

Personal protective equipment use by healthcare workers in intensive care unit during the early phase of COVID-19 pandemic in Italy: a secondary analysis of the PPE-SAFE survey

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Abstract

Background: Italy was the first Western country to be heavily affected by COVID-19. Healthcare workers (HCWs) were exposed to a high risk of occupational infection, partially due to insufficient personal protective equipment (PPE) supplies. This study aimed to describe the practices, availability, training, confidence in PPE use and the adverse effects due to extended PPE use, as reported by HCWs in Italy. We also aimed to provide a comparison between Italian data and those from other countries.

Methods: This study was a secondary analysis of a previously published international study, the PPE-SAFE Survey, conducted in April 2020. Data were analysed from the original study database.

Results: We analysed the responses from 380 healthcare workers based in Italy, out of the 2711 respondents to the international survey. Among the Italian respondents, FFP2 and FFP3 respirators or equivalent were the most used masks for routine tasks [respectively 188/380, 50%; and 163/380, 43%]. The median time of wearing PPE without taking a break was 5 h [interquartile range (IQR) 4–6], with statistically significant difference from other countries [median 4 h (IQR 2–5) $p < 0.0001$]. In Italy, 249 out of 380 (65%) HCWs had never performed a formal fit test for a N95 mask or equivalent and 91/380 (24%) never had a partner for donning and doffing procedures. Most of the respondents (299/380, 79%) had received formal training in PPE use at any time.

Conclusion: Most of the surveyed Italian HCWs reported working at above usual capacity, long shifts with PPE without breaks and routine use in intensive care unit of aerosol protection (e.g. FFP2/FFP3), hazmat suits and face shields/visors. The correct adherence to safety procedures (e.g. donning/doffing in pairs, performing fit test) has substantial scope for improvement in the future.

Keywords: COVID-19, Italy, personal protective equipment, PPE-SAFE, survey

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Introduction

The coronavirus disease 2019 (COVID-19) pandemic, caused by the SARS-CoV-2 virus, has become a global public health emergency that has

caused more than 60 million confirmed cases and more than one million deaths.¹ In some areas, a large number of deaths has been recorded among healthcare workers (HCWs).² HCWs have been

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exposed to a high risk of occupational infection, heightened by lack of personal protective equipment (PPE) supplies. Evidence and recommendations regarding the use of PPE as a preventive measure for COVID-19 have been controversial.³ However, there is broad agreement that PPE provides important protection for HCWs when caring for patients with COVID-19.⁴

The PPE-SAFE survey is an international survey conducted in April 2020.⁵ The study evaluated responses from 2711 HCWs involved in the management of patients with COVID-19, in the setting of critical care. The survey provided important information regarding PPE supplies, the adequacy of HCWs' training in PPE use and the occurrence of adverse events related to their prolonged use.⁵

Italy was the first Western country to be heavily affected by COVID-19, just after the emergence of the disease in China.⁶ The unpreparedness to the pandemic exerted various effects in the country, especially in terms of lack of resources and supplies needed for patients' care and HCWs' safety.⁷ Thus, the primary aim was to describe the practices, availability, training, confidence in PPE use and adverse effects due to extended PPE use, as reported by HCWs in Italy. Moreover, we also aimed to provide a comparison between Italian data and those from other countries participating in the PPE-SAFE survey.

Methods

This study was conducted as a secondary analysis of the PPE-SAFE,⁵ an international survey that was conducted in April 2020 among HCWs involved in the management of patients with COVID-19 in the setting of critical care worldwide. It was approved by the Royal Brisbane and Women's Hospital Human Research Ethics Committee (LNR/2020/QRBW/63041), Brisbane, Australia.

