Vol. 37 N. 1 - JANUARY-FEBRUARY 2025

ANNALI DI IGIENE

Medicina Preventiva e di Comunità

Bimonthly scientific publication founded by A.Celli in 1889 as
ANNALI DELL'ISTITUTO DI IGIENE SPERIMENTALE DELLA UNIVERSITÀ DI ROMA

Editor-in-chief: Prof. G.M. Fara

since 1889

SOCIETÀ EDITRICE UNIVERSO
Via G.B. Morgagni 1 - 00161 Roma

ISSN (online) 3035-5559
ISSN (print) 1120-9135

VOL. 37 N. 1 - JANUARY-FEBRUARY 2025

ANNALI DI IGIENE

MEDICINA PREVENTIVA E DI COMUNITÀ

Bimonthly scientific publication founded by A. Celli in 1889 as “ANNALI DELL'ISTITUTO DI IGIENE SPERIMENTALE DELLA UNIVERSITÀ DI ROMA”, became “ANNALI DI IGIENE” with G. Sanarelli in 1914, “NUOVI ANNALI DI IGIENE E MICROBIOLOGIA” with V. Puntoni, A. Tizzano, V. Del Vecchio and S.U. D'Arca in 1941, and “ANNALI DI IGIENE, MEDICINA PREVENTIVA E DI COMUNITA'” with G.M. Fara in 1989

Management and Editorial Office
Dept. of Public Health and Infectious Diseases
Sapienza Università di Roma
Piazzale Aldo Moro, 5 - 00185 Roma
Tel. 0649914680 Fax 064454845
E-mail: rosella.delvecchioigiene@gmail.com

Publisher
Società Editrice Universo srl
Via G.B. Morgagni, 1 - 00161 Roma
Tel 0644231171 - 064402053/4 Fax 064402033
E-mail: annali@seu-roma.it

Contents

Ann Ig. 2025 Jan-Feb; 37(1): 1-13 doi: 10.7416/ai.2024.2641. Epub 2024 May 30.

The prevention of medication errors in the home care setting: a scoping review

Sara Dionisi[1], Noemi Giannetta[2], Gloria Liquori[3], Aurora De Leo[3,4], Nicolò Panattoni[4,5], Mariasole Caiafa[1], Marco Di Muzio[6], Emanuele Di Simone[4,6]

Keywords: Home care; Patient safety; Medication errors; Strategies; Scoping Review.
Parole chiave: Assistenza domiciliare; Sicurezza del paziente; Errori da terapia; Strategie di prevenzione.

Abstract

Background. *The changes in health, social and demographic needs impose new approaches to cures and care without giving up patients' safety. Although several studies analysed the patient safety approach and strategies, the literature considering the home care setting seems still scarce. The analysis of the phenomenon of medication errors in the primary care setting highlights the necessity of exploring the specific variables to understand how to prevent or reduce the occurrence of a medication error in the home context. This review investigates the main preventive strategies implemented at the patient's home to prevent and/or limit the possibility of a medication error.*
Design. *The scoping review was conducted under the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) statement and based on the guidelines of the Joanna Briggs Institute.*
Methods. *No time or language limit was set to obtain the most comprehensive results possible. The following databases were queried: PubMed, Cochrane, CINAHL, ERIC and PsycINFO via EBSCO. All literature published up to 31 December 2022 was considered for data collection.*
Results. *The main preventive strategies implemented in the patient's home to prevent a medication error are: Multidisciplinary teams, therapeutic reconciliation and computerised systems that improve information sharing. As evidenced by all of the included studies, no educational intervention or preventive strategy individually reduces the risk of making a medication error.*
Conclusions. *It would be desirable for healthcare professionals to be constantly updated about their knowledge and understand the importance of introducing the aforementioned preventive strategies to guarantee safe care that protects the person from medication errors even at the patient's home.*

[1] *Nursing, Technical and Rehabilitation Department – DaTeR, Azienda Unità Sanitaria Locale di Bologna, Italy*
[2] *UniCamillus-Saint Camillus International University of Health and Medical Sciences, Rome, Italy*
[3] *Department of Biomedicine and Prevention, University Tor Vergata of Rome, Italy*
[4] *Nursing, Technical, Rehabilitation, Assistance and Research Direction, IRCCS Istituti Fisioterapici Ospitalieri – IFO, Rome, Italy*
[5] *Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy*
[6] *Department of Clinical and Molecular Medicine, Sapienza University, Rome, Italy*

Annali di Igiene : Medicina Preventiva e di Comunità (Ann Ig)
ISSN (print) 1120-9135 ISSN (online) 3035-5559

https://www.annali-igiene.it

1. Introduction

If it is true that to err is considered human, as suggested by the title of - To err is human - one of the international scientific literature milestones (1), it is nevertheless true that it remains necessary to implement every possible strategy of errors prevention, especially when concern people's lives and health. As Reason stated, if human error cannot be completely eliminated, it is essential to put in place actions that make it hard to make mistakes (2).

The scientific literature is rich in studies that investigate the phenomenon of medication errors (3,4), analysing their typology and prevalence (5,6) and also providing numerous strategies that healthcare professionals can concretely implement to reduce events, ensure patient safety and consequently decrease the extent of complications that can derive from such errors (7,8). However, most of the studies seem to focus on the hospital setting, returning a lower scientific production regarding the primary care setting and specifically home care (8,9).

Even in the home care setting, medication errors can be made, mainly due to the nature of the setting and the dynamics of caring for people at home. In fact, the errors that can be made are linked to the main causes of errors such as the lack of pharmacological reconciliation, the difficult communication between the different actors caring for the person, which is reflected in the process of prescribing and administering therapy (10-12). If, to date, territorial assistance still needs to be explored, this happens because health assistance is almost always associated exclusively with hospitals (13).

Although many risks and adverse events exist in hospital and home settings, the latter is characterised by different variables and often requires unique and specific solutions (14). This means that the risks that may arise in the various characteristic settings of primary care, including people's homes, and the solutions needed to mitigate them may differ from those in the hospital setting (15). Just think of the very nature of the hospital system in the event of a possible therapeutic error and the possibility to act specific strategies and tools to prevent or manage it. And to the possibility of implementing specific procedures can drastically reduce the probability that an error reaches the patient or has severe adverse effects (16,17).

Therefore, identifying and applying such strategies during home health care would allow not only patients not to experience adverse events that can compromise their safety and health but also health professionals to provide these patients with the best services and clinical care.

1.1. Aim and research question

This scoping review aims to identify the primary strategies aimed at reducing and/or preventing medication errors in the home care setting. Specifically, it intends to map the main characteristics of the possible preventive strategies and investigate which are the most involved professionals.

The PCC (Population, Concept, Context) approach developed by Peters and colleagues was (18) used to elaborate the research question and the inclusion and exclusion criteria. The PCC framework used was "medication errors in home care settings" (Population), "strategies for preventing medication errors" (Concept), and "home care setting" (Context). The questions that this scoping review aims to answer are the following:

What are the main strategies to prevent or reduce medication errors in treating adult patients in the home care setting?

What are the main characteristics of the preventive interventions and strategies implemented at the patient's home to prevent medication errors?

1.2. Key Explanations

Below are the definitions chosen in the following scoping review to identify medication errors and care provided at home. The definitions do not constitute an inclusion criterion for the studies but are rather reported as there is no unambiguous definition of these terms in the literature. The definitions are therefore given below to provide a better understanding of the definitions that guided the scoping review.

Medication errors

Medication error is defined as "*any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing; order communication; product labelling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use*" (10).

Home care setting

For the definition of home care setting, reference is made to that provided by Meyer-Massetti and

colleagues, according to whom "*assistance to patients living at home with the support of health professionals (mainly nurses) engaged by a professional home care organization*" (8).

2. Methods

This scoping review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) statement (19) and based on the guidelines of the Joanna Briggs Institute (20).

2.1. Inclusion criteria

2.1.1. Type of participants

All studies whose study population was represented by healthcare professionals responsible for the therapy management process in the home care setting (nurses, medical doctors, pharmacists) were included.

2.1.2. Type of interventions

All primary studies in which strategies for the prevention of medication errors in the user's home were specified and evaluated were considered relevant.

2.1.3. Setting

All primary studies that analysed implementing preventive strategies in the home setting were evaluated as eligible. Furthermore, studies focused on *transitional care* were also considered suitable, as this phase is crucial for a possible harmful event.

2.1.4. Evidence sources tipology

All the primary studies, quantitative (experimental and observational studies), qualitative (phenomenological, ethnographic, grounded theory and focus group studies) that were conducted to reduce the incidence of medication errors that occur at the patient's home thanks to the intervention of the healthcare personnel responsible for managing the therapy.

2.2. Exclusion criteria

2.2.1. Types of participants

Studies involving students and/or trainees of any healthcare discipline and those conducted in the pediatric field were not considered eligible. Student-focused studies were not considered eligible as, during training, the level of responsibility in managing therapy may differ from that of professionals. Furthermore, the pediatric population was not considered eligible as it is characterised by variables and approaches different from those for adults and, therefore, worthy of a separate analysis.

2.2.2. Setting

On the other hand, the analysis did not include all the studies that implied prevention interventions for medication errors within hospital settings, healthcare facilities (such as rest homes, residential care homes, etc.) and other places that were not the patient's home.

2.2.3. Evidence sources tipology

Studies involving students and/or trainees of any healthcare discipline and those conducted in the pediatric field were excluded. Student-focused studies were not included because the level of responsibility for managing therapy during training may differ from that of professionals. The pediatric population was excluded as characterised by variables and approaches different from those for adults and, therefore, worthy of a separate analysis.

2.3. Data sources and research strategy

For the search string elaboration, a previous search of the principal terms used in the literature was conducted, and the main synonyms of the following terms were chosen: medication errors also inserting the synonyms of the terms that indicate the phase of therapy management; home care setting and strategy or intervention. The keywords identified were combined using the Boolean operators "OR" and "AND", adapting each search string to the corresponding database (Tables 1,2,3). The databases consulted were: PubMed, Cochrane, CINAHL, ERIC and PsycINFO via EBSCO. No temporal or linguistic limit was set to obtain the most exhaustive results possible, and all the literature published up to 31 December 2022 was considered. Two independent researchers (SD, EDS) conducted the screening phase, assessing the relevance of the studies by reading the title and abstract. The articles deemed pertinent were subjected to eligibility through the reading of the entire text to confirm their pertinence concerning the criteria for inclusion and satisfaction of the research objective. Equivocal studies were evaluated by a third reviewer independently (NG).

2.4. Data extraction

The information in the studies deemed relevant will be described in aggregate according to the type

Table 1 - Search strategy on PubMed

#1	“medication error” ti/ab
#2	“medication errors” ti/ab
#3	“Medication errors” [MeSh Term]
#4	“drug error*” ti/ab
#5	“medication incident*” ti/ab
#6	#1 OR #2 OR #3 OR #4 OR #5
#7	“adverse drug reaction*” ti/ab
#8	“adverse drug event*” ti/ab
#9	“adverse event*” ti/ab
#10	#7 OR #8 OR #9
#11	“drug-related problem*” ti/ab
#12	“medication related problem*” ti/ab
#13	“drug related adverse event*” ti /ab
#14	“preventable adverse drug event*” ti/ab
#15	“preventable adverse event*” ti/ab
#16	#11 OR #12 OR #13 OR #14 OR #15
#17	“near miss” ti /ab
#18	“medication safety” ti/ab
#19	“drug safety” ti/ab
#20	#17 OR #18 OR #19
#21	“prescribing error*” ti/ab
#22	“administration error*” ti/ab
#23	“dispensing error*” ti/ab
#24	“transcription error*” ti/ab
#25	“medication prescribing error*” ti/ab
#26	“medication transcription error*” ti/ab
#27	“medication administration error*” ti/ab
#28	“medication dispensing error*” ti/ab
#29	#21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28
#30	#6 OR #10 OR #16 OR #20 OR #29
#31	“intervention” ti/ab
#32	“interventions” ti/ab
#33	“strategy” ti/ab
#34	“strategies” ti/ab
#35	“system” ti/ab
#36	#31 OR #32 OR #33 OR #34 OR #35
#37	“home care” ti/ab
#38	“home health care” ti/ab
#39	“home care servic*” ti/ab
#40	#37 OR #38 OR #39
#41	#30 AND #36 AND #40

Table 2 - Search strategy on Cochrane

#1	(“medication error”):ti,ab,kw OR (“medication errors”):ti,ab,kw
#2	(“adverse drug reaction*”):ti,ab,kw OR (“adverse drug event*”):ti,ab,kw OR (“adverse event*”):ti,ab,kw
#3	(“drug related prblem*”):ti,ab,kw OR (“medication related problem*”):ti,ab,kw OR (“drug related adverse event*”):ti,ab,kw OR (“preventable adverse drug event*”):ti,ab,kw OR (“preventable adverse event*”):ti,ab,kw
#4	(“drug error*”):ti,ab,kw OR (“medication incident*”):ti,ab,kw
#5	(“prescribing error*”):ti,ab,kw OR (“administration error*”):ti,ab,kw OR (“dispensing error*”):ti,ab,kw OR (“transcription error*”):ti,ab,kw
#6	(“medication prescribing error*”):ti,ab,kw OR (“medication administration error*”):ti,ab,kw OR (“medication dispensing error*”):ti,ab,kw OR (“medication transcription error*”):ti,ab,kw
#7	(“near miss”):ti,ab,kw OR (“medication safety”):ti,ab,kw OR (“drug safety”):ti,ab,kw
#8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7
#9	(“intervention”):ti,ab,kw OR (“interventions”):ti,ab,kw OR (“strategy”):ti,ab,kw OR (“strategies”):ti,ab,kw OR (“system”):ti,ab,kw
#10	(“home care”):ti,ab,kw OR (“home health care”):ti,ab,kw OR (“home care servic*”):ti,ab,kw OR (“home assistance”):ti,ab,kw
#11	#8 AND #9 AND #10

Table 3 - Search strategy on EBSCO

S1	TI “medication error” ORAB “medication error”OR TI medication errors”OR AB “medicationerrors”
S2	TI “drug error*” OR AB”drug error*”
S3	TI “medication incident*”OR AB “medicationincident*”
S4	TI “adverse drugreaction*” OR AB”adverse drug reaction*”OR TI “adverse drugevent*” OR AB “adversedrug event*” OR TI”adverse event*” OR AB”adverse event*”
S5	TI “drug-relatedproblem*” OR AB “drug-related problem*” OR TI”medication relatedproblem*” OR AB”medication relatedproblem*” OR TI “drugrelated adverse event*”OR AB “drug relatedadverse event*” OR TI”preventable adversedrug event*” OR AB “preventable adversedrug event*” OR TI”preventable adverseevent*” OR AB”preventable adverseevent*”
S6	TI “near miss” OR AB”near miss”
S7	TI “medication safety”OR AB “medicationsafety”
S8	TI “drug safety” OR AB”drug safety”
S9	TI “prescribing error*” OR AB “prescribingerror*” OR TI”administration error*”OR AB “administrationerror*” OR TI “dispensingerror*” OR AB”dispensing error*” OR TI”transcription error*” ORAB “transcription error*”OR TI “medicationprescribing error*” ORAB “medicationprescribing error*” OR TI”medication transcriptionerror*” OR AB”medication transcriptionerror*”
S10	TI “medicationadministration error*” ORAB “medicationadministration error*” ORTI “medicationdispensing error*” ORAB “medicationdispensing error*”
S11	S1 OR S2 OR S3 OR S4OR S5 OR S6 OR S7OR S8 OR S9 OR S10
S12	TI “intervention” OR AB”intervention” OR TI”interventions” OR AB”interventions” OR TI”strategy” OR AB”strategy” OR TI”strategies” OR AB”strategies” OR TI”system” OR AB”system”
S13	TI “home care” OR AB”home care” OR TI”home health care” ORAB “home health care”OR TI “home careservic*” OR AB “homecare servic*” OR TI”home assistance” ORAB “home assistance”
S14	S11 AND S12 AND S13

of intervention or strategy used to reduce or prevent medication errors.

In this regard, the following information will be extracted for each study:

the name of the author(s) and the year of publication of the study, as bibliographic reference;

the aim of the study;

the study type;

the intervention/preventive strategy description;

the sample under analysis and relative reference population;

the health professional[s] involved;

the main results;

limitations of the study (where present)

the examined strategies’ practice implications.

The data extraction chart has organised and reported this information (Table 4).

3. Results

The present scoping review included ten studies reporting strategies for facing medication errors in the home care setting.

Totally 488 articles were found. All identified bibliographic sources were imported into the bibliographic management software, Mendeley®. After the deletion of duplicates (n=97), 391 articles were obtained. In the first screening phase, all those articles were considered irrelevant or not pertinent based on reading the title and the abstract, and the inclusion and exclusion criteria were eliminated. 331 articles were eliminated; the remaining 39 articles considered adequate or doubtful were analysed in full text. In conclusion, 10 articles were selected. Figure 1 shows the article selection process.

It is important to point out that many of the studies included proposed different strategies but that, by integrating synergistically, met the objective described by the authors and allowed to obtain excellent results after the practical application of the strategies themselves.

To be able to summarise the results of the review more clearly, three main categories of interest were identified considering the main preventive strategy used to reduce the possibility of a medication error occurring. The three main categories identified were: the first concerning the multi-professional team, the second referring to the support of the pharmacist, and the third concerning the use of computerised systems. The organisation in different categories was carried out, considering the primary implemented

Table 4 - Summary of the main findings of the studies included in the review

Authors and year	Aim	Study type	Intervention	Study population	Healthcare professionals	Main results	Limitation of the study	Implications for clinical practice
Auvinen et al., 2021	Investigate whether multi-professional therapy assessment may affect the quality of care (and therapeutic) for elderly patients at home.	Randomized controlled trial	The FIMA method provides multi-professional assistance with a team formed by a doctor, a nurse and a pharmacist to perform an accurate therapeutic reconciliation. The intervention using the FIMA method was evaluated in the experimental group, while the control group received standard care.	512 patients. Inclusion criteria were: patients over 65, suffering from vertigo or orthostatic hypotension, or having had a recent fall episode, or taking more than 6 medications per day.	Nurses, doctors and pharmacists	The use of the FIMA methodology in the patients enrolled in the study who took more than 15 drugs each per day had excellent results. Specifically, a reduction in impairment of renal function, a reduction in the risk of bleeding, a decrease in anticholinergic effects, a decrease in constipation and, in a more general sense, a decrease in the probability for patients to take potentially inappropriate drugs were found.	The study reports the following limitations: the lack of risk analysis based on drug doses or the number of drugs affecting risk loads. and the complete implementation of the FIMA procedure.	FIMA's intervention has improved the quality of pharmacological therapy of patients assisted at home, confirming the importance of a multidisciplinary approach and the role of therapeutic reconciliation.
Brito et al., 2017	Evaluate how the integration of the pharmacist in the home care team affects the reduction of medication errors and patient safety.	Observational study	The pharmacist performs the medication review, evaluates medication regimen information, and develops medication schedules in collaboration with the doctor and nurse.	199 patients	A multidisciplinary team composed of doctor, nurse, social worker, nutritionist and pharmacist	The drug reconciliation performed by the pharmacist included in the multi-professional team is a way to avoid involuntary therapeutic discrepancies, especially in setting transitions.	The study reports as a limitation the difficulty in implementing new services in different healthcare systems and thus the limitation of extrapolating the results to other countries.	The pharmacist's intervention's importance is fundamental in improving the patient's health and reducing the risk of error.
Clark et al., 2019	To analyze the long-term impact of a pharmacist consultation service on home health care services.	Retrospective study	The pharmacist manages the therapeutic plan through telephone calls, home visits, and communication with the doctors of the home health agency.	1263 patients	A multidisciplinary team that also involves the pharmacist and the prescriber.	Identify the reason for the referral, the possible resolution methods, the number and type of drug-related problems, and the response rate of the attending physician. The pharmacy team resolved them by seeing 421 patients, calling 261 patients, and collaborating with the clinical team on 323 patients; a further 265 interventions have been planned by the patient's doctors and home care doctors.	The authors report as a limitation of the study the reliance of documentation on those involved in the practice rather than designated researchers. Although training was provided, the rotation of residents and students in a teaching service introduces the possibility of inconsistencies in the documentation of some items.	Home care is an appropriate setting for the participation of pharmacists in multi-professional teams.
Johansson et al., 2010	Evaluate the use of the drug barcode reading system as a tool to reduce medication errors.	Observational study	PDA (digital personal assistant) tool scans drug packaging, LIFE-reader® obtains drug profiles and information, and checks drug interactions and therapeutic duplications.	15 nurses, 67 patients	The professionals involved are home nurses, while the instrument used is LIFE-reader®.	Through a digital personal assistant, the LIFE-reader®, the medical decision support system provides information on drug-drug interactions, therapeutic duplications and warning systems for assisted persons with inappropriate drugs. Support identified 11 therapeutic duplications and 125 reports for inappropriate medications.	The need for LIFe-reader® to increase the intervention time and all functions should be available for use in order to optimise use and acceptability is highlighted as a limitation. Furthermore, in order to increase user involvement, participants should keep the PDA for further use in their work after the study. For further research, randomised controlled trials and larger sample sizes should be sought.	Regular scanning of patients' medications in their homes can support nurses and physicians in reducing inappropriate medication use and the risk of medication error.
Slugget et al., 2019	Apply a multidimensional intervention to simplify treatment regimens for people receiving community-based home care.	Observational study	Pharmacist performs medication reconciliation to streamline patient regimens; the multi-professional team provides health education to patients.	N.A.; 50 patients	Drug review; pharmacists, nurses and geriatricians	Evaluate the feasibility of the study and patients' benefit from applying this system, and improve therapeutic adherence, quality of life, patient satisfaction, and therapeutic errors.	The authors point out as a limitation of the study the fact that self-efficacy and medication adherence is self-reported by the sampled users.	Improving the drug administration to elderly people cared for at home, providing information strategies to improve the management of medicines in this care setting.

Sorensen et al., 2004	Examine the effectiveness of multidisciplinary care that provides a pharmacological review to patients most at risk of committing or receiving MEs in the home setting.	Randomized controlled trial	Therapeutic education performed by the general practitioner; visits to the patient's home; drug review by the pharmacist; team conferences with representatives of primary care services.	N.A.; 400 patients	Multi-professional teams; general practitioner and pharmacist	54.4% of the health recommendations were implemented, and 23.9% of them were implemented in practice with all the specific recommendations indicated by the pharmacological review. 92% of the interventions implemented by doctors improved home care, reduced adverse drug events, reduction of disease severity and also an improvement in costs, follow-up visits had a good impact on health.	The authors report the following limitations: the sponsor's priority of demonstrating efficacy within a certain time period precluded conducting a classic clinical trial; a longer follow-up period could have shown a greater difference in outcome measures and confirmed reported trends.	This pharmacological review model has been successfully tested; the participants stated they had excellent satisfaction levels.
Toivo et al., 2019	Coordinate the health care provided to the elderly about managing pharmacological risk in the home setting. A care coordination intervention would reduce the number of risks among medications.	Randomized controlled trial	Education for nurses on home pharmacological risk; sending the information from the nurse to the pharmacist to evaluate the interventions undertaken with the multidisciplinary team.	N.A.; 129 patients	Pharmacist drug review with an automated system to detect drug-related problems, drug interactions and patients at risk; resolution of issues with the team doctor.	Outcomes were measured as changes in the use of potentially inappropriate and psychotropic medications on the anticholinergic and serotonergic load and drug interactions. Half of the participants did not implement the suggestions received; 45.5% had no DRP; of the remainder, 29.6% needed a prescription review, 63% a pharmacological review, and 7.4% a comprehensive review of the treatment plan.	The authors report the relatively small sample size as a major limitation, which may have influenced the low effectiveness of the intervention. Furthermore, half of the eligible residents did not provide written consent for participation. The high workload of the recruiting nursing staff and the fragile and multi-morbid clients of the home care were evaluated as limiting factors especially with regard to the drop-out rate of the study.	More studies are needed on correctly managing therapeutic regimens to reduce the MEs that older people experience in home care.
Wang et al., 2019	Evaluate the reduction in the number of medications/ drug interactions experienced by ICU patients after pharmacists' home consultations and evaluate the intervention's effectiveness.	Randomized controlled trial	The pharmacist performs the drug review with the "PharmaCloud System" to record the drugs the patient takes at home, view his previous drug prescriptions and report drug-related problems.	N.A.; 469 patients	The number of kinds of drugs taken by the patient decreased by 1.89 times ($p < 0.001$), the number of drugs decreased by 61.6%, and the incidence of drug interaction decreased by 0.6-fold ($p < 0.001$).	Thanks to the intervention, there was a significant reduction in DRP and drug interactions, consequently reducing the number of drugs the patient takes at home. Home pharmaceutical assistance can improve drug safety thanks to the intervention of therapeutic reconciliation.	The main limitation of this study is that the population examined consisted of patients with high healthcare utilisation and excessive polypharmacy, and the characteristics of the drug interaction in this group may not be applicable to other groups.	Applying such a system to deliver home care services can improve patient outcomes.
Nauton et al., 2003	To evaluate pharmacist-conducted follow-up at home of high-risk elderly patients discharged from hospital	Randomized controlled trial	Patients in the intervention group were visited at home by a pharmacist five days after discharge. The pharmacist educated patients on their medication, encouraged compliance, assessed for drugrelated problems, intervened when appropriate and communicated all relevant findings to community health professionals.	121 patients	Nurses, and pharmacists	The study results showed 90 days after the follow-up visit: a decrease in issues related to drug therapy and increased patient adherence to treatment	The study has the following limitations: the pharmacist (who was not blinded to patient assignment) assessed DRPs in the intervention group and in the control group at 90 days, introducing a possible bias towards the intervention group in the identification of possible DRPs; the question asked about compliance may have overestimated actual compliance; finally, the relatively small sample limited some of the interpretations and made it impossible to determine exactly which patients could benefit most from the home visit.	A pharmacist-conducted follow-up at home of high-risk elderly patients discharged from hospital is valuable in identifying and addressing drug-related problems and reducing the risk of readmission to hospital.

Authors and year	Aim	Study type	Intervention	Study population	Healthcare professionals	Main results	Limitation of the study	Implications for clinical practice
Josendal et al., 2021	Investigate whether an electronically Shared Medication List (eSML) reduced discrepancies between medication lists in primary care.	Controlled pre-post study	The eSML System allows direct input into the HER System by the general prescription and the possibility of communication between the different profesionals (doctor, nurse, pharmacist). The intervention provided for the reconciliation of the doctor, pharmacist and/or home care before generating the eSML	267 patients	Multi-professional teams; general practitioner nurse and pharmacist	The intervention group had on average 3.9 discrepancies in their medication lists before the intervention, while the control group had 5.9. For both groups, when comparing the GP and the home care service list, the most frequent types of discrepancies were that medication was lacking or that different dosages were listed. Discrepancies in the intervention group were significantly reduced after the implementation of eSML.	The authors report the way the eSML was implemented as the main limitation. In fact, when the eSML was implemented, the GPs in the intervention groups were recommended to perform a medication reconciliation. GPs enrolled in the control group were given no such recommendation. It is therefore difficult to separate the effect of reconciliation from that of the presence of an eSML. However, previous studies have shown that even after reconciliations, discrepancies remain or recur rapidly, and reconciliations must be repeated regularly to keep drug lists up-to-date	The transition from the paper-based to the electronic system can thus lead to unintended changes in the patient's medication treatment if these discrepancies are not resolved before implementation.

strategy. Finally, a critical appraisal of the individual sources of evidence was not conducted, as this was not appropriate for the purpose of the scoping review, as defined in the PRISMA-ScR checklist (19).

3.1. Preventive strategies related to the multi-professional team

Auvinen and colleagues, in their study, support the importance of the multi-professional evaluation of therapeutic plans by doctors, nurses, and pharmacists to implement a synergy to improve the management of the therapeutic process, ensuring patient safety (21). The intervention chosen to evaluate the proposed strategy is the Finnish Interprofessional Medication Assessment (FIMA), based on multi-professional collaboration and designed to optimise the number of drugs the patient takes. Thanks to this intervention, it was possible to appreciate the reduction of various side effects and the decrease in the probability of patients taking potentially inappropriate drugs. The study by Sorensen and colleagues also obtained very encouraging data following the intervention of the multi-professional home care team (22). Through the collaboration with the nurses responsible for home care, the multi-professional team performed therapeutic reconciliation alongside therapeutic education interventions for patients and caregivers. The data testify that 92% of the interventions implemented have improved the assistance provided to the patient, with a reduction in adverse drug events and an improvement in the management of the therapeutic regimen. Finally, in support of what has been stated, the study by Toivo and colleagues (23) shows that implementing a multi-professional team in evaluating the therapeutic plan can contribute to reducing the number of drugs taken by the patient and the risk of error. The study involved 129 patients divided into two groups. The experimental group received an initial evaluation of the therapeutic plan by the nurse responsible for the patient's home care, who shared any problems with the multi-professional team [doctors and pharmacists] to identify the best intervention. The results showed that: in 45.5% of cases, no drug-related risks were identified which would require a review of the treatment plan; 29.6% of the patients required a revision of the therapeutic prescriptions; 63% required adequate treatment reconciliation, and 7.4% needed a complete review of the treatment plan. Finally, in the intervention group, following the multi-professional evaluation, the number of drugs decreased from 14.1 to 13.5, while in the control group, it increased from 12.7 to 13.

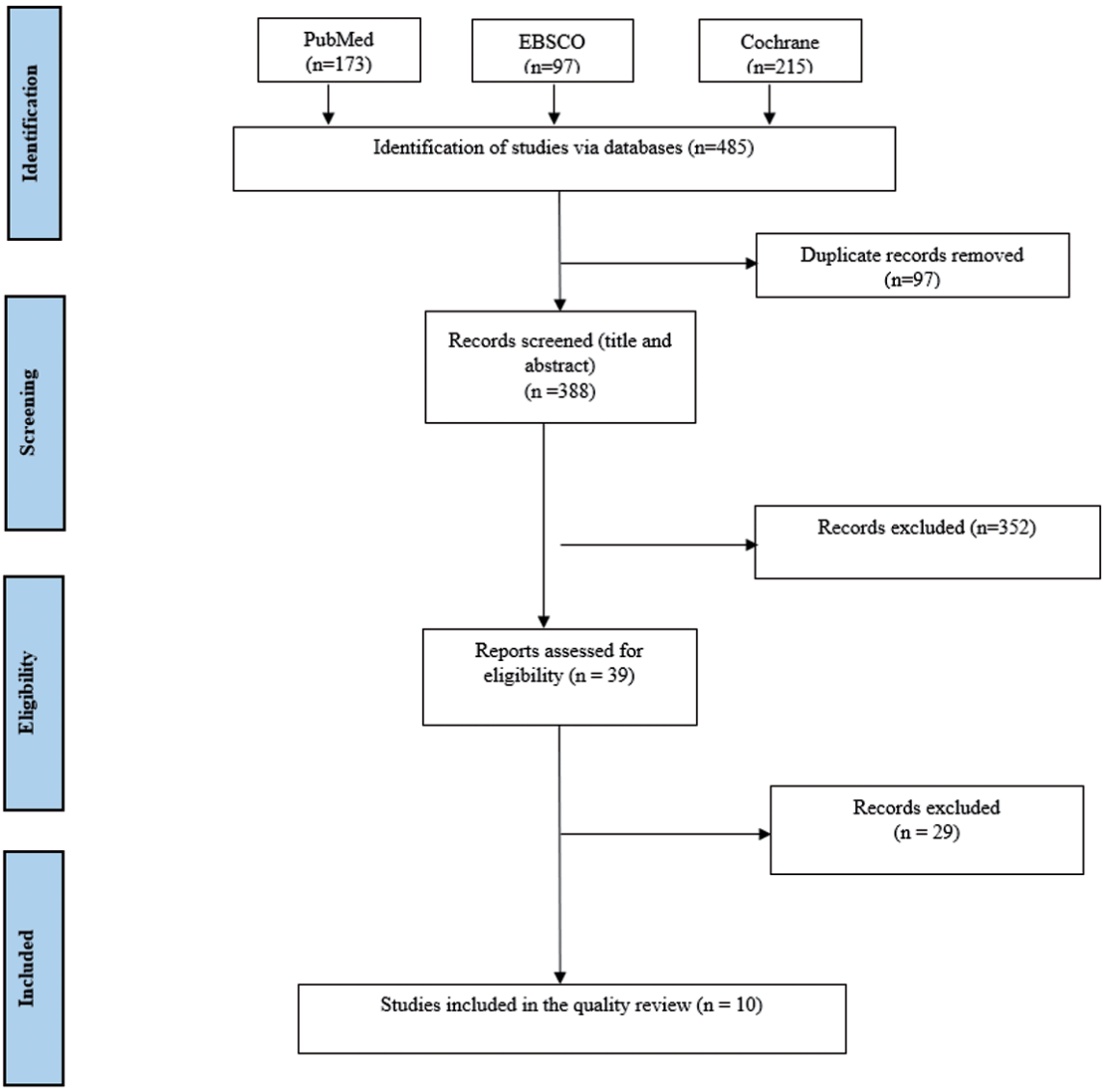


Figure 1 - PRISMA Flow diagram

3.2. Preventive strategies related to the pharmacist intervention

Within the multi-professional team, the importance of the role played by the pharmacist in evaluating the therapy is the object of interest of the studies by Brito (24) e and Clark and colleagues (25). The latter has estimated that the pharmacological reconciliation implemented by the multi-professional team, with the support of the pharmacist, reduces medication errors in the home care setting. Out of 1,263 reports of problems associated with drug therapy, the team solved: 421 through visits to patients' homes, 261 through telephone interventions with the patient and 323 by collaborating with the multi-professional team (26).

The study by Slugget and colleagues emphasises the importance of the pharmacist's contribution to drug reconciliation, evaluating the patient's therapeutic history, thanks to the information obtained from the home care nurses and the general practitioner (26). In the specifics of the intervention, the authors include, in addition to the pharmacist's role, the assessment of each patient's ability to self-manage their therapeutic regimen to adapt a plan aligned with the person's health literacy level.

Even Naunton & Peterson, in their study, argue that to reduce home medication errors of elderly patients, the presence of the pharmacist in the multi-professional team is essential (27). The study evaluated

the impact of home follow-up visits by nurses and pharmacists. These visits were aimed at educating patients on the characteristics of the drugs, supporting their therapeutic compliance and evaluating all patient problems related to drug therapy. The study results showed that 90 days after the follow-up visit, there was a decrease in issues related to drug therapy and increased patient adherence to treatment.

3.3. Preventive strategies related to the use of computerised systems

The use of computerised systems as an error prevention strategy was investigated by 3 of the studies deemed pertinent.

In 2010, Johansson and colleagues conducted an observational study recruiting 15 home care nurses to evaluate the implementation of a *medical decision support system* (MDSS), the LIFE-reader® consisting of a barcode reader of therapy (28). This tool implements a genuine automated therapeutic reconciliation, showing the patient's therapeutic profiles, reporting possible interactions between drugs, therapeutic duplications and alert messages for unsuitable medications for the patient's clinical situation. Thanks to the LIFE-reader® tool, nurses have identified 11 therapeutic duplications, received 125 reports of inappropriate medications and intercepted 58 drug interactions.

The study conducted in 2019 by Wang and colleagues provided therapeutic reconciliation by the pharmacist through the computerised tool "*PharmaCloud System*" (29). Postoperatively, the number of medications the patient took decreased 1.89 times ($p < 0.001$), with a 19.9% reduction in drug interactions. These data testify to the good impact that a technological system can have on the safety of care and patients.

Finally, the study by Josendal and colleagues evaluates the effect of the eSML (*electronically shared medication list*), i.e. the electronic updating of therapeutic prescriptions (30). Specifically, this list, which shows the drugs used by the patient, is visible to the various professionals (in charge of the user) but can be modified and used for prescription only after the general practitioner has approved the treatment plan. Therefore, the eSML is a list of the therapy that the patient assumes, a complete and shared tool between the various actors. Use in the pre-post study demonstrated the reduction of therapeutic discrepancies, reducing them from 383 to 122 ($p < 0.001$).

4. Discussion and conclusions

Considering therapeutic discrepancies, drug interactions and the inadequacy of particular categories of drugs that patients have to take at home, one of the main error prevention strategies shared in most of the studies is therapeutic reconciliation (21,22,24-27). The nurse and pharmacist can conduct this process together, using computerised supports, which allow information to be obtained in real-time regarding the patient's clinical history, therapeutic plans and patient diagnostic profiles, getting answers and comprehensive solutions that improve continuity of care and patient safety (30).

A further and fundamental preventive strategy identified concerns the evaluation of the patient's drug therapy by the multi-professional team. Specifically, this affects the implementation of care teams involving figures such as general practitioners, pharmacists, nurses, physiotherapists, geriatricians, speech therapists and other health professionals. Several authors have followed this line (21,23-26). The *quid* behind the importance of this strategy is the possibility of implementing global patient management, carrying out detailed assessments from every medical, specialist and assistance point of view, and implementing synergistic interventions aimed at all for the same purpose: the patient's safety.

Health education interventions are another essential strategy for preventing medication errors in the home setting. In particular, the study by Sluggett emphasises the importance of calibrating one's therapeutic intervention based on the person's ability to understand (26). Therefore, if the healthcare professional involved in the assessment of the patient's cognitive levels assumes that this parameter does not reach a value sufficiently adequate, he can autonomously decide to involve the formal or informal caregiver who takes charge of daily health assistance to protect the health and safety of the patient himself about taking medicines (31).

The primary objective to be achieved, therefore, within this particular healthcare delivery system, such as the home one, is certainly to improve the safety of the care that the patient receives and to reduce the incidence with which medication errors tend to register themselves in the homes of the assisted persons (32).

The authors are conscious of the limits of this review. First of all, the setting analyzed in conducting this research. The home care setting is still understudied for patient safety approaches and strategies by

experts. Furthermore, to our knowledge, it is possible to find only a few systematic reviews or primary studies specific to this context. All of these reasons contribute to the necessity of analyzing the efficacy of the strategies elevated in this research.

Although the international literature exploring the prevention of *medication errors* is rich in studies conducted within hospital settings, with particular attention to intensive settings (17,33), the literature shows a probable change of trend, shifting the attention of researchers in primary care and home care settings. As evidenced by the studies included, no univocal educational intervention or preventive strategy reduces the risk of making a medication error. It would therefore be desirable that health professionals not only were constantly updated concerning their knowledge but also understood the importance of introducing the aforementioned preventive strategies to guarantee, even at the patient's home, safe assistance that protects the person from therapy failure (34).

Finally, new studies that assess the outcomes from the practical application of specific preventive strategies and educational interventions, would contribute to evaluate efficiency, offering new ideas for research and analysis to achieve the main objective of every health action, i.e., the protection of the health and safety of patients.

Acknowledgments: Not applicable
Funding Statement: None external fundings.
Conflicts of interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Riassunto

La prevenzione degli errori terapeutici in ambito domiciliare: una scoping review

Background. I cambiamenti nei bisogni sanitari, sociali e demografici impongono nuovi approcci alle cure e all'assistenza senza rinunciare alla sicurezza dei pazienti. Sebbene diversi studi abbiano analizzato l'approccio e le strategie per la sicurezza del paziente, la letteratura che considera l'ambito dell'assistenza domiciliare sembra essere ancora scarsa. L'analisi del fenomeno degli errori terapeutici in ambito di cure primarie evidenzia la necessità di esplorare le variabili specifiche per comprendere come prevenire o ridurre il verificarsi di un errore terapeutico, nel contesto domiciliare. Questa revisione indaga le principali strategie preventive attuate a domicilio del paziente per prevenire e/o limitare la possibilità di un errore terapeutico.

Disegno dello studio. La scoping review è stata condotta secondo la dichiarazione PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) e sulla base delle linee guida del Joanna Briggs Institute.

Metodi Al fine di ottenere risultati quanto più complete, non è stato fissato alcun limite di tempo o di lingua. Sono stati interrogati i seguenti database: PubMed, Cochrane, CINAHL, ERIC e PsycINFO tramite EBSCO. Tutta la letteratura pubblicata fino al 31 dicembre 2022 è stata considerata per la raccolta e l'analisi dei dati.

Risultati. Le principali strategie preventive attuate a domicilio del paziente per prevenire un errore terapeutico sono: team multidisciplinari, riconciliazione terapeutica e sistemi computerizzati che migliorano la condivisione delle informazioni. Come evidenziato da tutti gli studi inclusi, nessun intervento educativo o strategia preventiva riduce individualmente il rischio di commettere un errore terapeutico.

Conclusioni. Sarebbe auspicabile che gli operatori sanitari fossero costantemente aggiornati in merito alle proprie conoscenze e comprendessero l'importanza di introdurre le suddette strategie preventive per garantire un'assistenza sicura che tuteli la persona da errori terapeutici anche a domicilio.

References

1. Institute of Medicine (US) Committee on Quality of Health Care in America, Kohn LT, Corrigan JM, Donaldson MS. To Err is Human: Building a Safer Health System. Washington (DC): National Academies Press (US); 2000.
2. Reason J. Human error: models and management. BMJ. 2000 Mar 18;**320**(7237):768-70. doi: 10.1136/bmj.320.7237.768. PMID: 10720363.
3. Bond CA, Raehl CL, Franke T. Medication errors in United States hospitals. Pharmacotherapy. 2001 Sep;**21**(9):1023-36. doi: 10.1592/phco.21.13.1023.34617. PMID: 11560192.
4. Giannetta N, Dionisi S, Tonello M, Di Simone E, Di Muzio M. A Worldwide Bibliometric Analysis of Published Literature on Medication Errors. J Patient Saf. 2022 Apr 1;**18**(3):201-209. doi: 10.1097/PTS.0000000000000894. PMID: 35026796.
5. Almanasreh E, Moles R, Chen TF. The medication reconciliation process and classification of discrepancies: a systematic review. Br J Clin Pharmacol. 2016 Sep;**82**(3):645-58. doi: 10.1111/bcp.13017. Epub 2016 Jun 29. PMID: 27198753.
6. Dionisi S, Giannetta N, Liquori G, De Leo A, D'Inzeo V, Orsi GB, et al. Medication Errors in Intensive Care Units: An Umbrella Review of Control Measures. Healthcare (Basel). 2022 Jun 29;**10**(7):1221. doi: 10.3390/healthcare10071221. PMID: 35885748.
7. Giannetta N, Dionisi S, Tonello M, Cappadona R, Di Muzio M, Di Simone E. Educational intervention to improve the safety medication process: A review using the GRADE approach. Journal of Pharmaceutical Health Services Research 2021;**12**(3):434-443. doi: 10.1093/jphsr/rmab014.
8. Meyer-Massetti C, Meier CR, Guglielmo BJ. The scope of drug-related problems in the home care setting. Int J Clin Pharm. 2018 Apr;**40**(2):325-334. doi: 10.1007/s11096-017-0581-9. Epub 2018 Jan 11. PMID: 29322475.
9. World Health Organization (WHO). Medication Errors. Geneva: License: CC BY-NC-SA 3.0 IGO; 2016.

