	81.6	89.7	58.5
Yes				43.7	20.0	18.4	10.3	41.5
Number of worked hours per week				$P < 0.0001$				
Increased				35.1	33.3	23.3	15.5	29.0
Unchanged				36.5	33.3	40.2	20.7	47.4
Decreased				28.5	33.3	36.5	63.8	23.7
Salary variation	$P = 0.0053$							
Increased	1.2	0.0	4.4					
Unchanged	97.3	94.4	94.8					
Decreased	1.5	5.6	0.9					
Phase2								
Institute research activities resumed	$P = 0.0457$							
No	18.3	14.8	27.1					
Yes	81.7	85.2	72.9					
Involvement in the drafting of internal guidelines for research activities during phase 2	$P = 0.0141$			$P < 0.0001$				
No	82.8	93.4	89.0	75.7	93.3	91.1	91.1	92.7
Yes	17.2	6.6	11.0	24.3	6.7	9.0	8.9	7.3

GL, Group Leader; JGL, Junior Group Leader; TAC, Technician/Administrative/Consultant.

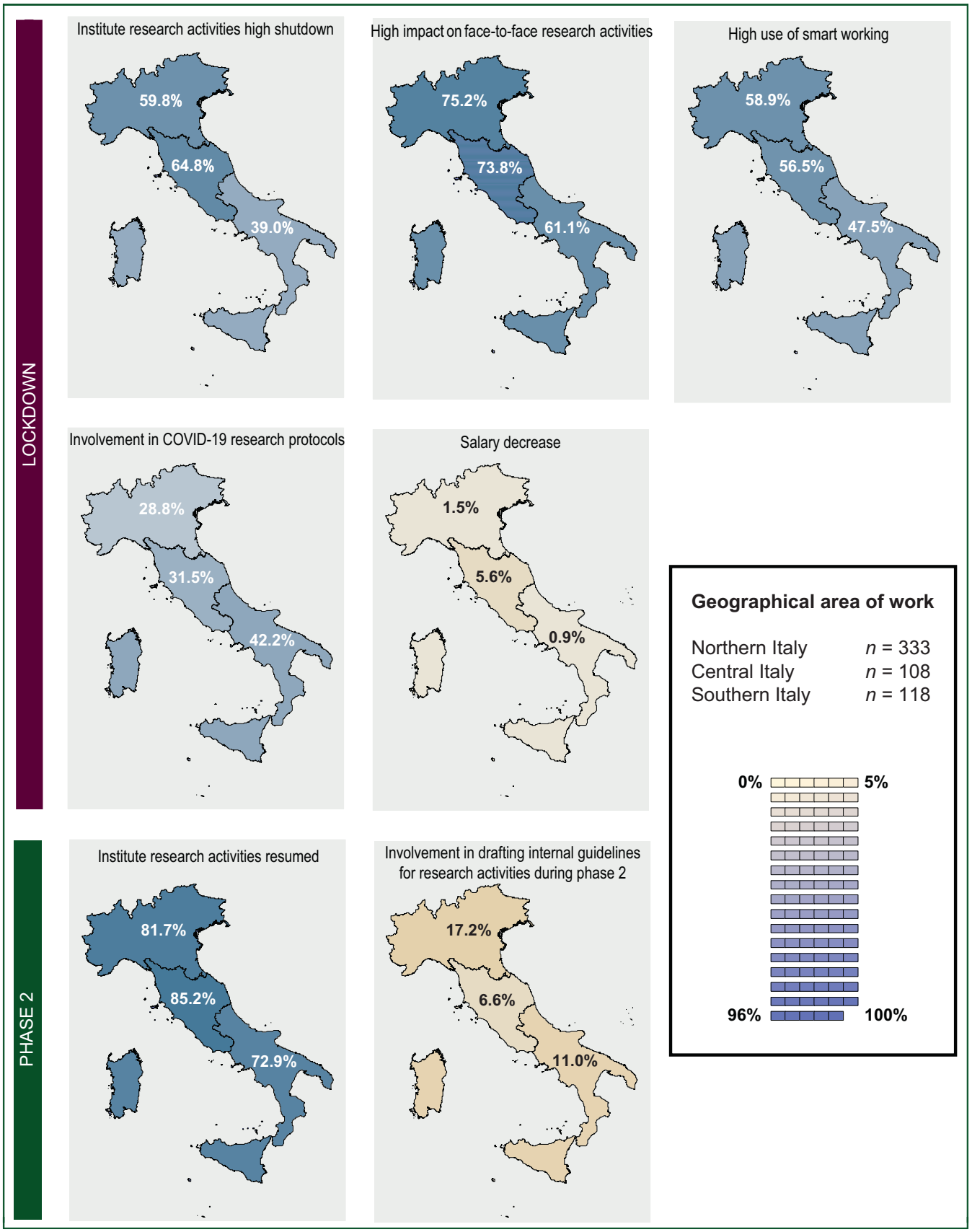

Figure 2. Distribution of research activities during lockdown phase 1 and phase 2, according to Italian geographical area of work.
Absolute numbers of survey participants distributed in the geographical areas are also shown.