The complete description of the survey instrument and administration methods is available from the report of the primary analysis.⁵

The survey was translated using a language localization tool within the SurveyMonkey platform. Respondents were presented with the survey in their language, based on the language of their web browser. There was at the top of the survey webpage a dropdown menu with available languages

from where the respondents could change the language should they want to. The survey was self-administered anonymously by the HCWs who were directly involved in the management of patients with COVID-19 in a critical care setting. The first binary question of the survey aimed to ask the respondent if he/she was caring for COVID-19 patients in the intensive care unit ICU setting. If yes, the survey was continued and the response validated. In the opposite case the survey was terminated, and the response categorized as invalid. Validity of responses was ensured at both the steps of data collection and of data management. All data identifiers were checked for duplicates, but there was no possible control to block a respondent from coming back to the survey and responding again at a later date.

The survey included questions regarding HCWs' basic demographic characteristics and about their institutions, followed by questions regarding their routine care, the availability of PPE, the training received and the perceived level of confidence about their knowledge on how to safely use the recommended PPE. The type of adverse effects experienced during their shifts, if any, was also asked of the respondents. The respondents could select Italian among the language options. The answers could be given as multiple choice; a free text was instead allowed for questions related to durations (e.g. years of experience, hours of PPE duration). The respondents had the possibility to select more than one option for the questions directly regarding the type of PPE used. The full text questionnaire is available in English and Italian versions as Supplemental Material 1 and Supplemental Material 2 online.

The questionnaire was publicized using the mailing list of the members of the European Society of Intensive Care Medicine and further shared *via* various other mailing lists and on social media by the members and other national societies who gave their endorsement to the project and was administered through a web-based platform (please see Acknowledgments below). Respondents were asked to forward the survey to other ICU-HCWs within their networks. In Italy, the survey was endorsed by the Italian Society of Anaesthesiology (Società Italiana di Anestesia Analgesia Rianimazione e Terapia Intensiva – SIAARTI), the Italian Society of Critical Care Nurses (Associazione Nazionale Infermieri di Area Critica – ANIARTI) and the Italian Society

of Anti infective Therapy (Società Italiana di Terapia Antinfettiva – SITA), who circulated the invitation among their members *via* email and social media. The survey responses were recorded based on convenience sampling.

Data management and analysis

For the purpose of this study, we analysed the results from Italian dataset and then we compared these data with those from other countries, once extracted from the database of PPE-SAFE survey study as separated groups of data. No record was excluded because of missing data to one or more questions of the survey. For questions about the type of PPE in use, in the case of multiple selection, we considered only the highest level of indicated protection for reporting and calculations. The data were then exported and analysed using Prism 7 (GraphPad software; San Diego, CA, USA) and Microsoft Excel (version 2013; Microsoft Corporation, Redmond, CA, USA). The data were mostly presented as descriptive statistics, including number and percentages. Medians and interquartile ranges (IQRs) were adequately used in the case of continuous variables. The chi-square test for independence was used to compare two or more categorical variables and the Mann–Whitney *U* test was used to compare continuous variables, as appropriate. *p* values < 0.05 were considered statistically significant.

Results

Data from Italy

There were 380 respondents from Italy. The main characteristics of the respondents and a comparison with those from other countries are shown in Table 1. Most were doctors (194/380, 51%), of whom 140/380 (37%) reported a senior level of experience; 169/380 (44%) were nurses. The median age was 40 years (IQR 32–48) and 196/380 (51%) were female. Most (326/380, 86%) worked in a dedicated or repurposed ICU, that is, admitting only patients with COVID-19 at the time of completing the survey. A total of 270 (71%) usually worked in intensive care. The median time of wearing PPE without taking a break was 5 h (IQR 4–6).

Information about routine use, shortages and reuse of disposable PPE are shown in Table 2. The percentages of routinely used PPE in Italy are presented as a chart in Figure 1. Approximately

half of the respondents used FFP2 and FFP3 respirators or equivalent for their routine tasks (respectively 188/380, 50%; and 163/380, 43%). Only 1% did not use aerosol protection for routine care. Re-use was very rarely reported, with 3/380 (1%) respondents reporting re-use of FFP2 respirators and 6/380 (2%) FFP3 respirators. Hazmat suits were the most used gowns in Italy (73%) and face shields were more frequently used than goggles (86% *versus* 14%) as eye protection.