10. Dionisi S, Di Simone E, Liquori G, De Leo A, Di Muzio M, Giannetta N. Medication errors' causes analysis in home care setting: A systematic review. Public Health Nurs. 2022 Jul;**39**(4):876-897. doi: 10.1111/phn.13037. Epub 2021 Dec 30. PMID: 34967458.
11. Baker GR, Flintoft V, Wojtak A, Blais R. Contributing causes to adverse events in home care and potential interventions to reduce their incidence. Healthc Manage Forum. 2018 Sep;**31**(5):178-185. doi: 10.1177/0840470418782261. Epub 2018 Aug 22. PMID: 30133330.
12. Meyer-Massetti C, Hofstetter V, Hedinger-Grogg B, Meier CR, Guglielmo BJ. Medication-related problems during transfer from hospital to home care: baseline data from Switzerland. Int J Clin Pharm. 2018 Dec;**40**(6):1614-1620. doi: 10.1007/s11096-018-0728-3. Epub 2018 Oct 5. PMID: 30291577.
13. Cain CH, Neuwirth E, Bellows J, Zuber C, Green J. Patient experiences of transitioning from hospital to home: an ethnographic quality improvement project. J Hosp Med. May-Jun;**7**(5):382-7. doi: 10.1002/jhm.1918. Epub 2012 Feb 29. PMID: 22378714.
14. Harrison MB, Keeping-Burke L, Godfrey CM, Ross-White A, McVeety J, Donaldson V, et al. Safety in home care: a mapping review of the international literature. Int J Evidence-Based Healthcare. 2013 Sep;**11**(3):148-160. doi: 10.1111/1744-1609.12027.
15. World Health Organization (WHO). Medication Without Harm - WHO Global Patient Safety Challenge. 2017. Available from: https://www.who.int/initiatives/medication-without-harm [Last accessed: 2024 Feb 2].
16. Dionisi S, Di Simone E, Franzoso V, Caldarola E, Cappadona R, Di Muzio F, et al. The application of the Theory of Planned Behaviour to prevent medication errors: a scoping review. Acta Biomed. 2020 Jun 20;**91**(6-S):28-37. doi: 10.23750/abm.v91i6-S.9290. PMID: 32573504.
17. Giannetta N, Dionisi S, Stievano A, Eltaybani S, Abdelgawad ME, Katigri MR, et al. Comparison across 12 countries on knowledge, attitude, and behavior scores about medication errors in Intensive Care Units: an international study. Eur Rev Med Pharmacol Sci. 2021 Dec;**25**(23):7223-7230. doi: 10.26355/eurrev_202112_27415. PMID: 34919221.
18. Peters MDJ, Marnie C, Tricco AC, Pollock D, Munn Z, Alexander L, et al. Updated methodological guidance for the conduct of scoping reviews. JBI Evid Synth. 2020 Oct;**18**(10):2119-2126. doi: 10.11124/JBIES-20-00167. PMID: 33038124.
19. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med. 2018 Oct 2;**169**(7):467-473. doi: 10.7326/M18-0850. Epub 2018 Sep 4. PMID: 30178033.2018.
20. Jordan Z, Lockwood C, Munn Z, Aromataris E. The updated Joanna Briggs Institute Model of Evidence-Based Healthcare. Int J Evid Based Healthc. 2019 Mar;**17**(1):58-71. doi: 10.1097/XEB.0000000000000155. PMID: 30256247.
21. Auvinen KJ, Räisänen J, Voutilainen A, Jyrkkä J, Mäntyselkä P, Lönnroos E. Interprofessional Medication Assessment has Effects on the Quality of Medication Among Home Care Patients: Randomized Controlled Intervention Study. J Am Med Dir Assoc . 2021 Jan;**22**(1):74-81. doi: 10.1016/j.jamda.2020.07.007. Epub 2020 Sep 3. PMID: 32893136.
22. Sorensen L, Stokes JA, Purdie DM, Woodward M, Elliott R, Roberts MS. Medication reviews in the community: results of a randomized, controlled effectiveness trial. Br J Clin Pharmacol. 2004 Dec;58(6):648-64. doi: 10.1111/j.1365-2125.2004.02220.x. Erratum in: Br J Clin Pharmacol. 2005 Mar;**59**(3):376. PMID: 15563363.
23. Toivo T, Airaksinen M, Dimitrow M, Savela E, Pelkonen K, Kiuru V, et al. Enhanced coordination of care to reduce medication risks in older home care clients in primary care: a randomized controlled trial. BMC Geriatr. 2019 Nov 27;**19**(1):332. doi: 10.1186/s12877-019-1353-2. PMID: 31775650.
24. Brito AM, Simões AM, Alcobia A, Alves da Costa F. Optimising patient safety using pharmaceutical intervention in domiciliary hospitalization. Int J Clin Pharm. 2017 Oct;**39**(5):980-984. doi: 10.1007/s11096-017-0512-9. PMID: 28840436.
25. Clark JA, Shen D, Shelden MR, Anderson KD, Koller NJ, Gates BJ. Analysis of a Long-Standing Consultant Pharmacy Service in Home Health Care. Sr Care Pharm. 2019 Jun 1;**34**(6):370-383. doi: 10.4140/TCP.n.2019.370. PMID: 31164184.
26. Sluggett JK, Page AT, Chen EYH, Ilomäki J, Corlis M, Van Emden J, et al. Protocol for a non-randomised pilot and feasibility study evaluating a multicomponent intervention to simplify medication regimens for people receiving community-based home care services. BMJ Open 2019 -07-19;**9**(7):e025345.
27. Naunton M, Peterson GM. Evaluation of home-based follow-up of high-risk elderly patients discharged from hospital. J PharmPract Res. 2003 Sep;**33**(3):176-182. https://doi.org/10.1002/jppr2003333176.
28. Johansson PE, Petersson GI, Nilsson GC. Personal digital assistant with a barcode reader--a medical decision support system for nurses in home care. Int J Med Inform. 2010 Apr;**79**(4):232-42. doi: 10.1016/j.ijmedinf.2010.01.004. Epub 2010 Feb 6. PMID: 20138577.
29. Wang T, Trezise D, Ku P, Lu H, Hsu K, Hsu P. Effect of Pharmacist Intervention on a Population in Taiwan with High Healthcare Utilization and Excessive Polypharmacy. Int J Environ Res Public Health. 2019 Jun 21;**16**(12):2208. doi: 10.3390/ijerph16122208. PMID: 31234455.
30. Josendal AV, Bergmo TS, Granas AG. Implementation of a shared medication list in primary care - a controlled pre-post study of medication discrepancies. BMC Health Serv Res. 2021 Dec 13;**21**(1):1335. doi: 10.1186/s12913-021-07346-8. PMID: 34903215.
31. Koper D, Kamenski G, Flamm M, Böhmdorfer B, Sönnichsen A. Frequency of medication errors in primary care patients with polypharmacy. Fam Pract. 2013 Jun;**30**(3):313-319. doi: 10.1093/fampra/cms070. Epub 2012 Nov 6. PMID: 23132894.
32. Alqenae FA, Steinke D, Keers RN. Prevalence and Nature

of Medication Errors and Medication-Related Harm Following Discharge from Hospital to Community Settings: A Systematic Review. Drug Saf. 2020 Jun;**43**(6):517-537. doi: 10.1007/s40264-020-00918-3. PMID: 32125666.
33. Hodkinson A, Tyler N, Ashcroft DM, Keers RN, Khan K, Phipps D, et al. Preventable medication harm across health care settings: a systematic review and meta-analysis. BMC Med. 2020 Nov;**18**(1):313. doi: 10.1186/s12916-020-01774-9. PMID: 33153451
34. Dionisi S, Giannetta N, Maselli N, Di Muzio M, Di Simone E. Medication errors in homecare setting: An Italian validation study. Public Health Nurs. 2021 Nov;**38**(6):1116-1125. doi: 10.1111/phn.12946. Epub 2021 Jul 7. PMID: 34231262.

Corresponding author: Dr. Nicolò Panattoni, Nursing, Technical, Rehabilitation, Assistance and Research Direction – IRCCS Istituti Fisioterapici Ospitalieri – IFO, Rome, Italy
e-mail: nicolo.panattoni@uniroma1.it

ORCIDs
Sara DIONISI 0000-0001-7933-8490
Noemi GIANNETTA 0000-0003-4575-1898
Gloria LIQUORI 0000-0001-8689-3740
Aurora DE LEO 0000-0003-1519-6299
Nicolò PANATTONI 0000-0002-4162-937X
Mariasole CAIAFA NA
Marco DI MUZIO 0000-0003-2641-4044
Emanuele DI SIMONE 0000-0002-6373-8163

Author contributions

Criteria	**Author Initials**
Made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data;	S.D., N.G., G.L., A.D.L., N.P., M.C., M.D.M., E.D.S.
Involved in drafting the manuscript or revising it critically for important intellectual content;	S.D., E.D.S., N.G., N.P., M.D.M.
Given final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content;	S.D., N.G., G.L., A.D.L., N.P., M.C., M.D.M., E.D.S.
Agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.	S.D., N.G., G.L., A.D.L., N.P., M.C., M.D.M., E.D.S.

Ann Ig. 2025 Jan-Feb; 37(1): 14-24. doi: 10.7416/ai.2024.2643. Epub 2024 Jun 20.

Training in infection prevention and control: survey on the volume and on the learning demands of healthcare-associated infections control figures in the Emilia-Romagna Region (Northern Italy)

Eleonora Ferrari[1], Patrizia Scannavini[2], Lucia Palandri[1], Elisa Fabbri[3], Grazia Tura[4], Catia Bedosti[5], Angela Zanni[6], Daniela Mosci[7], Elena Righi[1], Elena Vecchi[2]

Keywords: Healthcare associated infections; HAI; Infection prevention and control; training; Italy
Parole chiave: Rischio infettivo; infezioni correlate all'assistenza; formazione; Italia

Abstract

Background. *In the context of Infections Prevention and Control activities, the training of healthcare-associated infection control figures is crucial; the COVID-19 pandemic further emphasized the necessity of ensuring a widespread and stable level of skills over time for such professionals. The present work aims to identify the number and training needs of the personnel working in the Emilia-Romagna Region's healthcare facilities as "healthcare-associated infection control figures".*
Methods. *Data were collected through a survey created by experts from the Regional Group "Training in the prevention and control of antibiotic resistance". The questionnaire explored the number, professional and educational background, and training requirements of Healthcare-associated infections control figures in Emilia-Romagna.*
Results. *With 73 figures dedicated to Healthcare-associated infections control, the Emilia-Romagna Region appears to be in line with the European standard ratio (1 professional every 125 beds). Professionals with a nursing background, over 50 years old and of female sex prevail in the group, while the training needs expressed include both theoretical and practical aspects.*
Conclusions. *Healthcare assistants and nursing staff represent a fundamental resource for the implementation of infection prevention and control programs in our healthcare facilities; continuous, multidisciplinary and targeted training of these professionals is confirmed as necessary.*

[1] *Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy*
[2] *Collective Prevention and Public Health Section - Directorate General for Personal Care, Health and Welfare - Emilia Romagna Region, Bologna, Italy*
[3] *Regional Health and Social Innovation Section-Emilia Romagna Region, Bologna, Italy*
[4] *Romagna Local Health Unit, Rimini, Italy. Now retired.*
[5] *Imola Local Health, Imola, Italy*
[6] *Bologna Local Health, Bologna, Italy*
[7] *Bologna University Hospital, Bologna, Italy*

Elena Righi and Elena Vecchi have contributed equally to this work and share the senior authorship

Annali di Igiene : Medicina Preventiva e di Comunità (Ann Ig)
ISSN (print) 1120-9135 ISSN (online) 3035-5559

https://www.annali-igiene.it

Introduction

Health care-associated infections (HAIs) are a major public health issue (1): in 2016-17 the prevalence of patients with at least one HAI was 5.9% in European countries and 8% in Italy (2). The most frequently reported types of HAI are respiratory tract infections, urinary tract infections, surgical site infections, and bloodstream infections. As infection prevention and control (IPC) programmes represent key strategies for dealing with such public health issue, education and training of HAI control figures is crucial (1).

In Italy, the figure dedicated to HAI control originated with Circulars n. 52/1985 (3) and n. 8/1988 (4) issued by the Ministry of Health. Such documents defined the skills profile of HAI control figures and fixed the minimum staff standards - as defined by the US Centers for Disease Control and Prevention (5,6) - as one HAI control figure every 25 beds, or, depending on the type of ward, every 9,000-10,000 admissions per year.

The introduction of HAI control figures in the Italian National Health Service was gradual and not always homogeneous throughout the country (7). In the Emilia-Romagna region (Northern Italy) the HAI control figures were set shortly after the issuing of a circular, however the training of HAI control figures has been a major concern for decades (8,9); a few "infection-control nurse" (Italian acronym: ICI) professional training courses started in the '90s (10) and, more recently, several dedicated first-level Masters courses have been activated (11).

According to the Regional Council decision n.318/2013 (8), each public health authority (University Hospital or Local Health Facility) must designate a multidisciplinary Strategic Committee dedicated to clinical risk management, in charge of developing both antimicrobial stewardship (AS) and IPC programs. These strategies are operationalized by two sub-groups of experts focused respectively on AS and IPC and highly integrated. HAI control figures (nurses or health assistants) are important non-medical members of the IPC working group. Further, inside each ward of each health facility, specifically designated health professionals promote the development of AS and IPC activities, acting as a link between the Risk Management Strategic Committee and their ward.

COVID-19 pandemic severely hit the Emilia-Romagna region (12,13) and emphasized further the importance of maintaining a widespread and consistent level of knowledge on IPC. Thus, the regional council decision n. 832/2022 (14) set up a regional multi-professional board of experts (the "HAI control figures board"), aimed at defining and implementing regional training activities for HAI control and responsible antibiotic use.

The HAI control figures board includes representatives of hygienists, of infectious disease specialists), microbiologists, pharmacists, and HAI control nurses from the whole Region. Further, in each public health service, an Infectious Risk Manager was designated as a point of contact between the local HAI control figures and the the regional board. The board is divided into smaller working groups; one is focused on the training requirements of nurses and healthcare assistants involved in IPC activities.

Considering both the high turnover of staff also due to COVID-19 emergency and the different educational and professional backgrounds of HAI control figures, in order to better understand their future training needs, the working group designed and carried out a survey with the following specific objectives:

to record the number of health professionals employed as HAI control figures in Emilia-Romagna Region and to map their formal roles, training backgrounds and working place;

to explore HAI control figures training needs in the main technical domains.

Methods

1. Setting

On 1 January 2023, the Emilia-Romagna Region counted 4,460,030 inhabitants. The functional articulation of Healthcare in the Emilia-Romagna Region includes 8 Local Health Authorities (LHAs), and 4 University/Regional Hospitals (Bologna, Ferrara, Modena, Parma). Further, three highly specialized facilities are currently classified as "IRCCS" (Intitutes for scientific hospitalization and treatment" in Italian, a network of hospitals, public or privately owned) approved by the Ministry of Health and sharing the compulsory duty to be additionally involved in applied research in their special field, financed by the same Ministry: the Montecatone Rehabilitation Institute (Imola, BO), the Rizzoli Orthopaedics Institute in Bologna, and the Romagna Scientific Institute for the Study and Treatment of Cancer (Meldola, FC).

2. Survey design and data collection

This cross-sectional study was carried out in 2022. During the first months of 2022, the regional multi-

professional board of experts focused on the training requirements of different professionals involved in IPC activities (14) designed a survey to explore the following issues:

- total number of HAI control figures;
- demographic, organisational and training characteristics of HAI control figures;
- their training needs.

The survey was planned to be carried out in two steps. Firstly, infectious risk managers of each regional public health service were asked to fill a form describing the amount of employees working as HAI control figures within their organization.

The amount of HAI control figures was expressed both as absolute numbers and as Full time equivalents (FTE) which is defined as total hours worked as HAI control figure divided by the total number of compensable hours worked by a healthcare professional.

Then, each HAI control figure was asked to fill in a qualitative questionnaire investigating organizational, training, and demographic aspects. The survey was managed through Microsoft Forms survey tool.

The questionnaire was composed of 4 parts: the first one collected data on gender, age category and institution of employment for each participant. The second section included questions on the service of work, the executive position, and the possible coordination role of each professional; the third part explored the professional and educational background of the respondents, and their job seniority. The last section investigated the training needs of the respondents and consisted of 7 items with a dichotomous closed answer (yes/no). Each item represented a specific domain of competences, and the professional was required to express his/her need for further training in it. The seven domains of the "training needs" section (Table 1) were based on both Italian and international guidelines (15-17).

Data collection was carried out from 12/07/2022 to 26/09/2022. Out of the 15 public healthcare institutions in the Emilia-Romagna Region, only one did not take part in the survey.

3. Statistical analysis

Data analysis was performed using the Software IBM SPSS Statistics Version 28. Categorical variables were summarized by absolute and relative frequencies and compared using Pearson's chi-square test or

Table 1 - IPC training domains as suggested by national and international guidelines (15-17). An acronym and some examples of the domain's essential topics are also reported.

Training domain	Acronym	Examples of essential knowledge and competences
1. Organizational process and care bundles evaluation domain	VAL	Promoting and participating in the evaluation of compliance to the procedures and contributing to the improvement of compliance by monitoring parameters regarding process or outcome.
2. Technical-professional domain	TEC	Isolating and activating special (barrier) precautions, skin disinfecting, patient preoperative preparing, decontaminating and sterilizing medical devices and addingother technical issues.
3. Preparedness for pandemic/ epidemic events domain	PREP	Contributing to the design and implementation of procedures for crisis management in infection control: alerting management, recalling patients, recalling potentially contaminated equipment and supplies, reporting and exchanging with relevant healthcare professionals.
4. Training/research domain	F/R	Collecting and analyzing the relevant documentation for the development of an infection control procedure. Adopting principles and methods of adult education and learning (participatory strategies, including bedside and simulation training). Giving priority IPC domains to be included in training and education programs according to the target audience and context.
5. Organizational-programmatic domain	PO	Planning strategies for the design of healthcare procedures. Setting a program for the implementation and the revision of infection control guidelines and recommendations; disseminating appropriate policies and procedures to clinical departments and helping clinicians in their implementation.
6. Antimicrobial stewardship domain	AMS	Taking part in AMR surveillance programs. Formulating and proposing appropriate indicators concerning the identification of AMR. Participating in periodic audits. Contributing to clinicians' training in antimicrobials use.
7. Communication/ relationships domain	COM	Facilitating the implementation of infection control procedures within the clinical care organization. Identifying barriers to compliance with procedures and involve clinicians.

Table 2 - HAI control figures in the surveyed healthcare institutions, Emilia Romagna region (Northern Italy), 2022.

Healthcare institution	Infectious risk manager		HAI control figures		Total		Number of beds [a]	Total admissions [a]	Human resources / bed ratio	Human resources /10.000 admissions ratio
	n	FTEs	n	FTEs	n	FTEs				
# 1	1	0.75	3	2.25	4	3	706	27,860	1/235	1.08
# 2	1	1	1	1	2	2	331	13,316	1/166	1.5
# 3	1	0.5	15	14.5	16	15	2,976	130,677	1/198	1.15
# 4	1	0.5	8	8	9	8.5	1,512	51,878	1/178	1.64
# 5	1	1	9	9	10	10	1,498	53,392	1/150	1.87
# 6	1	1	7	6	8	7	1,306	57,043	1/187	1.23
# 7	1	1	5	4.83	6	5.83	1,156	51,332	1/198	1.14
# 8	2	2	2	1	4	3	891	38,616	1/297	0.78
# 9	1	0.75	4	3	5	3.75	720	30,718	1/192	1.22
# 10	1	1	3	3	4	4	484	11,805	1/121	3.39
# 11	0	0	2	2	2	2	349	14,401	1/175	1.39
# 12 [b]	0	0.5	1	0.5	1	1	314	15,127	1/314	0.66
# 13 [b,c]	0	0.5	1	0.5	1	1	158	1,321	1/158	N/A
# 14	0	0	1	0.25	1	0.25	42	1,521	1/168	1.64
Total	11	10.5	62	55.83	73	66.33	12,443	499,007	1/188	1.33

[a] Number of beds and total admissions are referred to the year 2021.
Human resources/bed ratio and Human resources /10,000 admissions ratio are calculated based on FTEs.
[b] In institutions #12 and #13, the same person carries out the functions of Infectious risk manager and HAI control figure.
[c] In institution #13, the resources/10,000 admissions ratio has not been reported and is excluded from the calculation of the regional average value, as it is out of scale due to the rehabilitative and long-term care nature of the facility.

Fischer's exact test. Continuous variables were summarized by median and interquartile range (IQR).

Human resources FTEs/ bed ratio and Human resources FTEs/10,000 admissions ratio were calculated both in overall terms and for each individual institution, to provide both an overview of the regional situation and a measure of the variability among units.

Data on acute-care beds and hospital admissions of each institution were obtained from the regional databases.

This paper was written in accordance with Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (18).

Results

1. HAI control figures census and main features

Out of the 15 public healthcare institutions in the Region, 14 provided information on the number and FTEs of the HAI control figures (Table 2).

Overall, the reported total number of HAI control figures was equal to 73 (ranging from 1 to 16 per facility). Among them, 11 were infectious risk managers and 62 were HAI control figures.

The global human resources (HR) /bed ratio was 1/188 (ranging from 1/324 to 1/121), while the overall HR/10,000 admissions ratio was 1.33 (ranging from 0.66 to 3.39).

As reported in Table 3, a total of 66 professionals (90% of the total number of HAI control figures in the Region) took part in the survey. Among them, 15% were males and 85% females and the most represented age category was 51-60 years old (56%).

The professionals worked mainly in the Medical Management or in the Nursing Management Department (44% and 42%, respectively), and most of them were employed in the LHAs (65%) or University Hospitals (30%).

Respondents were nurses (95%) or healthcare assistants (5%) and many did not hold an organizational/ functional position (71%).

Half of the professionals dedicated to HAI control in the region have less than five years of experience in the specific function. More specifically, at the moment of the survey, 28% of professionals had less than 2 years of experience (newly employed professionals recruited after COVID-19 pandemic outbreak), 26% of professionals had 2-5 years of experience, and 34% of professionals had more than 10 years of experience are present in the region.

Considering the educational background, the Pre-

Table 3 - Demographic and professional features of HAI control figures, Emilia-Romagna region, Italy, 2022. Data are expressed as n (%).

	Sample features (n= 66)	
Demographic dimension	***Age category (years)***	
	<30	4 (6%)
	31-40	8 (12%)
	41-50	15 (23%)
	51-60	37 (56%)
	>60	2 (3%)
	Gender	
	Female	56 (85%)
	Male	10 (15%)
Organizational and operational dimension	***Healthcare institution of work***	
	Local Health Authority	43 (65%)
	University Hospital	20 (30%)
	IRCCS [a] or other highly specialised facility	3 (5%)
	Service of work	
	Public Health Department	2 (3%)
	Medical Management	29 (44%)
	Nursing Management	28 (42%)
	Clinical Governance	2 (3%)
	Hospital Hygiene	3 (5%)
	Missing	2 (3%)
	Executive position	
	Organizational position holder	19 (29%)
	Non organizational position holder	47 (71%)
	Coordination function	
	Coordination position holder	19 (29%)
	Non coordination position holder	47 (71%)
Professional and Formative dimension	***Professional qualification***	
	Healthcare assistant	3 (5%)
	Nurse	63 (95%)
	Educational level	
	Practical nursing diploma (before Law 251/00)	25 (38%)
	University degree (3 years training)	25 (38%)
	Master degree (5 years)	16 (24%)
	Any IPC training received	
	Yes	34 (52%)
	No	32 (48%)
	Specific IPC training received	
	"ICI" [b] Regional Course	4 (6%)
	"ISRI" [c] Master	29 (44%)
	Master in Public Health	1 (2%)
	Years of activity as HAI control figure	
	<2	18 (28%)
	2-5	17 (26%)
	6-10	8 (12%)
	>10	22 (34%)

[a] IRCCS - "Scientific Institute for Treatment and Research", Italian acronym
[b] ICI - "Infectious risk control nurse", Italian acronym
[c] ISRI - "Infectious Risk Specialist Nurse", Italian acronym

Table 4 - Professionals specifically trained in IPC in relation to their age category and in relation to their years of specific activity as HAI control figures. Emilia Romagna Region, Italy, 2022.

		Any IPC training received		p
		No (N=31)	Yes (N=34)	
Age category	<30	2 (50%)	2 (50%)	0.264
	31-40	6 (75%)	2 (25%)	
	41-50	4 (27%)	11 (73%)	
	51-60	19 (51%)	18 (49%)	
	>60	1 (50%)	1 (50%)	
Years of activity as HAI control figure	<2	9 (50%)	9 (50%)	0.373
	2-5	7 (41%)	10 (59%)	
	6-10	2 (25%)	6 (75%)	
	>10	13 (59%)	9 (41%)	

Reformation Course (Practical Nursing Diploma) and the University Degree were the most reported. In particular, University education was more frequently reported by younger health workers (less than 50 years of age), while the Diploma was held by more than half of the over-50s. 52% of the sample received specific post-graduated training in the field of HAIs. Among them, only a small proportion attended the Regional course focused on the training of an Infectious risk control nurse (ICI) or the master's degree course in Public Health. On the other hand, 44% of the sample stated that they attended (or were attending) the Master course for "Infectious Risk Specialist Nurse (ISRI)" (Table 3).

No statistically significant difference was observed in the distribution of professionals who received specific training either according to the age of the subjects or according to the years of employment as HAI control figures (Table 4).

2. HAI control figures training needs

Overall, organizational processes and care bundles evaluation domain (VAL), technical-professional domain (TEC) and preparedness for pandemic/epidemic

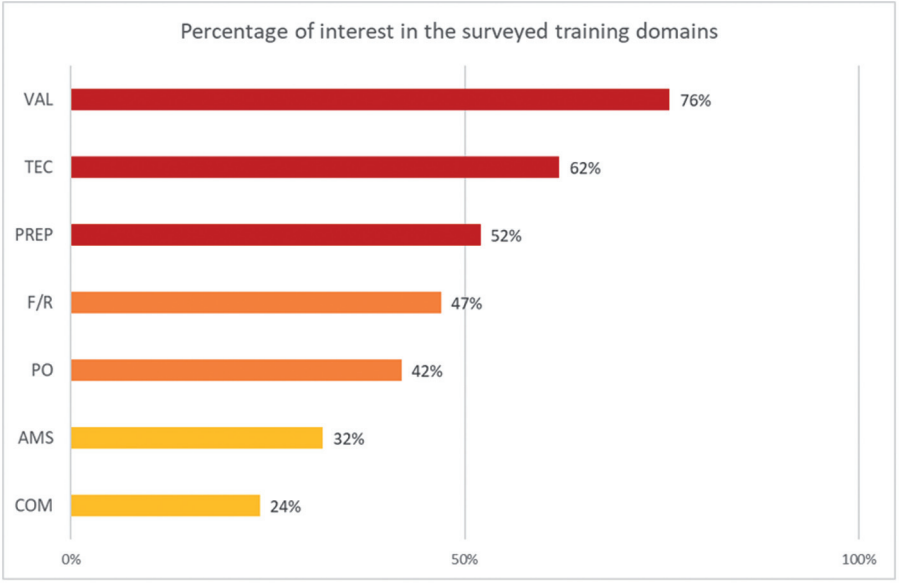


Figure 1 -Training needs of HAI control figures. Emilia Romagna Region, Italy, 2022

[a] VAL (organizational process and care bundles evaluation domain); TEC (technical-professional domain); PREP (preparedness for pandemic/epidemic events domain); F/R (training/research domain); PO (organizational-programmatic domain); AMS (antimicrobial stewardship domain); COM (communication/relationships domain).

Table 5 - Training domains required, by stratifying the sample according to years of HAI control activity and possession or not of specific IPC training. Emilia Romagna region, Italy, 2022

Training field	Whole sample (n=66)	<5 years of HAI control activity	>5 years of HAI control activity	p	Specific IPC training [a] not received	Specific IPC training [a] received	p
TEC	41	22 (55%)	18 (45%)	0.507	28 (68%)	13 (32%)	<0.001
PO	28	14 (50%)	14 (50%)	0.386	9 (32%)	19 (68%)	0.021
VAL	50	28 (57%)	21 (43%)	0.259	24 (48%)	26 (52%)	0.558
AMS	21	12 (57%)	9 (43%)	0.460	9 (43%)	12 (57%)	0.360
PREP	34	19 (57%)	14 (43%)	0.358	18 (53%)	16 (47%)	0.309
COM	16	8 (50%)	8 (50%)	0.472	4 (25%)	12 (75%)	0.029
F/R	31	17 (55%)	14 (45%)	0.538	12 (39%)	19 (61%)	0.106

[a] The specific IPC trainings received referred to "ISRI" Master, Public Health Master, or "ICI" Regional Course. VAL (organizational process and care bundles evaluation domain); TEC (technical-professional domain); PREP (preparedness for pandemic/epidemic events domain); F/R (training/research domain); PO (organizational-programmatic domain); AMS (antimicrobial stewardship domain); COM (communication/relationships domain).

events domain (PREP) were the three most requested training domains, representing the training needs respectively for 76%, 62% and 52% of the investigated professionals (Figure 1).

About a half of the interviewees were interested in the training/research domain (F/R) and in the organizational-programmatic domain (PO). On the other hand, professionals felt to have reached some consolidated knowledge in the domain of antimicrobial stewardship (AMS) and in the communication/relationships domain (COM).

When investigating job seniority across training needs (Table 5), no statistically significant differences emerged.

On the contrary, having received a specific IPC training seemed to affect the choice among the 7 training fields. The technical-professional domain was required predominantly by those who did not undergo specific training in IPC (p<0.001). The organizational-programmatic domain and the communication-relationship domain, on the other hand, were preferred by those who had received IPC training (p=0.021 and p=0.029, respectively).

Discussion and conclusions

Appropriate infectious risk prevention and control practices represent crucial activities for any healthcare system, globally and locally (19). As IPC teams need to have a sufficient number of employees adequately educated and trained, the multi-professional board of experts of the Emilia-Romagna region designed a regional survey to assess the volume, features and training needs of HAI control professionals in Emilia-Romagna.

According to our data, the number of HAI control figures in the region is 73. The regional median HR/bed ratio is 1 HAI control figure every 188 beds, and it appears to be higher than the Italian national ratio (about 1/415) (7)(20), but lower than the European ratio (1/125) (21).

If compared with the ratio of 1 IPC nurse/250 beds proposed in the eighties by CDC (6), the situation in our region respects international standards; still, the 1/250 ratio standard appears outdated. Several recently published national and international documents (7,21) suggest boosting these numbers, reaffirming that 1/250 is a minimum standard that can be considered as a useful starting benchmark in contexts where a proper IPC culture is still missing (22). At European level, standards such as 1 HAI control figure / 100 beds in Acute Care Hospitals and 1 per 150-200 beds in Long Term Care Facilities should be applied (21).

According to our findings, the demographic features of the samples (85% females mainly 51-60 years old) are in line with the nursing sector's main characteristics recorded in other Western countries (23). The distribution of professionals working in the LHAs or University Hospitals (about 2/3 and 1/3, respectively) is representative of the organization of public healthcare institutions in the Emilia-Romagna region (8 LHA and 4 University Hospitals, respectively). The percentages of professionals belonging to the different services (44% for the Medical Directorates, 42% for the Nursing Directorate) and those of professionals holding organizational positions (29%) are comparable with national data (7). Coordination position holders

are, on the contrary, more present in Emilia-Romagna than the national average (7). The prevalence of nurses (95%) over health assistants in the exercise of HAI control functions reflects the respective numbers of the two professional profile holders in our country. Although the figure of the health assistant (a profession dedicated to prevention and health promotion) has existed in Italy for more than a century, the number of health assistants in Italy today is only the 0.1% of the total number of nurses (24). Finally, the educational backgrounds seem to be consistent with the distribution of respondents in different age groups: the academic nursing degree has been established only in 1991,.à therefore the majority of the over-50s hold the previously established diploma.

A remarkable amount of HAI control professionals was actually recruited in our region during the pandemic period (28%); from a quantitative point of view, this number is much higher than the increase in recruitments (approximately +2%) that took place in the Italian National Health Service between 2019 and 2021 (25), and seems to account for a renewed focus on the importance of HAI control activities stimulated by the advent of the COVID-19 pandemic (26).

Additionally, our data indicate that only 52% of our responders received a specific post-degree training in the IPC field. The frequency of professionals who underwent specific training does not show any significant difference based on the subjects' age or years of experience as IPC nurses/health assistants; still, professionals 41-50 years old and professionals who have been in service for 6-10 years seem to have particularly low percentages of specific IPC training. These findings highlight the need to increase the offer both at regional and at local levels of post-degree specialized training activities for HAI control professionals and to monitor this educational process carefully and actively (8,15,16). Further, it is crucial to include Academia in the educational process in order to increase the offer of education in IPC and AMR in academic courses in the medical/veterinary area, and to take them up constantly in post-graduate training programs. (27, 28). Recent evidence suggests (29-31) that adult healthcare training (both early in the recruitment phase and subsequently on a regular schedule) should:

- prioritize blended learning (combining experiential and transmissive approaches)
- individualize teaching and learning strategies;
- focus on peer support initiatives.

As for our sample's learning needs, the most requested training fields are:

- organizational processes and care bundles evaluation domain (VAL);
- technical-professional domain (TEC);
- preparedness for pandemic/epidemic events domain (PREP).

A technical-specialistic education is especially required by those who did not receive any IPC training, while knowledge and competences in VAL and PREP domains lack both in trained and non-trained professionals. This finding confirms that healthcare professionals require practical skills (e.g., process evaluation and epidemic event preparedness) as well as academic and theoretical expertise (32-34).

Educational needs in the organizational-programmatic (PO), training/research (F/R) and communication/relationships domain (COM) are more expressed by IPC professionals who already received a specific training. Until the Seventies, IPC competences used to belong to the skill set of the physician who specialized in Hygiene and Preventive Medicine (19); as a result, many nurses and health assistants eventually got interested in the IPC field after attending specific courses (ICI course, Master degree).

Furthermore, it is important to highlight that, overall, the training in the communication and relationship area is the least requested (24%). (35), professionals seem to struggle recognizing their own communicative inadequacy. We should read this finding keeping in mind that medical education does not historically include soft skills, such as communication.

Finally, Emilia-Romagna Region, which has a great tradition in infectious disease monitoring and surveillance (36-37), paid great attention to the AMR problem over the last decades (38), since most of the antimicrobial resistance (AMR) burden is caused by microorganisms acquired in healthcare as HAIs (39). These training activities seem to be effective as our findings indicate that HAI control professionals in Emilia-Romagna ask very rarely to be further trained in the AS/AMR field.

The results of our survey should be read in light of the study limitations. Firstly, given the lack of a validated questionnaire to investigate the educational needs of HAI control figures, the survey was set up *ad hoc* for the study and not previously validated. Nevertheless to improve its validity, it was designed considering national and international guidelines on HAI control figures training needs (15-17). Secondly, due to the local nature of our investigation and the significant differences existing among regional health services (40), our results could have a relatively poor generalizability in the Italian context. On the other

hand, the very high response rate of the structures (14 out of 15) and of the healthcare professionals (90%) allow our data to be representative of the characteristics and training needs of HAI professionals in Emilia-Romagna.

In conclusion, the number of professionals employed as HAI control figures in the Emilia-Romagna region appeared to be sufficient, however it could be improved to reach high international quality standards. Despite the large number of professionals hired with COVID, our data do not show differences in terms of educational background or training needs between junior and senior professionals. We advocate, therefore, that IPC training should be standardized and continuous, even after academic/specialistic training, and not limited to the moment of hiring. Lastly, the training needs of our professionals appear to be strongly oriented towards managerial skills, preparedness and training and research skills. These findings will be useful to set up future training based on the actual needs of health professional involved in Infection prevention and control.

Acknowledgements

The present work was possible thanks to the infectious risk managers and the Healthcare Associated Infections control figures from the healthcare institutions of the Emilia-Romagna Region, who took part in the survey. We further want to thank our colleagues Diletta Priami, Federica Borsari, Alice Benini, Enrico Ricchizzi, Carlo Gagliotti, Rossella Buttazzi and Maria Luisa Moro from the Emilia-Romagna Region's Health Policies Department for their constant willingness to collaborate with the multidisciplinary group that conducted the survey and the other professionals belonging to the multidisciplinary working group "Training in the prevention and control of antibiotic resistance" (Regional Council Determination Num. 832 of 19/01/2022) - Working Subgroup 2 "Dedicated figures": Edoardo Carretto, Laura Cavazzuti, Sandra Monalti, Sara Tedeschi and Annamaria Valcavi.

We finally want to thank Prof. Elena Righi and Dr. Elena Vecchi from University of Modena and Reggio-Emilia for supervising our work from a methodological point of view.

Riassunto

Prevenzione e controllo del rischio infettivo nelle attività assistenziali: volume e bisogni formativi del personale dedicato nella Regione Emilia-Romagna (Italia)

Background. La formazione del personale per il Governo del Rischio infettivo nelle attività assistenziali è fondamentale nel contesto delle attività Prevenzione e Controllo del Rischio Infettivo; la pandemia COVID-19 ha ulteriormente evidenziato la necessità di garantire un livello di competenze diffuso e stabile nel tempo per il personale dedicato. L obiettivo di questo lavoro è inquadrare il volume e i bisogni formativi del personale specializzato nella prevenzione delle infezioni correlate all'assistenza nelle aziende sanitarie della Regione Emilia-Romagna.

Metodi. La raccolta dati è stata effettuata attraverso un questionario ideato da professionisti appartenenti al Gruppo Regionale "Formazione in tema di prevenzione e controllo

dell'antibioticoresistenza". Le diverse sezioni del questionario indagavano numero, retroterra educativo e professionale e bisogni formativi delle figure dedicate al controllo del rischio infettivo nelle Aziende Sanitarie della Regione Emilia-Romagna.

Risultati. Con 73 figure dedicate al controllo delle Infezioni correlate all'assistenza, la Regione Emilia-Romagna appare in linea rispetto agli standard europei (1 professionista ogni 125 letti). Prevalgono nel gruppo professionisti con formazione di natura infermieristica, di oltre 50 anni e di sesso femminile, mentre i bisogni formativi espressi includono sia aspetti teorici sia aspetti pratici.

Conclusioni. Assistenti sanitari e personale infermieristico rappresentano una risorsa fondamentale per l'implementazione di programmi per il controllo del rischio infettivo oggi nelle strutture sanitarie; si conferma come necessaria la formazione continua, multidisciplinare e mirata di tali professionisti.

References

1. World Health Organization (WHO). Guidelines on core components of infection prevention and control programmes at the national and acute health care facility level [Internet]. Geneva: World Health Organization; 2016. Available from: https://iris.who.int/handle/10665/251730 [Last accessed: 2024 Apr 30].
2. Suetens C, Kärki T, Plachouras D. Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals: 2016-2017. Stockholm: ECDC; 2023.
3. Circular of the Ministry of Health n. 52/1985: Lotta contro le infezioni ospedaliere. (Rome, 1985).
4. Circular of the Ministry of Health n. 88/1988: Lotta contro le infezioni ospedaliere: la sorveglianza (Rome, 1988).
5. Eickhoff TC, Brachman PW, Bennett JV, Brown JF. Surveillance of nosocomial infections in community hospitals. I. Surveillance methods, effectiveness, and initial results. J Infect Dis. 1969 Sep;**120**(3):305-17. doi: 10.1093/infdis/120.3.305.
6. Haley RW, Culver DH, White JW, Morgan WM, Emori TG, Munn VP, et al. The efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals. Am J Epidemiol. 1985 Feb;**121**(2):182–205. doi: 10.1093/oxfordjournals.aje.a113990.
7. Società Scientifica Nazionale Infermieri Specialisti Rischio Infettivo (ANIPIO). Le Infezioni Correlate all'Assistenza (ICA): una pandemia silente. Roma: Ufficio Stampa e Comunicazione Federazione nazionale degli ordini delle professioni infermieristiche; 2021.
8. Deliberazione della Giunta Regionale n.318/2013: Linee di indirizzo alle aziende per la gestione del rischio infettivo: infezioni correlate all'assistenza e uso responsabile di antibiotici. (Emilia-Romagna, Italy; 2013).