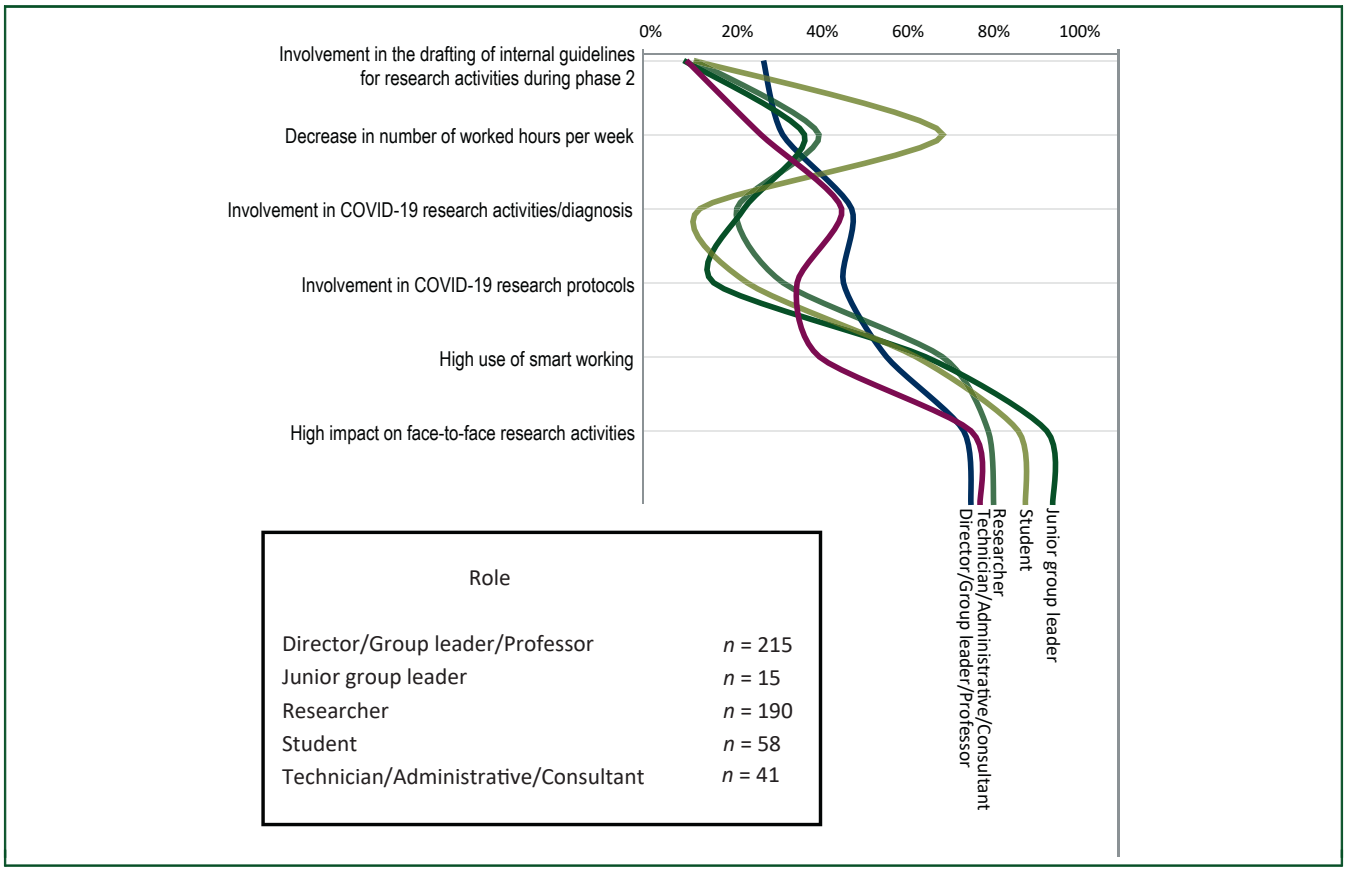

Figure 3. Distribution of research activities during lockdown phase 1 and phase 2 according to job role.
Absolute numbers of survey participants stratified by role are also shown.

this makes results more generalizable and representative of COVID-19's detrimental impact on Italian cancer research activities.

The results of this survey are in agreement with previous studies that have described the significant impact of the pandemic on clinical practice and clinical research activities in oncology in Italy. Clinical oncology departments had to adapt their organization and treatment protocols taking into account the risk/benefit ratio for each individual patient.[14-17] These precautions were also necessary because patients with cancer who develop COVID-19 have a high probability of mortality.[18] The impact on clinical research activities was also significant, with reductions reported by 80% of clinicians.[16] Finally, a survey among 53 thoracic pathology centers from 18 European countries reported that clinical and molecular pathology activities decreased dramatically by 31% and 26%, respectively.[19]

CONCLUSION

The pandemic has now lasted for more than a year and is continuing to negatively impact cancer patient management and both experimental and clinical cancer research. Activities resumed in almost all the institutions, but the problems related to the reorganization of spaces, the preparation of risk plans and the monitoring of epidemic

Table 4. Research activities during phase 2 ($N = 570$)

	N (%)			
	No	Partially	Yes	NA
Institute research activities resumed	111 (19.5)	—	458 (80.4)	1 (0.2)
Internal guidelines for research activities during phase 2 provided	103 (18.1)	—	440 (77.2)	27 (4.7)
Involvement in the drafting of internal guidelines for research activities during phase 2	485 (85.1)	—	81 (14.2)	4 (0.7)