The results regarding the duration of wearing PPE and related adverse effects are shown in Table 3. Heat, thirst and pressure areas were the most frequent adverse effects, occurring even for shift duration less than 3 h (respectively in 36%, 50% and 31% of the respondents).

Most respondents (299/380, 79%) had received formal training in PPE use at some time. Interestingly, only 82/380 (21%) of the Italian respondents declared to have received training at the time of employment. One hundred and eighty-two Italian respondents (48%), had received training just because of the COVID-19 pandemic, in the 2 months preceding the survey, 35/380 (9%) had received training at some other time but not in the precedent 2 months and 81/380 (21%) had not received training.

In Italy, 249 out of 380 (65%) HCWs reported never having formal fit testing for a N95 mask or equivalent and 91/380 (24%) never used a two-persons technique (i.e. the worker donning or doffing PPE plus a supervisor responsible for the correct execution of the procedures) for donning and doffing PPE. Nevertheless, around 73% (277/380) of the Italian respondents felt somewhat confident, confident or very confident about the safe use of the recommended PPE.

Data from other countries

This analysis considered the responses of the 2331 HCWs working in 89 countries and five continents, other than Italy. The characteristics of the respondents, the information about routine use, shortages and reuse of disposable PPE with full details are shown in Tables 1 and 2.

Some differences were noted between the two groups (Italy *versus* other countries). The proportion of Italian HCWs working in COVID-19 dedicated or re-purposed ICU, in comparison with

Table 1. Comparison of demographic and workplace attributes among respondents working in Italy and other countries.

	PPE-SAFE Italy n = 380	PPE-SAFE other than Italy n = 2331	
Age, median in years (IQR)	40 (32–48)	41 (35–49)	$p = 0.0219$
Female, <i>n</i> (%)	196 (51)	1058 (45)	$p = 0.02878$
ICU experience, median in years (IQR)	8 (2–16)	10 (4–18)	$p < 0.001$
COVID-19 dedicated or re-purposed ICU, <i>n</i> (%)	326 (86)	1239 (53)	$p < 0.001$
PPE shift duration without breaks, median in hours (IQR)	5 (4–6)*	4 (2–5)**	$p < 0.001$
Position, <i>n</i> (%)			$p < 0.001$
Registered nurse	169 (44)	547 (23)	
Doctor	194 (51)	1601 (69)	
Senior level	140 (37)	1231 (53)	
In training – specialist/senior training levels	40 (10)	298 (13)	
In training – initial levels, intern/resident	14 (4)	72 (3)	
Allied HCW	17 (5)	183 (8)	
Specialty, <i>n</i> (%)			$p < 0.001$
Emergency	21 (5)	51 (2)	
Intensive care	270 (71)	1749 (75)	
Anaesthesia	48 (13)	382 (16)	
Hospital ward – surgical	12 (3)	10 (~0)	
Hospital ward – medical	6 (2)	77 (3)	
Other	23 (6)	62 (3)	
Type of hospital, <i>n</i> (%)			$p < 0.001$
Remote/regional	19 (5)	167 (7)	
Private	16 (4)	221 (10)	
Tertiary	214 (56)	1334 (57)	
Community/urban	131 (34)	609 (26)	
Running capacity, <i>n</i> (%)			$p < 0.001$
Well above	157 (41)	533 (23)	
Above	121 (32)	465 (20)	
Below	31 (8)	632 (27)	
Usual	65 (17)	634 (27)	
Unsure	6 (2)	51 (2)	
Missing data	0	16 (1)	
Data are reported as raw (<i>n</i>), percentages and median (interquartile range), as appropriate.			
*Data missing in 23 responses to the survey.			
**Data missing in 212 responses to the survey.			
HCW, healthcare worker; ICU, intensive care unit; IQR interquartile range; PPE, personal protective equipment.			

Table 2. Shortages and reuse of single use PPE.