9. Deliberazione della Giunta Regionale n.1079/2021: Approvazione delle "Linee di indirizzo regionali per l'implementazione dei programmi di uso razionale degli antibiotici" (Emilia-Romagna, Italy; 2021).
10. Centro di documentazione per la salute, Agenzia sanitaria regionale dell'Emilia-Romagna. Dossier "Infezioni Ospedaliere" – Rapporto tecnico per la definizione di obiettivi e strategie per la salute. Ravenna: Centrostampa Azienda USL di Ravenna; 2001. Available from: https://assr.regione.emilia-romagna.it/pubblicazioni/dossier/doss055 [Last accessed: 2024 Apr 30].
11. ANIPIO - Master universitari di I e II livello. [Internet]. Bologna. Available from: https://www.rischioinfettivo.it/flex/cm/pages/ServeBLOB.php/L/IT/IDPagina/161 [Last accessed: 2024 Feb 3].
12. Serafini A, Palandri L, Kurotschka PK, Giansante C, Sabattini MR, Lavenia MA, et al. The effects of primary care monitoring strategies on COVID-19 related hospitalisation and mortality: a retrospective electronic medical records review in a northern Italian province, the MAGMA study. Eur J Gen Pract. 2023 Dec;**29**(2):2186395. doi: 10.1080/13814788.2023.2186395. Epub 2023 Apr 20.
13. Ferrari E, Palandri L, Lucaccioni L, Talucci G, Passini E, Trevisani V, et al. The Kids Are Alright (?). Infants' Development and COVID-19 Pandemic: A Cross-Sectional Study. Int J Public Health. 2022Jun **20**;67:1604804. doi: 10.3389/ijph.2022.1604804.
14. Determinazione del Direttore Generale Cura della Persona, Salute e Welfare n. 832/2022: Costituzione del gruppo di lavoro multidisciplinare "Formazione in tema di prevenzione e controllo dell'antibioticoresistenza" (Emilia-Romagna, Italy; 2022).
15. World Health Organization (WHO). Core competencies for infection prevention and control professionals. Geneva: World Health Organization; 2020. Available from: https://iris.who.int/bitstream/handle/10665/335821/9789240011656-eng.pdf?sequence=1 [Last accessed: 2024 Apr 30].
16. European Centre for Disease Prevention and Control (ECDC). Core competencies for infection control and hospital hygiene professionals in the European Union. Stockholm: ECDC; 2013. Available from: https://www.ecdc.europa.eu/sites/default/files/media/en/publications/Publications/infection-control-core-competencies.pdf [Last accessed: 2024 Apr 30].
17. Piano Nazionale di Contrasto dell'Antimicrobico-Resistenza (PNCAR) 2017–2020. Roma: Ministero della salute; 2017. Available from: https://www.salute.gov.it/imgs/C_17_pubblicazioni_2660_allegato.pdf [Last accessed: 2024 Apr 30].
18. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. The Lancet. 2007 Oct;**370**(9596):1453–7. doi: 10.1016/S0140-6736(07)61602-X.
19. Tsioutis C, Birgand G, Bathoorn E, Deptula A, Ten Horn L, Castro-Sánchez E, et al. Education and training programmes for infection prevention and control professionals: mapping the current opportunities and local needs in European countries. Antimicrob Resist Infect Control. 2020 Nov;**9**(1):183. doi: 10.1186/s13756-020-00835-1.
20. Posti letto per Regione e disciplina 2020 [Internet]. Roma: Ministero della salute; 2022. Available from: www.dati.salute.gov.it/dataset/posti_letto_per_regione_e_per_disciplina_2020.jsp [Last accessed: 2024 Apr 30].
21. Dickstein Y, Nir-Paz R, Pulcini C, Cookson B, Cookson B, Beovi B, Tacconelli E, et al. Staffing for infectious diseases, clinical microbiology and infection control in hospitals in 2015: results of an ESCMID member survey. Clin Microbiol Infect. 2016 Sep;**22**(9):812.e9-812.e17. doi: 10.1016/j.cmi.2016.06.014. Epub 2016 Jun 29.
22. World Health Organization (WHO). Global report on infection prevention and control. Geneva: World Health Organization; 2022. Available from: https://iris.who.int/bitstream/handle/10665/354489/9789240051164-eng.pdf?sequence=1 [Last accessed: 2024 Apr 30].
23. Mao A, Cheong PL, Van IK, Tam HL. "I am called girl, but that doesn't matter" -perspectives of male nurses regarding gender-related advantages and disadvantages in professional development. BMC Nurs. 2021 Jan 20;**20**(1):24. doi: 10.1186/s12912-021-00539-w.
24. Dettaglio numeriche - Infermiere [Internet]. Roma: Professional Knowledge Empowerment, 2023 [updated 2023 Nov 26]. Available from: https://www.pke.it/html/pag/dettaglio-numeriche.asp?id=30 [Last accessed: 2024 Apr 30].
25. Boldrini R, Di Cesare M, Basili F, Campo C, Moroni R, Romanelli M, et al. Personale delle A.S.L. e degli Istituti di ricovero pubblici ed equiparati Anno 2021. Roma: Ministero della Salute, Direzione Generale della Digitalizzazione, del Sistema Informativo Sanitario e delle Statistica; 2023.
26. Loveday H, Wilson J. Pandemic preparedness and the role of infection prevention and control – how do we learn? J Infect Prev. 2021 Mar;**22**(2):55–7. doi: 10.1177/17571774211001040. Epub 2021 Mar 29.
27. Piano Nazionale di Contrasto dell'Antimicrobico-Resistenza (PNCAR) 2022-2025. Roma: Ministero della salute; 2022. Available from: https://www.epicentro.iss.it/antibiotico-resistenza/pncar-2022 [Last accessed: 2024 Apr 16].
28. Seligardi M, Bassi E, Mongardi M. Esiti sensibili alle cure infermieristiche e staffing: le infezioni correlate all'assistenza. Revisione della letteratura. Assist Inferm Ric. 2017;**36**(4):172-178. doi 10.1702/2817.28483
29. Knowles MS, Formenti L. La formazione degli adulti come autobiografia: il percorso di un educatore tra esperienza e idee. Milano: Raffaello Cortina Editore; 2004. 178 p.
30. Holton EF, Swanson RA, Knowles MS. Quando l'adulto impara: andragogia e sviluppo della persona. 9 ed. Milano: Franco Angeli; 2016. 352 p.
31. Agenzia Sanitaria e Sociale Regionale. Accompagnare le persone nei processi di cambiamento. Linee di indirizzo regionali per progettare e realizzare la formazione continua in sanità. [Internet]. Bologna: Centrostampa Regione Emilia-Romagna; 2017 [Updated 2020 Feb]. Available from: https://assr.regione.emilia-romagna.it/pubblicazioni/

dossier/doss262 [Last accessed: 2024 Apr 30].
32. Palandri L, Urbano T, Pezzuoli C, Miselli F, Caraffi R, Filippini T, et al. The key role of public health in renovating Italian biomedical doctoral programs. Ann Ig. 2024 May-Jun;**36**(3):353-362. doi: 10.7416/ai.2024.2592. Epub 2024 Mar 17.
33. Zingg W, Holmes A, Dettenkofer M, Goetting T, Secci F, Clack L, et al. Hospital organisation, management, and structure for prevention of health-care-associated infection: a systematic review and expert consensus. Lancet Infect Dis. 2015 Feb;**15**(2):212–24. doi: 10.1016/S1473-3099-(14)70854-0. Epub 2014 Nov 11.
34. Brusaferro S, Arnoldo L, Cattani G, Fabbro E, Cookson B, Gallagher R, et al. Harmonizing and supporting infection control training in Europe. J Hosp Infect. 2015 Apr;**89**(4):351–6. doi: 10.1016/j.jhin.2014.12.005. Epub 2015 Jan 7.
35. Sancho-Cantus D, Cubero-Plazas L, Botella Navas M, Castellano-Rioja E, Cañabate Ros M. Importance of Soft Skills in Health Sciences Students and Their Repercussion after the COVID-19 Epidemic: Scoping Review. Int J Environ Res Public Health. 2023 Mar 10;**20**(6):4901. doi: 10.3390/ijerph20064901.
36. Veronesi L, Colucci ME, Capobianco E, Bracchi MT, Zoni R, Palandri L, et al. Immunity status against poliomyelitis in young migrants: a seroprevalence study. Acta Biomed. 2019;**90**(Suppl 9):28–34. doi: 10.23750/abm.v90i9-S.8700.
37. Palandri L, Morgado M, Colucci ME, Affanni P, Zoni R, Mezzetta S, et al. Reorganization of Active Surveillance of Acute Flaccid Paralysis (AFP) in Emilia-Romagna, Italy: a two-step Public Health intervention. Acta Biomed. 2020;**91**(Suppl 3):85–91.
38. Innovazione sanitaria e sociale Regione Emilia-Romagna. Pubblicazioni | Antibioticoresistenza e infezioni correlate all'assistenza [Internet]. Bologna; 2024 [Updated 2024 Jan 14]. Available from: https://assr.regione.emilia-romagna.it/pubblicazioni/documenti-antibioticoresistenza-infezioni [Last accessed: 2024 Apr 30].
39. Addressing the burden of infections and antimicrobial resistance associated with health care. Geneva: OECD/WHO; 2022. Available from: https://www.oecd.org/health/Addressing-burden-of-infections-and-AMR-associated-with-health-care.pdf [Last accessed 2024 Apr 16].
40. Cartabellotta N, Cottafava E, Luceri R, Mosti M. Il regionalismo differenziato in sanità. Bologna: Fondazione GIMBE; 2023. Available from: www.gimbe.org/regionalismo-differenziato-report [Last accessed: 2024 Apr 30].

Corresponding author: Eleonora Ferrari, MD, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, 41125 Modena, Italy
e-mail: eleonora.ferrari149@gmail.com

Ann Ig. Jan-Feb; 37(1): 25-36. doi: 10.7416/ai.2024.2642. Epub 2024 May 23

Prevalence and predictors of hand hygiene compliance in clinical, surgical and intensive care unit wards: results of a second cross-sectional study at the Umberto I teaching hospital of Rome

Mariateresa Ceparano[1], Antonio Covelli[1], Valentina Baccolini[1], Claudia Isonne[1], Antonio Sciurti[1], Giuseppe Migliara[2], Maria De Giusti[1], Carolina Marzuillo[1], Paolo Villari[1]

Keywords: Hand hygiene compliance; public health; patient safety
Parole chiave: Compliance all'igiene mani; sanità pubblica; sicurezza del paziente

Abstract

Introduction. *Hand hygiene is the most cost-effective procedure for the prevention of healthcare-associated infections, but healthcare worker compliance is often insufficient.*
Research design. *The objective of this second cross-sectional study was to quantify hand hygiene compliance among the healthcare workers of a large teaching hospital, to explore associated factors and to compare results to those of the 2021 study.*
Methods. *In 2022, educational sessions were conducted within each hospital department during which hospital healthcare workers received tailored feedback on the hand hygiene compliance registered in the previous year. Then, one month later, direct observations of hand hygiene compliance with five World Health Organization recommendations were collected again by anonymous observers in each ward. Data were grouped by healthcare area (clinical, surgical and intensive care), and three multivariable logistic regression models were built to identify predictors of hand hygiene compliance.*
Results. *Overall, 5,426 observations were collected by 73 observers in three weeks. Hand hygiene compliance was 79.7%, 73.5% and 63.1% in clinical, surgical and intensive care areas, respectively, increasing in clinical wards but decreasing in surgical departments compared to the 2021 study. The multivariable analyses showed that hand hygiene compliance after patient contact was consistently higher than before patient contact, while there was some variability in compliance with other factors across the three areas.*
Conclusion. *The study found suboptimal adherence to good hand hygiene practice, with the lowest rates observed before patient interaction, which, together with the variability recorded across departments, underscores the challenges involved in achieving a uniform level of compliance. Hence, additional training is essential to raise awareness among healthcare workers, while repeating this survey over time will also be crucial, so that hand hygiene compliance can be monitored and any major issue identified.*

[1] *Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy*
[2] *Department of Life Sciences, Health and Healthcare Professions, Link Campus University, Rome, Italy*

Annali di Igiene : Medicina Preventiva e di Comunità (Ann Ig)
ISSN (print) 1120-9135 ISSN (online) 3035-5559

https://www.annali-igiene.it

Introduction

The prevention and control of healthcare-associated infections (HAIs) is fundamental to the maintenance of patient safety and the quality of care in hospitals (1,2). Because most nosocomial infections are often spread through direct contact, particularly on the hands of healthcare workers (HCWs), targeted efforts to reduce the frequency and burden of these infections have focused on improving hand hygiene (HH) practice (3,4). Indeed, handwashing is considered the simplest, cheapest and least expensive measure to minimize the spread of pathogens and thus control and prevent HAIs (5,6). Although adherence to good HH practice has the potential to prevent up to 50% of HAIs (7) and reduce the cross-transmission of antibiotic-resistant pathogens (8,9), non-adherence is still a major issue in hospital care. Several studies document that HH remains insufficient, with compliance levels as low as 9% reported in low-income countries, while compliance levels rarely exceed 70% even in high-income countries (10).

Within this context, research suggests that the HH monitoring systems can produce measurable improvements in HH adherence among HCWs, with a consequent lower incidence of HAIs (11–13). Furthermore, HH monitoring allows us to understand the determinants of HH compliance, which may differ depending on the settings and the role of healthcare personnel (14). For instance, a recent systematic review reported that HH compliance was lower in ICUs (30–40%) than in other departments (50-60%), lower among physicians (32%) than nurses (48%), and before (21%) rather than after (47%) touching a patient, with an overall median compliance rate of 40% (15). Numerous factors may contribute to poor compliance, including physical infrastructure and institutional support, availability of materials and human resources, and professional behaviour (16,17).

Thus, it is essential to monitor the reasons for HH non-adherence in healthcare institutions to allow strategies for the improvement of HH compliance among hospital staff to be formulated (18). In Italy, several studies have monitored adherence to HH guidelines in different healthcare settings, reporting HH compliance rates among HCWs usually between 60% and 70% (19–21), values slightly lower than the 71.9% registered at the Umberto I teaching hospital of Rome in 2021 (22). In this study, we now report the results of a second cross-sectional study conducted in the same hospital using the same methodology a year after the previous one, in 2022, with the aim of estimating HH compliance again, analysing its determinants and highlighting any changes (23).

Methods

Study design and observation strategy

This study included two phases: a first phase during which feedback sessions were conducted with hospital HCWs, and a second phase of three weeks to elaborate data collection on HH compliance. Specifically, in the first phase, ten educational sessions were carried out (one within each hospital department) between September and October 2022, during which the hospital staff attended a lecture on the definition, impact and burden of HAIs, and were presented with both the methodology and the results of the data collected during the previous study (22) on hospital and ward HH compliance.

The second phase was conducted between November 28th and December 19th, 2022, as part of the annual plan for HAIs at the Umberto I teaching hospital of Rome. As previously, two HCWs on each hospital ward served as anonymous observers of HCWs' compliance with HH guidelines. They were recruited from those who had been previously identified by formal communication with the hospital management and who had taken part in the previous study (22). Each participant was asked to carry out up to 100 direct observations of HH compliance (i.e., 200 observations per ward) through the completion of a multiple-choice paper checklist, designed according to World Health Organization (WHO) guidelines (3): this checklist was the same as that used for the 2021 data collection and is described in (22). Briefly, it consisted of two sections (the first to determine information on the observer, and the second relating to the observations), with a total of 11 items. The observations covered the five moments where appropriate HH is critical according to WHO guidelines: before touching a patient (indication I), before a clean/aseptic procedure (indication II), after body fluid exposure (indication III), after touching a patient (indication IV) and after touching a patient's surroundings (indication V) (3). The study protocol was approved by the Ethics Committee of the hospital (reference number: 4707/2021).

Statistical analysis

Data collected were analysed according to the type of care delivered. Specifically, taking into

account the potential influence of the intensity and complexity of care on HH opportunities (23), and considering the past research that showed differences in adherence between ward types (24,25), the analysis was conducted separately for each ward category, i.e., distinguishing between clinical, intensive care and surgical areas. Mean and standard deviation (SD) were calculated for continuous variables, while proportions were used for dichotomous and categorical variables. HH compliance – overall and stratified by factors of interest – was calculated as the proportion of recorded opportunities for HH in which HCWs followed the guidelines (i.e., the sum of the number of HH actions performed using soap and water plus those performed using an alcohol-based formulation against the total number of opportunities recorded). For each area, changes in HH compliance between the 2021 and 2022 studies were tested using the Z-test for proportions and expressed as percentage difference, overall and by stratified analyses. Then, three multivariable logistic regression models were built, one for each area, to identify factors independently associated with overall HH compliance. The following variables were included in the models, based on expert knowledge (26): HH indication (I to V), observed HCW gender, observed HCW job category, observed HCW type (internal or external), work shift, day of the week, observer gender, and observer job category. Adjusted odds ratios (aORs) and their 95% confidence intervals (CIs) were estimated. The Hosmer-Lemeshow test was used to evaluate the goodness of fit of the models. A two-tailed p-value less than 0.05 was considered statistically significant. Statistical analyses were performed with Stata version 17.0 (StataCorp LLC, 4905 Lakeway Drive, College Station, Texas, USA).

Results

Key characteristics of observers and observations by area

Of 48 wards included in the study, 56.2% belonged to the clinical area, 25.0% to the surgical area and 18.8% to the intensive care area (Table 1). Observations were carried out by 52 observers in the clinical, 12 in the surgical and 9 in the intensive care areas, with an average of 1.7 observers per ward. In each area, the majority of the observations were performed by female staff and nurses. A total of 5426 observations were collected, 3008 in the clinical area, 1602 in the surgical area and 816 in the intensive care area, with the highest number of observations per ward in intensive care units (approximately 134).

Regarding HH indications, those before and after touching a patient were the most observed (for indication I: 40.7% in clinical, 36.6% in surgical and 46.1% in intensive care wards; and for indication III: 28.8% in clinical, 30.7% in surgical and 25.5% in intensive care wards) (Supplementary Table 1). Hospital staff were more likely to use an alcohol-based formulation to perform HH in clinical wards (41.5%) and intensive care units (38.0%), whereas in surgical areas they used soap and water more frequently (38.6%). Gloves were worn without performing HH in 12-15% of cases across all areas, whereas no action (i.e., neither HH nor glove use) was recorded mostly in intensive care units (21.3%), followed by surgical (11.4%) and clinical (7.7%) wards. In all the three areas, physicians and nurses were the subject of approximately three-quarters of the observations, followed by healthcare assistants (16.4% and 13.4% among clinical and surgical staff, respectively) and others in intensive areas (5.0%). The HCWs observed were mostly females (from 58.1% in intensive care units to 62.0% in clinical areas) and internal to the ward (from 81.9% to 87.4% in surgical and clinical areas, respectively). In all areas, observations were mostly collected during weekdays (80-90%) and morning shifts (around 60%) by female HCWs (approximately 75%), who were more often nurses in surgical and intensive care areas (52.4% and 58.6%, respectively), but were more likely to be physicians in clinical wards (51.4%).

HH compliance and comparison to the previous study by area

In the clinical area, overall HH compliance was 79.7% (Table 2). Regarding HH recommendations, indications III (after touching a patient) and IV (after body fluid exposure) were found to have the highest HH compliance: 90.6% and 96.6%, respectively. Midwives were the most compliant among HCWs (93.5%), followed by nurses (82.2%), physicians (79.5%) and healthcare assistants (77.7%). Moreover, HH compliance was higher for female staff (81.5%) and internal staff (80.8%), and during the afternoon work shift (80.8%) and weekdays (81.6%). In comparison with the 2021 study, we found that there was a significant 17.0% increase in HH compliance ($p<0.001$) in the clinical area. Moreover, indication I, "before touching a patient", showed the greatest increase (+46.2%, $p<0.001$) among the five WHO recommendations, going from 50.0% to 73.1%. In general, there was a significant improvement of more

Table 1 - Key characteristics of observers and observations by area. Results are expressed as numbers (percentage) or mean ± standard deviation.

	Clinical area	Surgical area	Intensive care area
Wards	27	12	9
Observers	52	22	15
Observers per ward, mean ± SD	1.7 ± 0.6	1.8 ± 0.4	1.7 ± 0.5
Observer gender, n (%)			
Male	16 (30.8)	7 (28.0)	3 (20.0)
Female	36 (69.2)	18 (72.0)	12 (80.0)
Observer role, n (%)			
Physician	24 (46.2)	11 (44.0)	6 (40.0)
Nurse	27 (51.9)	12 (48.0)	9 (60.0)
Midwife	0 (0.0)	1 (4.0)	0 (0.0)
Healthcare assistant	1 (1.9)	1 (4.0)	0 (0.0)
Observations	3008	1602	816
Observations per ward, mean ± SD	111.4 ± 63.3	90.7 ± 56.8	133.5 ± 53.8

SD: standard deviation

than 15% in most of the variables analyzed, except for indication V, which showed a decrease of 11.3% (p=0.006) (Table 2).

In the surgical area, overall HH compliance was 73.5% (Table 2). Regarding the specific recommendations, indication III ("after touching a patient") and IV ("after body fluid exposure") were again found to have the highest HH compliance (88.4% and 89.1%, respectively). Nurses were the most compliant among HCWs (76.7%), followed by healthcare assistants (75.6%), physicians (73.0%) and midwives (69.2%). Similarly to the clinical area, HH compliance was higher for females (75.4%) and internal staff (75.0%) and during weekdays (73.7%), while on the contrary morning work shifts showed the highest compliance (74.2%). Compared to 2021, in 2022 there was a significant reduction in overall compliance (-5.6%, p=0.007), especially in indications I (-12.1%, p=0.006), IV (-8.0%, p=0.004) and V (-19.0%, p=0.005), while for indication II there was an increase of 18.4% (p=0.022). HH compliance during night shifts showed the largest decrease (-21.2%, p=0.006), but a decrease was also found in the compliance rates of physicians (-9.1%, p=0.003), male staff (-7.3%, p=0.040) and during weekend days or holidays (-19.7%, p<0.001) (Table 2).

Finally, in the intensive care area, the overall HH compliance was 63.1% (Table 2). Indications II and IV showed the highest HH compliance rates (73.5% and 83.6%, respectively). Nurses were the most compliant HCW category (69.3%), while the other job categories had HH compliance rates lower than 60%. Like other areas, female staff were the most compliant (70.3%), along with internal staff (67.1%), while higher compliance was reached during night shifts (67.9%) and weekend days or holidays. In 2022 there were no significant changes compared to 2021 in total HH compliance (p=0.185), as well as in the various indications. By contrast, a significant reduction in HH compliance from 2021 to 2022 was found among nurses (-12.2%, p=0.005), male staff (-23.4%, p<0.001) and during night shifts (-30.4%, p<0.001) (Table 2).

Predictors of hand hygiene compliance by area

The multivariable analysis (Table 3, Model 1) showed that, in clinical areas, compared to physicians, being a midwife was associated with higher HH compliance (aOR=4.7, 95% CI: 1.2-18.8). Likewise, indications III and IV were associated with a higher likelihood of HH compliance compared to indication I (aOR: 3.3, 95% CI: 1.9-5.5; aOR: 14.7, 95% CI: 5.4-40.2, respectively). The observer's gender and role, the gender and staff type of the HCWs observed, day type and work shift showed no association with the outcome.

Conversely, in surgical areas (Table 3, Model 2), being a midwife was associated with a lower HH compliance (aOR=0.3, 95% CI: 0.1-0.8), while indications III and IV and being female were positively associated with the outcome (aOR=5.7,

Table 2 - Hand hygiene (HH) compliance - 2022 versus 2021

	Clinical area				Surgical area				Intensive care area			
	2021 n/N (%)	2022 n/N (%)	Δ	*p-value*	2021 n/N (%)	2022 n/N (%)	Δ	*p-value*	2021 n/N (%)	2022 n/N (%)	Δ	*p-value*
Overall HH compliance	1522/2235 (68.1)	2398/3008 (79.7)	+ 17.0	<0.001	1006/1292 (77.9)	1178/1602 (73.5)	- 5.6	0.007	369/554 (66.6)	515/816 (63.1)	- 5.3	0.185
HH Indication												
Indication I	407/814 (50.0)	895/1225 (73.1)	+ 46.2	<0.001	318/469 (67.8)	350/587 (59.6)	- 12.1	0.006	139/235 (59.2)	195/376 (51.9)	- 12.3	0.078
Indication II	106/138 (76.8)	152/222 (68.5)	- 10.8	0.088	106/168 (63.1)	124/166 (74.7)	+ 18.4	0.022	40/53 (75.5)	61/83 (73.5)	- 2.6	0.797
Indication III	502/656 (76.5)	786/868 (90.6)	+ 18.4	<0.001	286/316 (90.5)	435/492 (88.4)	- 2.3	0.349	121/166 (72.9)	152/208 (73.1)	+ 0.3	0.968
Indication IV	178/201 (88.6)	308/318 (96.9)	+ 9.4	<0.001	183/189 (96.8)	164/184 (89.1)	- 8.0	0.004	38/46 (82.6)	61/73 (83.6)	+ 1.2	0.892
Indication V	329/426 (77.2)	257/375(68.5)	- 11.3	0.006	113/150 (75.3)	105/173 (61.0)	- 19.0	0.005	31/54 (57.4)	46/76 (60.5)	+ 5.4	0.721
Observed HCW role												
Physician	629/927 (67.9)	843/1061 (79.5)	+ 17.1	<0.001	469/584 (80.3)	422/578 (73.0)	- 9.1	0.003	118/201 (58.7)	157/266 (59.0)	+ 0.5	0.945
Nurse	526/755 (69.7)	977/1188 (82.2)	+ 17.9	<0.001	330/420 (78.6)	427/557 (76.7)	- 2.4	0.479	206/261 (78.9)	302/436 (69.3)	- 12.2	0.005
Midwife	2/2 (100.0)	29/31 (93.5)	- 6.5	0.711	20/22 (90.6)	18/26 (69.2)	- 23.9	0.065	NA	1/2 (50.0)	NA	NA
Healthcare assistant	193/310 (62.3)	379/488 (77.7)	+ 24.7	<0.001	91/128 (71.1)	158/209 (75.6)	+ 6.3	0.361	8/29 (27.6)	12/32 (37.8)	+ 37.0	0.410
Observed HCW gender												
Male	586/920 (64.0)	873/1139 (76.7)	+ 19.8	<0.001	352/461 (76.4)	453/640 (70.8)	- 7.3	0.040	121/172 (70.4)	182/338 (53.9)	- 23.4	<0.001
Female	914/1287 (71.0)	1515/1858 (81.5)	+ 14.8	<0.001	654/829 (78.9)	722/958 (75.4)	- 4.4	0.077	247/381 (64.8)	329/468 (70.3)	+ 8.5	0.090
Observed ward staff												
Internal	1416/2065 (68.6)	2068/2561 (80.8)	+ 17.8	<0.001	918/1174 (78.2)	964/1286 (75.0)	- 4.1	0.059	326/466 (70.0)	431/642 (67.1)	- 4.1	0.319
External	106/170 (62.4)	265/369 (71.8)	+ 15.1	0.028	88/118 (74.6)	190/285 (66.7)	- 10.6	0.118	43/88 (48.9)	52/125 (41.6)	- 14.9	0.294
Day type												
Weekday	1291/1911 (67.6)	2079/2548 (81.6)	+ 20.7	<0.001	812/1068 (76.0)	1052/1428 (73.7)	- 3.0	0.180	344/524 (65.6)	419/684 (61.2)	- 6.7	0.117
Weekend day / holidays	231/324 (71.3)	232/295 (78.6)	+ 10.2	0.035	194/224 (86.6)	105/151 (69.5)	- 19.7	<0.001	25/30 (83.3)	96/132 (72.7)	- 12.7	0.228
Work shift												
Morning	844/1274 (66.3)	1479/1865 (79.3)	+ 19.6	<0.001	505/657 (76.9)	713/961 (74.2)	- 3.5	0.221	247/381 (64.9)	299/479 (62.4)	- 3.9	0.466
Afternoon	566/806 (70.2)	798/988 (80.8)	+ 15.1	<0.001	413/526 (78.5)	399/541 (73.8)	- 6.0	0.068	81/130 (62.3)	173/276 (62.7)	+ 0.6	0.942
Night	105/142 (74.0)	114/147 (77.6)	+ 4.9	0.474	79/95 (83.2)	61/93 (65.6)	- 21.2	0.006	39/40 (97.5)	38/56 (67.9)	- 30.4	<0.001

Indication I: before touching a patient; Indication II: before clean/aseptic procedure; Indication III: after touching a patient; Indication IV after body fluid exposure; Indication V: after touching a patient's surroundings.
HCW: Healthcare workers; NA: not assessable; Δ: percentage difference between 2022 and 2021 study.

95% CI: 2.5-13.2; aOR=6.5, 95% CI: 2.9-14.4 and aOR= 1.4, 95% CI: 1.1-1.7, respectively). Regarding the observer's job category, compared to physicians, both nurses and midwives were more likely to report compliant observations (aOR=2.9, 95% CI: 1.3-6.3; and aOR=7.7, 95% CI: 4.6-12.9, respectively), while the observer's gender, the HCW staff observed, day type and work shift did not affect the likelihood of the outcome.

Lastly, the multivariable model for intensive care areas (Table 3, Model 3) showed a higher HH compliance for female staff (aOR=1.9, 95% CI: 1.2-2.9) and during weekends or holidays (aOR=1.8, 95% CI: 1.0-3.1), while external staff showed a lower compliance than internal staff (aOR=0.4, 95% CI: 0.2-0.8). Compared to indication I, indication III (aOR=2.9, 95% CI: 1.9-4.5), indication IV (aOR=4.7, 95% CI: 1.6-13.9) and indication V (aOR=2.5, 95% CI: 1.2-5.2) were all associated with higher HH compliance. The observer's gender and job category, the job category of the staff observed and work shift showed no association with the outcome.

Discussion

In this second cross-sectional study, we found HH compliance rates of 79.7%, 73.5%, and 63.1% in the clinical, surgical and intensive care wards, respectively, values that align with the literature in underlining the difficulty, even in developed countries, of achieving the 80% adherence rate recommended by the WHO (27). Notably, albeit slightly surpassing the literature's reported rate of 59.6% (28), intensive care units exhibited the least satisfactory compliance level (28). Potential explanations for this result may include factors such as an elevated workload and a high patient-to-nurse ratio, which make it difficult for HCWs to uphold proper HH practices (29). However, these findings are of particular concern, especially considering the increase in HAIs observed during the COVID-19 pandemic (30,31), and they advocate a strengthening of hygiene practices in these wards, which, together with other measures such as actively monitoring HAIs (2), will contribute to a reduction in infection rates and to an improvement in the quality of care.

Compliance with good HH practice was not uniform across the five moments defined by the WHO. Indeed, multivariable analyses consistently showed that HCWs were more compliant after touching a patient (indication IV) and after body fluid exposure (indication III), suggesting that these actions were more likely to be directed at safeguarding themselves rather than patients, as already shown (4). By contrast, the lowest levels of compliance were recorded before patient contact (indication I), which was as low as 52% in intensive care units. Likewise, the compliance rates before aseptic procedures (indication II) did not exceed 75.0% in any area, findings that together are particularly worrisome, considering they are those that require the utmost caution to prevent cross-contamination (32). Regarding the characteristics of the HCWs observed, no job category was associated with higher HH compliance, apart from midwives, who - despite the limited number of observations - were found to be more compliant than physicians in clinical wards. However, midwives were less compliant than physicians in surgical departments, perhaps due to the more intense workload that midwives experience in the surgical area, potentially impacting the quality of care (33); nevertheless, the result is difficult to interpret. It is clear that our results do not align with the existing literature, which usually reports higher adherence rates in nurses than physicians (34,35), at least before the COVID-19 emergency. Indeed, as previously hypothesized (36), the COVID-19 pandemic may have made HH compliance rates more similar across HCW job categories, in particular increasing the awareness of physicians of correct HH practice (37). Interestingly, and in accordance with previous research demonstrating that females in the general population show a higher level of knowledge and a more appropriate HH behaviour than males (38), our findings also suggest that female staff, particularly from surgical and intensive care wards, are more likely to pay attention to good HH practice. Again, in line with previous research (19), we found that in intensive care areas the external staff had a lower HH compliance than internal HCWs, a factor that may be explained by a lower psychological commitment (39) or awareness of the extreme importance of performing HH practices in critically ill patients (40).

Notably, HH compliance did not seem to change in relation to the day and shift of observation in any area except for intensive care units, in which HCWs were found to perform HH routines more frequently during weekend days or holidays, indicating a potentially positive effect of reduced workload and fewer external consultations, which allowed more time for HH procedures (41). In addition, across all three areas there was no association between HH compliance and gender or job category of the observers with the sole exception of surgical wards, where nurses and

Table 3 - Multivariable logistic regression model for compliance with hand-hygiene (HH) procedures by area

	Model 1 (Clinical area) HH compliance		**Model 2** (Surgical area) HH compliance		**Model 3** (Intensive care area) HH compliance	
	aOR (95% CI)	p-value	aOR (95% CI)	p-value	aOR (95% CI)	p-value
Indication						
Indication I	Ref.		Ref.		Ref.	
Indication II	0.7 (0.4-1.4)	0.354	1.6 (0.9-2.8)	0.117	2.3 (1.0-5.4)	0.051
Indication III	3.3 (1.9-5.5)	<0.001	5.7 (2.5-13.2)	<0.001	2.9 (1.9-4.5)	<0.001
Indication IV	14.7 (5.4-40.2)	<0.001	6.5 (2.9-14.4)	<0.001	4.7 (1.6-13.9)	0.005
Indication V	0.7 (0.4-1.3)	0.251	1.2 (0.6-2.4)	0.656	2.5 (1.2-5.2)	0.019
Observed HCW role						
Physician	Ref.		Ref.		Ref.	
Nurse	0.9 (0.7-1.3)	0.769	1.0 (0.7-1.4)	0.884	1.1 (0.7-1.9)	0.688
Midwife	4.7 (1.2-18.8)	0.028	0.3 (0.1-0.8)	0.010	1.5 (0.2-15.9)	0.714
Healthcare assistant	0.7 (0.4-1.0)	0.060	0.8 (0.4-1.4)	0.408	0.5 (0.2-1.2)	0.138
Student	2.0 (0.5-8.0)	0.314	1.2 (0.5-3.1)	0.658	3.2 (0.5-21.5)	0.232
Relative	0.6 (0.2-2.2)	0.452	0.2 (0.0-3.3)	0.249	0.6 (0.2-1.6)	0.320
Other	0.8 (0.3-2.0)	0.641	0.7 (0.2-2.5)	0.598	0.6 (0.2-2.6)	0.541
Observed HCW gender					-	-
Male	Ref.		Ref.		Ref.	
Female	1.1 (0.9-1.5)	0.278	1.4 (1.1-1.7)	0.002	1.9 (1.2-2.9)	0.007
Observed ward staff						
Internal	Ref.		Ref.		Ref.	
External	0.6 (0.3-1.2)	0.130	0.6 (0.3-1.5)	0.294	0.4 (0.2-0.8)	0.011
Day						
Weekday	Ref.		Ref.		Ref.	
Weekend day/Holiday	0.9 (0.4-1.7)	0.708	0.9 (0.5-1.7)	0.866	1.8 (1.0-3.1)	0.037
Work shift						
Morning	Ref.		Ref.		Ref.	
Afternoon	1.0 (0.7-1.5)	0.836	0.8 (0.6-1.2)	0.308	1.0 (0.5-2.0)	0.969
Night	1.0 (0.6-1.7)	0.997	0.4 (0.2-1.1)	0.084	1.0 (0.5-1.9)	0.930
Observer gender						
Male	Ref.		Ref.		Ref.	
Female	2.0 (0.8-5.3)	0.137	0.5 (0.3-1.0)	0.063	1.6 (0.7-3.3)	0.240
Observer role						
Physician	Ref.		Ref.		Ref.	
Nurse	1.0 (0.5-2.3)	0.967	2.9 (1.3-6.3)	0.007	1.1 (0.5-2.4)	0.851
Midwives	-	-	7.7 (4.6-12.9)	<0.001	-	-
Healthcare assistant	-	-	1.1 (0.7-1.7)	0.787	-	-

Indication I: before touching a patient; Indication II: before clean/aseptic procedure; Indication III: after touching a patient; Indication IV: after body fluid exposure; Indication V: after touching a patient's surroundings; Ref.: Reference

midwives more frequently observed good HH practice. This result suggests some inter-observer variability in the surgical area.

In comparison to the previous study, while we witnessed an increase in observer participation compared to 2021, we did not collect the expected 200 observations per ward, meaning that additional training is needed to improve the commitment of observers to the study. However, we found a significant improvement in overall HH rates in clinical wards. Conversely, we recorded a decline in overall HH compliance (5.6%) in surgical departments, that may be linked to the rising workload in these units following the pandemic (42) and the resumption of surgical worklists (29). Lastly, our study allowed us to highlight the indications for which there was a decrease in compliance compared to the previous year, namely the indications "before touching a patient" and "after touching a patient's surroundings". These results underscore how important it is to structure specific training interventions, both to return feedback from the surveys conducted and to improve behaviours that recorded lower HH compliance by diversifying them for different areas (43–45). To effectively control infections in healthcare settings, it's crucial to provide detailed and ongoing training along with continuous guidance (46). Solid leadership and a flexible organizational culture are necessary to overcome resistance to change (47). Given that patients have diverse medical conditions, adopting personalized infection control strategies is vital rather than a standardized approach (46). This requires a deep understanding of diseases and their modes of transmission. Investing in ongoing training and education for healthcare workers is essential to ensure effective infection control.

However, caution is strongly warranted in interpreting the changes in compliance rates between 2021 and 2022, due to both the cross-sectional nature of the study and the methodology used to observe HH compliance (22).

This study has some strengths and limitations. The major strength is that we adopted a consolidated methodology to quantify HH compliance one year after the previous study. Furthermore, we were able to closely examine predictors of HH compliance across three distinct types of wards, accounting for the different settings, and to highlight any differences with the previous year. The main limitation of this study is that, like most HH observational studies, both observer bias and inter-observer variability may have affected the accuracy of our results. For example, internal observers may have been more inclined to rate their co-workers differently than external observers would (43). In addition, despite direct observation being considered the "gold standard" method of monitoring HH compliance, our results may suffer from the observer effect, whereby HCWs may improve their practice under observation (14). For this reason, we recruited the same observers as the previous study, who had been trained to maintain anonymity, so that the HCWs did not know the identities of the observers and which practices were recorded. While this should reduce these biases, annual training is still needed to make HH observations more consistent across observers and to promote their commitment to the study.

Conclusion

This second study found suboptimal HH compliance rates in all healthcare areas, with values that were lower before approaching patients than after patient contact. Some variability across department types was registered for other predictors, underlining the difficulty in achieving uniform HH compliance rates. For these reasons, despite recording some improvements compared to the previous year, especially in relation to observers' participation, additional training is needed to increase HCW awareness of the topic and to improve the observation strategy of observers. Finally, it will be crucial to repeat this survey regularly, so as to enable monitoring of HH compliance and allow the identification of any major issues.

Acknowledgments: We thank the residents of the Residency School of Hygiene and Preventive Medicine, Department of Public Health and Infectious Diseases, Sapienza University of Rome, 00185 Rome, Italy for their cooperation.

Riassunto

Prevalenza e fattori predittivi della compliance all'igiene delle mani nei reparti medici, chirurgici e di terapia intensiva: risultati del secondo studio trasversale presso il Policlinico Umberto I di Roma

Introduzione. L'igiene delle mani è la procedura più efficace dal punto di vista dei costi per prevenire le infezioni correlate all'assistenza, ma la compliance degli operatori sanitari è spesso insufficiente.

Disegno dello studio. L'obiettivo di questo secondo studio trasversale è stato quello di quantificare la compliance all'igiene delle mani tra gli operatori sanitari di un grande ospedale universitario,

esplorare i fattori associati e confrontare i risultati con quelli di uno studio del 2021.

Metodi. Nel 2022 sono state tenuti incontri educativi con ogni reparto dell'ospedale, durante i quali gli operatori sanitari hanno ricevuto un feedback personalizzato sulla compliance all' igiene delle mani registrata nell'anno precedente. Poi, un mese dopo, sono state raccolte osservazioni dirette della compliance dell'igiene delle mani nei cinque momenti dell'Organizzazione Mondiale della Sanità da parte di osservatori anonimi in ogni reparto. I dati sono stati raggruppati per area sanitaria (medica, chirurgica e terapia intensiva) e sono stati costruiti tre modelli di regressione logistica multivariabile per identificare i fattori predittivi della compliance all'igiene delle mani.

Risultati. Complessivamente, sono state raccolte 5.426 osservazioni da 73 osservatori in tre settimane. La compliance all'igiene delle mani è stata del 79,7%, 73,5% e 63,1% rispettivamente nell'area medica, chirurgica e di terapia intensiva, aumentando nei reparti medici e diminuendo in quelli chirurgici rispetto allo studio del 2021. Le analisi multivariabili hanno dimostrato che le indicazioni all'igiene delle mani dopo il contatto con il paziente erano associate a una maggiore compliance rispetto alle indicazioni prima del contatto con il paziente, mentre c'era una certa variabilità tra le aree in alcuni degli altri fattori.

Conclusioni. Lo studio ha rilevato un'aderenza non ottimale alle pratiche dell'igiene delle mani con bassi tassi di compliance osservati prima dell'interazione con il paziente e che, insieme alla variabilità registrata tra i vari reparti, sottolinea le difficoltà nel raggiungere un livello uniforme di conformità. Pertanto, è essenziale una formazione aggiuntiva per sensibilizzare gli operatori sanitari, mentre la ripetizione dell'indagine nel tempo è fondamentale per monitorare la conformità all'igiene delle mani ed identificare eventuali problemi.

References

1. Yokoe DS, Classen D. Introduction : Improving Patient Safety Through Infection Control: A New Healthcare Imperative . Infect Control Hosp Epidemiol. 2008 Oct;**29**(S1):S3–11. doi: 10.1086/591063. PMID: 18840086.
2. Migliara G, Di Paolo C, Barbato D, Baccolini V, Salerno C, Nardi A, et al. Multimodal surveillance of healthcare associated infections in an intensive care unit of a large teaching hospital. Ann Ig. 2019;**31**(5):399–413. doi: 10.7416/ai.2019.2302. PMID: 31304521.
3. World Health Organization. Patient Safety. WHO guidelines on hand hygiene in health care : first global patient safety challenge clean care is safer care. World Health Organization; 2009. Available from: https://www3.paho.org/hq/dmdocuments/2010/WHO-Guidelines-on-hand-hygiene.pdf [Last accessed: 2024 Mar 12].
4. Allegranzi B, Gayet-Ageron A, Damani N, Bengaly L, McLaws ML, Moro ML, et al. Global implementation of WHO's multimodal strategy for improvement of hand hygiene: A quasi-experimental study. Lancet Infect Dis. 2013 Oct;**13**(10):843–51. doi: 10.1016/S1473-3099(13)70163-4. Epub 2013 Aug 23. PMID: 23972825.
5. Boyce JM, Larson EL, Pittet D. Hand hygiene must be enabled and promoted. Am J Infect Control. 2012;**40**(4 SUPPL.). doi: 10.1016/j.ajic.2012.03.001. PMID: 22546270.
6. Al-Tawfiq JA, Pittet D. Improving Hand Hygiene Compliance in Healthcare Settings Using Behavior Change Theories: Reflections. Teach Learn Med. 2013 Oct;**25**(4):374–82. doi: 10.1080/10401334.2013.827575. PMID: 24112209.
7. World Health Organization (WHO). Report on the Burden of Endemic Health Care-Associated Infection Worldwide Clean Care is Safer Care [Internet]. 2011. Available from: www.who.int [Last accessed: 2024 Mar 12].
8. Grayson ML, Jarvie LJ, Martin R, Johnson PDR, Jodoin ME, Mcmullan C, et al. Significant reductions in methicillin-resistant Staphylococcus aureus bacteraemia and clinical isolates associated with a multisite, hand hygiene culture-change program and subsequent successful statewide roll-out. Med J Aust [Internet]. 2008;**188**(2). Available from: www.mja.com.au [Last accessed: 2024 Mar 12].
9. Rosenthal VD, Guzman S, Safdar N. Reduction in nosocomial infection with improved hand hygiene in intensive care units of a tertiary care hospital in Argentina. Am J Infect Control. 2005 Sep;**33**(7):392–7. doi: 10.1016/j.ajic.2004.08.009. PMID: 16153485.
10. de Kraker MEA, Tartari E, Tomczyk S, Twyman A, Francioli LC, Cassini A, et al. Implementation of hand hygiene in health-care facilities: results from the WHO Hand Hygiene Self-Assessment Framework global survey 2019. Lancet Infect Dis. 2022 Jun 1;**22**(6):835–44. doi: 10.1016/S1473-3099(21)00618-6. Epub 2022 Feb 23. PMID: 35202600.
11. The Joint Commission. Measuring Hand Hygiene Adherence: Overcoming the Challenges [Internet]. 2009. Available from: http://www.jointcommission.org. [Last accessed: 2024 Mar 12].
12. Lee SS, Park SJ, Chung MJ, Lee JH, Kang HJ, Lee J a., et al. Improved hand hygiene compliance is associated with the change of perception toward hand hygiene among medical personnel. Infect Chemother. 2014;**46**(3):165–71. doi: 10.3947/ic.2014.46.3.165. Epub 2014 Sep 24. PMID: 25298905.
13. Gould DJ, Moralejo D, Drey N, Chudleigh JH, Taljaard M. Interventions to improve hand hygiene compliance in patient care. Cochrane Database of Systematic Reviews. 2017 Sep 1;(9). CD005186. doi: 10.1002/14651858.CD005186.pub4. PMID: 28862335.
14. van der Kooi T, Sax H, Grundmann H, Pittet D, de Greeff S, van Dissel J, et al. Hand hygiene improvement of individual healthcare workers: results of the multicentre PROHIBIT study. Antimicrob Resist Infect Control. 2022 Oct 5;**11**(1):123. doi: 10.1186/s13756-022-01148-1. PMID: 36199149.
15. Elia F, Calzavarini F, Bianco P, Vecchietti RG, Macor AF, D'Orazio A, et al. A nudge intervention to improve hand hygiene compliance in the hospital. Intern Emerg Med. 2022 Oct 1;**17**(7):1899–905. doi: 10.1007/s11739-022-03024-7. Epub 2022 Jul 19. PMID: 35852676.
16. Marra AR, Edmond MB. New technologies to monitor healthcare worker hand hygiene. Clinical Microbiology and Infection. 2014;**20**(1):29–33. doi: 10.1111/1469-0691.12458. PMID: 24245809.