Workplace space reorganization during phase 2	149 (26.1)	—	345 (60.5)	76 (13.3)
Work shifts modified during phase 2	22 (3.9)	3 (0.5)	470 (82.5)	75 (13.2)
PPE provided by research institute	33 (5.8)	4 (0.7)	486 (85.3)	47 (8.2)
COVID-19 testing during phase 2	163 (28.6)	8 (1.4)	277 (48.6)	122 (21.4)
Collaboration with facilities	13 (2.3)	154 (27.0)	244 (42.8)	159 (27.9)

Percentages do not add up to 100% due to rounding.
PPE, personal protective equipment.

spread in the research community were only partially addressed. This unprecedented situation has, however, forced us to think of and develop new ways of working and communicating, to alternate work in the laboratory with smart working and perhaps to plan laboratory activities better. However, it is undeniable that the progress of research is based on idea exchange among collaborators, among researchers of different backgrounds and on constant mentoring between lab heads and trainees. The limitation of these activities will certainly affect above all the training and personal growth of the youngest researchers.

Among the effects of the pandemic, there is a fear of a considerable decrease in funding for research in general and for cancer research in particular. Yet, if there is one thing we should have learned from the pandemic, it is precisely the relevance of research: research was able to provide the first answers and possible ways out of this situation, with the contribution of many cancer researchers that sacrificed their research programs to help overcome the pandemic by offering their knowledge and technologies. Finally, a more adequate organization of research centers will be urgently required and necessary to assure the continuity of laboratory activities in a safe environment.

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DISCLOSURE

The authors have declared no conflicts of interest.

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