	Italian ICU			PPE-SAFE survey – other than Italy		
	Used for routine care – allowed to select more than one	Reported as missing* – allowed to select more than one	Washed or reused** – allowed to select more than one	Used for routine care – allowed to select more than one	Reported as missing – allowed to select more than one	Washed or reused – allowed to select more than one
Mask – <i>n</i> = 379 [§]				Mask – <i>n</i> = 2300 [§]		
Surgical mask, <i>n</i> (%)	4 (1)	0 (0)	0 (0)	285 (12)	11 (~0)	13 (1)
N95/FFP2 respirator, <i>n</i> (%)	188 (50)	3 (1)	3 (1)	1369 (59)	124 (5)	264 (11)
FFP3 respirator, <i>n</i> (%)	163 (43)	14 (4)	6 (2)	486 (21)	64 (3)	101 (4)
PAPR, <i>n</i> (%)	24 (6)	1 (~0)	N/A	160 (7)	15 (1)	N/A
Gown – <i>n</i> = 360 [§]				Gown – <i>n</i> = 2072 [§]		
Sleeveless apron, <i>n</i> (%)	1 (~1)	0 (0)	0 (0)	192 (9)	3 (~0)	5 (~0)
Full sleeve waterproof gown, <i>n</i> (%)	95 (26)	2 (~0)	11 (3)	1528 (74)	113 (5)	172 (8)
Hazmat suits, <i>n</i> (%)	264 (73)	19 (5)	3 (1)	352 (17)	54 (3)	63 (3)
Eye protection – <i>n</i> = 372 [§]				Eye protection – <i>n</i> = 2147 [§]		
Goggles, <i>n</i> (%)	52 (14)	0 (0)	8 (2)	893 (41)	28 (1)	318 (15)
Face shield or visor, <i>n</i> (%)	321 (86)	10 (3)	208 (55)	1253 (58)	121 (6)	612 (29)
Head protection – <i>n</i> = 348 [§]				Head protection – <i>n</i> = 1727 [§]		
Hair cover, <i>n</i> (%)	221 (63)	3 (1)	2 (~0)	1415 (82)	40 (2)	39 (2)
Balaclava, <i>n</i> (%)	95 (27)	6 (2)	0 (0)	222 (13)	20 (1)	8 (~0)
Impervious hood, <i>n</i> (%)	33 (9)	0 (0)	0 (0)	89 (5)	5 (~0)	11 (1)

Data are reported as raw (*n*) and as percentages. *N* is different from 380 when data were missing (i.e. respondents who did not select any option for the considered question). PAPR are shown as not applicable (N/A) for reuse as they are reusable devices.

*Reported as missing shows the number of PPE that would normally be used but was declared as not available at the time of the survey.

**Washed or reused shows single use PPE washed or reused due to stock or availability issues at the time of the survey.

§Number of valid responses (i.e. at least one of the options selected) for PPE used for routine care.

ICU, intensive care unit; PAPR, powered air purifying respirators; PPE, personal protective equipment.

those from other countries, was significantly higher (86% *versus* 53%, $p < 0.001$). With regard to running capacity at time of survey completion, 41% of the Italian respondents and 23% from other countries declared a capacity “well above” usual, plus 32% of the Italian respondents and 20% from other countries declaring a capacity “above” usual. A chi-square test of independence was performed, confirming the statistically significant heterogeneity of the distribution of the HCWs’ role [$\chi (2) = 74.98$; $p < 0.001$], the usual specialty [$\chi (5) = 62.46$; $p < 0.001$], the declared

type of hospital [$\chi (3) = 21$; $p < 0.001$] and the running capacity of the centres [$\chi (5) = 129.2$; $p < 0.001$] between the two groups (Italy *versus* other countries).