17. Kingston L, O'Connell NH, Dunne CP. Hand hygiene-related clinical trials reported since 2010: a systematic review. Journal of Hospital Infection. 2016 Apr 1;**92**(4):309–20. doi: 10.1016/j.jhin.2015.11.012. Epub 2015 Dec 17. PMID: 26853369.
18. Al Sawafi KM. Examining the Importance of Hand Hygiene Policy and Patient Safety Culture on Improving Healthcare Workers' Adherence to Hand Hygiene Practice in Critical Care Settings in the Sultanate of Oman: A Scoping Review. Cureus. 2021 Nov 20; **13**(11): e19773. doi: 10.7759/cureus.19773. PMID: 34950551.
19. Baccolini V, D'Egidio V, De Soccio P, Migliara G, Massimi A, Alessandri F, et al. Effectiveness over time of a multimodal intervention to improve compliance with standard hygiene precautions in an intensive care unit of a large teaching hospital. Antimicrob Resist Infect Control. 2019 May 31;**8**:92. doi: 10.1186/s13756-019-0544-0. PMID: 31164981.
20. Bert F, Giacomelli S, Ceresetti D, Zotti CM. World Health Organization Framework: Multimodal Hand Hygiene Strategy in Piedmont (Italy) Health Care Facilities. J Patient Saf [Internet]. 2019;**15**(4):317–21. Available from: www.journalpatientsafety.com [Last accessed: 2024 Mar 12].
21. Ragusa R, Giorgianni G, Lupo L, Sciacca A, Rametta S, La Verde M, et al. Healthcare-associated Clostridium difficile infection: role of correct hand hygiene in cross-infection control. J Prev Med Hyg. 2018 Jun;**59**(2):E145–E152. PMID: 30083622.
22. Antinozzi M, Ceparano M, Cammalleri V, Baccolini V, Tufi D, De Giusti M, et al. Compliance with hand-hygiene guidelines among healthcare workers: a cross-sectional study at the Umberto I teaching hospital of Rome, Italy. Ann Ist Super Sanita. 2023 jul-Sep;**59**(3):204–12. doi: 10.4415/ANN_23_03_06. PMID: 37712238.
23. Han A, Conway LJ, Moore C, McCreight L, Ragan K, So J, et al. Unit-Specific Rates of Hand Hygiene Opportunities in an Acute-Care Hospital. Infect Control Hosp Epidemiol. 2017 Apr 1;**38**(4):411–6. doi: 10.1017/ice.2016.308. Epub 2016 Dec 28. PMID: 28029336.
24. Scheithauer S, Haefner H, Schwanz T, Schulze-Steinen H, Schiefer J, Koch A, et al. Compliance with hand hygiene on surgical, medical, and neurologic intensive care units: Direct observation versus calculated disinfectant usage. Am J Infect Control. 2009 Dec;**37**(10):835–41. doi: 10.1016/j.ajic.2009.06.005. PMID: 19775774.
25. Steed C, Kelly JW, Blackhurst D, Boeker S, Diller T, Alper P, et al. Hospital hand hygiene opportunities: Where and when (HOW2)? the HOW2 Benchmark Study. Am J Infect Control. 2011 Feb;**39**(1):19–26. doi: 10.1016/j.ajic.2010.10.007. PMID: 21281883.
26. Talbot D, Massamba VK. A descriptive review of variable selection methods in four epidemiologic journals: there is still room for improvement. Eur J Epidemiol. 2019 Aug 15;**34**(8):725–30. doi: 10.1007/s10654-019-00529-y. Epub 2019 Jun 3. PMID: 31161279.
27. Mouajou V, Adams K, DeLisle G, Quach C. Hand hygiene compliance in the prevention of hospital-acquired infections: a systematic review. Journal of Hospital Infection. 2022 Jan 1;**119**:33–48. doi: 10.1016/j.jhin.2021.09.016. Epub 2021 Sep 25. PMID: 34582962.
28. Lambe KA, Lydon S, Madden C, Vellinga A, Hehir A, Walsh M, et al. Hand hygiene compliance in the ICU: A systematic review. Crit Care Med. 2019;**47**(9):1251–7. doi: 10.1097/CCM.0000000000003868. PMID: 31219838.
29. Ahmadipour M, Dehghan M, Ahmadinejad M, Jabarpour M, Mangolian Shahrbabaki P, Ebrahimi Rigi Z. Barriers to hand hygiene compliance in intensive care units during the COVID-19 pandemic: A qualitative study. Front Public Health . 2022 Aug 18;**10**:968231. doi: 10.3389/fpubh.2022.968231. PMID: 36062108.
30. Isonne C, Baccolini V, Migliara G, Ceparano M, Alessandri F, Ceccarelli G, et al. Comparing the Occurrence of Healthcare-Associated Infections in Patients with and without COVID-19 Hospitalized during the Pandemic: A 16-Month Retrospective Cohort Study in a Hospital Intensive Care Unit. J Clin Med. 2022 Mar 1;**11**(5):1446. doi: 10.3390/jcm11051446. PMID: 35268538.
31. Ceparano M, Sciurti A, Isonne C, Baccolini V, Migliara G, Marzuillo C, et al. Incidence of Healthcare-Associated Infections in a Neonatal Intensive Care Unit before and during the COVID-19 Pandemic: A Four-Year Retrospective Cohort Study. J Clin Med. 2023 Apr 1;**12**(7):2621. doi: 10.3390/jcm12072621. PMID: 37048704.
32. Mathur P. Hand hygiene: Back to the basics of infection control. Indian J Med Res. 2011;**134**(5):611–20. doi: 10.4103/0971-5916.90985. PMID: 22199099.
33. García LG, Llor AMS, Gil MFH, Valcárcel MDR, Cerezo PP, Cano E de la I, et al. Analysis of midwives' situation and the need to measure their workloads. Rev Bras Enferm. 2022 Nov 11;**75**(Suppl 3):e20210920. English, Spanish. doi: 10.1590/0034-7167-2021-0920. PMID: 36383900.
34. Aragon D, Mary F; Outcomes of an Infection Prevention Project Focusing on Hand Hygiene and Isolation Practices. AACN Clin Issues [Internet]. 2005;**16**(2):121–32. Available from: www.jcaho.org [Last accessed: 2024 Mar 12].
35. Centers for Disease Control and Prevention (CDC). Guideline for Hand Hygiene in Health-Care Settings Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. MMWR Recomm Rep. 2002 Oct 25;**51**(RR-16). Available from: https://www.cdc.gov/mmwr/pdf/rr/rr5116.pdf [Last accessed: 2024 Mar 12].
36. Wang Y, Yang J, Qiao F, Feng B, Hu F, Xi Z ang, et al. Compared hand hygiene compliance among healthcare providers before and after the COVID-19 pandemic: A rapid review and meta-analysis. Am J Infect Control. 2022 May 1;**50**(5):563–71. doi: 10.1016/j.ajic.2021.11.030. Epub 2021 Dec 7. PMID: 34883162.
37. Zhang X, Ma Y, Kong L, Li Y, Wang J, Li N, et al. The impact of COVID-19 pandemic on hand hygiene compliance of healthcare workers in a tertiary hospital in East China. Front Med (Lausanne). 2023 Jun 22;**10**:1160828. doi: 10.3389/fmed.2023.1160828. PMID 37425301.

38. Suen LKP, So ZYY, Yeung SKW, Lo KYK, Lam SC. Epidemiological investigation on hand hygiene knowledge and behaviour: A cross-sectional study on gender disparity. BMC Public Health. 2019 Apr 11;**19**(1): 401. doi: 10.1186/s12889-019-6705-5. PMID: 30975130.
39. Montagnani C, Cocchi P, Lega L, Campana S, Biermann KP, Braggion C, et al. Serratia marcescens outbreak in a neonatal intensive care unit: Crucial role of implementing hand hygiene among external consultants. BMC Infect Dis. 2015 Jan 13;**15**:11. doi: 10.1186/s12879-014-0734-6. PMID: 25582674.
40. Roche SD, Reichheld AM, Demosthenes N, Johansson AC, Howell MD, Cocchi MN, et al. Measuring the quality of inpatient specialist consultation in the intensive care unit: Nursing and family experiences of Communication. PLoS One. 2019 Apr 1;**14**(4): e0214918. doi: 10.1371/journal.pone.0214918. PMID: 30973891.
41. Chang NCN, Schweizer ML, Reisinger HS, Jones M, Chrischilles E, Chorazy M, et al. The impact of workload on hand hygiene compliance: Is 100% compliance achievable? Infect Control Hosp Epidemiol. 2022 Sep 14;**43**(9):1259–61. doi: 10.1017/ice.2021.179. Epub 2021 May 14. PMID: 33985603.
42. Abdullah HR, Lam SSW, Ang BY, Pourghaderi A, Nguyen FNHL, Matchar DB, et al. Resuming elective surgery after COVID-19: A simulation modelling framework for guiding the phased opening of operating rooms. Int J Med Inform. 2021 Dec 14;**158**:104665. doi: 10.1016/j.ijmedinf.2021.104665. Epub ahead of print. PMID: 34923449.
43. Wilson KB, Satchell L, Smathers SA, Goff LFL, Sammons JS, Coffin SE. The power of feedback: Implementing a comprehensive hand hygiene observer program. Am J Infect Control. 2023 Feb 1;**51**(2):142–8. doi: 10.1016/j.ajic.2022.06.003. Epub 2022 Jun 10. PMID: 35691447.
44. Ojanperä H, Kanste OI, Syrjala H. Hand-hygiene compliance by hospital staff and incidence of health-care-associated infections, Finland. Bull World Health Organ. 2020 Jul 1;**98**(7):475–83. doi: 10.2471/BLT.19.247494. Epub 2020 May 26. PMID: 32742033.
45. Qureshi M, Chughtai A, Seale H. Supporting the Delivery of Infection Prevention and Control Training to Healthcare Workers: Insights from the Sector. Healthcare (Switzerland). 2022 May 18;**10**(5):936. doi: 10.3390/healthcare10050936. PMID: 35628072.
46. Kubde D, Badge AK, Ugemuge S, Shahu S. Importance of Hospital Infection Control. Cureus. 2023 Dec 22;**15**(12):e50931. doi: 10.7759/cureus.50931. PMID: 38259418; PMCID: PMC10801286.
47. Sodhi K, Shrivastava A, Arya M, Kumar M. Knowledge of infection control practices among intensive care nurses in a tertiary care hospital. J Infect Public Health. 2013 Aug;**6**(4):269-75. doi: 10.1016/j.jiph.2013.02.004. Epub 2013 May 8. PMID: 23806701.

Supplementary Table 1. Characteristics of observations by area

		Clinical area (n= 3008) N (%)	**Surgical area** (n=1602) N (%)	**Intensive care area** (n=816) N (%)
HH Indication				
	Indication I	1225 (40.7)	587 (36.6)	376 (46.1)
	Indication II	222 (7.4)	166 (10.4)	83 (10.2)
	Indication III	868 (28.8)	492 (30.7)	208 (25.5)
	Indication IV	318 (10.6)	184 (11.5)	73 (8.9)
	Indication V	375 (12.5)	173 (10.8)	76 (9.3)
Action type				
	Soap and water	1149 (38.2)	619 (38.6)	205 (25.1)
	Alcohol-based formulation	1249 (41.5)	559 (34.9)	310 (38.0)
	Gloves	378 (12.6)	242 (15.1)	127 (15.6)
	Nothing	232 (7.7)	182 (11.4)	174 (21.3)
Observed HCW role				
	Physician	1061 (35.6)	578 (37.1)	266 (33.7)
	Nurse	1188 (39.8)	557 (35.8)	436 (55.2)
	Midwife	31 (1.0)	26 (1.7)	2 (0.3)
	Healthcare assistant	488 (16.4)	209 (13.4)	32 (4.0)
	Students	71 (2.4)	91 (5.8)	12 (1.5)
	Relative	5 (0.2)	4 (0.3)	2 (0.3)
	Other	138 (4.6)	93 (5.9)	40 (5.0)

		Clinical area (n= 3008) N (%)	Surgical area (n=1602) N (%)	Intensive care area (n=816) N (%)
Observed HCW gender				
	Male	1139 (38.0)	640 (40.1)	338 (41.9)
	Female	1858 (62.0)	958 (59.9)	468 (58.1)
Observed ward staff				
	Internal	2561 (87.4)	1286 (81.9)	642 (83.7)
	External	369 (12.6)	285 (18.1)	125 (16.3)
Day				
	Weekday	2548 (89.6)	1428 (90.4)	684 (83.8)
	Weekend day/holidays	295 (10.4)	151 (9.6)	132 (16.2)
Work shift				
	Morning	1865 (62.2)	961 (60.3)	479 (59.1)
	Afternoon	988 (32.9)	541 (33.9)	276 (34.0)
	Night	147 (4.9)	93 (5.8)	56 (6.9)
Observer gender				
	Male	695 (23.1)	376 (23.5)	208 (25.8)
	Female	2313 (76.9)	1226 (76.5)	608 (74.5)
Observer role				
	Physician	1545 (51.4)	661 (41.3)	338 (41.4)
	Nurse	1458 (48.5)	839 (52.4)	478 (58.6)
	Midwife	0 (0.0)	97 (6.1)	0 (0.0)
	Healthcare assistant	5 (0.2)	5 (0.3)	0 (0.0)

Indication I: before touching a patient; Indication II: before clean/aseptic procedure; Indication III: after touching a patient; Indication IV: after body fluid exposure; Indication V: after touching a patient's surroundings.

Corresponding Author: Dr Antonio Covelli, Department of Public Health and Infectious Diseases, Sapienza University of Rome, Piazzale Aldo Moro 5, 00185 Rome, Italy
e-mail: antonio.covelli@uniroma1.it

Ann Ig. 2025 Jan-Feb; 37(1): 37-48 doi: 10.7416/ai.2024.2645. Epub 2024 Jul 17.

The role of citizenship in the acceptance and completion of COVID-19 vaccine cycle in the resident population with foreign citizenship registered with the Umbrian Health Care System - An analysis of regional data

Irene Giacchetta[1], Chiara Primieri[2], Manuela Chiavarini[3], Chiara de Waure[4], Carla Bietta[2]

Keywords: Vaccine Hesitancy; Citizenship; COVID-19
Parole chiave: Esitazione vaccinale; cittadinanza; COVID-19

Abstract

Introduction. *Non-italian citizens experienced less access to anti-COVID-19 vaccination, compared to the native population. Literature has found differences in adherence to anti-COVID-19 vaccination among these groups; however, there are apparently no studies that investigated the role of citizenship. Our objective was to investigate the role of citizenship in vaccine hesitancy toward anti-COVID-19 vaccination and the completion of vaccine cycle, in the non-Italian citizens resident in the Umbria Region.*
Study design. *This is a population study, performed on resident population in Umbria.*
Methods. *Population data were obtained thanks to a record linkage between the Regional Health Information System and the regional DBCOVID Umbria database. On this dataset, a descriptive and logistic regression analyses were performed.*
Results. *The 19.2% of non-Italian citizens did not take even one dose, 2.1% did not complete it and 40.6% did not take the additional dose. The range of values of which these results are an average, however, is very wide, suggesting important differences in COVID-19 vaccine up taking, among different citizenships. The logistic regression shows that citizenships with the highest probability of non-adherence to vaccination, compared to Philippine, was Romanian (OR=7.8), followed by Macedonian (OR=7.3) and Polish (OR=5.9).*
Conclusions. *The study provides evidence of differences among citizenships that pinpoint the importance of understanding the reasons behind these behaviours, to support decisions around health policies tailored to each citizenship.*

[1] *Local Health Unit of Bologna, Department of Hospital Network, Hospital Management of Maggiore and Bellaria, Bologna, Italy*
[2] *Local Health Unit 1 of Umbria, Prevention Department, Epidemiology Service, Perugia, Italy*
[3] *Department of Biomedical Sciences and Public Health, Section of Hygiene, Preventive Medicine and Public Health, Polytechnic University of the Marche Region, Ancona, Italy*
[4] *Department of Medicine and Surgery, University of Perugia, Italy*

Chiara De Waure and Carla Bietta contributed equally to the manuscrip

Annali di Igiene : Medicina Preventiva e di Comunità (Ann Ig)
ISSN (print) 1120-9135 ISSN (online) 3035-5559

https://www.annali-igiene.it

Introduction

Vaccination hesitancy was defined as "the delay in accepting or refusing vaccinations despite the availability of vaccination services" (1), and is a complex phenomenon linked to personal, social, political and geographical factors. Recognizing the significance of this phenomenon, the Strategic Advisory Group of Experts (SAGE) on Immunization of the World Health Organization (WHO), has developed the following recommendations: 1. understanding the determinants of vaccine hesitancy; 2. highlighting organisational aspects that facilitate adherence; 3. evaluating the tools needed to counter this phenomenon (2). During the COVID-19 pandemic many countries have collected large-scale cross-sectional data regarding people's self-reported perceptions, intentions and behaviours about COVID-19 vaccination, to investigate reasons behind vaccine hesitancy. In describing the phenomenon of vaccine hesitancy, it is necessary to mention that, for some populations, healthcare services are considered hard to reach; in particular, non-Italian citizens have experienced less access to COVID-19 vaccination, compared with the native population (3-8). Expanding the scenario, non-Italian citizens generally record lower rates of utilisation of preventive services, including vaccinations, than native populations across the European Union member states (4,9, 10-19).

In respect to COVID-19, as stated above, international literature has found differences in adherence to vaccination among different groups of non-Italian citizens present in the study populations (3-8,9,20-25). A recent systematic review revealed that the overall COVID-19 vaccine hesitancy among migrants, refugees and foreign workers was 71.9% in the WHO European region, 36.5% in the Eastern Mediterranean region, and 31.0% in the Western Pacific region (4).

The literature has offered interesting insights into the differences between ethnic groups, which do not seem to behave in the same way about vaccination (3,26), also in relation to the religious beliefs that characterise each ethnic group (27). One study, in particular, found a greater vaccine hesitancy in sub-Saharan African and Eastern Europe people (26), in line with another systematic review that found a greater association with vaccine hesitancy among Eastern Europeans and Muslims (3).

The Italian literature seems to confirm that COVID-19 vaccination acceptance is uneven among non-Italian citizens (25, 28). Referring to the Umbrian scenario, the study by Primieri et al., 2023 (29) confirmed that, even in Umbria, non-Italian subjects were more likely neither to start nor to complete the vaccination cycle.

However, there are no studies investigating the citizenship role in vaccine hesitancy, even if it could be a proxy for the cultural identity to which people feel to belong. Indeed, the scientific literature either refers to "country of birth" and "minority ethnicity", however, these characteristics do not permit a comprehensive description of the identity that the individual chooses and with which he or she identifies, nor any changes in marital status chosen by the individual, such as the decision to apply for a change of residence or citizenship. The rationale of this study is precisely to further describe, with particular attention to the role of citizenship, the phenomenon of vaccine hesitancy in the population with foreign citizens of the study of Primieri et al., 2023 (29). This is necessary in order to further understand determinants of vaccine hesitancy and to tailor vaccination policies and strategies within one country that could facilitate vaccination adherence.

Objective

To investigate the role of citizenship in the phenomenon of hesitancy toward the uptake of COVID-19 vaccine and the completion of cycle, in the population with foreign citizens residing in Umbria.

Materials e Methods

For the selection of the study population, we started from the population with non-Italian citizenship, resident in Umbria as of February 28th, 2021 (N=90,714). In order to identify the population that was integrated with the territorial healthcare system, subjects not attended by a General Practitioner or Family Paediatrician in Umbria or with a health card that was not active during the study period (N=7,039) and subjects domiciled outside the region (N=351) were excluded from the study population. To allow for a proper assessment of outcomes, those exempted from COVID-19 vaccination (N=36) and minors (age <18 years) who could not independently choose whether to vaccinate or not (N=17,618) were excluded. Finally, to allow a better understanding of the role of citizenship, all those who belonged to a citizenship represented by fewer than 1,000 subjects were excluded (N=15,035) (Figure 1).

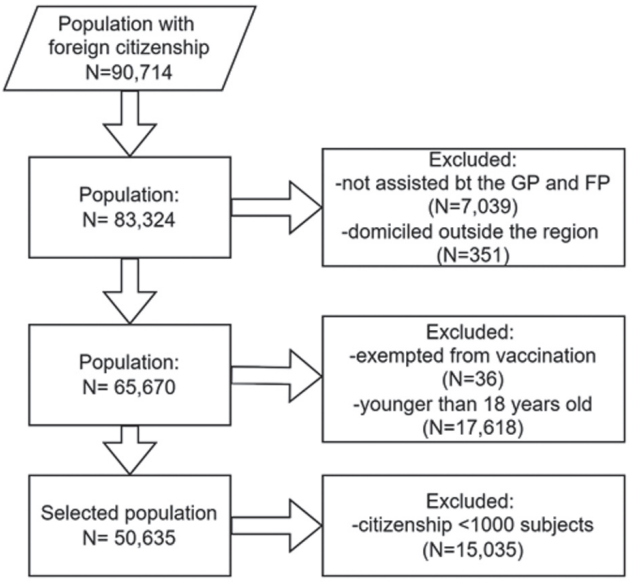


Figure 1 - Selection of the Study Population

1. Data Source

A record linkage was performed between the Regional HIS and the Regional DBCOVID Umbria database, using people's regional ID codes.

The Regional DBCOVID Umbria database collects individual data from the Regional SARS-CoV-2 Integrated Surveillance System as of February 2020; from DBCOVID Umbria we extracted data on doses of the vaccine administration in a year, as of February 28th, 2022. The HIS contains the personal data of the population served by the regional health service; from HIS we extracted: gender, age, residence, citizenship, possession of an "exemption" for chronic or rare disease or disability from medical causes. "Exemption" means that to some people, because of their disability or presence of the above described diseases no participation to the cost of the services is requested.

Data processing was carried out at the Epidemiology Service of the Prevention Department of the Umbria USL 1, which ensured the processing in compliance with privacy regulations. Vaccination coverages as of February 28th, 2022 in countries of origin of the citizenships present in Umbria were also retrieved from the Our World in Data website for elaborating the findings.

The study was conducted in accordance with the Declaration of Helsinki and approved by the Umbrian Regional Ethics Committee (ERC Umbria) (ERC N 4183/19, protocol code: 23155/21/ON; approval date: 27/10/2021). We extracted data about one dose vaccination coverage recorded in countries of origin as of February 28th, 2022 to compare it with one dose vaccination coverage recorded in our study (30).

2. Endpoint and covariates

Non-adherence to vaccination as of February 28th, 2022 was assessed as the primary endpoint, with adherence being defined as the administration of at least one dose of any COVID-19 vaccine.

As secondary endpoints, the following were considered:

- The failure to complete the primary vaccine cycle - understood as the administration, in various possible combinations, of two doses of Pfizer-BioNTech, Moderna or Vaxzevria vaccines, or as the administration of a single dose of Johnson&Johnson or as the administration of a single dose of any vaccine within one year of SARS-CoV-2 infection (previous or subsequent) - in those who had at least one dose of vaccine.
- Failure to uptake the booster dose in those who completed the primary vaccine cycle.

Possible delays in adherence, due to possible SARS-CoV-2 infections, were not considered in the assessment of endpoints.

As additional variables, the following were considered:

- sex (male or female);
- age (18-29, 30-39, 40-49, 50-59, 60+);
- citizenship (categorical variable with all citizenships as long as they were represented by at least 1,000 subjects);
- possession of a chronic or rare disease exemption or officially recognized disability from medical causes as a proxy for frailty (present or absent).

3. Statistical Analysis

Absolute and percentage frequencies and mean ± standard deviation (SD) were used to describe categorical variables and quantitative variables. A logistic regression model was used to investigate the role of individual citizenship by estimating odds ratios (OR) and associated 95% confidence intervals (95% CIs). All variables collected were included in the full-adjusted model. For each variable, the one with the lowest non-adherence rate was chosen as the reference category.

Statistical significance was set at $p<0.05$. All analyses were performed with Stata 18.0 statistical software.

Table 1 - Study population characteristics

Citizenship	N	%	Mean age	SD	Female		Male		Exemption for disease or invalidity	
					N	%	N	%	N	%
Romania	16,148	31.9	44.5	±12.6	11,024	68.3	5,124	31.7	2,415	15.0
Albania	9,467	18.7	44.0	±15.8	4,847	51.2	4,620	48.8	1,507	15.9
Morocco	6,515	12.9	43.6	±14.1	3,138	48.2	3,377	51.8	1,099	16.9
Ukraine	4,293	8.5	51.3	±14.0	3,559	82.9	734	17.1	780	18.2
North Macedonia	2,345	4.6	41.7	±13.3	1,023	43.6	1,322	56.4	337	14.4
Ecuador	2,117	4.2	42.6	±13.8	1,342	63.4	775	36.6	416	19.7
Moldova	1,829	3.6	44.7	±13.8	1,300	71.1	529	28.9	325	17.8
Poland	1,529	3.0	47.8	±13.0	1,204	78.7	325	21.3	304	19.9
Philippines	1,387	2.7	45.4	±135	788	56.8	599	43.2	224	16.1
Nigeria	1,382	2.7	36.7	±10.3	676	48.9	706	51.1	187	13.5
China	1,272	2.5	40.9	±12.11	698	54.9	574	45.1	114	9.0
Peru	1,202	2.4	44.7	±14.7	720	59.9	482	40.1	206	17.1
India	1,149	2.3	40.6	±12.7	476	41.4	673	58.6	179	15.6
Total	50,635	100	44.4	±14.0	30,795	60.8	19,84	39.2	8,093	16.0

Results

1. Description of the study population

The total population with non-Italian citizenship residing in Umbria as of February 28th, 2021 (henceforth just "non-Italian population") was found to consist of 90,714 subjects, divided into 160 different citizenships. The population selected for the study was represented by 50,635 subjects divided into 13 citizenships. Table 1 summarises the citizenships considered in the study and their characteristics (Table 1). Within the study population 30,795 (60.8%) were female subjects, while 19,840 (39.2%) were males. The mean age was 44.4 years, with a standard deviation of 14.0. The mean age of females was 45.7 (SD 14.0), while that of males was 42.4 years (SD 13.7) (Table 1). The most represented age group was 40-49 years old, namely the 25.3% of the total population. The middle age groups (30 to 59 years old) accounted for 68.7% of the population, with the remainder equally distributed between the 18-29 years old and 60 years and older age groups (Table 2). Out of the total of 50,635 individuals, 8,093 (16%) had a disability or chronic condition exemption. The most represented citizenships were Romanian (31.9%), Albanian (18.7%), Moroccan (12.9%), Ukrainian (8.5%) and, with almost the same number of subjects, Macedonian (4.6%) and Ecuadorian (4.2%).

Table 2 - Age groups of the study population

Age group	N	%
18 - 29	8,184	16.2
30 - 39	11,505	22.7
40 - 49	12,825	25.3
50 – 59	10,500	20.7
60 and older	7,621	15.1
Total	50,635	100

2. The role of citizenship in the uptake of vaccination

Out of the total study population (50,635), 9,717 subjects (19.2%) did not take even one dose, while 867 out of 40,918 people who started the vaccination cycle (2.1%) did not complete it and 16,257 out of 40,051 people eligible to receive the booster dose (40.6%) did not take the additional dose. The percentage of the unvaccinated population varies within the different citizenships from as low as 4.7% in the Filipino population, to as high as 27.3% in the Romanian population. Regarding the secondary endpoints, the rate of failure to complete the vaccination cycle ranged from 0.5% of Polish and Peruvian citizenships, to 3.8% of Ecuadorian citizenship and the failure to uptake the booster dose ranged from 21.1% in Poland to 58.2% in Ecuador. More results for the primary endpoint and secondary endpoints are shown in Table 3.

Table 4 shows the vaccination coverage, for those who have had at least one dose, recorded in our study

Table 3 - N (%) of non-adherent to vaccination by citizenship

Citizenship	Non adherence to vaccination ∑.N mnj°v		Failure to complete the vaccination cycle		Failure to uptake the booster dose	
	N	(% on those eligible)	N	(% on those eligible)	N	(% on those eligible)
Romania	4,409	27.3%	302	2.6%	4,751	41.5%
Albania	1,435	15.2%	151	1.9%	3,475	44.1%
Morocco	957	14.7%	163	2.9%	2,313	42.9%
Ukraine	815	19.0%	56	1.6%	1,188	34.7%
North Macedonia	611	26.1%	19	1.0%	699	35.8%
Ecuador	148	7.0%	66	3.8%	970	58.2%
Moldova	343	18.8%	19	1.3%	621	42.3%
Poland	348	22.8%	7	0.5%	278	21.1%
Philippines	65	4.7%	21	1.8%	323	27.8%
Nigeria	227	16.4%	36	3.1%	606	54.2%
China	152	11.9%	7	0.6%	373	33.4%
Peru	78	6.5%	6	0.5%	354	31.8%
India	129	11.2%	14	1.4%	306	30.4%
Total	9,717	19.2%	867	2.1%	16,257	40.6%

Table 4 - Comparison of vaccination coverage (at least one dose) of the citizenships of the study population with those of the countries of origin

Citizenship	National coverage (at least one dose) of the country of origin (%)	Umbrian data (%)
Romania	27.7	72.7
Albania	44.7	84.8
Morocco	66.3	85.3
Ukraine	39.7	81.0
North Macedonia	40.5	73.9
Ecuador	82.0	93.0
Moldova	32.8	81.2
Poland	56.5	77.2
Philippines	59.4	95.3
Nigeria	8.12	83.6
China	89.0	88.1
Peru	81.8	93.5
India	68.1	88.8

and the vaccination coverage, again for at least one dose, recorded in the countries of origin as of February 28th, 2022 (Table 4). The lowest national coverage was described among Nigerians (8.12%), followed by Romanians (27.7 %), while the highest national coverage was described in Chinese citizen (89%) an Ecuadorians (82%).

From the logistic analysis on the primary endpoint, a significant association for all citizenships considered, except for Peruvian, was highlighted. The citizenship with the highest probability of non-adherence to vaccination, compared to Philippine citizenship (that had the lowest non-adherence rate), was Romanian (OR=7.8), followed by Macedonian (OR=7.3) and Polish (OR=5.9). There was no evidence of differences between the two sexes. Regarding age, belonging to the over-60 class was associated with the higher risk of not adhering (OR=1.9) to vaccination. Finally, not having a disease exemption was found to be associated with a higher significant likelihood of non-adherence to vaccination (OR=1.2) (Table 5).

From the logistic analysis performed considering the secondary endpoint "not having completed the primary vaccine cycle," it turned out that Ecuadorian, Chinese, and Peruvian people did not have a significantly different risk of failing to complete the vaccination

Table 5 - Sociodemographic characteristics associated with nonadherence to vaccination in the study population (N=50,635)

Variables	OR	95%CI		p-value
Sex				
Male	(Reference)			
Female	1.012	0.964	1.062	0.626
Age				
18-29	1.203	1.111	1.302	<0.001
30-39	1.352	1.26	1.45	<0.001
40-49	1.054	0.983	1.131	0.141
50-59	(Reference)			
60+	1.935	1.794	2.087	<0.001
Citizenship				
Romania	7.784	6.051	10.014	<0.001
Albania	3.489	2.702	4.505	<0.001
Morocco	3.473	2.681	4.499	<0.001
Ukraine	4.334	3.337	5.63	<0.001
North Macedonia	7.316	5.607	9.547	<0.001
Ecuador	1.561	1.156	2.108	0.004
Moldova	4.582	3.477	6.039	<0001
Poland	5.95	4.51	7.849	<0.001
Philippines	(Reference)			
Nigeria	4.008	3.006	5.344	<0.001
China	2.804	2.074	3.792	<0.001
Peru	1.384	0.986	1.942	0.061
India	2.596	1.904	3.539	<0.001
Exemption for disease/invalidity				
Yes	(Reference)			
No	1.295	1.208	1.388	<0.001

cycle in respect to Filipinos. The citizenships with a higher risk of not completing the vaccine cycle were Macedonian (OR=7.2), Moroccan (OR=5.6), Nigerian (OR=5.5) and Romanian (OR=4.9). With regard to gender, being female showed a 17% significant increased probability of not completing the vaccination cycle. Regarding the age, 18-29 years old class showed a significant higher risk of not completing the cycle whereas the 40-49 years olds class a significant lower risk (OR=0.7) as compared to 50-59 years old people. Also, for this endpoint, not having a disease or disability exemption was associated with a higher, but not significant, probability of not completing the vaccine cycle (Table 6).

Finally, in the analysis for the endpoint "failure to uptake the booster dose" all citizenships showed a significant association, and the citizenships most at risk of not uptalking the booster dose were Macedonian (OR=4.9), Nigerian (OR=3.5), Albanian (OR=2.8), Moldavian (OR=2.8), Romanian (OR=2.7), Moroccan (OR=2.7), and Ukrainian (OR=2.5), the remainder having an OR less than 2. Regarding gender, females were significantly 8.7% less likely not to uptake the booster dose. Finally, with regard to age groups, compared with the 50-59 age group, the age group with a higher significant risk of not completing the booster dose was 18-29 years (OR=2.9), followed by the 30-39 (OR=2.2) and 40-49 (OR=1.4), while the over-60 had a 7% significant lower probability of not uptaking the booster dose. Finally, people not having a disease or disability exemption still depicted a higher significant risk of not receiving the booster dose as compared to the counterpart (OR=1.2) (Table 7).

Discussion

This study investigated the role of "citizenship" in the uptake of COVID-19 vaccines in order to study how this variable works in comparison to other

Table 6 - Socio-demographic characteristics associated with failure to complete the primary vaccine cycle in the study population (N=40,918).

Variables	OR	95%CI		p-value
Sex				
Male	(Reference)			
Female	1.177	1.02	1.359	0.026
Age				
18-29	1.484	1.205	1.827	<0.001
30-39	1.105	0.902	1.354	0.334
40-49	0.721	0.582	0.895	0.003
50-59	(Reference)			
60+	0.936	0.731	1.199	0.6
Citizenship				
Romania	4.913	2.317	10.421	<0.001
Albania	3.492	1.633	7.471	0.001
Morocco	5.65	2.644	12.073	<0.001
Ukraine	3.028	1.374	6.674	0.006
North Macedonia	7.259	3.317	15.884	<0.001
Ecuador	1.738	0.728	4.148	0.213
Moldova	2.346	0.983	5.601	0.055
Poland	3.508	1.485	8.291	0.004
Philippines	(Reference)			
Nigeria	5.51	2.439	12.451	<0.001
China	0.987	0.331	2.947	0.981
Peru	1.147	0.401	3.282	0.798
India	2.549	1.024	6.346	0.044
Exemption for disease/invalidity				
Yes	(Reference)			
No	1.169	0.945	1.446	0.15

characteristics more frequently used in the national and international literature, such as the individual's place of birth or ethnicity. As shown in the results, among the citizenships analysed, three had an adherence below 80%, namely Romanian (72.7%), Macedonian (73.9%), and Polish (77.2%), while all others showed adherence above 80%. In particular, three had an adherence above 90%: Ecuadorian (93%), Peruvian (93.5%), and Filipinos (95.3%). When considering that Italy, as of February 28th, 2022, had a vaccination coverage of at least one dose of 86% (30) it can be seen that the citizens did behave differently toward the COVID-19 vaccination. Only six out of thirteen citizenships (Moroccan, Chinese, Indian, Ecuadorian, Peruvian, and Filipino) have comparable or higher coverage than Italian citizenships. Regarding the secondary endpoints, as underlined in the results (see Table 3), there is a wide variability too, especially when compared to the Italian second dose uptake of 80% (30). In addition, the citizenships that show a higher percentage of vaccination up-take of at least one dose, are not always the same ones that also have higher up-take of second dose and booster dose. An example is Ecuadorian citizenship, which reports a 93% of population with at least one dose, but also reports a high percentage of population who refused the second and the booster dose: 3.8% and 58.2%, respectively. On the other hand, the citizenship that has a low percentage of at least one dose, such as the Romanian, also has a low rate of up-take of second dose and booster dose. The observed differences in vaccination adherence, across different citizenships and for different outcomes, highlight that the phenomenon of vaccination hesitancy is complex and suggests that citizenship plays a significant role in the behavior toward vaccination among the foreign populations. For such reason, it would not be correct to use a single variable which describes only

Table 7 - Socio-demographic characteristics associated with failure to uptake the booster dose in the eligible foreign study population (N=40,051)

Variables	OR	95%CI		p-value
Sex				
Male	(Reference)			
Female	0.913	0.875	0.954	<0.001
Age				
18-29	2.9	2.706	3.108	<0.001
30-39	2.23	2.092	2.376	<0.001
40-49	1.394	1.311	1.483	<0.001
50-59	(Reference)			
60+	0.93	0.862	1.004	0.062
Citizenship				
Romania	2.758	2.398	3.173	<0.001
Albania	2.812	2.439	3.241	<0.001
Morocco	2.682	2.318	3.102	<0.001
Ukraine	2.465	2.114	2.874	<0.001
North Macedonia	4.974	4.207	5.882	<0.001
Ecuador	2.015	1.709	2.376	<0.001
Moldova	2.808	2.366	3.334	<0.001
Poland	1.62	1.343	1.955	<0.001
Philippines	(Reference)			
Nigeria	3.486	2.911	4.176	<0.001
China	1.536	1.275	1.85	<0.001
Peru	1.85	1.537	2.227	<0.001
India	1.39	1.147	1.684	0.001
Exemption for disease/invalidity				
Yes	(Reference)			
No	1.206	1.134	1.284	<0.001

if a person is Italian or not. The reasons behind such different behaviors could improve the knowledge of the phenomenon and thus support decisions around health policies tailored to each citizenship.

Comparing the adherence to vaccination in our study population with the coverage of countries of origin, we appreciated that the citizenships that showed lower adherence had also very low coverage in their countries of origin. Nevertheless, while this is true, the contrary is not verified. In fact, citizenships such as Albanian, Ukrainian, Moldavian, as well as Moroccan and Indian, which had low national vaccination coverage, showed good adherence to vaccination in Italy. One bizarre percentage is the one referring to Nigeria's national coverage, which is 8.12 %, much lower than the Umbrian data of 83.6 %; although there is no literature or information to help explaining this, it is possible that it is related to data collection and reporting problems. The coverage (at least one dose) of Italian residents of Umbria, in the same period, was of 88.1% (29), a data higher than most of the national coverage of non-Italian citizenship, but lower than the national coverage of China (89,0%) and comparable to Ecuador (82,0%). Comparing instead the coverage of Italian residents of Umbria to non-Italian population of our study, 5 citizenships had a comparable or higher than Italian's vaccination coverage: Ecuador (93,0%), Philippines (95,3%), China (88,1%), Peru (93,5%) and India (88,8%).

This comparison prompted us to consider some characteristics of the countries of origin and some characteristics of the foreign populations living in Italy, which could contribute to explain this variability. We classified these factors into 3 macro-groups.

The first is the influence of the country of origin, which includes all factors, including the role that politicians and public figures played during the vaccination, that resulted in low adherence in

the country of origin, and which could have also influenced the community living in Italy. In Romania, for example, the role of politics, as well as the no vax community (31,32), seemed to have been central in deterring vaccination (33-35). It is rational, therefore, to assume that the Romanian population residing in Italy was also affected by the political situation in their country, which was characterised by distrust of institutions and media, to the point of being influenced in their choices about vaccination during the Italian vaccination campaign. A second factor, which may have indirectly influenced foreign communities in Italy, may have been a reduced risk perception related to increased natural immunity due to delayed distribution of vaccine doses in the country of origin, as was the case in Macedonia, for example (36-38). The vaccination campaign in Macedonia, in fact, started only in March 2021, finding a population which had already contracted COVID-19 and had had a low risk perception.

The second macro area is the level of integration of different citizenships within the Italian community. One of the factors describing the level of integration is definitely the length of time spent in Italy: actually, migrants with shorter stays record lower rates of access/use of health services. (12,39). In this respect it should be considered that 32.3% of the community members with Filipinos citizenship have been staying in Italy for more than 20 years, followed by Albanian, Chinese, Moroccan, and Peruvian, showing longer residence times than other citizenships (40). Similarly, the employment situation of non-Italian citizens allows us to open a point of view to read the phenomenon of vaccination adherence among different citizenships. In fact, the Ministry of Labor and Social Policy found that different communities had different employment rates in 2020 (41), and again, employment rates show Filipinos, Chinese and Peruvian citizenships at the top, which are the only ones to exceed 70% of employed, among both males and females. The type of occupation, in addition, could help to explain the adherence of some citizens to vaccination: in fact, since May 16th, 2021, the Green Pass has been introduced in Italy and it has allowed access to almost any activity or job that involves public or contact with people. It is reasonable to assume that for those communities primarily employed in Human Services, such as the Filipinos, being vaccinated probably meant being able to work or not (41).

The third macro area is represented by the socio-economic indicators, such as wealth and education level. With this respect, Filipinos citizens have a medium-high level of education: more than half of the workers belonging to that community have at least a high school diploma (50.8%), which is significantly higher than the percentage found among the non-EU population (40.4%). Peruvian citizenship also saw the number of Peruvian students increase by 2.4% in the 2020/2021 school year, against a slight average decline in non-EU students (-0.4 %) (42). Similarly, the Ecuadorian community, which accounts for 2% of the non-European population in Italy, in the same year, had a higher number of students in secondary school, accounting for 2.6% of enrolment out of the total number of non-EU students (43).