Most of the respondents reported using FFP2 and FFP3 or equivalent respirators for routine care (respectively 50% in Italy *versus* 59% in other countries for FFP2 and 43% in Italy *versus* 21% in other countries for FFP3). A level higher than or equal to FFP2 was then used by the 99% of the respondents from Italy and by the 87% of the

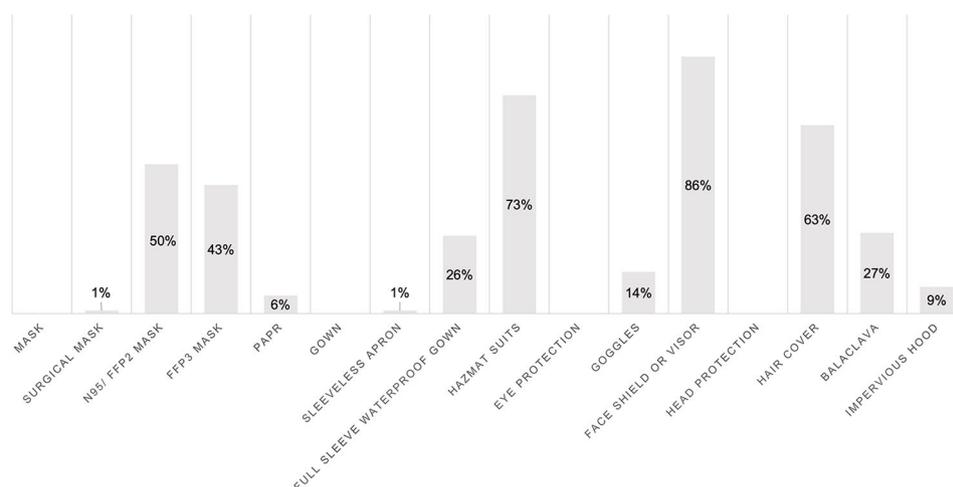


Figure 1. Personal protective equipment used for routine care in Italy. The chart shows the frequencies distribution of routinely used personal protective equipment in Italy. PAPR, powered air purifying respirators; PPE, personal protective equipment.

Table 3. Adverse effects according to PPE shift duration among Italian respondents.

Adverse effects	PPE shift duration			
	<3 h n = 26	3–5.9 h n = 188	6–8.9 h n = 134	≥9 h n = 9
Extreme exhaustion, n (%)	4 (15)	30 (16)	29 (21)	0 (0)
Inability to use the bathroom, n (%)	4 (15)	46 (24)	48 (35)	7 (78)
Headaches, n (%)	3 (11)	79 (42)	52 (38)	7 (78)
Thirst, n (%)	9 (36)	90 (48)	63 (47)	6 (67)
Heat, n (%)	13 (50)	100 (53)	62 (46)	5 (55)
Pressure areas, n (%)	8 (31)	101 (54)	80 (59)	3 (33)

Data are reported as raw (n) and percentages.
PPE, personal protective equipment.

respondents from other countries. The median PPE shift duration was 5 h (IQR 4–6) in Italy, slightly but significantly higher than in the other countries group, with a median duration of 4 h.^{2–5} Full sleeve waterproof gown was the most used gown (74%) in countries other than Italy. A χ^2 test of independence was also performed on data about the type of routinely used PPE, showing a statistically significant heterogeneity of the distribution of masks [$\chi^2(3) = 108.7$; $p < 0.001$], gowns [$\chi^2(2) = 518.7$; $p < 0.001$], eye protections [$\chi^2(1) = 98.16$; $p < 0.001$] and head protections [$\chi^2(2) = 36.1$; $p < 0.001$] among the two groups (Italy *versus* other countries). Comparisons were

not performed for missing and re-used PPE because of small numbers.

Respondents from other countries reported never performing a formal fit test in 1022/2331 (44%) of the cases, a statistically significant difference from the Italian group [249/380, 65%; $\chi^2(1) = 60.82$; $p < 0.01$]. A total of 548/2331 (23%) of the respondents had never performed donning and doffing of PPE in a two persons team. Eighty-three per cent (1946/2331) had received formal training in PPE use at any time, a statistically significant difference from the Italian group [299/380, 79%; $\chi^2(1) = 4.95$, $p = 0.026$].

Discussion

This study was the first to report data on the use of PPE in the setting of ICUs during the first COVID-19 outbreak in Italy. It reports data on availability, usage, training, and on adverse effects related to PPE. Additionally, it provides a comparison with countries of the PPE-SAFE survey.⁵

The most relevant findings were the running capacity of the centres and other organizational issues, possibly reflecting the changes put in place by the Italian healthcare system to face the pandemic in the early phase as the first Western country to be heavily affected by COVID-19.⁸ Our data have to be put in context with the earliest phase of the pandemic, during which Italy was extensively involved. The high proportion of Italian respondents (14%) to the main survey probably reflected the greater healthcare system burden registered in the country at that time.

The high frequency of dedicated or repurposed ICUs (86%) and above usual running capacity confirm that Italian ICUs were unprepared to provide care to such a high number of patients with COVID-19.^{9,10} At the time of survey dissemination, Italy counted approximately 105,700 confirmed cases and 12,430 deaths, being first highest for number of cases in Europe and third highest worldwide, just behind China and the United States of America.¹¹ Despite this, PPE re-use was not a common practice in Italy, probably due to the uncertainty and controversial data about its safety.^{12,13} We describe that extended use of PPE was common, with a median PPE shift duration of 5 h (IQR 4–6), higher than in the other countries.^{5,14} The Chinese outbreak caused a lack of supplies in non-producer countries, like Italy, and this could explain the need for an extended use of PPE, in order to prevent stock failures. Avoiding shortages of supplies is pivotal, especially during public health emergencies, when risky phenomena, such as counterfeiting or use of unregistered PPE, may rapidly spread and further reduce safety.¹⁵ The data may also indicate a discrete adherence to recommendations with a preference for prolonged or extended use rather than re-use or reprocessing procedures.^{16–18} In the setting of an ICU, different routine care tasks (e.g. non-invasively ventilated patients, high flow oxygen therapy, orotracheal intubation) may determine aerosolization,¹⁹ thus reasonably explaining the high percentage (99%) of the surveyed HCWs

using a level of protection equal to FFP2 or higher for routine care.

The most evident difference between the two cohorts in terms of type of PPE used was the significant difference in the frequency of use between hazmat suits in Italy compared with other countries; reasons for this difference may be related to different availability, or lack of evidence regarding best practice for infection prevention and control measures at the time. In Italy, 79% of respondents received formal training but the recommended performance of donning and doffing procedures²⁰ was infrequent, with 24% never having performed the procedures with a partner supervisor and 65% never having performed a fit test. Nevertheless, the survey seems to indicate a gap between the reported practice and how the involved workers perceived it. In total, the 73% (277/380) of Italian respondents and 74% (1724/2331) of those from other countries felt somewhat confident, confident or very confident about their safe use of PPE. The frequency of the reported adverse events seems to suggest the need for monitoring or self-monitoring tools to prevent their occurrence and to rapidly adopt countermeasures, thus minimizing the potential occurrence of severe complications.

In general, the timing of the survey in relation to peak Italian cases and to the early uncertainty in how to handle COVID-19, together with early burden of demand for PPE, may have led to the differences between the Italian cohort and the other countries.

A recent cross-sectional study was conducted by Savoia *et al.*⁷ in the same period (April 2020), and evaluated the use of PPE through the self-administration of an online survey to Italian physicians involved in the care of patients with COVID-19. The study reported only 13% of respondents declaring to have access to PPE every time they need it, a result in contrast with our study. The differences between the two cohorts could have arisen because this study included physicians from various settings, including territorial medicine and independent contractors, while our study specifically focused on ICUs. It is possible that in the context of global shortages, ICUs were prioritized for delivery of supplies compared with community (or non-hospital) healthcare settings. No information was provided about formal training, but the

authors reported on the information received on the use of PPE, mostly reported as being either clear (47%) or complete (54%) by the respondents.