Strengths and limitations of the study

The innovative feature of the study is that it considered citizenship as a variable associated with the behaviour towards COVID-19 vaccination among Umbria's foreign population. Among the strengths of the study is the use of individual data derived from institutional and reliable information systems. Moreover, the data were considered over a sufficiently large time span to allow all subjects included in the study to be able to vaccinate.

Limitations include:

those related to the information system itself, such as the possibility that data from out-of-region vaccinations may not have moved into the regional system in a timely manner;

the absence of other relevant information in the data sources that could have been diriment in explaining the results, such as occupation and type of work or how long the subjects considered had been residing in Italy.

Finally, it should be considered that the analysis included only regular migrants, with recidency permit or citizency and Umbrian residence, excluding asylum seekers and refugees, whose conditions, therefore, are not described by this study.

It is necessary, in any case, to interpret the results with caution, because migrant populations in different countries differ in many respects, particularly with regard to rules for the acquisition of citizenship and migrants' rights regarding access to healthcare, so that findings have little transferability to different countries and social contexts. However, these results, in addition to being interesting because of the nature of the phenomenon they describe, with adequate accommodations, may be transferable to other Italian regional realities.

Conclusions

This study is the first to describe the role of citizenship in the adherence to COVID-19 vaccination. It provides evidence of relevant differences among different citizenships that pinpoint the importance of avoiding flattening ethnic groups and non-Italian citizens into inadequate categories that neither respect their diversity nor help in adapting health interventions to the multifaceted subpopulations that make up contemporary societies. However, further studies, both quantitative and qualitative, are needed to fully investigate the different causes that may have led to the observed differences among different citizenships.

Riassunto

Il ruolo della cittadinanza nell'accettazione e nel completamento del ciclo vaccinale anti-COVID-19 nella popolazione con cittadinanza non italiana, residente in Umbria e registrata nell'anagrafe sanitaria regionale umbra – un'analisi di dati regionali

Introduzione. I soggetti con cittadinanza non italiana hanno avuto meno accesso alla vaccinazione anti-COVID-19 rispetto alla popolazione italiana. La letteratura ha riscontrato differenze nell'adesione alla vaccinazione anti-COVID-19 tra gruppi di stranieri, tuttavia non esistono studi che indaghino il ruolo della cittadinanza. L'obiettivo è stato quello di indagare il ruolo della cittadinanza nell'esitazione alla vaccinazione anti-COVID-19 e nel completamento del ciclo vaccinale, nella popolazione con cittadinanza straniera residente in Umbria.

Disegno dello studio. Questo è uno studio di popolazione condotto sulla popolazione residente in Umbria.

Metodi. I dati di popolazione sono stati ottenuti con un record linkage tra l'Anagrafe Sanitaria Regionale e il database DBCOVID Umbria. Sul dataset ottenuto sono state effettuate analisi descrittive e di regressione logistica.

Risultati. Il 19,2% della popolazione non-italiana non ha effettuato nemmeno una dose, il 2,1% non ha completato il ciclo primario e il 40,6% non ha assunto la dose aggiuntiva. Il range di queste misure medie, tuttavia, è ampio, suggerendo importanti differenze legate alle cittadinanze. La regressione logistica mostra che le cittadinanze con una probabilità più alta di non aderire alla vaccinazione, rispetto alla Filippina, sono state la Rumena (OR=7.8), la Macedone (OR=7.3) e la Polacca (OR=5.9).

Conclusioni. Lo studio fornisce un riscontro delle differenze esistenti tra le diverse cittadinanze, differenze che evidenziano l'importanza di comprendere le ragioni alla base di questi comportamenti, per supportare le decisioni sulle politiche sanitarie adatte a ciascuna cittadinanza.

References

1. SAGE Working Group on Vaccine Hesitancy. Report of The SAGE Working Group On Vaccine Hesitancy 12 November 2014. Available from: https://www.asset-scienceinsociety.eu/sites/default/files/sage_working_group_revised_report_vaccine_hesitancy.pdf [Last accessed: 2024 Jun 30].
2. WHO Recommendations Regarding Vaccine Hesitancy. Available from: https://www.sciencedirect.com/journal/vaccine/vol/33/issue/34 [Last accessed: 2024 Jun 30].
3. Crawshaw AF, Farah Y, Deal A, Rustage K, Hayward SE, Carter J, et al. Defining the determinants of vaccine uptake and undervaccination in migrant populations in Europe to improve routine and COVID-19 vaccine uptake: a systematic review. Lancet Infect Dis. 2022 Sep;**22**(9):e254-e266. doi: 10.1016/S1473-3099(22)00066-4. Epub 2022 Apr 13. PMID: 35429463; PMCID: PMC9007555.
4. Hajissa K, Mutiat HA, Kaabi NA, Alissa M, Garout M, Alenezy AA, et al. COVID-19 Vaccine Acceptance and Hesitancy among Migrants, Refugees, and Foreign Workers: A Systematic Review and Meta-Analysis. Vaccines (Basel). 2023 Jun 6;**11**(6):1070. doi: 10.3390/vaccines11061070. PMID: 37376459; PMCID: PMC10302060.
5. Abba-Aji M, Stuckler D, Galea S, McKee M. Ethnic/racial minorities' and migrants' access to COVID-19 vaccines: A systematic review of barriers and facilitators. J Migr Health. 2022;**5**:100086. doi: 10.1016/j.jmh.2022.100086. Epub 2022 Feb 18. PMID: 35194589; PMCID: PMC8855618.
6. Nichol AA, Parcharidi Z, Al-Delaimy WK, Kondilis E. Rapid Review of COVID-19 Vaccination Access and Acceptance for Global Refugee, Asylum Seeker and Undocumented Migrant Populations. Int J Public Health. 2022 Dec 22;**67**:1605508. doi: 10.3389/ijph.2022.1605508. PMID: 36618432; PMCID: PMC9812946.
7. Jimenez ME, Rivera-Núñez Z, Crabtree BF, Hill D, Pellerano MB, Devance D, et al. Black and Latinx Community Perspectives on COVID-19 Mitigation Behaviors, Testing, and Vaccines. JAMA Netw Open. 2021 Jul 1;**4**(7):e2117074. doi: 10.1001/jamanetworkopen.2021.17074. PMID: 34264327; PMCID: PMC8283554
8. Shearn C, Krockow EM. Reasons for COVID-19 vaccine hesitancy in ethnic minority groups: A systematic review and thematic synthesis of initial attitudes in qualitative research. SSM Qual Res Health. 2023 Jun;**3**:100210. doi: 10.1016/j.ssmqr.2022.100210. Epub 2022 Dec 22. PMID: 36573229; PMCID: PMC9771578.
9. Knights F, Carter J, Deal A, Crawshaw AF, Hayward SE, Jones L, et al. Impact of COVID-19 on migrants' access to primary care and implications for vaccine roll-out: a national qualitative study. Br J Gen Pract. 2021 Jul 29;**71**(709):e583-e595. doi: 10.3399/BJGP.2021.0028. PMID: 33875420; PMCID: PMC8216266.
10. Rosano A, Dauvrin M, Buttigieg SC, Ronda E, Tafforeau J, Dias S. Migrant's access to preventive health services in five EU countries. BMC Health Serv Res. 2017 Aug 23;**17**(1):588. doi: 10.1186/s12913-017-2549-9. PMID: 28830423; PMCID: PMC5568253.
11. Vermeer B, Van den Muijsenbergh ME. The attendance of migrant women at the national breast cancer screening in the Netherlands 1997-2008. Eur J Cancer Prev. 2010 May;**19**(3):195-8. doi: 10.1097/CEJ.0b013e328337214c.

PMID: 20150815.
12. Francovich L, Gargiulo L, Giordani B, Giorgi Rossi P, Petrelli A. Prevention of female tumors among foreign women. Rapporto Osservasalute 2015. Milan: Prex; 2016: 302–307. Available from: http://www.inmp.it/index.php/ita/content/download/25682/172492/ file/La%20prevenzione%20dei%20tumori%20femminili%20nelle%20donne%20straniere.pdf [Last accessed: 2024 Jun 30].
13. van Leeuwen AW, de Nooijer P, Hop WC. Screening for cervical carcinoma. Cancer. 2005 Oct 25;**105**(5):270-6. doi: 10.1002/cncr.21153. PMID: 15937918.
14. Anson O. Inequality in the access to preventive health care: the case of immigrants in Belgium. Arch Public Health. 2001;**59**(5-6):265-79.
15. Riccardo F, Dente MG, Kojouharova M, Fabiani M, Alfonsi V, Kurchatova A, et al. Migrant's access to immunization in Mediterranean Countries. Health Policy. 2012 Apr;**105**(1):17-24. doi: 10.1016/j.healthpol.2012.02.004. Epub 2012 Mar 3. PMID: 22385905.
16. Campari C, Fedato C, Iossa A, Petrelli A, Zorzi M, Anghinoni E, et al; GISCi Migrant Working Group. Cervical cancer screening in immigrant women in Italy: a survey on participation, cytology and histology results. Eur J Cancer Prev. 2016 Jul;**25**(4):321-8. doi: 10.1097/CEJ.0000000000000173. PMID: 26207563.
17. Vallesi G, Bietta C, Marri M, Petrella M. Provenienza da Paesi a forte pressione migratoria e partecipazione allo screening citologico nell'AUSL2 dell'Umbria. Impatto sulla probabilità di presentare lesioni di alto grado e tumori del collo dell'utero [Immigration from countries with a strong migratory pressure and participation in cervical cancer screening program in the Local Health Unit 2, Umbria Region. Impact on the probability of high-grade lesions and cervical cancer]. Epidemiol Prev. 2012 Mar-Apr;**36**(2):95-9. Italian. PMID: 22706359.
18. Di Napoli A, Rossi A, Battisti L, Cacciani L, Caranci N, Cernigliaro A, et al. Valutazione dell'assistenza sanitaria della popolazione immigrata in Italia attraverso alcuni indicatori di un sistema nazionale di monitoraggio [Evaluating health care of the immigrant population in Italy through indicators of a national monitoring system]. Epidemiol Prev. 2020 Sep-Dec;**44**(5-6 Suppl 1):85-93. Italian. doi: 10.19191/EP20.5-6.S1.P085.077. PMID: 33415950.
19. Petrelli A, Di Napoli A, Rossi A, Costanzo G, Mirisola C, Gargiulo L. The variation in the health status of immigrants and Italians during the global crisis and the role of socioeconomic factors. Int J Equity Health. 2017 Jun 12;**16**(1):98. doi: 10.1186/s12939-017-0596-9. PMID: 28606147; PMCID: PMC5468957.
20. Bajaj SS, Stanford FC. Beyond Tuskegee - Vaccine Distrust and Everyday Racism. N Engl J Med. 2021 Feb 4;**384**(5):e12. doi: 10.1056/NEJMpv2035827. Epub 2021 Jan 20. PMID: 33471971; PMCID: PMC9908408.
21. Javadi D, Murchland AR, Rushovich T, Wright E, Shchetinina A, Siefkas AC, et al. Systematic review of how racialized health inequities are addressed in Epidemiologic Reviews articles (1979-2021): a critical conceptual and empirical content analysis and recommendations for best practices. Epidemiol Rev. 2023 Jun 29:mxad008. doi: 10.1093/epirev/mxad008. Epub ahead of print. PMID: 37386694
22. Deal A, Hayward SE, Huda M, Knights F, Crawshaw AF, Carter J, et al; ESCMID Study Group for Infections in Travellers and Migrants (ESGITM). Strategies and action points to ensure equitable uptake of COVID-19 vaccinations: A national qualitative interview study to explore the views of undocumented migrants, asylum seekers, and refugees. J Migr Health. 2021;**4**:100050. doi: 10.1016/j.jmh.2021.100050. Epub 2021 May 27. PMID: 34075367; PMCID: PMC8154190.
23. Benavides-Melo J, Rojas-Bautista L, Jaramillo-Arellano A, Montenegro-Coral FA, Rosero-Galindo CY, Salas-Zambrano A, et al. COVID-19 vaccination intention among Venezuelan migrant populations in Colombia, 2021. Travel Med Infect Dis. 2022 May-Jun;**47**:102250. doi: 10.1016/j.tmaid.2021.102250. Epub 2021 Dec 23. PMID: 34954111; PMCID: PMC8695514.
24. Page KR, Genovese E, Franchi M, Cella S, Fiorini G, Tlili R, et al. COVID-19 vaccine hesitancy among undocumented migrants during the early phase of the vaccination campaign: a multicentric cross-sectional study. BMJ Open. 2022 Mar 17;**12**(3):e056591. doi: 10.1136/bmjopen-2021-056591. PMID: 35301211; PMCID: PMC8931801.
25. Cesaroni G, Calandrini E, Balducci M, Cappai G, Di Martino M, Sorge C, et al. Educational Inequalities in COVID-19 Vaccination: A Cross-Sectional Study of the Adult Population in the Lazio Region, Italy. Vaccines (Basel). 2022 Feb 25;**10**(3):364. doi: 10.3390/vaccines10030364. PMID: 35334995; PMCID: PMC8950687
26. Bentivegna E, Di Meo S, Carriero A, Capriotti N, Barbieri A, Martelletti P. Access to COVID-19 Vaccination during the Pandemic in the Informal Settlements of Rome. Int J Environ Res Public Health. 2022 Jan 10;**19**(2):719. doi: 10.3390/ijerph19020719. PMID: 35055541; PMCID: PMC8776102.
27. Shaw J, Anderson KB, Fabi RE, Thompson CA, Harris M, Aljabbarin N, et al. COVID-19 vaccination intention and behavior in a large, diverse, U.S. refugee population. Vaccine. 2022 Feb 23;**40**(9):1231-1237. doi: 10.1016/j.vaccine.2022.01.057. Epub 2022 Feb 1. PMID: 35125223; PMCID: PMC8806127.
28. Russo AG, Tunesi S, Consolazio D, Decarli A, Bergamaschi W. Evaluation of the anti-COVID-19 vaccination campaign in the Metropolitan Area of Milan (Lombardy Region, Northern Italy). Epidemiol Prev. 2021;**45**(6):568-579. English. doi: 10.19191/EP21.6.114. PMID: 34791867.
29. Primieri C, Chiavarini M, Giacchetta I, de Waure C, Bietta C. COVID-19 Vaccination Actual Uptake and Potential Inequalities Due to Socio-Demographic Characteristics: A Population-Based Study in the Umbria Region, Italy. Vaccines (Basel). 2023 Aug 9;**11**(8):1351. doi: 10.3390/vaccines11081351. PMID: 37631919; PMCID: PMC10458483.
30. Our World in Data. Coronavirus (COVID-19) Vaccinations. Available from: https://ourworldindata.org/covid-vaccina-

tions [Last accessed: 2024 Jun 30].
31. Il 72% dei medici in Romania contro la vaccinazione obbligatoria negli ospedali. EuropaToday 2021 October 14. Available from: https://europa.today.it/attualita/medici-romania-contro-vaccinazione-obbligatoria.html [Last accessed: 2024 Jun 30].
32. Vaccinazione Covid. I medici europei molto favorevoli. Unica eccezione i romeni. Il sondaggio della Fems. Quotidiano Sanità, 2021 October 13. Available from: https://www.quotidianosanita.it/studi-e-analisi/articolo.php?articolo_id=99009 [Last accessed: 2024 Jun 30].
33. Italia-Romania: scambio di vedute su campagna vaccinale. Ministero degli Affari Esteri e della Cooperazione internazionale, 2021. Available from: https://www.esteri.it/it/sala_stampa/archivionotizie/retediplomatica/2021/10/italia-romania-scambio-di-vedute-su-campagna-vaccinale/ [Last accessed: 2024 Jun 30].
34. Vaccini nel mondo. Il Sole 24 Ore, ultimo aggiornamento September 2023. Available from: https://lab24.ilsole24ore.com/vaccinazioni-mondo/ [Last accessed: 2024 Jun 30].
35. European Centre for Disease Prevention and Control (ECDC). Due to ongoing changes in COVID-19 surveillance in the EU/EEA, this dashboard for EU/EEA daily cases and deaths will be retired from 1 November 2022. Available from: https://vaccinetracker.ecdc.europa.eu/public/extensions/COVID-19/vaccine-tracker.html#uptake-tab [Last accessed: 2024 Jun 30].
36. Iniziata la campagna di vaccinazione in Macedonia del Nord. Confindustria, 2021. Available from: https://www.confindustriamacedonia.mk/iniziata-la-campagna-di-vaccinazione-in-macedonia-del-nord, 2021 [Last accessed: 2024 Apr 15].
37. Macedonia del Nord, vaccinazione a rilento. Osservatorio Balcani e Caucaso, 2021. Available from: https://www.balcanicaucaso.org/aree/Macedonia-del-Nord/Macedonia-del-Nord-vaccinazione-a-rilento-209704 [Last accessed: 2024 Jun 30].
38. Stamatovska K, Kirijas M, GnjatovićM, ćujićD, Trajkov D, Cvetkovska E, et al. Prevalence of anti-sars-cov-2 igg antibodies in Skopje, North Macedonia: two-time points population-based cross-sectional study. Acad Med J. 2023; **3**(2): 19-31. https://www.doi.org/10.53582/AMJ2332019s.
39. Lebrun LA. Effects of length of stay and language proficiency on health care experiences among immigrants in Canada and the United States. Soc Sci Med. 2012 Apr;**74**(7):1062-72. doi: 10.1016/j.socscimed.2011.11.031. Epub 2012 Jan 25. PMID: 22326103.
40. Focus statistiche ISTAT 2023. Stranieri e naturalizzati nel mercato del lavoro italiano. Available from: https://www.istat.it/it/files//2023/02/Focus_stranieri-e-naturalizzati-nel-mondo-del-lavoro.pdf [Last accessed: 2024 Jun 30].
41. La comunità filippina in Italia-Rapporto annuale sulla presenza dei migranti. Ministero del Lavoro e delle Politiche Sociali, 2022. Available from: https://www.lavoro.gov.it/documenti-e-norme/studi-e-statistiche/rapporto-annuale-sulla-presenza-dei-migranti-2022-filippine [Last accessed: 2024 Jun 30].
42. La comunità peruviana- Rapporto annuale sulla presenza dei migranti. Ministero del Lavoro e delle Politiche Sociali, 2021. Available from: https://www.lavoro.gov.it/documenti-e-norme/studi-e-statistiche/Documents/Rapporti%20annuali%20sulle%20comunit%C3%A0%20migranti%20in%20Italia%20-%20anno%202021/Peru-rapporto-2021.pdf [Last accessed: 2024 Jun 30].
43. La comunità ecuadoriana- Rapporto annuale sulla presenza dei migranti. Ministero del Lavoro e delle Politiche Sociali, 2021. Available from: https://www.lavoro.gov.it/documenti-e-norme/studi-e-statistiche/Documents/Rapporti%20annuali%20sulle%20comunit%C3%A0%20migranti%20in%20Italia%20-%20anno%202021/Ecuador-rapporto-2021.pdf [Last accessed: 2024 Jun 30].

Corresponding author: Irene Giacchetta, Local Health Unit of Bologna, Department of Hospital Network, Hospital Management of Maggiore and Bellaria, L.go Bartolo Nigrisoli 2, 40133 Bologna (BO), Italy
e-mail: irene.giacchetta@gmail.com

Ann Ig. 2025 Jan-Feb; 37(1): 49-73 doi: 10.7416/ai.2024.2647. Epub 2024 Jul 17.

The impact of the COVID-19 pandemic on academic performance among developmental age students: a systematic review with meta-analysis

Vincenza Gianfredi[1], Simona Scarioni[1], Luca Marchesi[1], Elena Maria Ticozzi[1], Martina Ohene Addo[1], Valeriano D'errico[1], Lorenzo Fratantonio[1], Ludovica Liguori[1], Alberto Pellai[1], Silvana Castaldi[1,2]

Keywords: Academic performance; systematic review; meta-analysis; COVID-19; developmental age students
Parole chiave: Prestazioni accademiche; revisione sistematica; meta-analisi; COVID-19; studenti in età evolutiva

Abstract

Objective. *The COVID-19 pandemic has disrupted educational systems worldwide, raising concerns about its impact on academic performance, particularly among developmental age students.*
Methods. *A systematic review with meta-analysis aimed to evaluate the association between the COVID-19 pandemic and the academic performance in this population was performed according to PRISMA 2020 guidelines. PubMed/MEDLINE, Scopus and Embase were searched on December 2023 to identify relevant studies. Both fixed and random effect models were performed. The Effect size was reported as Cohen's d with a 95% Confidence Interval. Studies' quality was assessed using the Newcastle-Ottawa scale. The protocol was registered in PROSPERO.*
Results. *A total of 30 studies met the inclusion criteria, but only 13 could be combined in the meta-analysis. Based on a sample size of 4,893,499 students, pooled Cohen's d was -0.07 [(95% CI = -0.10; -0.03); p-value <0.001]. Subgroup analyses by subject suggested that performance in math was affected the most, Cohen's d= -0.14 [(-0.18; -0.10); p-value <0.001].*
Conclusion. *The findings revealed a significant negative association between the COVID-19 pandemic and academic performance among developmental age students. Interventions to mitigate the adverse effects of the pandemic on educational outcomes in this population are needed.*

[1] *Department of Biomedical Sciences for Health, University of Milan, Italy*
[2] *Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*

Annali di Igiene : Medicina Preventiva e di Comunità (Ann Ig)
ISSN (print) 1120-9135 ISSN (online) 3035-5559

https://www.annali-igiene.it

Introduction

Due to the novel nature and the coronavirus disease 2019 (COVID-19) (1) and its rapid spread, the World Health Organization (WHO) declared a pandemic situation in November 2020 (2,3). As a consequence, and considering the high burden of the disease (4), many countries worldwide quickly adopted preventive measures, including social distancing, that ended up in full lockdowns, including schools' closure and distance-based learning activities (5,6).

The sudden shift from in-person to online education altered the relationship between children and school, making it more challenging for both students and teachers to adapt adequately. This shift has affected not only the need to readjust teaching techniques but also instrumental aspects (7). In fact, several potential responses have been implemented by each country and schools, adopting remote learning policies based on the available resources and offering a combination of broadcast media, online platforms and paper-based delivery (8). In this context, students in more socially and economically disadvantaged conditions, faced greater difficulties (9). Thereby, these realities amplified pre-existing inequalities in learning, and schoolchildren who lacked access to distance-based learning had limited means to continue their education, increasing social discomfort, socio-economic disparities, and potentially even academic performance (10,11). Moreover, distance-based learning, together with general social distance, have largely impacted on perceived levels of stress and loneliness in young that affected their physical, mental and social health, in turn potentially associated with their academic performance (12-14). Moreover, United Nations Children's Fund (UNICEF) estimates that COVID-19 restrictive measures on the education system may have caused a loss of $17 trillion in future earnings for the involved generations (15).

On the other hand, the availability of alternative teaching methods has several potential strengths. Firstly, the need to adapt to the temporary situation might have contributed to innovating the learning methods, improving, and enforcing the traditional educational systems (16). Secondly, this situation has provided a teaching opportunity that enabled the continuation of educational activities and prevented a complete isolation of students from their peers and teachers. Such isolation would undoubtedly have resulted in a loss of educational opportunities for the children. Therefore, distance-based learning has offered a necessary form of social interaction essential for carrying on with learning activities (17).

Although some studies evaluated the consequences on academic performance, results appear to be inconsistent. Therefore, the goal of this systematic review is to retrieve all the available evidence assessing the association between the COVID-19 pandemic and the school performance among developmental age students.

Methods

The current systematic review with meta-analysis was conducted according to the guidelines of the Cochrane Collaboration (18), and the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines (19). The results were reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 (PRISMA-2020) (20). The research protocol was registered in the international database of prospectively registered systematic reviews (PROSPERO; registration number: CRD 42023452490).

Literature search strategy

The literature search was conducted simultaneously on PubMed/MEDLINE, Scopus and Embase on December 2023, based on the following research question: "What is the impact of the COVID-19 pandemic on academic performance of developmental age students?". Hence, the search strategy was developed considering three aspects: students of developmental age (as population), any type of teaching methods adopted during the COVID-19 pandemic (as exposure), and academic performance (as outcome of interest). Selected keywords, both MeSH terms and Title/Abstract, were combined using the Boolean operators "AND" and "OR". The search strategy was first developed in PubMed/MEDLINE and therefore adopted for Scopus and Embase. The search strategy used for each database is presented in the Supplementary Material: Table S1. Potential additional relevant articles were searched by screening the reference lists of the included articles and consulting experts in the field.

Inclusion/exclusion criteria

Inclusion/exclusion criteria were defined according to the following guidelines: Population (P), Exposure (E), Comparison (C), Outcome (O), Study design (S). Only observational epidemiological studies in developmental age students (6-18 years), assessing the

Table 1 - Inclusion/exclusion criteria based on Population, Exposure, Comparators/Controls, Outcome, Study design (PECOS) strategy

	Details
Search query	What is the impact of the COVID-19 pandemic on academic performance of developmental age students?
Inclusion criteria	P: Developmental age students (6-18 years), of both sexes. E: Any type of teaching methods adopted during the COVID-19 pandemic C: academic performance before and after COVID-19 pandemic O: Learning abilities and academic performance status and progression throughout the remote school year during COVID-19 pandemic S: Observational studies (cross-sectional or prospective or retrospective or ecological)
Exclusion criteria	P: preschool children, college students and above E: other interventions different than teaching methods adopted during the COVID-19 pandemic C: academic performance not related to COVID-19 pandemic O: Assessing different outcomes not listed in our inclusion criteria (as for instance resilience, stress, etc.) S: not original (reviews with or without meta-analysis), not performed among humans, not observational (as for instance trials), not published as peer-reviewed articles in international scientific journals (book, book chapter, thesis), no full-text papers (abstract, conference paper, letter, commentary, note)
Language	English
Time filter	After December, 01st, 2019
Databases searched	PubMed/MEDLINE Embase Scopus
Search date	December 2023

association between teaching methods adopted during the COVID-19 pandemic (any type) and academic performance (any type), published in English in international, peer-reviewed scientific journals, were considered eligible. In contrast, non-original or interventional studies assessing the association between any teaching methods and an outcome other than academic performance in people younger than 5 years or older than 18 years, not published in English and not in a peer-reviewed journal were excluded. A detailed description of the inclusion/exclusion criteria, defined according to PECOS, is provided in Table 1.

Study selection and data extraction

The selection of studies was carried out in two stages. First, titles and abstracts of records retrieved using the search strategy and those retrieved from additional sources were screened independently by two reviewers using the inclusion/exclusion criteria above. Secondly, the full-text was searched and downloaded only for potentially eligible articles. These were then assessed independently by two reviewers. Any disagreements about the eligibility and inclusion of articles were resolved by discussion between the reviewers. If disagreement persisted, a third senior researcher was involved to make the final decision. The extracted data were collected using a standardized, and pre-defined spreadsheet using Excel (Microsoft Excel® for Microsoft 365 MSO, USA, 2019). To improve the quality of data extraction, the spreadsheet was pre-tested on 5 randomly selected studies. The following information was extracted from each included study: first author, year of publication, study period, country in which the study was conducted, study design, number of participants, main population characteristics, age and sex, type of teaching method, measurement of academic performance, maximally adjusted effect size measurements along with the corresponding 95% CIs, variables used for adjustment, whether funding was received for conducting the original study, and declared conflicts of interest. Data extraction was performed in duplicate and discrepancies were resolved by discussion. Missing data were obtained by contacting the corresponding author.

Data synthesis

Following the PRIMA 2020 guidelines (20), the selection process was documented using a “flow diagram” showing the number of references excluded at each step. In addition, the extracted data were tabulated and summarized in text. Moreover, the results of the statistical analysis are presented in both tables, forest and funnel plots (detailed below).

Quality assessment

The methodological quality of the cohort and the case control studies was determined by the Newcastle–Ottawa Scale (NOS) (21), while, cross-sectional studies were assessed through the NOS adapted version for cross-sectional studies developed by Herzog et al (22). The NOS is a star system that assesses three main domains: the selection and comparability of the study groups, and the ascertainment of either the exposure or the outcome of interest. Based on previously adopted cut-offs (23), articles which had a NOS ≥ 7 were considered high quality, the ones with 4 ≤ NOS≤ 6 were considered as moderate quality and the ones with NOS ≤ 3 were considered low quality.

The ecological studies' quality was determined by the 15-item quality assessment tool proposed by Dufault et al for ecological studies (24). This scale evaluates three main domains: study design that can assign maximum 12 points, statistical methodology that can assign maximum 6 points and quality of reporting with a maximum of 3 points for a total of 21 points. Studies which had a quality score (QS) ≤ 7 were considered low quality, the ones with 7 < QS ≤ 14 were considered moderate quality, and the ones with QS >14 were considered high quality.

Statistical analysis

The Effect Size (ES) was calculating based on the mean and standard deviation (SD) or differences between means and SD, and sample size provided for each study. The most common descriptive statistics used in literature for continuous variables, following the normal distribution, is mean and SD (25). In the current meta-analysis, the pooled ES was expressed as standardized mean difference and measured as Cohen' s d with a 95% Confidence Interval (CI) (26). Cohen's d served as a representation of the distinctions in group averages, accounting for deviations in standard measures. This metric is commonly defined as minor (d = 0.2), intermediate (d = 0.5), and substantial (d = 0.8) (27). Nevertheless, Hattie (28) scrutinized the utility of Cohen's effect sizes in evaluating educational results, highlighting that seemingly trivial effect sizes could exert significant influences on certain students' learning. Keith (29) subsequently adjusted these criteria for academic learning: when d < 0.05, the effect is deemed too inconsequential to be deemed meaningful; d > 0.05 denotes a small yet meaningful effect, while d > 0.10 indicates a moderate effect, and d > 0.25 signifies a considerable effect.

Academic mean performance and its SD during pre-pandemic era were compared to academic mean performance and its SD during pandemic era. Both fixed and random effect models were used. We opted for this approach as the fixed effect model is typically employed when studies are considered to be similar. In other words, fixed effect model considered the individual studies as samples drawn from the same population, opposite to the random effect model where individual studies are intended as drawn from different populations. Conversely, the random effect model is recommended in cases of moderate or high heterogeneity. An I^2 test was conducted to assess the heterogeneity among the included studies, with the heterogeneity categorized into four distinct levels: high if I^2 values exceeded 75%, moderate for values ranging between 50% and 75%, low for values between 25% and 50%, and no heterogeneity if values were below 25% (30).

To assess potential publication bias, both graphical evaluation of the Funnel plot and Egger's regression asymmetry test were employed, with statistical significance set at $p < 0.10$ (31). In the event of publication bias, and to account for it, the trim and fill method, which involves searching for missing studies to the right of the overall, was implemented (32). Statistical analyses were performed using Prometa3® software (Internovi, Cesena, Italy).

Sensitivity and subgroup analyses

In our review protocol, we a priori defined two types of subgroup analyses: by teaching method, and by study design. Moreover, additional analyses were performed in order to explain high heterogeneity. In particular analysis only including studies that reported results as composite measure of academic performance and by subject (math or reading) were conducted. Further, a sensitivity analysis based on quality assessment (only studies with high methodological quality (33)) was performed.

Results

Literature search

A total of 3671 records were identified by searching Pubmed/MEDLINE (n = 1185), Scopus (n = 830) and Embase (n = 1656). Moreover, based on references screening 17 additional articles were preliminary included. However, 1218 records were immediately removed because duplicates. Therefore, 2470 records were further assessed. After the first screening, based on title/abstract, 2410 records were removed due to different language (n = 66), publication date before

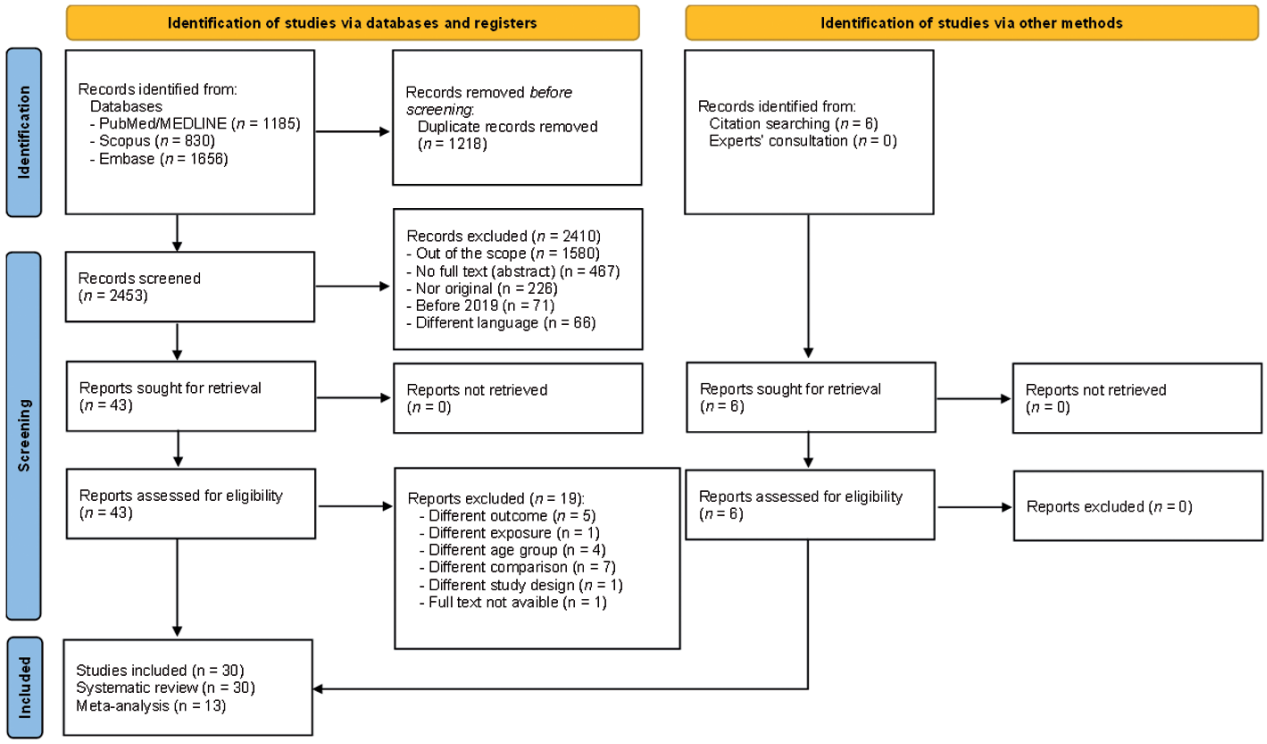


Figure 1 - Flow diagram of selection process

2019 (n = 71), non-original work (n = 226), no full text (n = 467) and focus on different topics (n = 1580), leaving 49 records eligible for inclusion. Based on full-text assessment, 19 records were excluded with reason (details are shown in Supplementary Material: Table S2) (34-52). At the end of the screening process 30 articles were included in the systematic review (53-82). The selection process is shown in Figure 1.

Main characteristics of included studies

All the studies included data regarding school closures and teaching methods following the COVID-19 pandemic in 2020, 2021, and 2022, with 12 studies also including data collected before 2020, within a timeframe ranging from 2008 to 2019.

The selected articles include twenty cohort studies (68.9%), five cross-sectional studies (17.2%), four ecological studies (13.8%), and one case-control study (3.4%). The most represented continent was Europe, with half of the included studies (n= 15, 50%). In detail, three studies were conducted in the Netherlands, three in Norway, two in Germany, two in Italy, one in Flanders, one in Spain, one in Austria, one in Finland, and one in Switzerland. Nine studies (27.6%) took place in the Americas, with 8 in the USA and one in Mexico. Four studies (13.8%) were designed in Asia, two in India, one in China, and one in Indonesia. Lastly, two studies (6.8%) took place in Africa, with one study conducted in Ethiopia and one in South Africa. Overall, there is good global representation, with the notable exception of the Australian-New Zealand region. Qualitative data extracted from included studies are detailed in Table 2.

Main characteristic of studied population

Approximately 33% of the included studies (10/30) included mixed in person and online learning, the remaining 66% of the studies (20/30) included distance learning during school closure. The age of included children ranged between 7 and 19 years. Moreover, the smallest sample size reported was 92 subjects (54), whereas the largest was 2,248,194 subjects (55).

All the included studies assessed the academic performance among a representative sample of the target population, only two studies specifically included students with diagnosis of specific learning disorders (dyslexia and/or dysorthography and/or dyscalculia) (54); and with diagnosis of attention deficit hyperactivity disorder (ADHD) (57). Details are reported in Table 2.

Table 2 - Qualitative characteristics of included studies, reported in alphabetical order

Author name	Study period	Country	Study design	Sample size	Main characteristics of the population	Age and gender	Type of teaching method
Ardington, 2021	2018-2021	South Africa	panel data cohort study	Grade 2: 566 (pre) 435 (post pandemic); Grade 4: 2910 (pre) 1899 (post pandemic)	Grade 2-4 students in under-resourced school contexts	n.a.	school closure, no further details
Bayley, 2023	2019-2021	Ethiopia	panel data cohort study	2741 in 2019, 2416 in 2021	Ethiopian students enrolled in grade 4 in 2019 and in grade 6 in 2021 in 138 schools.	11-13 y M: 51.0% in 2019, M: 51.6% in 2021.	Distance learning during school closure, with the inclusion of educational radio programs broadcasted by the government for primary school pupils, mixed with in person traditional learning
Battisti, 2022	2020	Italy	cross-sectional study	92 parents-student pairs	Students between 11-19 yrs old, with diagnosis of SLD (dyslexia and/or dysorthography and/or dyscalculia), and non-verbal Intelligence Quotient (nvIQ) ≥ 70 (±5 points allowing for measurement error)	11-19 y M: 52,2%	Distance learning, no further details
Battisti, 2023	2020-2021	Italy	panel data cohort study	2,248,194	Nationwide data	10-18 y gender n.a.	Mixed in person and online learning (following school closures)
Breaux, 2022	2020-2021	USA	panel data cohort study	238	Adolescents, 49.6% with ADHD	15-17 y M: 55.5%	Remote, hybrid and in person learning
Cingel, 2022	2020–2021	USA	cross-sectional study	1,256	US adolescents with 47.9% identifying as White/Caucasian	14–16 y F: 65%	In-person in the school building", "hybrid model where some school is in-person and some is virtual/online", "completely virtual/online"
Domingue, 2022	2018-2021	USA	panel data cohort study	78,429 in 2018-2019; 52,280 in 2020-2021	Grades 1-4, in advantaged set of districts	n.a.	n.a.
Engzell, 2020	2017-2020	Netherlands	panel data cohort study	358,379	15% of all primary schools	8-11 y gender n.a.	Nationwide school closures that lasted 8 weeks, no further details
Engzell, 2021	2017-2020	Netherlands	panel data cohort study	358,379	15% of all primary schools	8-11 y gender n.a.	Nationwide school closures that lasted 8 weeks, no further details
Fisher, 2022	2020-2021	USA	cross-sectional study	2,152	Students attending a US-based public, private or charter middle or high school	13-18 y M: 1081	In person 425(19,8%), Hybrid 884 (41,1%), Remote/virtual 843(39,2%)
Förster, 2023	2019-2021	Germany	panel data cohort study	19,500 second grade students	Grade 2 students, boys and girls, between students with and without a migration background	7-11 y F: 47.12%	Mixed home-based virtual learning, face-to-face instruction with spacing rules and masks (in periods of relatively low incidence), and alternating instruction, in which half of the class attended school for a week and then received a week of distance instruction.
Guariso, 2023	2018-2022	India (Assam)	panel data cohort study	4,998	Grades 2- 4	7-12 y F: 51%	Remote learning, WhatsApp
Haelermans, 2022	2013-2020	Netherlands	panel data cohort study	263,553	Grades 1-5	age n.a. F: 49.75%	In person and remote

Hevia, 2022	2018-2021	Mexico	panel data cohort study	3161	Students selected from multistage, probabilistic stratified cluster sampling	12.07 (mean) y M: 49.64%	Remote learning via the internet (2020) and via television (2021)
Kuhfeld, 2022	2019-2021	USA	panel data cohort study	845,222	Grades 3–8 students	age n.a. M: 51%	Home-based virtual learning
Lerkkanen, 2023	2008-2011, 2016-2020	Finland	ecological study	pre-COVID: 378 during COVID: 198	Children from First Steps study (pre covid) and from Teacher and Student Stress and Interaction in Classroom study	from grade 1 to 4, no further data	remote for 8 weeks
Liao, 2022	2020	China	cross-sectional study	7,202	Junior high school students from Shaanxi province	12-15 M: 50,8%	In person and remote
Mælan, 2021	2018-2020	Norway	cross-sectional study	1,755 in 2020 4,875 in 2018	Grades 8-10	age n.a. M: 47.3%	Remote learning through homeschooling during the two-month school lockdown
Maldonado, 2022	2015-2020	Netherlands (Flanders)	panel data cohort study	5,691	Grade 6 (last year of primary school)	n.a.	Distance teaching consisted of the first three weeks focused on reviewing and practicing previously taught materials, followed by four weeks dedicated to previewing new material that will be covered once schools reopen
Pandango, 2023	2018-2022	Indonesia	panel data cohort study	2,222	Grades 4-6, in six elementary schools	n.a.	Online and in person learning
Relyea, 2023	2018-2021	USA	panel data cohort study	52,525	Grade 3–5 students in a large urban school district in North Caroline; 8% of students with disabilities	age n.a M: 50.2%	Home-based virtual learning
Rishitha, 2022	n.a.	India	case-control	cases: 120; control: 88	Students with IQs above 70, excluding children having autism, other disabilities and with neurological disorders.	8-14 y gender n.a.	Computer-based education in a virtual classroom
Skar, 2022	2019-2020	Norway	panel data cohort study	817 in 2019 1,636 in 2020	15,8% bilingual, 77,5% native Norwegian speaker, 6,7% non-native Norwegian speaker	age n.a. M: 48.5%	Emergency remote instruction via digital meeting platforms
Skar, 2023	2019-2021	Norway	panel data cohort study	1,668	Students come from four municipalities, two of them represented major urban areas, whereas the other two municipalities represented more rural areas. Grade 2	age n.a. M: 46.8%	Emergency remote instruction via digital meeting platforms
Spitzer and Moeller, 2023	2017-2020	Austria	panel data cohort study	168	no details	n.a.	Intelligent tutoring system designed for learning mathematics (Bettermarks system)
Spitzer and Musslick, 2021	2019-2020	Germany	ecological study	2,556	Students from all states in Germany and all types of schools from grades 4-10	n.a.	Intelligent tutoring system designed for learning mathematics (Bettermarks system)
Sun, 2023	2019-2020	USA	panel data cohort study	237	95 monolingual, 75 Spanish–English, and 67 Chinese–English bilingual children	age n.a. M: 53.4%	Home-based virtual learning
Tapia-Serrano, 2022	2018-2021	Spain	ecological study	844 in 2018 501 in 2021	Two groups of students similar in terms of age, sex, and socio-economic status, as all schools included belonged to neighbourhoods with similar socio-demographic characteristics	11-16 y M: 51%	Remote virtual learning
Tomasik, 2021	2020	Switzerland	panel data cohort study	28,685	Grades 3-9	9-15 y M: 49.7%	Distance and in person learning
Uthappa, 2023	2018-2021	USA	ecological study	704,929	Students from urban districts	from kindergarten through 8th grade no further data	Hybrid and fully in person learning

ADHD: attention deficit hyperactivity disorder; 95% CI: 95% confidence interval; ES: effect size; M: male; n.a.: not available; OR: odd ratio; SD: standard deviation; SLD: Specific Learning Disorders; USA: United States of America; y: years

Quality assessment

The overall quality of the cohort, case-control and cross-sectional studies, evaluated with the NOS scale system, was generally high. More in depth, 20 of the studies were considered high quality, 4 were assessed as moderate quality (58,62,74,77), and 2 as low quality (54,70). The main reasons for low quality were primarily attributed to the assessment of academic achievement through self-reporting. Additionally, Battisti's study focused on a selected group of students, and Maelan's study did not account for any factors when analyzing the results. On the other hand, the quality of all the ecological studies was high. Supplementary Material: Table S3 reports the item-by-item quality assessment for each included study. Inter-rater reliability was assessed, and discrepancy among the two reviewers was around 5%. Disagreements were. solved through discussion, and a final agreement was reached for all included studies. Supplementary Material: Table S4 shows the quality of each of the included articles.