The use of PPE was regulated by Italian Health Institute, whose document of recommendations suggested rational use of PPE. It was suggested to provide an increasing level of protection along with an increasing risk (i.e. FFP3 for aerosol generating procedures or FFP2 if highest level unavailable, FFP2 to care for patients with non-invasive ventilation or continuous positive airway pressure and surgical masks for the other conditions). Gloves, disposable gowns and goggles or face shields were suggested for all the levels of care. The document also highlighted the need for specific training.²¹

Strengths and limitations

Our analysis has limitations, although most of them are related to the cross-sectional nature of this research that limits the generalizability of our results.^{4,12} First, due to a non-systematic dissemination of the survey, it was not possible to calculate a denominator to evaluate the response rate. Second, unless a screening question was included at the beginning of the survey to check the professional profile of the respondent, we cannot exclude that the survey might have reached people out of the addressed professional categories through social media. We did not perform corrections for multiple comparisons or any adjustment for confounding factors, so the results must be considered exploratory. In addition, even if the Italian cohort represented the main contributor to the main study,⁵ the sample size was small and, together with the voluntary inclusion of the participants and self-administration of the survey, may have biased the findings in both directions (e.g. dramatic lack of PPE or efficient organization and full availability of PPE). The relatively high proportion of Italian respondents in comparison with those from other countries respondents may suggest that Italian participants were over-represented in the survey. This higher participation by Italian HCWs may have caused selection bias. Although efforts were made to disseminate the survey widely, the peculiar clinical context may also have limited and biased the response to the survey, as most of the includable HCWs were involved in exhausting shifts, thus potentially lowering the response rate of those working in overwhelmed centres. If this occurred, the survey may have overestimated the proportion of HCWs with

appropriate self-reported PPE use. There was a one-week delay between the availability of the English version and other languages. This delay may also have slightly biased the selection of the respondents. Finally, the comparison between Italian data with those from other countries should be considered in light of the heterogenous dynamic of the pandemic in different countries.

Nevertheless, the study has the merit of presenting data on a high number of respondents working in ICUs in Italy, with a high rate of responses coming from COVID-19 dedicated ICUs. Thus, it provides a snapshot of a pivotal setting involved in the pandemic. Given that new respiratory pandemics may emerge in the future, our study results may provide insights for future COVID-19-related policies and infection prevention and control measures and trainings (e.g. broadly implementing fit testing) by policy-makers, infection prevention and control practitioners and other stakeholders. Of note, at the time of the diffusion of our survey (April 2020), around 71% of the HCWs resulting positive to SARS-COV-2 in Italy had contracted COVID-19 while serving in hospitals or in emergency care services.²² However, it should be noted that the current situation of PPE availability and infection control measures may be significantly different from that at the time of data collection.

Conclusions

This study provided valuable data on the availability, usage, training and adverse events related to the use of PPE during the early phase of the COVID-19 pandemic in Italy. The centres were described as mostly dedicated to the care of patients with COVID-19 and working at above usual capacity. Facing the pandemic at an early phase, Italian HCWs spent long shifts wearing PPE without a break. Most respondents reported routine use in ICUs of aerosol protection (FFP2/FFP3), hazmat suits and face shields/visors. The correct adherence to safety procedures (such as donning/doffing in pairs, performing fit test) have substantial scope for improvement in the future. Updated data on implementation of COVID-19-related policies and infection prevention and control measures and trainings are needed.

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Author contributions

MI made a substantial contribution to the concept, analysed the data, drafted the article and approved the final version to be published; MR made a substantial contribution for the interpretation of data, revised the article critically for important intellectual content and approved the final version to be published; DB, GC, PI, ADG, GG, AG, MB, AT made a substantial contribution to acquisition of the data, revised the article critically for important intellectual content and approved the final version to be published; AC conceived the content, analysed the data and made a substantial contribution for

the interpretation of data, revised the article critically for important intellectual content and approved the final version to be published.

Availability of data

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Conflict of interest statement

Outside the submitted work, MB has participated in advisory boards and/or received speaker honoraria from Achaogen, Angelini, Astellas, Bayer, Basilea, Biomerieux, Cidara, Gilead, Menarini, MSD, Nabriva, Paratek, Pfizer, Roche, Melinta, Shionogi, Tetrphase, VenatoRx and Vifor and has received study grants from Angelini, Basilea, Astellas, Shionogi, Cidara, Melinta, Gilead, Pfizer and MSD, AC has received honoraria for lectures from Thermofisher and Pfizer. All the other authors declare that there is no conflict of interest.

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Supplemental material

Supplemental material for this article is available online.

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