The item that affected the quality of most of the articles was the adjustment. The most important factor selected in our assessment was academic year. In this perspective, 13.3% (n=4) of the articles adjusted their results just for the academic year, 13.3% (n=4) of the studies did not adjust by academic year but took in account other forms of adjustments; while 36.7% (n=11) articles did not use any adjustment factor in the evaluation of their result. Additionally, information regarding conflict of interests, and funds were collected (Table 3). Details on the conflict of interests were reported by 46.7% (n=14) of the articles, 2 of them declared some form of conflict of interests. Information concerning fundings was available for 60% (n=18) of the articles, 16 of them reported to have received funding, while two declared to not have received any funding.

Meta-analysis

Among the 30 studies included in the systematic review, four reported data as beta coefficients without 95%CI (75-78), two studies expressed the results as odds ratios (OR) (62, 74), one study presented results as the number of corrected words read per minute (59), one study reported results are z-score and p-value (56), in four studies data were not extractable (58, 63, 66, 68), while the remaining studies (n= 18) presented the data as the mean of academic performance before the pandemic and the mean during the pandemic or differences between the means (53-55,57,60,61,64, 65,67,69-73,79-82). However, among the studies

Table 3 - Quantitative characteristics of included studies, reported in alphabetical order

Author name	Measurement of academic performance	Maximally adjusted ES 95%CI	Type of ES	Meta-analysis	Adjustment	CoI	Funds
Ardington, 2021	Oral reading in Nguni home languages (isiXhosa, Siswati and isiZulu) and English (e Early Grade Reading Assessment) letter sound and fluency (number of words read correctly per minutes)	Grade 2 letter sound: –16.00 (p<0.001), home language fluency: –7.339 (p<0.001); Grade 4 home language fluency: -6.900 (p<0.001), English fluency: -6.537 (p<0.001)	mean difference	no	Difference in difference model. Participants come from the same school with no differences before/after. For grade 4 an exact matching method was used to match students' initial reading performance, gender and school quintile.	n.a.	yes
Bayley, 2023	Numeracy: correctness in a multiple-choice items test	z-score: 0.56 SD: 0.02, p<0.001	z-score	no	gender, age, class grade, primary caregiver's education, size and wealth of the household, learners' teacher's years of experience and highest qualification, school region and location, whether rural or urban	no	yes
Battisti, 2022	Adolescents' Academic Grades (up to 10) self-reported by parents	Italian: 6.55 ± SD 0.87 vs. 6.87 ± 0.98, Math: 6.48 ± 1.21 vs. 6.82 ± 1.22; English: 6.49 ± 1.16 vs. 6.79 ± 1.24	mean SD	yes	Bonferroni correction	no	yes
Battisti, 2023	INVALSI tests in Mathematics and Italian	Math: 0,19 p=0.00 Italian: 0,11 p= 0.00	mean difference	no	paired matched	n.a.	n.a.

Breaux, 2022	High school GPA (Grade Point Average)	ADHD: 3.51 ± 0.53 (2020); 3.28 ± 0.64 (2021); No ADHD: 3.76 ± 0.29 (202), 3.72 ± 0.42 (2021)	mean SD	yes	none	no	yes
Cingel, 2022	Self-reported pre and post pandemic grade	Bonferroni post-hoc analyses indicated that participants who were in virtual schooling reported a greater drop in grades relative to those attending in-person ($p < 0.0001$) or in hybrid format ($p = 0.014$). Data not shown	data not extractable	no	Bonferroni correction	n.a.	yes
Domingue, 2022	Oral reading fluency (number of words read correctly divided by the elapsed time)	slower growth in oral reading fluency	words correct per minutes/ month	no	person and book in order to eliminate individual-specific performance differences and text-specific differences	yes	yes
Engzell, 2020	Biannual national test scores in maths, spelling and reading (composite measure)	Composite: 0.28 ± 10.90 pre, -1.28 ± 11.83 post Math: 0.36 ± 15.00 pre, -1.79 ± 15.21 post; Reading: 0.66 ± 18.96 pre, -1.01 ± 18.94 post; Spelling: 0.05 ± 17.27 pre, -0.71 ± 17.07 post	mean SD	yes	time elapsed between testing dates and a linear trend in year	n.a.	n.a.
Engzell, 2021	Biannual national test scores in maths, spelling and reading (composite measure)	Composite: 0.28 ± 10.90 pre, -1.28 (11.83) post Math: 0.36 ± 15.00 pre, -1.79 ± 15.21 post; Reading: 0.66 ± 18.96 pre, -1.01 ± 18.94 post; Spelling (0.05 (17.27) pre, -0.71 (17.07) post	mean SD	yes	time elapsed between testing dates and a linear trend in year	no	yes
Fisher, 2022	Self-reported pre and post pandemic grade (dicotomized variable in "declined" or "same/improved")	Hybrid: OR= 0.58 (0.42, 0.80) p<0.001; Remote/virtual: OR= 0.50 (0.36, 0.69) p<0.001 Ref: having same/improved academic grade compared to pre-pandemic	OR (95%CI)	no	Census region, locality, Social Vulnerability Index, and SARS-CoV-2 transmission level	no	yes
Förster, 2023	Test series quop-L2 score	data not extractable (only reported in figure)	data not extractable	no	propensity score matching	n.a.	n.a.
Guariso, 2023	Standard ASER (Annual Status educational Report) test conducted yearly by the ASER Center across India for children	Maths= -0.30 (p=0.00); Reading= -0.39 (p=0.00)	mean difference	no	mean and standard deviation for students	n.a.	n.a.
Haelermans, 2022	Standardized test scores from Netherlands Cohort Study on Education project in the area of reading, spelling and math	Reading: -0.153 p<0.01 Spelling: -0.223 p<0.01 Math: -0.324 p<0.01	mean difference	no	school	no	yes
Hevia, 2022	4 items score in reading, 5 items score in math	no summary data, results are stratified by socio-economic status or gender. No composite measure for math or reading, only by item	data not extractable	no	none	n/a	yes
Kuhfeld, 2022	Measure of Academic Progress score	Math: 219.14 ± 18.16 (2020); 222.62 ± 18.08 (2019) Reading: 212.46 ± 16.88 (2020); 213.86 ± 16.12 (2019)	mean SD	yes	academic year	n.a.	n.a.
Lerkkanen, 2023	Tests for: reading fluency and reading comprehension (nationally normed reading test battery ALLU), arithmetic fluency and arithmetic reasoning (arithmetic reasoning test)	No summary data, results are stratified by grade, and by academic task	data not extractable	no		no	yes
Liao, 2022	Administrative data on students' test scores	222.111 ± 55.296 pre, 219.517 ± 55.586 post	mean SD	yes	academic year	n.a.	yes
Mælan, 2021	Teacher reported grade (from 1 to 6) and self-reported grade	homeschooling: mean 4.07 SD (0.89); regular 3.78 (1.04)	mean SD	yes	none	no	n.a.
Maldonado, 2022	Standardised tests that are administered every year by the network of Catholic schools in Flanders	Math: -0.15 ± 0.08 Dutch: -0.18 ± 0.05	mean difference SD	yes	test version, school characteristics, year 6 characteristics, teacher characteristics and year 4 scores	no	yes
Pandango, 2023	Mean scores in Mathematics, Indonesian Language and Science	87 ± 5.8 pre 84.7 ± 6.2 post	mean SD	yes	academic year	no	no
Relyea, 2023	Measure of Academic Progress score	201.66 ± 19.07 (2019); 202.74 ± 18.26 (2020)	mean SD	yes	none	n.a.	yes

Rishitha, 2022	Academic Performance Rating Scale: teacher survey on student's performance and behaviour	OR= 29.64 (no 95%IC data), p=0.05	OR	no	none	no	n.a.
Skar, 2022	Writing, handwriting fluency, and attitude toward writing	text quality: -2.131 p= 0.001; handwriting: –0.240 p<0.001; attitude writing: -0.056 p=0.036	beta coefficient	no	variance due to national test scores, school size, proportion of certified teachers, students per special education teacher, school hours per student, student gender, and native language	n.a.	yes
Skar, 2023	Writing performance rated individually by two trained raters	text quality: 0.074 p= 0.089; handwriting: –1.707 p= 0.055; attitude writing: -0.044 p=0.155	beta coefficient	no	national test result, school size, proportion of certified teachers, students per special education teacher, and school hours per student, gender and language background	n.a.	n.a.
Spitzer and Moeller, 2023	relative error rate indicating below or above average performance	0.01, p<0.001	beta coefficient	no	none	no	no
Spitzer and Musslick, 2021	relative error rate indicating below or above average performance	-1.21e-02 p< 0.001	beta coefficient	no	none	n.a.	n.a.
Sun, 2023	test score	Vocabulary: 106.85 ± 18.66 pre, 111.77 ± 17.78 post p<0.001; Phonological: 10.69 ± 2.91 pre, 10.46 ± 3.04 post p=0.11; Reading: 108.17 ± 17.33 pre, 109.69 ± 17.19 post p= 0.027; Passage comprehension: 102.17 ± 14.62, 100.58 ± 14.58 post p=0.040	mean SD	yes	none	n.a.	n.a.
Tapia-Serrano, 2022	school records at the end of the academic year (average score of Spanish, English, math and physical education)	7.16 ± 1.61 pre, 6.89 ± 1.64 post p<0.01	mean SD	yes	none	n.a.	n.a.
Tomasik, 2021	Teacher generated assessments in mathematics and German supplied by the MINDSTEPS system	8.86, p=0.001 primary school	mean difference	no	none	n.a.	n.a.
Uthappa, 2023	Grade level proficiency in mathematics and reading measured by two different state-issued standardized assessments and individual district administered standardized tests	Math: -0,12 (-0.16; -0.19) Reading: -0.19 (-0.11; -0.13)	mean difference SD	yes	none	yes	yes

ADHD: attention deficit hyperactivity disorder; 95% CI: 95% confidence interval; CoI: conflict of interest; ES: effect size; OR: odd ratio; SD: standard deviation

reporting mean or difference between the means (n=18), 5 did not provide standard deviation values, and for this reason, they could not be computed in the meta-analysis (53,55,64,65,81). Among the 13 studies that reported full data expressed as the mean of academic performance scores or the difference between means (54,57,60,61,67,69-73,79, 80,82), the majority of studies (n=8) reported data on academic performance as a composite measurement (57,60,61,69,70,72,73,80), while some authors presented results on academic performance divided by subject type (e.g., Italian, English, Mathematics, etc.) (54,60,67,71,82) or by task (e.g., comprehension, reading, etc.) (79). For this reason, studies in which results were reported for individual subjects or tasks were considered as independent studies. Similarly, the study conducted by Breaux et al reported separate data for students with and without attention deficit hyperactivity disorder (ADHD) (57). In this case as well, the data were treated as coming from

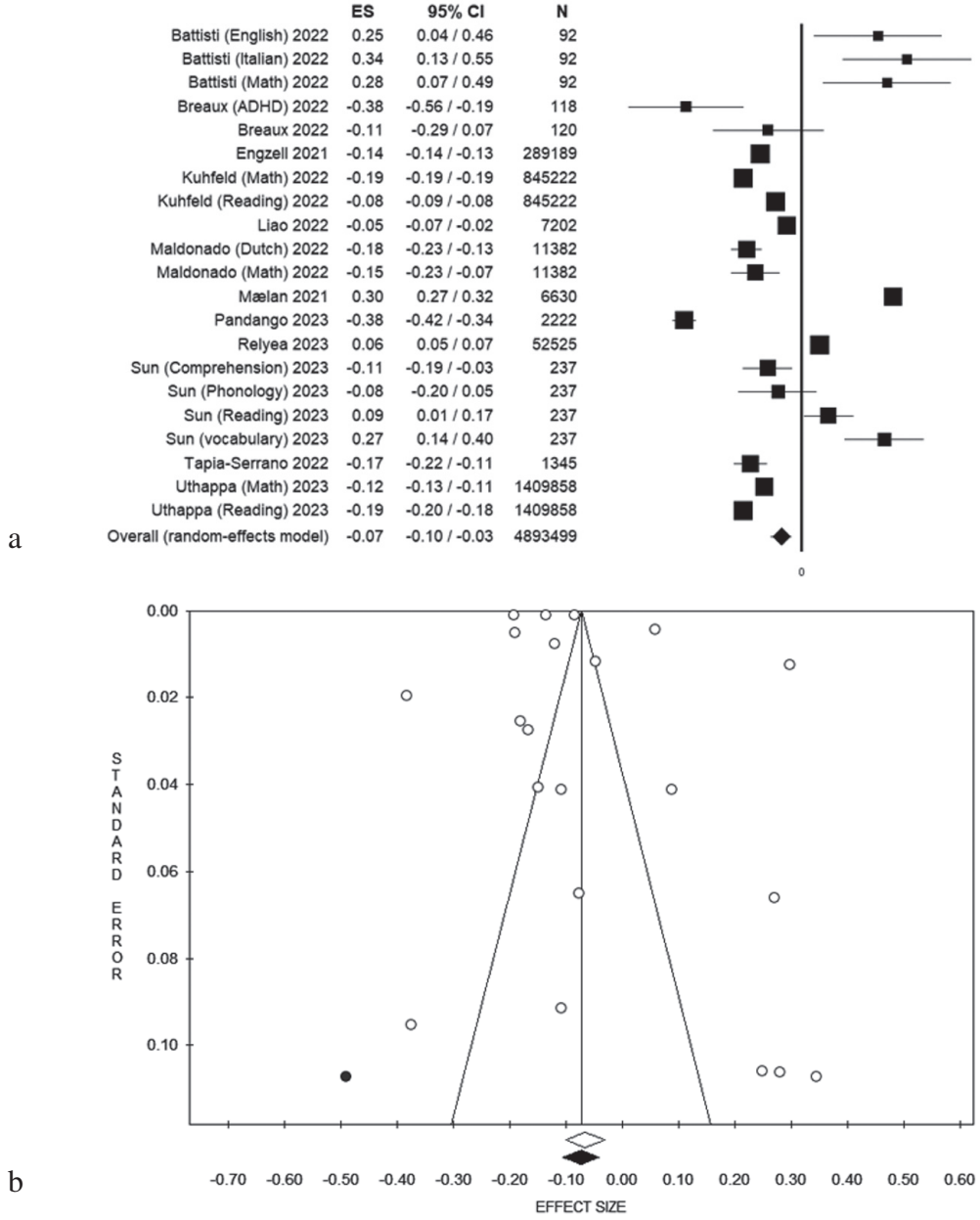


Figure 2 - Forest (a), and funnel plot (b) of the meta-analysis assessing the association between COVID-19 pandemic and academic performance. Random effect model. ES: Effect size

independent studies. Lastly, two studies conducted by the same authors were based on the same cohort (60,61). For this reason, to avoid overestimation, they were considered only once. In the end, the meta-analysis was conducted based on a total of 21 datasets. Quantitative data extracted from included studies are reported in Table 3.

Considering all the 21 data sets and using the random effect model, the pooled standardized mean difference measured as Cohen' s d was -0.07 [(95% CI = -0.10; -0.03); p-value <0.001] based on 4,893,499 students (Figure 2a) with high statistical heterogeneity (df = 19, I^2 = 99.76, p-value =< 0.001). Potential publication bias was identified by visual assessment of the funnel plot (Figure 2b) and confirmed by Egger's linear regression test (intercept 4.45, p-value = 0.404). After applying the trim and fill method, the estimated effect size did not materially change (Table 4). Full data for fixed and random effect model are reported in Table 4 (Supplementary Material: Figure 1a and 1b). Moreover, considering that one study reported data for ADHD students (57), and another focused-on students with specific learning disorders (54), we excluded these data to increase comparability. However, results remained similar (Table 4). Due to the high heterogeneity found, additional analyses aimed to find potential explanation for this were performed. In particular, when only studies reporting a composite measurement of academic achievement was considered, the pooled Cohen' s d was statistically significant only when fixed effect model was applied (Table 4, Supplementary Material: Figure 2a and 2b).

Subgroup and sensitivity analysis

Since all the included studies did not explicitly detailed teaching methods, but on the contrary, they generically described them as remote, hybrid, or distance learning, the subgroup analysis by teaching method was not possible. Instead, subgroup analysis by study design was conducted grouping cross-sectional studies or panel cohort studies. When cross-sectional and ecological studies were analyzed, the pooled Cohen' s d was not statistically significant when random effect model was performed, similarly when only cross-sectional studies were included; whereas a statistically significant association was found between COVID-19 pandemic and increased academic performance when fixed random effect was applied to only cross-sectional studies (Table 4). On the contrary, when only panel cohort studies were included, the Cohen' s d was -0.56 [(95% CI = -0.65; -0.47); p-value < 0.001]. Lastly, when only studies with high methodological quality were included, results remained stable.

Discussion

Interpretation of the results

In the current systematic review association between COVID-19 pandemic and academic performance among developmental age students (6-18 years) was assessed. Out of 3671 studies, retrieved form PubMed/ Medline, Scopus and Embase, 49 studies were considered eligible after the first screening, however, at the end of the full screening process 30 studies were included in qualitative synthesis, and 13 studies (with 21 data sets) were included in the meta-analysis. Main reasons for exclusion after full assessment was different outcome. Whereas the high variability trough which results were reported and incompleteness of data, largely impacted on the possibility to pool data in the meta-analytical evaluation. However, the total number of included studies is satisfactory, confirming that the topic has proven to be of particular interest within the scientific community.

The pooled standardized mean difference, based from 4,893,499 students, measured as Cohen's d, was -0.07 (95% CI = -0.10; -0.03), indicating a small but meaningful statistically significant negative association between the COVID-19 pandemic and academic performance. However, high statistical heterogeneity was found, and despite multiple subgroups or sensitivity analyses performed, none of them could statistically explain the heterogeneity. Nevertheless, it is important to note that although the studies considered for the meta-analysis all reported average values (or differences between averages), each study assessed academic performance using different methodologies. Additionally, some studies presented the evaluation as a composite measure, while in other cases, it was divided by subject or task. This varied measurement approach also implies different ranges within which the performance assessment could range. This was the reason why ES has been reported as standardized mean difference. Nevertheless, the approach presupposes that variations in standard deviations across studies signify distinctions in measurement scales rather than actual disparities in variability among study populations. This assumption could pose challenges in situations where real differences in variability between the participants in different studies are expected. For instance, in the current meta-analysis both cross-sectional, cohort

Table 4 - Summary statistics of main, sensitivity and subgroup analyses.

				Summary statistics		Publication bias	
Analysis	***Included studies [Ref]***	***Total sample size***	***Df***	***Cohen's d (95% CI); p-value***	***I^2; p-value***	***Intercept'; p-value***	***Estimated[a] ES; p-value***
Overall	55, 58, 61, 62, 68, 70-74, 80, 81, 83	4,893,499	20	FE: -0.13 (-0.13; -0.13); <0.001	99.76; <0.001	4.45; 0.404	FE: -0.13 (-0.14; -0.13); <0.001
				RE: -0.07 (-0.10; -0.03); <0.001			RE: -0.07 (-0.11; -0.04); <0.001
Removing ADHD and SLD students	58, 61, 62, 68, 70-74, 80, 81, 83	2,050,625	16	FE: -0.13 (-0.13; -0.13); <0.001	99.83; <0.001	4.92; 0.385	FE: -0.13 (-0.14; -0.13); <0.001
				RE: -0.08 (-0.11; -0.05); <0.001			RE: -0.08 (-0.11; -0.05); <0.001
Composite measure of academic performance	58, 61, 70, 71, 73, 74, 81	359,233	6	FE: -0.12 (-0.12; -0.12); <0.001	99.81; <0.001	5.14; 0.459	FE: -0.12 (-0.13; -0.12); <0.001
				RE: -0.07 (-0.18; 0.05); 0.268			RE: -0.07 (-0.18; 0.05); 0.268
Cross-sectional and ecological studies	56, 70, 71, 81, 83	2,835,169	7	FE: -0.11 (-0.12; -0.11); <0.001	99.49; <0.001	8.67; 0.270	FE: -0.15 (-0.16; -0.15); <0.001
				RE: 0.06 (-0.07; 0.19); 0.376			RE: -0.04 (-0.17; -0.09); 0.527
Only cross-sectional studies	56, 70, 71	14,108	4	FE: 0.12 (0.10; 0.13); <0.001	99.02;< 0.001	2.25; 0.789	FE: -0.04 (-0.06; -0.03); <0.001
				RE: 0.22 (-0.00; 0.44); 0.053			RE: 0. 19(-0.01; 0.39); 0.065
Only panel cohort studies	58, 61, 68, 72-74, 80	2,058,330	12	FE: -0.13 (-0.13; -0.13); <0.001	99.83;< 0.001	3.018; 0.710	FE: -0.13 (-0.13; -0.13); <0.001
				RE: -0.11 (-0.15; -0.07); <0.001			RE: -0.11 (-0.15; -0.07); <0.001
Only studies assessing Math performance	56, 61, 68, 72, 83	2,555,743	4	FE: -0.18 (-0.18; -0.18); <0.001	99.34;< 0.001	7.16; 0.413	FE: -0.19 (-0.19; -0.19); <0.001
				RE: -0.14 (-0.18; -0.10); <0.001			RE: -0.14 (-0.18; -0.10); <0.001
Only studies assessing Reading performance	61, 68, 80, 83	2,544,506	3	FE: -0.09 (-0.09; -0.09); <0.001	99.30;< 0.001	-6.99; 0.571	FE: -0.09 (-0.09; -0.09); <0.001
				RE: -0.10 (-0.13; -0.07); <0.001			RE: -0.12 (-0.15; -0.09); <0.001
High quality methodological studies	55, 58, 61, 62, 68, 70, 72-74, 80, 81, 8[3]	4,886,869	19	FE: -0.13 (-0.14; -0.13); <0.001	99.74;< 0.001	2.64; 0.615	FE: -0.13 (-0.14; -0.13); <0.001
				RE: -0.09 (-0.13; -0.06); <0.001			RE: -0.10 (-0.13; -0.07); <0.001

[a] after applying the Trim and Fill method; ADHD: attention deficit hyperactivity disorder; 95% CI: 95% confidence interval; df: degree of freedom; ES: effect size; FE: Fixed effect model, RE: random effect model; SLD: Specific Learning Disorders

and ecological studies were included. Ecological studies include a wider range of participants and may consequently have higher standard deviations, on the contrary cohort or cross-sectional studies include a sample of the whole population, which could imply potential selection bias. Moreover, the high heterogeneity could also be attributed to the type of comparison conducted. Specifically, some studies compared the pandemic year with the previous one, while others compared a longer time span. Furthermore, the high heterogeneity could be attributed to the type of teaching implemented during the pandemic. In fact, some schools conducted educational activities using the internet, while others relied on radio-television support. However, the level of detail provided by individual studies varied considerably and was partially incomplete, preventing us from conducting a subgroup analysis as hypothesized in the research protocol. Additionally, sensitivity analysis considering only studies with high methodological quality yielded consistent results. Moreover, subgroup analysis by study design revealed that cross-sectional and ecological studies did not show a statistically significant association, while panel cohort studies indicated a significant moderate negative effect (Cohen's d = -0.13). Further, an additional analysis by type of academic performance measure (composite or divided by subject) reviled that during COVID-19 pandemic academic performance in math was affected the most. Lastly, our results should be interpreted in light of the potential publication bias detected. However, after applying the trim and fill method, the estimated effect size remained relatively unchanged.

To summarize, the findings suggest from low to modest, but statistically significant negative impact of the COVID-19 pandemic on academic performance. Additional analyses, such as subgroup and sensitivity analyses, provided insights into the potential sources of heterogeneity and supported the robustness of the overall findings.

Implications for policies and practices

Various practical implications can be drawn. Firstly, becoming aware of the negative impact that the pandemic has had on academic performance is crucial for the development of targeted interventions to address learning gaps. From our results, it appears that mathematics is the subject that, more than others, has felt the challenges posed by the pandemic (83). Additionally, interventions that not only act on students but also on teachers, implementing initiatives to provide support and resources needed to train and enhance teachers' teaching skills, through platforms and technological methods are needed. Allocating resources to promote teacher training, with a focus on acquiring the necessary skills for effective remote or hybrid teaching, would enable educators to stay updated (84). This would enhance the learning experience for students and contribute to a less stressful teaching experience for educators. Indeed, according to the study conducted by Coman et al., in educational contexts insufficiently prepared for remote teaching, both in terms of technology and methodology, students face significant challenges (85). Among them, technical issues, followed by teachers' inadequate technical skills and teaching styles not appropriately adapted to the online environment were the three most frequently reported. In this context, the advantages of online learning might become futile in the unequipped and unprepared school systems. In addition, it is important to consider the parents' perspective in supporting children during remote learning activities. The data presented by Battisti et al. revealed a higher level of stress, among children with specific learning disorders, during online activities, both due to difficulties in following educational tasks, mainly related to homework, online lessons, written tests, oral exams, and device usage, as well as the social isolation (54). Furthermore, in the same study, the results highlight an association between the perceived stress levels of children in conducting remote learning activities and the stress levels of parents in supporting their children's learning and balancing daily home activities and/or smart-working. Similarly, Dong et al. found a negative feeling with distance-based learning among Chinese parents (86).

Equally, training must be accompanied by the enhancement of the infrastructure itself, allowing a transition from remote teaching, implemented in response to the pandemic urgency, to an e-learning approach capable of supporting and complementing traditional forms of teaching (84). This would allow for significant advantages to be gained from the pandemic-related restrictions, enabling the education system to mitigate the future impact of any subsequent disruptions caused by situations similar to those of the pandemic, and beyond (84). In the historical context we find ourselves in, with conflicts even in Europe and the need for greater sustainability in all systems, this time would represent a unique opportunity to reformulate and enhance the educational approach. In this perspective, future studies should recognize the multifaceted nature of teaching methods employed

during the COVID-19 pandemic, in order to understand and appreciate the diverse strategies and educative approaches employed. Assessing the efficacy of these strategies and make a comparison among them could be of extreme utility in order to identify the best teaching methods. At the same time, developing flexible educational systems (also intended as hybrid in which both traditional and electronic teaching methods are combined) would allow for greater resilience, enabling them to more effectively face potential future unforeseen challenges.

Furthermore, although studies selectively focusing on students with specific learning disorders or attention deficit hyperactivity disorder (ADHD) are limited, the gathered data suggests the need for a better understanding of the challenges and specific needs of these student populations. Embracing this awareness is crucial for developing tailored support systems, inclusive policies, and targeted interventions that address the individualized learning requirements of students with specific learning disorders or ADHD. This comprehensive approach aims to ensure that educational environments are welcoming, equitable, and supportive for all students, regardless of their unique learning profiles and needs.

Future perspective for research

Results of the current systematic review with meta-analysis have also important implications in future research. Firstly, in light of the diverse reporting methods and data extraction challenges observed across the 30 studies included in this systematic review, future research should prioritize standardization in the presentation of results. Moreover, the consideration of academic performance as a composite measurement versus individual subjects or tasks revealed potential nuances in the meta-analysis outcomes. Future studies should more deeply understand potential differences among subjects or specific tasks. Moreover, since in most countries there is already a monitoring system of academic performance in place, future studies should focus on continuous monitoring and evaluation of educational interventions, aimed at assessing their effectiveness and impact over an extended period, or in case of changes in the teaching system or even to evaluate the impact of an unpredicted event as the COVID-19 pandemic. This would be of extreme utility to inform and potentially update policies on emerging evidence and changing educational landscapes. Additionally, promoting a collaboration between researchers, policymakers and educators might help in understanding factors that influenced outcome the most. Lastly, it will enable the pooling of resources, expertise, and innovative ideas to promote effective solutions and advancements in the field of education.

Strengths and limitations

Before generalizing the results of the current systematic review, some limitations should be considered. Firstly, high heterogeneity was found, however, while efforts were made to explore potential explanations, the exact sources of this heterogeneity remain unclear potentially mining the reliability of the ES. Therefore, the high heterogeneity found could probably be due to the high variability in terms of measurement adopted in each single study. Nevertheless, in order to account for this variability, we estimated a standardized ES, which is typically used when the metrics of variables being studied do not have intrinsic meaning (e.g., a score on an arbitrary scale, as the multiple academic tests might have), some or all of the studies use different scales, or when, results from multiple studies are being combined. Lastly, despite multiple biomedical databases being assessed to retrieve eligible original articles, some studies that mainly focus on pedagogical aspects might not be indexed in biomedical databases, and therefore might not be included in the current systematic review.

However, the study has also important strengths. First, it is a systematic review with meta-analysis which follows rigorous methodology and international guidelines. Moreover, in order to increase transparency systematic review protocol was pre-registered in the international database for review protocol, PROSPERO. Moreover, several sensitivity and subgroups analyses have been conducted to disentangle and deeply understand the association detected. Similarly, having estimated publication bias using both visual assessment and the Egger's linear regression test highlight transparency and reliability in reporting. We also added the trim and fill method, which allowed us to address potential publication bias, enhancing the robustness of our meta-analysis. Furthermore, despite systematic reviews of literature having been previously conducted on the COVID-19 pandemic and academic performance (87,88), to the best of our knowledge, this is the first systematic review to include a meta-analysis, allowing for statistical pooling and estimation of the overall effect size.

Additionally, our main analysis was based on a very large sample size (more than 4 million students), which provides statistical power, contributing to the

robustness of our consideration drawn from results. Lastly, the absence of a geographical filter in the search allowed us to retrieve all conducted studies, enabling us to assess the association between the COVID-19 pandemic and academic performance on a global scale.

Conclusions

Our results demonstrate a negative impact of the pandemic on academic performance. The data obtained can inform us about the educational gap resulting from the COVID-19 pandemic. In this perspective, the data show that the generation of developmental age students, who had to undergo part of their education during the evolution of the COVID-19 pandemic, carries an educational gap. Future efforts should be aimed at trying to bridge this gap in order to limit potential negative effects due to the lack of acquisition of skills and education.

Conflict of interest: none
Funds: This study was supported in part by institutional funding (Ricerca corrente), Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

Riassunto

L'impatto della pandemia COVID-19 sulle prestazioni accademiche degli studenti in età evolutiva: una revisione sistematica con meta-analisi

Obiettivo. La pandemia COVID-19 ha impattato sui sistemi educativi in tutto il mondo, sollevando preoccupazioni riguardo al suo effetto sulle prestazioni accademiche, in particolare tra gli studenti in età evolutiva.

Metodi. È stata effettuata una revisione sistematica con meta-analisi per valutare l'associazione tra la pandemia di COVID-19 e le prestazioni accademiche in questa popolazione, secondo le linee guida PRISMA 2020. La ricerca è stata condotta su PubMed/MEDLINE, Scopus ed Embase a dicembre 2023. La meta-analisi è stata condotta usando modelli a effetto fisso e a effetto casuale. La dimensione dell'effetto è stata riportata come Cohen's d con un Intervallo di Confidenza del 95%. La qualità degli studi è stata valutata utilizzando la scala Newcastle-Ottawa. Il protocollo è stato registrato in PROSPERO.

Risultati. Un totale di 30 studi ha soddisfatto i criteri di inclusione, ma solo 13 sono stati inclusi nella meta-analisi. Su un totale di 4,893,499 studenti, il Cohen's d è risultato -0.07 [(95% CI = -0.10; -0.03); p-value <0.001]. Le analisi dei sottogruppi per materia hanno suggerito che le prestazioni in matematica sono state le più colpite, con Cohen's d= -0.14 [(-0.18; -0.10); p-value <0.001].

Conclusione. I risultati hanno rivelato un'associazione negativa significativa tra la pandemia COVID-19 e le prestazioni accademiche tra gli studenti in età evolutiva. Interventi futuri dovrebbero mitigare gli effetti negativi della pandemia sui risultati educativi di questa popolazione.

References

1. Zhu H, Wei L, Niu P. The novel coronavirus outbreak in Wuhan, China. Glob Health Res Policy. 2020 Mar 2;**5**:6. doi: 10.1186/s41256-020-00135-6. PMID: 32226823; PMCID: PMC7050114.
2. World Health Organization. Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV). 2020. Available from: https://www.who.int/news/item/30-01-2020-statement-on-the-second-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-(2019-ncov) [Last accessed: 2024 May 20].
3. World Health Organization (WHO). WHO Director-General's statement on IHR Emergency Committee on Novel Coronavirus (2019-nCoV). 2020. Available from: https://www.who.int/director-general/speeches/detail/who-director-general-s-statement-on-ihr-emergency-committee-on-novel-coronavirus-(2019-ncov) [Last accessed: 2024 May 20.]
4. Mauer N, Chiecca G, Carioli G, Gianfredi V, Iacoviello L, Bertagnolio S, et al. The First 110,593 COVID-19 Patients Hospitalised in Lombardy: A Regionwide Analysis of Case Characteristics, Risk Factors and Clinical Outcomes. Int J Public Health. 2022 May 11;**67**:1604427. doi: 10.3389/ijph.2022.1604427. PMID: 35645700; PMCID: PMC9131487.
5. Auger KA, Shah SS, Richardson T, Hartley D, Hall M, Warniment A, et al. Association Between Statewide School Closure and COVID-19 Incidence and Mortality in the US. JAMA. 2020 Sep 1;**324**(9):859-870. doi: 10.1001/jama.2020.14348. PMID: 32745200; PMCID: PMC7391181.
6. Signorelli C, Odone A, Gianfredi V, Balzarini F, Bucci D, Croci R, et al. Epidemiological assessment of the first COVID-19 epidemic wave in Lombardy. A systematic review. Acta Biomed. 2021 Oct 7;**92**(S6):e2021462. doi: 10.23750/abm.v92iS6.12340. PMID: 34739453; PMCID: PMC8851015.
7. Xia Y, Hu Y, Wu C, Yang L, Lei M. Challenges of online learning amid the COVID-19: College students' perspective. Front Psychol. 2022 Dec 22;**13**:1037311. doi: 10.3389/fpsyg.2022.1037311. PMID: 36619114; PMCID: PMC9815150.
8. Avanesian G, Mizunoya S, Amaro D. How many students could continue learning during COVID-19-caused school closures? Introducing a new reachability indicator for measuring equity of remote learning. Int J Educ Dev. 2021

Jul;**84**:102421. doi: 10.1016/j.ijedudev.2021.102421. Epub 2021 Jun 1. PMID: 36569542; PMCID: PMC9759655.
9. Sosa Díaz MJ. Emergency Remote Education, Family Support and the Digital Divide in the Context of the COVID-19 Lockdown. Int J Environ Res Public Health. 2021 Jul 28;**18**(15):7956. doi: 10.3390/ijerph18157956. PMID: 34360248; PMCID: PMC8345699.
10. Hevia FJ, Vergara-Lope S, Velásquez-Durán A, Calderón D. Estimation of the fundamental learning loss and learning poverty related to COVID-19 pandemic in Mexico. Int J Educ Dev. 2022 Jan;**88**:102515. doi: 10.1016/j.ijedudev.2021.102515. Epub 2021 Nov 18. PMID: 34812219; PMCID: PMC8599019.
11. United Nations Sustainable Development Group. Policy Brief: Education during COVID-19 and beyond. United Nations; 2020. Available from: https://unsdg.un.org/sites/default/files/2020-08/sg_policy_brief_covid-19_and_education_august_2020.pdf [Last accessed: 2024 May 20].
12. Peng X, Liang S, Liu L, Cai C, Chen J, Huang A, et al. Prevalence and associated factors of depression, anxiety and suicidality among Chinese high school E-learning students during the COVID-19 lockdown. Curr Psychol. 2022 Jan 27:1-12. doi: 10.1007/s12144-021-02512-x. Epub ahead of print. PMID: 35103039; PMCID: PMC8791692.
13. Wang J, Wang H, Lin H, Richards M, Yang S, Liang H, et al. Study problems and depressive symptoms in adolescents during the COVID-19 outbreak: poor parent-child relationship as a vulnerability. Global Health. 2021 Apr 6;**17**(1):40. doi: 10.1186/s12992-021-00693-5. PMID: 33823875; PMCID: PMC8022312.
14. Duan L, Shao X, Wang Y, Huang Y, Miao J, Yang X, et al. An investigation of mental health status of children and adolescents in china during the outbreak of COVID-19. J Affect Disord. 2020 Oct 1;**275**:112-118. doi: 10.1016/j.jad.2020.06.029. Epub 2020 Jul 2. PMID: 32658812; PMCID: PMC7329661.
15. Azevedo JPWD, Rogers FH, Ahlgren SE, Cloutier MH, Chakroun B, Chang GC, et al. The State of the Global Education Crisis : A Path to Recovery. Washington, D.C.: World Bank-UNESCO-UNICEF. 2021 Available from: http://documents.worldbank.org/curated/en/416991638768297704/The-State-of-the-Global-Education-Crisis-A-Path-to-Recovery [Last accessed: 2024 May 20].
16. Spitzer MWH, Musslick S. Academic performance of K-12 students in an online-learning environment for mathematics increased during the shutdown of schools in wake of the COVID-19 pandemic. PLoS One. 2021 Aug 3;**16**(8):e0255629. doi: 10.1371/journal.pone.0255629. PMID: 34343221; PMCID: PMC8330947.
17. Ferri F, Grifoni P, Guzzo T. Online Learning and Emergency Remote Teaching: Opportunities and Challenges in Emergency Situations. Societes. 2020;**10**(4): 86. https://doi.org/10.3390/soc10040086.
18. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al; Cochrane Bias Methods Group; Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011 Oct 18;**343**:d5928. doi: 10.1136/bmj.d5928. PMID: 22008217; PMCID: PMC3196245.
19. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA. 2000 Apr 19;**283**(15):2008-12. doi: 10.1001/jama.283.15.2008. PMID: 10789670.
20. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021 Mar 29;**372**:n71. doi: 10.1136/bmj.n71. PMID: 33782057; PMCID: PMC8005924.
21. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses 2014. Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp [Last accessed: 2024 May 20].
22. Herzog R, Álvarez-Pasquin MJ, Díaz C, Del Barrio JL, Estrada JM, Gil Á. Are healthcare workers' intentions to vaccinate related to their knowledge, beliefs and attitudes? A systematic review. BMC Public Health. 2013 Feb 19;**13**:154. doi: 10.1186/1471-2458-13-154. PMID: 23421987; PMCID: PMC3602084.
23. Nucci D, Santangelo OE, Provenzano S, Fatigoni C, Nardi M, Ferrara P, et al. Dietary Fiber Intake and Risk of Pancreatic Cancer: Systematic Review and Meta-Analysis of Observational Studies. Int J Environ Res Public Health. 2021 Nov 3;**18**(21):11556. doi: 10.3390/ijerph182111556. PMID: 34770068; PMCID: PMC8583332.
24. Dufault B, Klar N. The quality of modern cross-sectional ecologic studies: a bibliometric review. Am J Epidemiol. 2011 Nov 15;**174**(10):1101-7. doi: 10.1093/aje/kwr241. Epub 2011 Sep 22. PMID: 21940800.
25. Jaykaran. "Mean ± SEM" or "Mean (SD)"? Indian J Pharmacol. 2010 Oct;**42**(5):329. doi: 10.4103/0253-7613.70402. PMID: 21206631; PMCID: PMC2959222.
26. Lakens D. Calculating and reporting effect sizes to facilitate cumulative science: a practical primer for t-tests and ANOVAs. Front Psychol. 2013 Nov 26;**4**:863. doi: 10.3389/fpsyg.2013.00863. PMID: 24324449; PMCID: PMC3840331.
27. Cohen J. Statistical power analysis for the behavioral sciences. Routledge, 2013.
28. Hattie J. Visible learning: A synthesis of over 800 meta-analyses relating to achievement. Routledge, 2008.
29. Keith TZ. Multiple regression and beyond: An introduction to multiple regression and structural equation modeling. 3rd ed. Taylor & Francis, 2019.
30. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003 Sep 6;**327**(7414):557-60. doi: 10.1136/bmj.327.7414.557. PMID: 12958120; PMCID: PMC192859.
31. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997 Sep 13;**315**(7109):629-34. doi: 10.1136/bmj.315.7109.629. PMID: 9310563; PMCID: PMC2127453.

32. Duval S, Tweedie R. A nonparametric "Trim and Fill" method of accounting for Publication Bias in Meta-Analysis. J Am Stat Assoc. 2000; **95**(449): 89-98. https://doi.org/10.1080/01621459.2000.10473905.
33. Nucci D, Fatigoni C, Salvatori T, Nardi M, Realdon S, Gianfredi V. Association between Dietary Fibre Intake and Colorectal Adenoma: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health. 2021 Apr 15;**18**(8):4168. doi: 10.3390/ijerph18084168. PMID: 33920845; PMCID: PMC8071151.
34. Abdul-Majied S, Kinkead-Clark Z, Burns SC. Understanding Caribbean Early Childhood Teachers' Professional Experiences During the COVID-19 School Disruption. Early Child Educ J. 2023;**51**(3):431-441. doi: 10.1007/s10643-022-01320-7. Epub 2022 Feb 4. PMID: 35153465; PMCID: PMC8815388.
35. Ahn J. Exploring the Negative and Gap-Widening Effects of EdTech on Young Children's Learning Achievement: Evidence from a Longitudinal Dataset of Children in American K-3 Classrooms. Int J Environ Res Public Health. 2022 Apr 29;**19**(9):5430. doi: 10.3390/ijerph19095430. PMID: 35564827; PMCID: PMC9104322.
36. Alfonsi V, Carbone A, Scarpelli S, Gorgoni M, Luchini A, D'Andrea P, et al. The Impact of Delayed School Start Times During COVID-19 on Academic Performance: A Longitudinal Naturalistic Study in Italian High Schools. Nat Sci Sleep. 2023 Dec 23;**15**:1129-1138. doi: 10.2147/NSS.S437958. PMID: 38152440; PMCID: PMC10752017.
37. Angrist N, de Barros A, Bhula R, Chakera S, Cummiskey C, DeStefano J, et al. Building back better to avert a learning catastrophe: Estimating learning loss from COVID-19 school shutdowns in Africa and facilitating short-term and long-term learning recovery. Int J Educ Develop. 2021 Jul;**84**:102397. https://doi.org/10.1016/j.ijedudev.2021.102397.
38. Ashta JK, Weingart R, Gazmararian JA. The Impact of COVID-19 on Education Experiences of High School Students in Semi-Rural Georgia. J Sch Health. 2023 Apr;**93**(4):257-265. doi: 10.1111/josh.13269. Epub 2022 Nov 22. PMID: 36414540; PMCID: PMC10006293.
39. Balayar BB, Langlais MR. Parental Support, Learning Performance, and Socioemotional Development of Children and Teenagers During the COVID-19 Pandemic. Fam J Alex Va. 2022 Apr;**30**(2):174-183. doi: 10.1177/10664807211052496. PMID: 35399755; PMCID: PMC8980849.
40. Bao X, Qu H, Zhang R, Hogan TP. Modeling Reading Ability Gain in Kindergarten Children during COVID-19 School Closures. Int J Environ Res Public Health. 2020 Sep 1;**17**(17):6371. doi: 10.3390/ijerph17176371. PMID: 32882960; PMCID: PMC7504163.
41. Borges ÉPK, Koltermann G, Minervino CADSM, de Salles JF. The Role of Emergent Literacy Assessment in Brazilian Portuguese Literacy Acquisition during COVID-19. Behav Sci (Basel). 2023 Jun 19;**13**(6):510. doi: 10.3390/bs13060510. PMID: 37366762; PMCID: PMC10295449.
42. Colvin MK, Koven MR, Vuijk PJ, Fleming LE, Reese KL, Cassill C, et al. Differences in cognitive and academic performance during the COVID-19 pandemic in child psychiatric outpatients. Psychol Assess. 2023 Nov;**35**(11):1000-1009. doi: 10.1037/pas0001267. PMID: 37902668.
43. Crawfurd L, Evans DK, Hares S, Sandefur J. Live tutoring calls did not improve learning during the COVID-19 pandemic in Sierra Leone. J Dev Econ. 2023 Sep;**164**:103114. doi: 10.1016/j.jdeveco.2023.103114. Epub 2023 May 20. PMID: 37309536; PMCID: PMC10198741.
44. Levitt KJ, Munzer T, Torres C, Schaller A, McCaffery H, Radesky JS. Remote and Hybrid Schooling During COVID-19: Associations with Child Behavior and Sleep. J Dev Behav Pediatr. 2022 Jun-Jul 01;**43**(5):e288-e295. doi: 10.1097/DBP.0000000000001085. Epub 2022 May 18. PMID: 35583945; PMCID: PMC10186251.
45. Manuel Prieto J, Salas Sánchez J, Tierno Cordón J, Álvarez-Kurogi L, González-García H, Castro López R. Social anxiety and academic performance during COVID-19 in schoolchildren. PLoS One. 2023 Jan **12**;18(1):e0280194. doi: 10.1371/journal.pone.0280194. PMID: 36634072; PMCID: PMC9836262.
46. Puteikis K, Mameniškyt- A, Mameniškien- R. Sleep Quality, Mental Health and Learning among High School Students after Reopening Schools during the COVID-19 Pandemic: Results of a Cross-Sectional Online Survey. Int J Environ Res Public Health. 2022 Feb 23;**19**(5):2553. doi: 10.3390/ijerph19052553. PMID: 35270245; PMCID: PMC8909739.
47. Song HJ, Mu YF, Wang C, Cai J, Deng ZY, Deng AP, et al. Academic performance and mental health among Chinese middle and high school students after the lifting of COVID-19 restrictions. Front Psychiatry. 2023 Aug 14;**14**:1248541. doi: 10.3389/fpsyt.2023.1248541. PMID: 37645634; PMCID: PMC10461048.
48. Soriano-Ferrer M, Morte-Soriano MR, Begeny J, Piedra-Martínez E. Psychoeducational Challenges in Spanish Children With Dyslexia and Their Parents' Stress During the COVID-19 Pandemic. Front Psychol. 2021 May 28;**12**:648000. doi: 10.3389/fpsyg.2021.648000. PMID: 34122234; PMCID: PMC8193576.
49. Spitzer MWH, Moeller K, Musslick S. Assignment strategies modulate students' academic performance in an online learning environment during the first and second COVID-19 related school closures. PLoS One. 2023 May 3;**18**(5):e0284868. doi: 10.1371/journal.pone.0284868. PMID: 37134094; PMCID: PMC10155976.
50. Subirats L, Palacios Corral A, Pérez-Ruiz SI, Fort S, Sacha GMI. Temporal analysis of academic performance in higher education before, during and after COVID-19 confinement using artificial intelligence. PLoS One. 2023 Feb 27;**18**(2):e0282306. doi: 10.1371/journal.pone.0282306. PMID: 36848374; PMCID: PMC9970089.
51. Wang Y, Xia M, Guo W, Xu F, Zhao Y. Academic performance under COVID-19: The role of online learning readiness and emotional competence. Curr Psychol. 2022 Jan 13:1-14. doi: 10.1007/s12144-022-02699-7. Epub ahead of print. PMID: 35039738; PMCID: PMC8755984.

52. Zhang Y, Liu J, Liang J, Lang J, Zhang L, Tang M, et al. Online education isn't the best choice: evidence-based medical education in the post-epidemic era-a cross-sectional study. BMC Med Educ. 2023 Oct 10;**23**(1):744. doi: 10.1186/s12909-023-04746-8. PMID: 37817252; PMCID: PMC10563228.
53. Ardington C, Wills G, Kotze J. COVID-19 learning losses: Early grade reading in South Africa. Int J Educ Develop. 2021 Oct;**86**. https://doi.org/10.1016/j.ijedudev.2021.102480.
54. Battisti A, Lazzaro G, Varuzza C, Vicari S, Menghini D. Distance learning during COVID-19 lockdown: Impact on adolescents with specific learning disorders and their parents. Front Psychiatry. 2022 Oct 19;**13**:995484. doi: 10.3389/fpsyt.2022.995484. PMID: 36339862; PMCID: PMC9627200.
55. Battisti M, Maggio G. Will the last be the first? School closures and educational outcomes. Eur Econ Rev. 2023 May;**154**:104405. doi: 10.1016/j.euroecorev.2023.104405. Epub 2023 Mar 8. PMID: 36915618; PMCID: PMC9993736.
56. Bayley S, Wole Meshesha D, Rose P, Woldehanna T, Yorke L, Ramchandani P. Ruptured school trajectories: understanding the impact of COVID-19 on school dropout, socio-emotional and academic learning using a longitudinal design. Longit Life Course Stud. 2022 Nov 28;**14**(2):203-239. doi: 10.1332/175795921X16665759070534. PMID: 37022317.
57. Breaux R, Dunn NC, Langberg JM, Cusick CN, Dvorsky MR, Becker SP. COVID-19 Resulted in Lower Grades for Male High School Students and Students With ADHD. J Atten Disord. 2022 May;**26**(7):1011-1017. doi: 10.1177/10870547211044211. Epub 2021 Oct 26. PMID: 34696611; PMCID: PMC8943475.
58. Cingel DP, Lauricella AR, Taylor LB, Stevens HR, Coyne SM, Wartella E. U.S. adolescents' attitudes toward school, social connection, media use, and mental health during the COVID-19 pandemic: Differences as a function of gender identity and school context. PLoS One. 2022 Oct 27;**17**(10):e0276737. doi: 10.1371/journal.pone.0276737. PMID: 36301903; PMCID: PMC9612460.
59. Domingue BW, Dell M, Lang D, Silverman R, Yeatman J, Hough H. The Effect of COVID on Oral Reading Fluency During the 2020–2021 Academic Year. AERA Opn 2022; **8**: 23328584221120254. https://doi.org/10.1177/23328584221120254.
60. Engzell P, Frey A, Verhagen MD. Learning loss due to school closures during the COVID-19 pandemic. Proc Natl Acad Sci U S A. 2021 Apr 27;**118**(17):e2022376118. doi: 10.1073/pnas.2022376118. PMID: 33827987; PMCID: PMC8092566.
61. Engzell P, Frey A, Verhagen MDJS. Learning inequality during the COVID-19 pandemic. Center for Open Science, 2020.
62. Fisher HH, Hawkins GT, Hertz M, Sliwa S, Beresovsky V. Student and School Characteristics Associated With COVID-19-Related Learning Decline Among Middle and High School Students in K-12 Schools. J Sch Health. 2022 Nov;**92**(11):1027-1039. doi: 10.1111/josh.13243. Epub 2022 Aug 21. PMID: 35989509; PMCID: PMC9538687.
63. Förster N, Forthmann B, Back MD, Souvignier E. Effects of the COVID-19 pandemic on reading performance of second grade children in Germany. Read Writ. 2023;**36**(2):289-315. doi: 10.1007/s11145-022-10379-y. Epub 2022 Nov 16. PMID: 36406630; PMCID: PMC9668217.
64. Guariso A, Björkman Nyqvist M. The impact of the COVID-19 pandemic on children's learning and wellbeing: Evidence from India. J Dev Econ. 2023 Sep;**164**:103133. doi: 10.1016/j.jdeveco.2023.103133. Epub 2023 Jun 14. PMID: 37342545; PMCID: PMC10264163.
65. Haelermans C, Korthals R, Jacobs M, de Leeuw S, Vermeulen S, van Vugt L, et al. Sharp increase in inequality in education in times of the COVID-19-pandemic. PLoS One. 2022 Feb 2;**17**(2):e0261114. doi: 10.1371/journal.pone.0261114. PMID: 35108273; PMCID: PMC8809564.
66. Hevia FJ, Vergara-Lope S, Velásquez-Durán A, Calderón D. Estimation of the fundamental learning loss and learning poverty related to COVID-19 pandemic in Mexico. Int J Educ Dev. 2022 Jan;**88**:102515. doi: 10.1016/j.ijedudev.2021.102515. Epub 2021 Nov 18. PMID: 34812219; PMCID: PMC8599019.
67. Kuhfeld M, Soland J, Lewis K, Ruzek E, Johnson A. The COVID-19 school year: Learning and recovery across 2020-2021. 2022; AERA Open. 2022 Jan-Dec;**8**(1):233285842210993. https://doi.org/10.1177/23328584221099306.
68. Lerkkanen MK, Pakarinen E, Salminen J, Torppa M. Reading and math skills development among Finnish primary school children before and after COVID-19 school closure. Read Writ. 2023;**36**(2):263-288. doi: 10.1007/s11145-022-10358-3. Epub 2022 Sep 27. PMID: 36186514; PMCID: PMC9513002.
69. Liao H, Ma S, Xue H. Does school shutdown increase inequality in academic performance? Evidence from COVID-19 pandemic in China. China Econ Rev. 2022 Oct;**75**:101847. doi: 10.1016/j.chieco.2022.101847. Epub 2022 Aug 1. PMID: 35935032; PMCID: PMC9343064.
70. Mælan EN, Gustavsen AM, Stranger-Johannessen E, Nordahl T. Norwegian students' experiences of homeschooling during the COVID-19 pandemic. Eur J Special Needs Educ. 2021;**36**(1):5-19. https://doi.org/10.1080/08856257.2021.1872843.
71. Maldonado JE, De Witte K. The effect of school closures on standardised student test outcomes. British Educ Res J. 2022 Feb;**48**(1):49-94. https://doi.org/10.1002/berj.3754.
72. Pandango GC, Suryawan A, Irmawati M. The effect of school closure and online learning during the COVID-19 pandemic on the academic performance of elementary school-aged children. Bali Med J. 2023; **12**(2): 1362-7. https://doi.org/10.15562/bmj.v12i2.4384.
73. Relyea JE, Rich P, Kim JS, Gilbert JB. The COVID-19 impact on reading achievement growth of Grade 3-5 students in a U.S. urban school district: variation across student characteristics and instructional modalities. Read Writ. 2023;**36**(2):317-346. doi: 10.1007/s11145-022-

10387-y. Epub 2022 Nov 14. PMID: 36406628; PMCID: PMC9662133.
74. Rishitha AV, Subramanian S. A Retrospective Study of Specific Learning Disorders and Comparing the Effect on Academic Performances with Online Education among School Children Due to Covid-19 Pandemic Across Bangalore. J Ecophysiol Occup Health 2022 Dec;**22**(4):162-8. https://doi.org/10.18311/jeoh/2022/31966.
75. Skar GB, Graham S, Huebner A. The Long-Term Effects of the COVID-19 Pandemic on Children's Writing: a Follow-up Replication Study. Educ Psychol Rev. 2023;**35**(1):15. doi: 10.1007/s10648-023-09729-1. Epub 2023 Feb 2. PMID: 36747881; PMCID: PMC9893196.
76. Skar GB, Graham S, Huebner A. Learning loss during the COVID-19 pandemic and the impact of emergency remote instruction on first grade students' writing: A natural experiment. J Educ Psychol. 2022;**114**(7):1553-66. https://doi.org/10.1037/edu0000701.
77. Spitzer MWH, Moeller K. Performance increases in mathematics during COVID-19 pandemic distance learning in Austria: Evidence from an intelligent tutoring system for mathematics. Trends Neurosci Educ. 2023 Jun;**31**:100203. doi: 10.1016/j.tine.2023.100203. Epub 2023 May 3. PMID: 37308258; PMCID: PMC10154054.
78. Spitzer MWH, Musslick S. Academic performance of K-12 students in an online-learning environment for mathematics increased during the shutdown of schools in wake of the COVID-19 pandemic. PLoS One. 2021 Aug 3;**16**(8):e0255629. doi: 10.1371/journal.pone.0255629. PMID: 34343221; PMCID: PMC8330947.
79. Sun X, Marks RA, Eggleston RL, Zhang K, Lau C, Yu CL, et al. Impacts of the COVID-19 disruption on the language and literacy development of monolingual and heritage bilingual children in the United States. Read Writ. 2023;**36**(2):347-375. doi: 10.1007/s11145-022-10388-x. Epub 2022 Nov 20. PMID: 36438429; PMCID: PMC9676889.
80. Tapia-Serrano MA, Sánchez-Oliva D, Sevil-Serrano J, Marques A, Sánchez-Miguel PA. 24-h movement behaviours in Spanish youth before and after 1-year into the covid-19 pandemic and its relationship to academic performance. Sci Rep. 2022 Oct 5;**12**(1):16660. doi: 10.1038/s41598-022-21096-5. PMID: 36198729; PMCID: PMC9533995.
81. Tomasik MJ, Helbling LA, Moser U. Educational gains of in-person vs. distance learning in primary and secondary schools: A natural experiment during the COVID-19 pandemic school closures in Switzerland. Int J Psychol. 2021 Aug;**56**(4):566-576. doi: 10.1002/ijop.12728. Epub 2020 Nov 24. PMID: 33236341; PMCID: PMC7753520.
82. Uthappa DM, Pak J, McGann KA, Brookhart MA, McKinzie K, Abdelbarr M, et al; ABC Science Collaborative. In-Person Instruction and Educational Outcomes of K-8 Students During the COVID-19 Pandemic. Pediatrics. 2023 Jul 1;**152**(Suppl 1):e2022060352L. doi: 10.1542/peds.2022-060352L. PMID: 37394499; PMCID: PMC10312276.
83. Engelbrecht J, Borba MC, Kaiser G. Will we ever teach mathematics again in the way we used to before the pandemic? ZDM. 2023;**55**(1):1-16. doi: 10.1007/s11858-022-01460-5. Epub 2023 Jan 13. PMID: 36684476; PMCID: PMC9839221.
84. UNESCO International Bureau of Education. Hybrid education, learning, and assessment: a reader; an overview of frameworks, issues and developments in light of COVID-19 and the way forward. Switzerland: United Nations Educational, Scientific and Cultural Organization; 2023.
85. Coman C, -îru LG, Mese-an-Schmitz L, Stanciu C, Bularca MC. Online Teaching and Learning in Higher Education during the Coronavirus Pandemic: Students' Perspective. Sustainability. 2020;**12**(24):10367. https://doi.org/10.3390/su122410367.
86. Dong C, Cao S, Li H. Young children's online learning during COVID-19 pandemic: Chinese parents' beliefs and attitudes. Child Youth Serv Rev. 2020 Nov;**118**:105440. doi: 10.1016/j.childyouth.2020.105440. Epub 2020 Sep 8. PMID: 32921857; PMCID: PMC7476883.
87. Cortés-Albornoz MC, Ramírez-Guerrero S, García-Guáqueta DP, Vélez-Van-Meerbeke A, Talero-Gutiérrez C. Effects of remote learning during COVID-19 lockdown on children's learning abilities and school performance: A systematic review. Int J Educ Dev. 2023 Sep;**101**:102835. doi: 10.1016/j.ijedudev.2023.102835. Epub 2023 Jun 14. PMID: 37361921; PMCID: PMC10266495.
88. Panagouli E, Stavridou A, Savvidi C, Kourti A, Psaltopoulou T, Sergentanis TN, et al. School Performance among Children and Adolescents during COVID-19 Pandemic: A Systematic Review. Children (Basel). 2021 Dec 4;**8**(12):1134. doi: 10.3390/children8121134. PMID: 34943330; PMCID: PMC8700572.

Corresponding author: Vincenza Gianfredi, Department of Biomedical Sciences for Health, University of Milan, Via Pascal 36, 20133 Milan, Italy
e-mail: vincenza.gianfredi@unimi.it

Supplementary Material

Table S1. Search strategy for each database

Database	Search strategy	N of records
PubMed/Medline	(“Adolescent”[Title/Abstract] OR “Adolescent”[MeSH Terms] OR “Adolescents”[Title/Abstract] OR “Child”[Title/Abstract] OR “Child”[MeSH Terms] OR “Children”[Title/Abstract] OR “Adolescence”[Title/Abstract] OR “Teens”[Title/Abstract] OR “Teen”[Title/Abstract] OR “Teenagers”[Title/Abstract] OR “Teenager”[Title/Abstract] OR “Youth”[Title/Abstract] OR “Teenage”[Title/Abstract] OR “Teenages”[Title/Abstract] OR “Teenaged”[Title/Abstract]) AND (“Covid-19”[Title/Abstract] OR “Covid-19”[MeSH Terms] OR “Pandemics”[Title/Abstract] OR “Pandemics”[MeSH Terms] OR “Covid-19”[Title/Abstract] OR “2019-nCoV”[Title/Abstract] OR “2019-nCoV”[Title/Abstract] OR “SARS-CoV-2”[Title/Abstract] OR “SARS-CoV-2”[Title/Abstract] OR “2019 novel coronavirus”[Title/Abstract] OR “COVID19”[Title/Abstract] OR “coronavirus disease 2019”[Title/Abstract] OR “sars coronavirus 2”[Title/Abstract] OR “Pandemic”[Title/Abstract] OR “SARS-CoV-2”[MeSH Terms] OR “nCoV”[Title/Abstract]) AND (“Educational”[Title/Abstract] OR “Academic”[Title/Abstract] OR “Graduate”[Title/Abstract]) AND (“Performance”[Title/Abstract] OR “Performances”[Title/Abstract] OR “Assessment”[Title/Abstract] OR “assessments”[Title/Abstract] OR “Record”[Title/Abstract] OR “Records”[Title/Abstract] OR “Examination”[Title/Abstract] OR “Examinations”[Title/Abstract] OR “Measurement”[Title/Abstract] OR “Measurements”[Title/Abstract] OR “Achievement”[Title/Abstract] OR “Achievements”[Title/Abstract] OR “Test”[Title/Abstract] OR “Tests”[Title/Abstract] OR “Score”[Title/Abstract] OR “Scores”[Title/Abstract] OR “Success”[Title/Abstract] OR “Successes”[Title/Abstract] OR “grade”[Title/Abstract] OR “grades”[Title/Abstract] OR (“Academic performance”[MeSH Terms] OR “Academic success”[MeSH Terms] OR “educational measurement”[MeSH Terms]))	1185
Scopus	(TITLE-ABS-KEY (adolescen* OR child* OR teen OR teenage* OR youth)) AND (TITLE-ABS-KEY (covid-19 OR pandemic OR “2019-ncov” OR “sars-cov-2” OR “2019 novel coronavirus” OR covid19 OR “coronavirus disease 2019” OR “sars coronavirus 2” OR ncov)) AND (((KEY (educational OR academic OR graduate)) AND (KEY (performance OR assessment OR record OR examination OR measurement OR achievement OR test OR score OR success OR grade))) OR ((TITLE (educational OR academic OR graduate)) AND (TITLE (performance OR assessment OR record OR examination OR measurement OR achievement OR test OR score OR success OR grade))))	830
Embase	(adolescen* OR child* OR teenage* OR ‘youth’/exp OR youth OR adolescen*:ti,ab,kw OR child*:ti,ab,kw OR teen:ti,ab,kw OR teenage*:ti,ab,kw OR youth:ti,ab,kw) AND (‘covid 19’/exp OR ‘covid 19’ OR ‘pandemic’/exp OR pandemic OR ‘2019-ncov’/exp OR ‘2019-ncov’ OR ‘sars-cov-2’/exp OR ‘sars-cov-2’ OR ‘2019 novel coronavirus’/exp OR ‘2019 novel coronavirus’ OR ‘covid19’/exp OR covid19 OR ‘coronavirus disease 2019’/exp OR ‘coronavirus disease 2019’ OR ‘sars coronavirus 2’/exp OR ‘sars coronavirus 2’ OR ncov) AND (educational:ti,ab,kw OR academic:ti,ab,kw OR ‘graduate’/exp OR graduate:ti,ab,kw) AND (‘performance’/exp OR performance:ti,ab,kw OR ‘assessment’/exp OR assessment:ti,ab,kw OR record:ti,ab,kw OR ‘examination’/exp OR examination:ti,ab,kw OR ‘measurement’/exp OR measurement:ti,ab,kw OR ‘achievement’/exp OR achievement:ti,ab,kw OR ‘test’/exp OR test:ti,ab,kw OR ‘score’/exp OR score:ti,ab,kw OR ‘success’/exp OR success:ti,ab,kw OR ‘grade’/exp OR grade:ti,ab,kw)	1656

Table S2. Reasons of exclusion

Reason of exclusion	Number of studies	Reference
Different age group: <6 years old or >19 years old	3	Abdul-Majied, 2023; Subirats, 2023; Zhang, 2023
Different population: parents	1	Balayar, 2022
Different exposure: pre-COVID19	1	Ahn, 2022
Different outcome: healthy development of children, sleep quality, mental health, behaviour, sleep, anxiety, emotional competence	12	Alfonsi, 2023; Angrist, 2021; Ashta, 2023; Bao, 2020; Borges, 2023; Levitt, 2022; Manuel Prieto, 2023; Puteikis, 2022; Song, 2023; Soriano-Ferrer, 2021; Spitzer, 2023; Wang, 2022
Different study design	1	Crawfurd, 2023
Full text not available	1	Colvin, 2023

Table S3. Item-by-item quality assessment of each included study, reported in alphabetical order, and based on study design. Supplementary Table 4a shows cohort, case-control and cross-sectional studies. Supplementary table 4b shows ecological studies.

a)

Cohort	Author, year	Item 1	Item 2	Item 3	Item 4	Item 5a	Item 5b	Item 6	Item 7	Item 8	Total	Quality
	Ardington, 2021	*	*	*	*	*	*	*	*	*	9	high
	Bayley, 2023	*	*	*	*	*	*	*	*	*	9	high
	Battisti, 2023	*	*	*	*	*	*	*	*	*	9	high
	Breaux, 2022	*	*	*	*	/	/	*	*	*	7	high
	Domingue, 2022	*	*	*	*	/	*	*	*	*	8	high
	Engzell, 2021	*	*	*	*	*	*	*	*	*	9	high
	Engzell, 2020	*	*	*	*	*	*	*	*	*	9	high
	Förster, 2022	*	*	*	*	*	*	*	*	*	9	high
	Guariso, 2023	*	*	*	*	/	*	*	*	*	8	high
	Haelermans, 2022	*	*	*	*	*	*	*	*	*	9	high
	Hevia, 2022	*	*	*	*	/	/	*	*	*	7	high
	Kuhfeld, 2022	*	*	*	*	/	/	*	*	*	7	high
	Maldonado, 2022	*	*	*	*	*	*	*	*	*	9	high
	Pandango, 2023	*	*	*	*	*	/	*	*	*	8	high
	Relyea, 2023	*	*	*	*	/	/	*	*	*	7	high
	Skar, 2022	*	*	*	*	*	*	*	*	*	9	high
	Skar, 2023	*	*	*	*	*	*	*	*	*	9	high
	Spitzer and Moeller, 2023	/	/	*	*	/	/	*	*	*	5	moderate
	Tomasik, 2021	*	*	*	*	*	/	*	*	*	8	high
	Sun, 2023	*	*	*	*	/	/	*	*	*	7	high
Case Control	Author, year	Item 1	Item 2	Item 3	Item 4	Item 5a	Item 5b	Item 6	Item 7	Item 8	Total	Quality
	Rishitha, 2022	*	/	*	*	/	/	*	*	*	6	moderate
Cross Sectional	Author, year	Item 1	Item 2	Item 3	Item 4	Item 5a	Item 5b	Item 6	Item 7		Total	Quality
	Battisti, 2022	/	/	/	*	/	*	/	*		3	low
	Cingel, 2022	*	*	/	*	*	*	/	*		6	moderate
	Fisher, 2022	*	/	/	*	/	*	/	*		4	moderate
	Liao, 2022	*	*	*	*	*	/	**	*		8	high
	Mælan, 2021	*	/	/	*	/	/	/	*		3	low

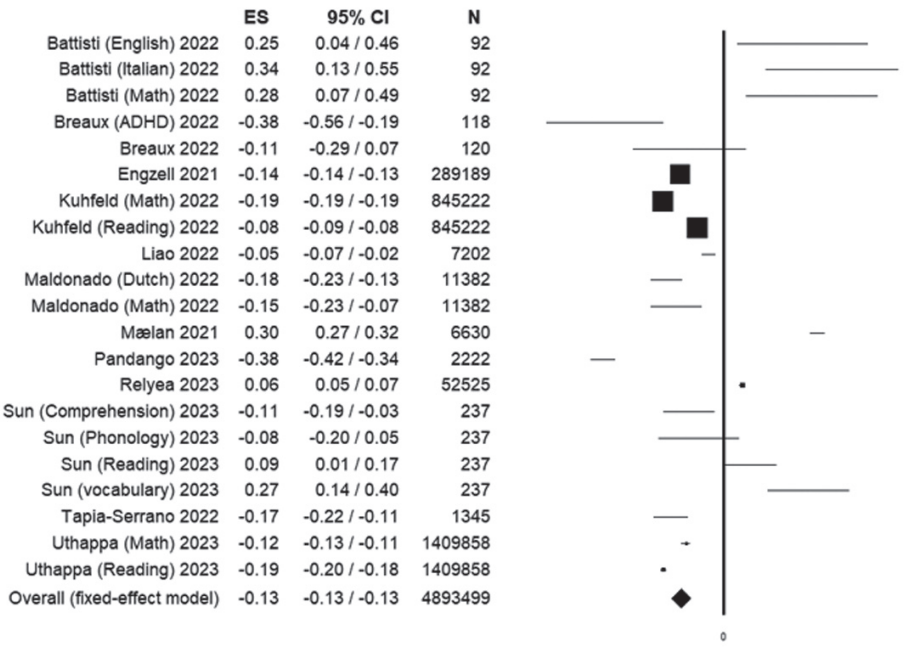
b)

Ecological Studies	Author, Year	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11		Item 13	Item 14	Item 15	Total	Quality
	Lerkkanen, 2022	2	0	1	3	1	1	2	1	1	1	1	1	1	1	1	18	high
	Spitzer and Musslick, 2021	2	0	1	3	1	1	2	1	1	1	0	0	1	1	1	16	high
	Tapia-Serrano, 2022	2	1	1	3	1	1	2	1	1	1	1	0	1	1	1	18	high
	Uthappa, 2023	2	1	1	2	1	1	2	1	1	1	1	0	1	1	1	17	high

Table S4. Quality assessment of the included studies. Green indicates high quality, orange indicates moderate quality, and red indicates low quality

COHORT STUDIES: Author, year	**Total score**	**Quality**
Ardington, 2021	9	
Bayley, 2023	9	
Battisti, 2023	9	
Breaux, 2022	7	
Domingue, 2022	8	
Engzell, 2020	9	
Engzell, 2021	9	
Förster, 2023	9	
Guariso, 2023	8	
Haelermans, 2022	9	
Hevia, 2022	7	
Kuhfeld, 2022	7	
Maldonado, 2022	9	
Pandango, 2023	8	
Relyea, 2023	7	
Skar, 2022	9	
Skar, 2023	9	
Spitzer and Moeller, 2023	5	
Tomasik, 2021	7	
Sun, 2023	7	
CASE CONTROL Author, year	**Total score**	**Quality**
Rishitha, 2022	6	
CROSS-SECTIONAL Author year	**Total score**	**Quality**
Battisti, 2022	3	
Cingel, 2022	6	
Fisher, 2022	4	
Liao, 2022	8	
Mælan, 2021	3	
ECOLOGICAL Author, year	**Total score**	**Quality**
Lerkkanen, 2022	18	
Spitzer and Musslick, 2021	16	
Tapia-Serrano, 2022	18	
Uthappa, 2023	17	

a)



b)

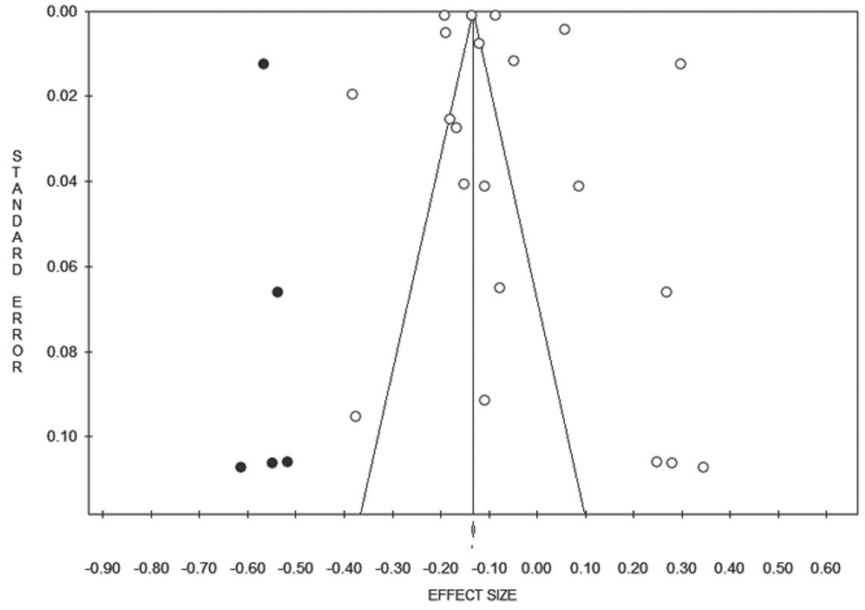
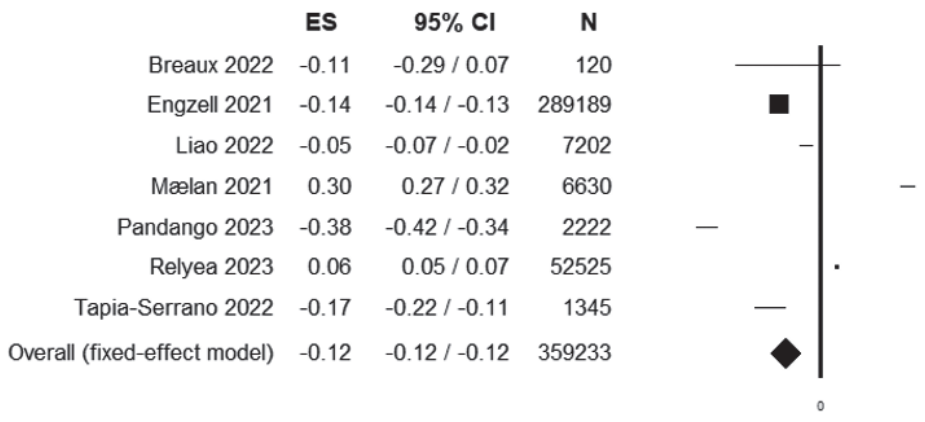


Figure S1. Forest (a), and funnel plot (b) of the meta-analysis assessing the association between COVID-19 pandemic and academic performance. Fixed effect model. ES: Effect size

a)



b)

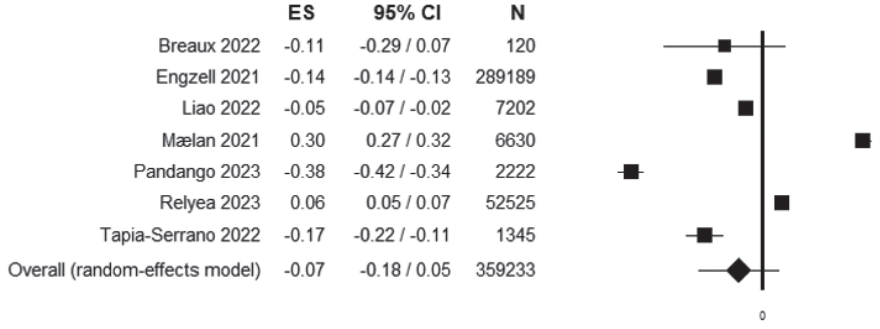


Figure S2. Forest plot after fixed effect model (a), and forest plot after random effect model (b) of the meta-analysis assessing the association between COVID-19 pandemic and academic performance reported as composite measure. ES: Effect size

Ann Ig. 2025 Jan Feb; 37(1): 74-83 doi: 10.7416/ai.2024.2650. Epub 2024 Sep 12.

Smart working during the COVID-19 pandemic: the prevalence of musculoskeletal and visual disorders in administrative staff of a large international company

Paolo Emilio Santoro[1,2,3], Carlotta Amantea[1], Martina Travaglini[3], Gianluca Salin[3], Ivan Borrelli[1], Maria Francesca Rossi[1], Dariush Khaleghi Hashemian[4], Maria Rosaria Gualano[5], Umberto Moscato[1,2]

Keywords: Smart working; White collar workers; Low back pain
Parole chiave: Smart working; Personale amministrativo; Dolore lombare

Abstract

Introduction. *During the COVID-19 Pandemic, the use of digital devices during work activities has increased with important repercussions on the psychological and physical well-being of the employees. The aim of this study was to investigate the prevalence of musculoskeletal and visual disorders related to the use of computers and home workstation.*
Methods. *The study is a cross-sectional study. A checklist, from the National Institute of Health, was administered to white collar workers of a large international pharmaceutical company based in Italy.*
Results. *Our study showed that postural breaks have a protective effect on neck/shoulder pain (OR 0.32, CI 0.16-0.62), back and lower extremity pain (OR 0.35, CI 0.18-0.69), and eye burning (OR 0.50, CI 0.27-0.94) of study participants.*
Conclusions. *The research recommends that remote employees who often change their workstations should establish a suitable work environment and obtaining enough risk training from an occupational physician. This is essential for maintaining their mental and physical well-being.*

[1] *Department of Health science and public health, Università Cattolica del Sacro Cuore, Rome, Italy*
[2] *Department of Women, children and public health sciences, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy*
[3] *Health, Safety & Environment Angelini Industries, Rome, Italy*
[4] *Laboratory of Medical Statistics, Biometry and Epidemiology "G. A. Maccacaro", Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy*
[5] *Saint Camillus International University of Health Sciences, UniCamillus, Rome, Italy*

Annali di Igiene : Medicina Preventiva e di Comunità (Ann Ig)
ISSN (print) 1120-9135 ISSN (online) 3035-5559

https://www.annali-igiene.it

Introduction

During the COVID-19 Pandemic, the use of digital devices during work activities has increased worldwide, creating an innovative challenge in workers of all ages, with important repercussions on the psychological and physical well-being of the employees (1). Remote working is preferred by some workers, due to a greater flexibility in the workday organization; however, it can also entail work-related difficulties and increased occupational risks for some categories of employees, including ergonomic and visual risks for video-terminal users (2). In Italy, the 'Shared Protocol for the Regulation of Measures to Combat and Contain the Spread of the Virus in the Workplace' was published and signed on 14 March 2020. This protocol, among other provisions, recommends the use of 'agile' or 'smart working' where feasible, to minimize contact among employees within the same company (3-4).

The pandemic scenario has required and continues to require changes in the organization of the working environment, as well as the need to adapt it to a new setting. While working remotely, employees may not respect health and safety regulations due to a lack of information or difficulties in monitoring the working environment and set-up by employers and supervisory authorities (5). Furthermore, it has been highlighted that, during the COVID-19 pandemic, workers have been spending more time sitting down and have been more susceptible to reduced sleep quality. In turn, the lack of sleep has been causing changes in mood and lack of concentration, resulting in reduced productivity, and worsened emotional well-being (6-7).

Due to the changes that shifting from presence to remote working entailed, it has been highlighted that new physical and mental health issues have been reported in workers; Xiao et al. conducted a study in employees working from home, highlighting 64.8% of respondents reported new physical health issues and 73.6% reported new mental health issues since they started working remotely (8).

The increased prevalence of musculoskeletal and oculo-visual disorders appears to be caused by both the increased use of digital devices and the changing working methods (working remotely and/or from home). Moreover, as reported in the study of Regmi A. et al., a higher prevalence of oculo-visual (43.1%) and musculoskeletal (45%) symptoms were found in workers who had to reorganize their working activities from home by using non-ergonomic chairs and digital devices for several hours during the day (9). Many literature studies show the consequences of remote working on the musculoskeletal apparatus (use of non-ergonomic chairs, inadequate postures, and an insufficiently organized workstation), such as a high prevalence of repetitive strain injuries (10-11).

In an Italian study, Moretti et al reported an increased incidence of musculoskeletal pain since participants started working remotely, with 70.5% of respondents reporting this type of pain in at least one site; the most frequent were low back pain (41.2%) or neck pain (23.5%), while 23.5% participants reported pain in multiple sites (12). Moretti et al also highlighted that 38.1% participants reported an increase of low back pain severity, and 50% reported the worsening of previous neck pain.

Another important consequence of shifting from working on site to working remotely is the workstation that may not be on par with ergonomic standards if employees are not appropriately informed about the desired characteristics. An ergonomic and adjustable workstation is instrumental in the prevention of musculoskeletal disorders. Seva et al. conducted a study in the Philippines, investigating the setup of the remote workstation that employees; most participants reported they had their keyboards, monitors, and mouse in the recommended positions, but the majority did not have their armrest at the same height as their keyboard, did not lean with their back against the backrest did not have their knees extending past their seat, and did not have a chair with adjustable/proper height (13).

The aim of this study was to investigate the prevalence of musculoskeletal and visual disorders related to the use of computers and related workstation, with reference to the activity carried out while working remotely during the COVID-19 pandemic, to assess and possibly suggest strategies to improve the worker's work comfort and psychophysical well-being.

Methods

Sample and questionnaire

The study is a cross-sectional study. A checklist was administered in Italian and English language to white collar workers of headquarters of a large international pharmaceutical company based in Italy. Using an online platform (Microsoft Forms), a specific invitation was sent from the company's occupational doctor (to maintain the anonymity of all personal and medical data) to all eligible employees. The participants were sent a link to participate in the survey but had to read through the information about the aim of

the study before they could access the questionnaire; if consent to participate was not given, the survey could not be filled out.

Information was collected through Microsoft Form and downloaded automatically in a Microsoft Excel spreadsheet by the occupational physician, gathering in this database all the survey responses. The questionnaire was completed anonymously; no data on name, e-mail address, or IP address was collected.

The aggregated health and risk data of workers undergoing health surveillance, who consented to participate in the study, were provided anonymously to the researchers by the occupational physician, following authorization from the company's Data Protection Officer (DPO).

The checklist was taken from the Computer Workstation Ergonomics: Self-Assessment Checklist of the National Institutes of Health, Office of Research Services, Division of Occupational Health and Safety (14) website and then modified.

The questionnaire included 35 questions and it was divided into 2 sections.

The first section consisted of six items. The first four assessed gender, age range, company affiliation, and work seniority. Two other questions asked where the work was carried out when smart working, whether at one's home or at another public place, and whether at one's home, in a dedicated environment for exclusive use or not.

The second part was taken from the National Institute of Health checklist. It was in turn divided into macro-topics that investigated the ergonomics of the workstation related to the use of the work chair (5 items) and the health status of the worker, i.e., whether the worker experienced pain/ discomfort in the neck/ shoulders due to the chair being used (1 item) or in the back/low limbs (1 item).

The remaining items investigated the ergonomics of the workstation related to the use of the keyboard and mouse (6 items) and the health status of the worker, i.e., whether the worker at the end of the workday experienced arms pain/discomfort (1items); and the use of the work surface (7items) and whether burning in the eyes and/or visual fatigue was experienced at the end of the workday (1 items).

The last questions investigated when and how work breaks were taken (2 items) and the use of accessories such as laptop, headset, and document holder (5 items).

Inclusion Criteria

To be included in the study, employees had to be working for the large international pharmaceutical company in which the study took place, had to be working remotely, and had to freely give their informed consent to participate in the study and to have their data processed according to the European and Italian legislation (see Ethical statement paragraph).

Exclusion Criteria

Employees who did not work remotely and those who did not provide informed consent to participate in the survey were excluded from the study.

Statistical Analysis

To assess the association between pain or disturbs in different districts of the body, logistic regression was performed. We selected the most common situations where office employees usually complain of pain or discomfort, that is neck and shoulders pain, back and lower limbs pain, pain to one or both arms, eye burning and/or lacrimation, and put this outcome against specific items of the *Computer Workstation Ergonomics: Self-Assessment Checklist of the National Institutes of Health*, based on current level of knowledge in occupational health.

First, we calculated the odds ratio (OR) and the corresponding confidence interval (CI) at 95% for each item of the checklist and the corresponding disturbance by itself, then we added biographical confounders to the model such as sex and age (divided in three equally distributed categories) and we added the information of if the place chosen for smart working was exclusively dedicated for working or not. We decided not to include the 'Seniority' variable because we notice a very close collinearity with the 'Age' factor (Spearman's rank correlation of 0.79 with a p-value <0.001). We didn't use the 'Company' variable because of the strong imbalance among the different companies and for the same reason we judged it appropriate not to add the 'Place of smart working' variable, as most of the participants (99.2%) answered they were using their own house for smart working. Finally, to complete the analysis we put all the "disturbance specific" variables in order to adjust the model.

For data analysis, we used RStudio 2022.07.01 Build 554 with R version 4.1.2 (2021-11-01).

Results

The sample included 506 employees, all part of administrative staff of headquarters of a large

international pharmaceutical company based in Italy, of whom 245 gave their consent to participate (response rate: 48.4%). Of the 245 who gave consent to complete the questionnaire, 5 were eliminated due to missing data. The final sample consisted of 240 participants. Of these, 77 (32%) were male and 163 (68%) were female. The age range was ≤ 40 years for 100 participants (42%), 41 to 50 for 67 participants (28%), and 51 and over for 73 (30%). In terms of seniority, there were 105 (44%) employees working from 0 to 10 years, from 11 to 20 years there were 59 (24%), and from 21 years onwards there were 76 (32%). 238 (99%) responded to us that in smart working they do their work in their own home, 2 (1%) in another public place. 122 (51%) in dedicated environment for their exclusive use, 118 (49%) no (Table 1).

Table 1 - Socio-demographic and occupational characteristics of the population (n=240)

Variables	n. (%)
Gender	
Male	77 (32.1)
Female	163 (67.9)
Age (years)	
≤ 40	100 (41.7)
41 – 50	67 (27.9)
≥ 51	73 (30.4)
Seniority (years)	
≤ 10	105 (43.7)
11 – 20	59 (24.6)
≥ 21	76 (31.7)
Place of smart working	
Home	238 (99.2)
Public Place	2 (0.8)
Exclusive use for smart working	
No	118 (49.2)
Yes	122 (50.8)

Among the 240 participants, 130 (54%) complained of neck/shoulder pain, while 110 (46%) participants did not complain of neck/shoulder pain. Of those who had neck/shoulder pain, 43 (33%) claimed to have a chair with no adjustable height, seat, and backrest, 30 (23%) reported to have no resting place for their feet, 50 (38%) had no lumbar support, 41 (31.5%) felt pressure on the back of their knees, 54 (41.5%) had no adjustable armrests, and 110 (84.6%) did not take postural breaks. Of the participants who did not complain of neck/shoulder pain, 85 (77%) claimed to have a chair with adjustable height, seat, and backrest, 98 (89%) claimed to have a place to rest their feet, 83 (75%) claimed to have lumbar support, 82 (74.5%) claimed not to feel pressure on the back of their knees, 80 (72.7%) claimed to have adjustable armrests, 41 (37.3%) claimed to take postural breaks. Postural breaks were found to have a protective effect on neck/shoulder pain, with a strongly significant value (OR 0.32, CI 0.16-0.62). As expected, having the feet rested also represents an ergonomic and protective posture for the onset of neck/shoulder pain with an OR that initially was 0.46 (CI 0.22-0.97) adjusted for some biographical data, significance is lost by adjusting for the other variables (OR 0.45, CI 0.20-1.00). Lumbar support was initially found to be a protective factor (OR 0.52, CI 0.29-0.93) for neck/shoulder pain, however, adjusting for the other variables lost significance (OR 0.64, CI 0.31-1.31) (Table 2).

Among the 240 participants, 121 (50.4%) reported back or lower limbs pain, 119 (49.6%) did not. Of those with back or lower limbs pain, 40 (33.1%) did not have a chair with adjustable height, 30 (24.8%) reported they did not have a support for their feet, 42 (34.7%) did not have a support for their back, 37 (30.6%) felt pressure behind their knees, 48 (39.7%) did not have armrests, 101 (83.5%) did not take postural breaks. Of the participants with no back or lower limbs pain, 91 (76.5%) had adjustable chair height, 107 (89.9%) had a support to lean their feet on, 84 (70.6%) had support for their back, 87 (73.1%) felt no pressure behind their knees, 83 (69.7%) had armrests, 41 (34.5%) took postural breaks.

Having a support to lean the feet was significantly correlated to the absence of back and lower limbs pain in participant (OR 0.33, CI 0.15-0.74); this remained significative even when adjusted for all other variables. Taking postural breaks was significantly related to not having back and lower limbs pain in participants (OR 0.35, CI 0.18-0.69); this remained significative even when adjusted for all other variables (Table 3).

Of the 240 participants, 55 (22.9%) reported arm pain, while 185 (77.1%) reported no pain. Seventeen (30.9%) of the participants with arm pain reported that the keyboard or mouse was not at elbow height, 2 (3.6%) did not have their usual work tools within reach, 32 (58.2%) did not keep their wrists properly straight and their arms relaxed, and 44 (80.0%) did not take postural breaks while using the video screen. With a highly significant value, keeping arms relaxed and keeping wrists properly rested was found to have a protective effect on arm pain (OR 0.26, CI 0.13-0.52) (Table 4).

Table 2 - Neck/shoulder pain (Odds ratios and 95% confidence intervals)

	Neck/shoulder pain				
	No n (%)	Yes n (%)	OR (95% CI)[a]	OR (95% CI)[b]	OR (95% CI)[c]
Adjustable height					
No	25 (22.7)	43 (33.1)	Ref.	Ref.	Ref.
Yes	85 (77.3)	87 (66.9)	0.60 (0.33-1.06)	0.65 (0.35-1.19)	1.11 (0.52-2.38)
Feet resting					
No	12 (10.9)	30 (23.1)	Ref.	Ref.	Ref.
Yes	98 (89.1)	100 (76.9)	0.41 (0.20-0.84)	0.46 (0.22-0.97)	0.45 (0.20-1.00)
Lumbar support					
No	27 (24.5)	50 (38.5)	Ref.	Ref.	Ref.
Yes	83 (75.5)	80 (61.5)	0.52 (0.30-0.91)	0.52 (0.29-0.93)	0.64 (0.31-1.31)
Knee pressure					
No	82 (74.5)	89 (68.5)	Ref.	Ref.	Ref.
Yes	28 (25.5)	41 (31.5)	1.35 (0.77-2.38)	1.45 (0.81-2.59)	1.72 (0.92-3.21)
Armrests					
No	30 (27.3)	54 (41.5)	Ref.	Ref.	Ref.
Yes	80 (72.7)	76 (58.5)	0.53 (0.31-0.91)	0.57 (0.32-1.01)	0.70 (0.37-1.33)
Postural breaks					
No	69 (62.7)	110 (84.6)	Ref.	Ref.	Ref.
Yes	41 (37.3)	20 (15.4)	0.31 (0.17-0.57)	0.32 (0.17-0.61)	0.32 (0.16-0.62)

[a]Unadjusted; [b]Adjusted estimates for sex, age, society of affiliation, work seniority, place of work (home or public place), if place for exclusive use or not; [c]Adjusted estimates for all other variables.

Table 3 - Back/lower limbs pain (Odds ratios and 95% confidence intervals)

	Back/lower limbs pain				
	No n (%)	Yes n (%)	OR (95% CI)[a]	OR (95% CI)[b]	OR (95% CI)[c]
Adjustable height					
No	28 (23.5)	40 (33.1)	Ref.	Ref.	Ref.
Yes	91 (76.5)	81 (66.9)	0.62 (0.35-1.10)	0.63 (0.35-1.15)	0.75 (0.35-1.59)
Feet resting					
No	12 (10.1)	30 (24.8)	Ref.	Ref.	Ref.
Yes	107 (89.9)	91 (75.2)	0.34 (0.16-0.70)	0.36 (0.17-0.75)	0.33 (0.15-0.74)
Lumbar support					
No	35 (29.4)	42 (34.7)	Ref.	Ref.	Ref.
Yes	84 (70.6)	79 (65.3)	0.78 (0.46-1.35)	0.77 (0.44-1.35)	1.09 (0.53-2.22)
Knee pressure					
No	87 (73.1)	84 (69.4)	Ref.	Ref.	Ref.
Yes	32 (26.9)	37 (30.6)	1.20 (0.68-2.10)	1.25 (0.71-2.22)	1.39 (0.75-2.56)
Armrests					
No	36 (30.3)	48 (39.7)	Ref.	Ref.	Ref.
Yes	83 (69.7)	73 (60.3)	0.66 (0.39-1.13)	0.68 (0.38-1.19)	0.86 (0.46-1.60)
Postural breaks					
No	78 (65.5)	101 (83.5)	Ref.	Ref.	Ref.
Yes	41 (34.5)	20 (16.5)	0.38 (0.20-0.69)	0.39 (0.20-0.72)	0.35 (0.18-0.69)

[a]Unadjusted; [b]Adjusted estimates for sex, age, society of affiliation, work seniority, place of work (home or public place), if place for exclusive use or not; [c]Adjusted estimates for all other variables.

Table 4 - Arm pain (Odds Ratios and 95% confidence intervals)

	Arm pain			OR (95% CI)b	OR (95% CI)c
	No	Yes	OR (95% CI)a		
	n (%)	n (%)			
Keyboard/Mouse elbow height					
No	23 (12.4)	17 (30.9)	Ref.	Ref.	Ref.
Yes	162 (87.6)	38 (69.1)	0.32 (0.15-0.65)	0.32 (0.15-0.67)	0.57 (0.25-1.33)
Neighboring objects					
No	1 (0.5)	2 (3.6)	Ref.	Ref.	Ref.
Yes	184 (99.5)	53 (96.4)	0.14 (0.01-1.62)	0.18 (0.02-2.03)	0.30 (0.02-4.21)
Wrists rested					
No	19 (10.3)	14 (25.5)	Ref.	Ref.	Ref.
Yes	166 (89.7)	41 (74.5)	0.34 (0.16-0.72)	0.31 (0.14-0.69)	0.54 (0.22-1.31)
Straight wrists and relaxed arms					
No	42 (22.7)	32 (58.2)	Ref.	Ref.	Ref.
Yes	143 (77.3)	23 (41.8)	0.21 (0.11-0.40)	0.20 (0.10-0.39)	0.26 (0.13-0.52)
Mouse near keyboard					
No	9 (4.9)	7 (12.7)	Ref.	Ref.	Ref.
Yes	176 (95.1)	48 (87.3)	0.35 (0.12-0.99)	0.32 (0.11-0.93)	0.55 (0.17-1.80)
Comfortable touchpad					
No	49 (26.5)	17 (30.9)	Ref.	Ref.	Ref.
Yes	136 (73.5)	38 (69.1)	0.81 (0.42-1.56)	0.79 (0.40-1.56)	1.07 (0.50-2.29)
Postural breaks					
No	135 (73.0)	44 (80.0)	Ref.	Ref.	Ref.
Yes	50 (27.0)	11 (20.0)	0.67 (0.32-1.41)	0.73 (0.34-1.55)	0.78 (0.35-1.78)
Laptop use					
No	42 (22.7)	7 (12.7)	Ref.	Ref.	Ref.
Yes	143 (77.3)	48 (87.3)	2.01 (0.85-4.78)	1.98 (0.83-4.76)	1.86 (0.71-4.88)

[a]Unadjusted; [b]Adjusted estimates for sex, age, society of affiliation, work seniority, place of work (home or public place), if place for exclusive use or not; [c]Adjusted estimates for all other variables.

Of the 240 participants, 170 (70,8%) reported burning eyes, while 70 (29,2%) reported no pain. 17 (10.0%), 41 (24.1%), 50 (29.4%) of the participants with burning eyes reported that the position, distance, and height of the monitor were not adjusted correctly. 38 (22.4%) and 13 (7,6%), of the participants with burning eyes have stated that they had the computer monitor with reflections and did not have adequate light connected to the workstation. Active visual breaks from computer work have been found to be a protective factor against the occurrence of eye burning (OR 0.50, CI 0.27-0.94) (Table 5).

Discussion

The COVID-19 pandemic has certainly brought about a significant shift in the way people work, with smart working or remote work becoming the norm for many. As a result, changing the workstation for those working from home has become a crucial aspect of ensuring productivity and well-being. One of the most significant challenges of working from home is finding a suitable space to work. Many people do not have a dedicated home office and have had to make do with setting up their workspace in shared living spaces or bedrooms. This can be detrimental to productivity and health, as these spaces are often filled with distractions, interruptions and are not adequate to work (15).

To combat this, it is essential to create a dedicated workspace, preferably in a quiet and well-lit area of the home. This space should be equipped with all the necessary tools and equipment to perform tasks efficiently, such as a comfortable chair, a desk, and a computer with a reliable internet connection. As shown in Figure 1, this should be the ergonomic posture and

Table 5 - Burning/lacrimation eyes (Odds Ratios and 95% confidence intervals)

	Burning/lacrimation eyes				
	No	Yes	OR (95% CI)[a]	OR (95% CI)[b]	OR (95% CI)[c]
	n (%)	n (%)			
Monitor position					
No	4 (5.7)	17 (10.0)	Ref.	Ref.	Ref.
Yes	66 (94.3)	153 (90.0)	0.55 (0.18-1.68)	0.45 (0.14-1.46)	0.49 (0.14-1.70)
Monitor distance					
No	17 (24.3)	41 (24.1)	Ref.	Ref.	Ref.
Yes	53 (75.7)	129 (75.9)	1.01 (0.53-1.93)	1.09 (0.55-2.13)	1.44 (0.69-3.00)
Monitor height					
No	17 (24.3)	50 (29.4)	Ref.	Ref.	Ref.
Yes	53 (75.7)	120 (70.6)	0.77 (0.41-1.46)	0.80 (0.42-1.54)	0.92 (0.46-1.83)
Reflection-free monitor					
No	9 (12.9)	38 (22.4)	Ref.	Ref.	Ref.
Yes	61 (87.1)	132 (77.6)	0.51 (0.23-1.13)	0.47 (0.21-1.05)	0.53 (0.23-1.24)
Adequate light					
No	6 (8.6)	13 (7.6)	Ref.	Ref.	Ref.
Yes	64 (91.4)	157 (92.4)	1.13 (0.41-3.11)	1.02 (0.36-2.88)	1.34 (0.45-3.97)
Visual breaks					
No	39 (55.7)	124 (72.9)	Ref.	Ref.	Ref.
Yes	31 (44.3)	46 (27.1)	0.47 (0.26-0.83)	0.48 (0.27-0.88)	0.50 (0.27-0.94)

[a]Unadjusted; [b]Adjusted estimates for sex, age, society of affiliation, work seniority, place of work (home or public place), if place for exclusive use or not; [c]Adjusted estimates for all other variables

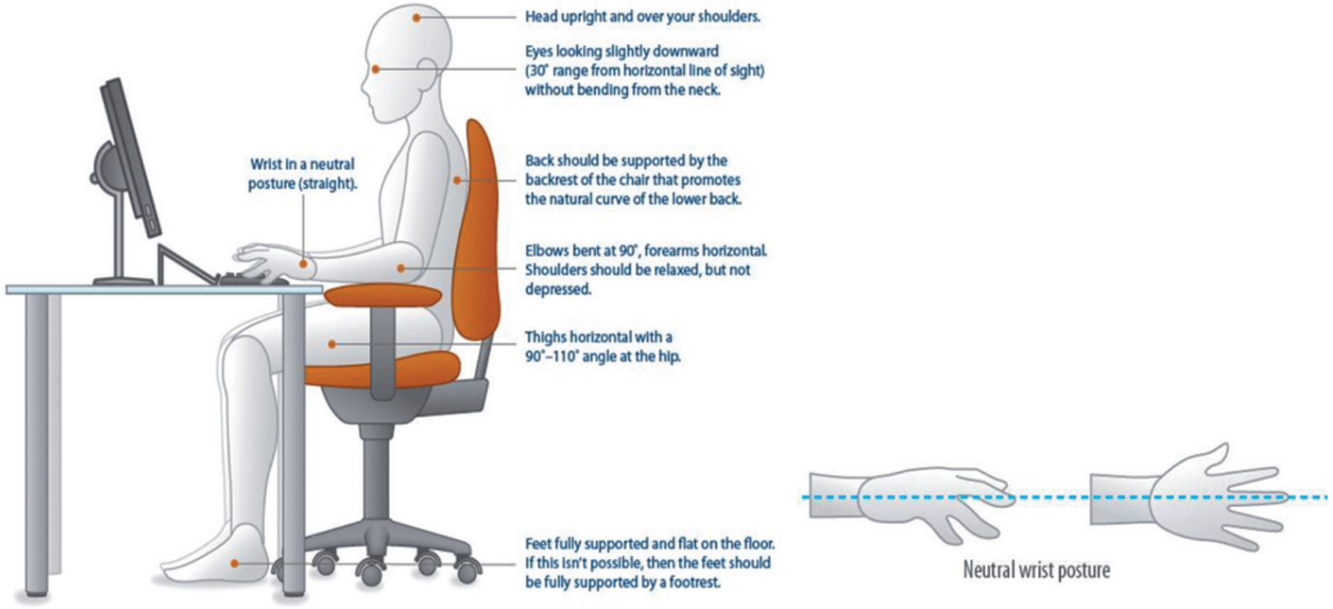


Figure 1 - From "Computer Workstation Ergonomics: Self-Assessment Checklist del National Institutes of Health, Office of Research Services, Division of Occupational Health and Safety website."

workstation organization, which employees should also adopt at home.

Among the 240 participants of the study, 130 (54%) complained of neck/shoulder pain, 121 (50.4%) reported back or lower limbs pain, 55 (22.9%) reported arm pain, 170 (70,8%) reported burning eyes. Of these, they took postural or visual breaks from the workstation or monitor, respectively, 20 (15.4%) of those who had neck/shoulder pain, 20 (16.5%) back/lower limbs pain, 11 (20.0%) arm pain, 46 (27.1%) burning eyes. Overall, it's important to take regular breaks and maintain good posture, as sitting for extended periods can have negative effects on one's health. Our study showed that, Postural breaks have a protective effect on neck/shoulder pain (OR 0.32, CI 0.16-0.62), back and lower extremity pain (OR 0.35, CI 0.18-0.69), and eye burning (OR 0.50, CI 0.27-0.94) of study participants. This effect was found to have a strongly significant value. Postural breaks are short, frequent pauses or adjustments in body position that help relieve the physical strain and tension that can build up when we sit or stand in the same position for extended periods. These breaks can be as simple as standing up and stretching or changing the angle of your chair or computer monitor. Neck/shoulder pain and back/lower extremity pain are common musculoskeletal disorders that can be caused by poor posture and prolonged periods of sitting or standing in one position. Postural breaks can help to prevent or alleviate these conditions by reducing the amount of time that the body spends in a static, uncomfortable position. One way that postural breaks protect against neck and shoulder pain is by reducing the tension that builds up in the neck and shoulder muscles when we hold our heads in a fixed position for long periods. When we work at a computer, for example, we tend to crane our necks forward to look at the screen, which can cause strain in the neck and shoulder muscles. Taking a postural break to stretch or adjust our position can help to relieve this tension and prevent the development of pain. Similarly, postural breaks can help to prevent and alleviate back and lower extremity pain by reducing the pressure that builds up in the spine and lower extremities when we sit or stand for long periods. When we sit, for example, the pressure on our spine increases as we compress our disks, and our hip flexors can become tight and shortened, leading to lower back pain. Taking a postural break to stand up and stretch can help to relieve this pressure and prevent the development of pain. In addition to relieving physical strain and tension, postural breaks also promote circulation and blood flow throughout the body. This increased circulation can help to prevent the development of pain by delivering oxygen and nutrients to the muscles and tissues that are at risk of becoming strained or overworked. Overall, postural breaks are an important protective factor for neck/shoulder pain and back/lower extremity pain. By reducing physical strain and tension, promoting circulation, and preventing the development of pain, postural breaks can help to keep the body healthy and pain-free even in the face of prolonged periods of sitting or standing (16-17).

In Italy, D. Lgs. 81/08 (18) stipulates that video screeners have a break from PC use of a quarter of an hour every 2 hours of work, to rest their eyesight and prevent damage from occurring in the long run. It is also important for the company's physician in charge to train and inform workers on this issue.

Our study also shows that holding correct posture such as straight wrists and relaxed arms (see Figure 1.) prevents arm pain (OR 0.26, CI 0.13-0.52), and those feet properly resting on the floor (see Figure 1.), prevent back and lower limb pain (OR 0.33, CI 0.15-0.74).

Moreover, across the cohort of individuals participating in the survey who engage in remote work, just 51% said that they operate inside a designated and well-equipped workspace exclusively devoted to business-related activities. This can have several consequences: firstly, the decrease in productivity, working in a dedicated workspace can help people maintain concentration. Those who do not have a dedicated workspace may find it more difficult to concentrate, resulting in lower productivity levels. Secondly, work-life balance problems; this can lead to burnout and increased stress levels. Third, security and privacy issues; if remote workers do not work in a secure and confidential environment, there may be data security risks. Confidential information could be exposed if family members or other people have access to their work area (19-20).

Results from this study highlighted that the workers with ergonomic chairs – and an ergonomic workstation in general – complained less musculoskeletal pain compared to those workers without ergonomic workstations. This raises the important question of social disparities in working from home. The employer can intervene improving the knowledge the workers have about the importance of ergonomics in the workplace, and formation and information programs are necessary to educate workers on the right set up when working remotely. However, some disparities can only be leveled intervening directly: the large

international pharmaceutical company investigated in this study, for example, had a fund accessible to all employees through which the employer would contribute to the purchase of an ergonomic chair for the home workstation, and other tools necessary for the ergonomic wellbeing of employees.

A difference has been reported for the average paycheck between jobs that can be performed remotely compared to jobs which need to be performed on site (21), however social disparities exist within these categories. Since results from this study showed that an ergonomic workstation can be instrumental in improving the wellbeing of employees, employers should take actions to ensure that all workers have the proper workstation when working from home. Interventions – both educational and economical by the employer – are instrumental in reducing social disparities affecting the physical wellbeing of workers. The role of the occupational physician is fundamental to ensure that all workers can recognize an unsafe set up and can participate in improving their home workstation (22).

Study limitations

This study has some limitations. One limitation is due to the study design, which is cross-sectional observational in nature, so there are no reevaluations of oculo-visual and musculoskeletal disorders related to computer use and related workstation in Angelini House employees after administration of the questionnaire. Another limitation of this study lies in the selection bias due to the enrollment of participants, so the questionnaire will be administered with prior consent, free and informed, on a voluntary basis only.

Conclusions

For people who work from home and change workstations, it is crucial to maintain their emotional and physical well-being, by creating an appropriate workspace and proper risk training by the occupational health physician.

Acknowledgments
The authors would like to express their gratitude to all the participants for their time and wonderful collaboration.

Riassunto

Smart working durante la pandemia da COVID-19: la prevalenza di disturbi muscoloscheletrici e visivi nel personale amministrativo di una grande azienda internazionale

Introduzione. Nel corso della pandemia da COVID-19, si è osservato un aumento dell'utilizzo dei dispositivi digitali durante le attività lavorative, con significative implicazioni per il benessere psicofisico dei lavoratori. Lo scopo di questo studio è stato quello di esaminare la prevalenza dei disturbi muscolo-scheletrici e visivi associati all'uso del computer e alla postazione di lavoro domestica.

Metodi. Lo studio è stato condotto utilizzando un disegno trasversale. Una checklist del National Institute of Health è stata somministrata ai dipendenti di una grande azienda farmaceutica internazionale con sede in Italia.

Risultati. I risultati del nostro studio hanno evidenziato che le pause posturali hanno un effetto protettivo sul dolore al collo/spalla (OR 0,32, IC 0,16-0,62), sul dolore alla schiena e agli arti inferiori (OR 0,35, IC 0,18-0,69) e sul bruciore agli occhi (OR 0,50, IC 0,27-0,94) dei partecipanti.

Conclusioni. Si raccomanda ai lavoratori che svolgono la propria attività in modalità smart working di predisporre un ambiente di lavoro ad uso esclusivo, dopo aver ricevuto una formazione specifica sui rischi correlati a cura del proprio medico del lavoro. Tale misura risulta fondamentale per preservare il loro benessero fisico e mentale.

References

1. Gualano MR, Santoro PE, Borrelli I, Rossi MF, Amantea C, Daniele A, et al. TElewoRk-RelAted Stress (TERRA), Psychological and Physical Strain of Working From Home During the COVID-19 Pandemic: A Systematic Review. Workplace Health Saf. 2022 Nov 16:21650799221119155. doi: 10.1177/21650799221119155. Epub ahead of print. PMID: 36382962; PMCID: PMC9672980.
2. Bouziri H, Smith DRM, Descatha A, Dab W, Jean K. Lavorare da casa ai tempi del COVID- come preservare al meglio la salute sul lavoro? Occup Environ Med. 2020;**77**:509-10. doi: 10.1136/oemed-2020-106599.
3. D.P.C.M. of 26 April, 2020. Shared Protocol for the Regulation of Measures to Combat and Contain the Spread of the COVID-19 Virus in the Workplace between the Government and the Social Partners. Available from: https://www.lavoro.gov.it/documenti-e-norme/normative/Documents/2020/DPCM-26-aprile-2020.pdf [Last accessed: 2024 May 20].
4. Cirrincione L, Rapisarda V, Mazzucco W, Provenzano R, Cannizzaro E. SARS-CoV-2 and the Risk Assessment Document in Italian Work; Specific or Generic Risk Even If Aggravated? Int J Environ Res Public Health. 2021 Apr 2;**18**(7):3729. doi: 10.3390/ijerph18073729. PMID: 33918369; PMCID: PMC8038281.
5. Ebert PRL. O teletrabalho na reforma trabalhista: Impactos na saúde dos trabalhadores e no meio ambiente do trabalho adequado. RED/UnB. 2018;**15**:163-72.
6. Barone Gibbs B, Kline CE, Huber KA, Paley JL, Perera S.

Covid-19 shelter-at-home and work, lifestyle and well-being in desk workers. Occup Med (Lond). 2021 Apr 9;**71**(2):86-94. doi: 10.1093/occmed/kqab011. PMID: 33598681; PMCID: PMC7928687.
7. Borrelli I, Santoro PE, Fiorilli C, Angelini G, Buonomo I, Benevene P, et al. A new tool to evaluate burnout: the Italian version of the BAT for Italian healthcare workers. BMC Public Health. 2022 Mar 9;**22**(1):474. doi: 10.1186/s12889-022-12881-y. PMID: 35264130; PMCID: PMC8906913.
8. Xiao Y, Becerik-Gerber B, Lucas G, Roll SC. Impacts of Working From Home During COVID-19 Pandemic on Physical and Mental Well-Being of Office Workstation Users. J Occup Environ Med. 2021 Mar 1;**63**(3):181-190. doi: 10.1097/JOM.0000000000002097. PMID: 33234875; PMCID: PMC7934324.
9. Regmi A, Suresh J, Asokan R. Changes in work patterns during COVID-19 lockdown and its impact on the eyes and body. Clin Exp Optom. 2022 Feb 14:1-7. doi: 10.1080/08164622.2022.2029682. Epub ahead of print. PMID: 35157810.
10. da Fonte ACFC, da Silva VM, Carvalho FLR, Freitas GA. Workplace exercise in telework: implementation of distance postural health actions in times of pandemic. Rev Bras Med Trab. 2021 Dec 30;**19**(4):553-559. doi: 10.47626/1679-4435-2021-833. PMID: 35733539; PMCID: PMC9162283.
11. de Almeida MLC, de Almeida MCC, de Carvalho MH. O meio ambiente do teletrabalho e as doenças do teletrabalhador. Consinter.. May-Jun 2018;**4**(6):421-431. https://doi.org/10.19135/revista.consinter.00006.19.
12. Moretti A, Menna F, Aulicino M, Paoletta M, Liguori S, Iolascon G. Characterization of Home Working Population during COVID-19 Emergency: A Cross-Sectional Analysis. Int J Environ Res Public Health. 2020 Aug 28;**17**(17):6284. doi: 10.3390/ijerph17176284. PMID: 32872321; PMCID: PMC7503869.
13. Seva RR, Tejero LMS, Fadrilan-Camacho VFF. Barriers and facilitators of productivity while working from home during pandemic. J Occup Health. 2021 Jan;**63**(1):e12242. doi: 10.1002/1348-9585.12242. PMID: 34181307; PMCID: PMC8238055.
14. Self-Assessment Checklist of the National Institutes of Health, Office of Research Services, Division of Occupational Health and Safety. Available from: https://ors.od.nih.gov/sr/dohs/Documents/Computer%20Workstation%20Ergonomics%20Self%20Assessment%20Checklist.pdf [Last accessed: 2024 May 20].
15. De Vincenzi C, Pansini M, Ferrara B, Buonomo I, Benevene P. Consequences of COVID-19 on Employees in Remote Working: Challenges, Risks and Opportunities An Evidence-Based Literature Review. Int J Environ Res Public Health. 2022 Sep 16;**19**(18):11672. doi: 10.3390/ijerph191811672. PMID: 36141948; PMCID: PMC9517495.
16. Michinov E, Ruiller C, Chedotel F, Dodeler V, Michinov N. Work-From-Home During COVID-19 Lockdown: When Employees' Well-Being and Creativity Depend on Their Psychological Profiles. Front Psychol. 2022 May 9;**13**:862987. doi: 10.3389/fpsyg.2022.862987. PMID: 35615185; PMCID: PMC9126181.
17. Bernaards CM, Ariëns GAM, Simons M, Knol DL, Hildebrandt VH. Improving Work Style Behavior in Computer Workers with Neck and Upper Limb Symptoms. J Occup Rehabil. 2008; **18**:87-101. https://doi.org/10.1007/s10926-007-9117-9.
18. Italian Republic. Gazzetta Ufficiale. D.lgs 81/08. Svolgimento quotidiano del lavoro. art. 175. Available from: https://www.gazzettaufficiale.it/atto/serie_generale/caricaArticolo?art.versione=1&art.idGruppo=33&art.flagTipoArticolo=0&art.codiceRedazionale=008G0104&art.idArticolo=175&art.idSottoArticolo=1&art.idSottoArticolo1=10&art.dataPubblicazioneGazzetta=2008-04-30&art.progressivo=0 [Last accessed: 2024 May 20].
19. Choudhury P, Foroughi C, Larson Barbara. Work-From-Anywhere: The Productivity Effects of Geographic Flexibility (August 7, 2019). Harvard Business School Technology & Operations Mgt. Unit Working Paper No. 19-054, Northeastern University School of Law Research Paper No. #3494473, Available from: https://ssrn.com/abstract=3494473 or http://dx.doi.org/10.2139/ssrn.3494473 [Last accessed: 2024 May 20].
20. Gualano MR, Santoro PE, Borrelli I, Rossi MF, Amantea C, Daniele A, Moscato U. TElewoRk-RelAted Stress (TERRA), Psychological and Physical Strain of Working From Home During the COVID-19 Pandemic: A Systematic Review. Workplace Health Saf. 2023 Feb;**71**(2):58-67. doi: 10.1177/21650799221119155. Epub 2022 Nov 16. PMID: 36382962; PMCID: PMC9672980.
21. Dingel JI, Neiman B. How many jobs can be done at home? J Public Econ. 2020 Sep; **189**:104235. doi: 10.1016/j.jpubeco.2020.104235. Epub 2020 Jul 9. PMID: 32834177; PMCID: PMC7346841.
22. Nwosu CO, Kollamparambil U, Oyenubi A. Socio-economic inequalities in ability to work from home during the coronavirus pandemic. The Economic and Labour Relations Review. 2022;**33**(2):290-307. https://doi.org/10.1177/10353046221085598.

Corresponding author: Ivan Borrelli, Università Cattolica del Sacro Cuore, Largo Francesco Vito 1, 00168 Rome, Italy
e-mail: ivan.borrelli@unicatt.it

Ann Ig. 2025 Jan-Feb; 37(1): 37(1): 84-96 doi: 10.7416/ai.2024.2659

Intentions to move abroad among medical students: a cross-sectional study to investigate determinants and opinions

Manuela Martella[1], Giuseppina Lo Moro[1], Giacomo Scaioli[1,2], Caterina Grisafi-Schittone[1], Gabriele Gebbia[1], Roberta Siliquini[1,3], Fabrizio Bert[1,2]

Keywords: Medical students; brain drain; career choice; physicians' migration
Parole chiave: Fuga di cervelli; studenti di medicina; carriera professionale; medici emigrati

Abstract

Aim. *The lack of health professionals and the physicians' migration trend represents a challenging issue for the health systems' sustainability worldwide. The current study aims to evaluate the intentions of Italian medical students to pursue their own careers abroad by investigating the push and pull factors of migration.*

Subject and Methods. *A cross-sectional study was performed among Italian medical students through a self-administered questionnaire. Primary and secondary outcomes were established as the intention of moving abroad after graduation and knowledge about residency programmes, application, quality training and remuneration in the country of interest. Descriptive analysis for all variables and univariable and multivariable regression for primary and secondary outcomes were performed.*

Results. *Overall, 307 medical students took part in the study. More than half of the sample considered moving abroad after graduation, mainly to find a higher quality training programme. Regression analysis highlighted a significant association between the primary outcome and general personal and professional reasons, as well as previous experiences abroad, whereas bureaucratic procedures were perceived as the main barrier. Perceived better knowledge about residency programmes and quality of training related to sources of information such as the Internet (blogs, forums, websites) and medical associations.*

Conclusion. *Retention policies are necessary to meet the expectations and requests of future generations of doctors by allocating financial resources to offer high-quality training and broad career opportunities, together with appropriate wages, as crucial factors for discouraging the migration of healthcare professionals.*

[1] *Department of Public Health Sciences and Paediatrics, University of Turin, Italy*
[2] *Azienda Sanitaria Locale di Collegno e Pinerolo TO3, Collegno (TO), Italy*
[3] *Azienda Ospedaliera Universitaria Città della Salute e della Scienza, Turin, Italy*

Annali di Igiene : Medicina Preventiva e di Comunità (Ann Ig)
ISSN (print) 1120-9135 ISSN (online) 3035-5559

https://www.annali-igiene.it

Introduction

Worldwide skilled healthcare workers (HCWs) as doctors and nurses have increased, reducing the global health workforce shortage (1). Nevertheless, the lack of health professionals remains a crucial issue in both high-income countries (HICs) and low-income and middle-income countries (LMICs), although graduates mostly come from HICs (2). Worldwide, about 15% of healthcare professionals have moved to a foreign country either to apply for a job or to pursue their education. Moreover, many countries experience a spotty distribution of health workforce (3,4). Recently, a report from the World Health Organization (WHO) promoted "The decent Employment Agenda" to improve the performance and motivation of health workers through attraction and retention policies addressing job security, a manageable workload, supportive supervision, and professional development opportunities (5).

For decades, physician migration flows have been an emerging issue across countries belonging to the Organization for Economic Cooperation and Development (OECD). Worldwide, catalyzing reasons are diverse, as training purposes, acquirement of additional professional qualifications, professional development opportunities, and financial incentives (1,3,6).

Recent findings revealed an increase in domestic medical graduates and the proportion of foreign-born or foreign-trained doctors across OECD countries (7). The extreme urgency to control the COVID-19 pandemic overflow pushed this trend further by inducing governments to foster policies for facilitating emigration flows of health professionals and providing for shortage of personnel and emerging workload (8).

Previous studies assessed several factors associated with health workforce migration, identifying the key ones as individual, organizational, healthcare system, and general environmental factors. Many potential reasons and conditions belong to these main categories, encompassing every aspect of personal and professional life, from age to compensation to human resource policies to health services funding (9).

In 2020, practicing physicians in the European Union (EU) were approximately 1.75 million, and 60% were recorded in Germany, Italy, Spain, and France. Nevertheless, Greece recorded the highest number of physicians (619.5) per 100,000 inhabitants, Italy recorded 400.1 per 100,000, and Germany 446.8 per 100,000. Between 2015 and 2020, the number of physicians per 100,000 inhabitants increased in all EU countries, due to a simultaneous increase in the absolute number of physicians and a decrease in population (10). This trend accounts for demographic shifts, such as the ageing of populations and higher demand for social and healthcare services.

Furthermore, in most EU Member States, physicians aged 55 years and over are between 22% and 37% of the overall, whereas in Italy, this age group represents more than 50% of the healthcare workforce (10).

Therefore, facing this massive shortage of HCWs and its forthcoming worsening in the coming years, every country should establish a national plan based on its population's healthcare needs. For instance, in Italy, the availability of residency training positions increased from 2019 to 2021 by 21%; however, this will be insufficient to address the demand for population health needs for the years to come (10,11). In this context, understanding the expectations and demands of the future healthcare workforce can contribute to depicting the current situation to find determinants of HCWs migration and the entity of such phenomenon. In this regard, the evaluation of opinions and intentions among medical students helps analyze the relationships between push and pull factors for looking for an excellent job position abroad (12).

The current study analyzed Italian medical students' intentions to pursue their professional qualification abroad. The primary purpose of this research was to understand the driving factors of moving to a foreign country, entailing personal, educational, and professional reasons, to explore prevalence and patterns across the medical undergraduate population. Secondarily, knowledge about training programmes, prerequisites, and applications for accessing a medical residency was explored. Identifying the pushing motivations of the youngest doctor generations is crucial to achieving effective interventions for strategic workforce planning and implementing attractive policies and training opportunities for both retention and immigration of health professionals.

Materials and methods

A cross-sectional study was carried out between the 21st of November and the 2nd of December 2022 among the students enrolled in the Medical School of the University of Turin. A paper-based self-administered questionnaire was disseminated during the immunisation campaign against influenza addressed to the medical students.

Attending the 4th, 5th, and 6th year and over (for those who had not completed all exams within the set period) of the School of Medicine was the inclusion criteria. International students attending the Erasmus+ programme at the Medical School of the University of Turin were excluded.

An invitation letter was delivered via email informing about the purpose of the study and clarifying that the questionnaire was completely anonymous and voluntary.

All procedures followed the 1964 Helsinki Declaration and its subsequent amendments. The Ethics Committee of the University of Turin granted ethical approval (Protocol no. 0183621 from 15 March 2023). Informed consent was necessary to access the questionnaire.

Overall, 307 participants completed a questionnaire with 24 items. Nobody refused to take part in the investigation.

The questionnaire was developed based on a review of the scientific literature and existing evidence about the main topic (13–16). The survey was divided into four sections, focusing on socio-demographics, intentions and preferences about residency programmes, attitudes regarding moving abroad for medical specialization, and perceived knowledge concerning foreign residency programmes.

Age, gender, nationality, socio-economic status, year of study, educational level and marital status were investigated. Specialty goals, reasons for specialty choice and previous experiences abroad were investigated in the second section. In the third section, questions focused on attitudes toward moving abroad after graduation, considering personal, educational, and professional factors for a variable period (from less than one year to lifelong). Peculiar personal reasons were reported, such as quality of life and social condition abroad, family support for moving abroad, and coming back at the end to one's own country of origin. Educational reasons were analyzed through specific questions, such as the availability of high-quality training and access to the medical speciality of choice in case of failing the Italian national exam for applying to a residency programme. Further questions focussed on professional reasons, such as engagement at work, higher career and research opportunities, health system management and salary. Such opinions and attitudes were measured through a 4-point like-Likert scale to rate the degree of agreement (from "1=at all" to "4=not at all"). Factors inducing medical students' migration were assessed by reviewing similar previous studies (13-20). In addition, perceived knowledge of foreign languages, application, structure, quality and remuneration of residency programmes abroad were explored. Finally, barriers to moving and working abroad were scrutinised (recognition of degree, language barrier, adaptability to different work environments, colleagues, weather conditions, separation from the family, and distance from social contacts). The fourth section was organised in 4-point like-Likert scale questions (scoring from "1=not at all" to "4=at all"). Finally, types of information sources consulted to find out details about such topics were investigated.

Data analysis

All variables were described through a descriptive quantitative analysis. For continuous variables, median and interquartile range (IQR) were reported by the significance of the Shapiro-Wilk test for normality assumption.

The study's primary outcome was the intention of working abroad after graduation for a variable period. The secondary outcomes focused on participants' knowledge about residency application, quality residency training, residency programmes and remuneration in the destination country. The primary and secondary outcomes were converted into binary variables by reorganising the 4-point like-Likert scale into dichotomous categories, where negative (1 and 2) and positive (3 and 4) responses were merged, respectively. Positive responses were associated with the willingness to move abroad for the primary outcome. Positive responses also outlined good perceived knowledge of foreign residency programmes, thus measuring the secondary outcomes.

Chi-square and Mann-Whitney tests were performed to detect differences between groups defined by primary and secondary outcomes for categorical and continuous variables, respectively.

Univariable and multivariable logistic regressions assessed relationships between independent variables and the binary outcomes. Using univariable logistic regression, p-value< .25 was the pre-filtering criterion for variable selection to the multivariable model (21). Two multivariable models were identified for the primary outcome: the first was about socio-demographic characteristics, and the second referred to reasons for emigration. Both models were adjusted for age and gender. The following independent variables were selected for the first model: age, gender, experiences abroad during high school and medical studies, socio-economic status, and marital status. The second model analyzed associations with personal, educational, and

professional reasons for moving abroad after graduation, perceived barriers and facilitators of moving abroad to attend the residency programme of choice. Secondary outcomes were analysed through multivariable models, adjusted for age and gender. The following independent variables were selected: socio-economic status, level of foreign language proficiency, experience abroad during high school and medical studies, intention to attend a surgery speciality or family medicine or others, and the information sources consulted, such as family and friends, social networks, blogs and forums, websites, and medical associations.

StataSE 17 (StataCorp. 2021. Stata: Release 17. Statistical Software. College Station, TX: StataCorp LLC.) Software was used for all analyses. Missing values were excluded. Statistical significance required *p-value*<.05.

Results

Overall, 307 responses were collected. Table 1 shows the main characteristics of participants. One foreign participant was attending the Erasmus+ project at the Medical School of the University of Turin and therefore was excluded.

Median age was 24 (IQR 23-25), and almost 70% of the interviewees were female. Participants attending the 4th, 5th and 6th academic year or over were homogeneously distributed. Participants' residency intent was unanimously stated, and medical specialities were the most popular compared with surgery, family medicine, and others (diagnostics, occupational medicine, anaesthesiology, etc.). However, 13% of them showed uncertainty. More than 40% of the sample had experienced already moving abroad temporarily during high school or college. Overall, 52% of the sample answered that they would consider moving abroad after graduation. Almost 70% considered it for a few years, like one or two, and less than 50% would stay till specialist certification. Scrutinizing reasons to move abroad, more than 80% of students mentioned better quality of life and social conditions. More than 90% of them were encouraged to migrate because of higher quality educational and training programmes. Furthermore, increased chances of getting into residency programmes and failing the Italian entrance exam were also considered worthy reasons to migrate.

Almost 54% considered personal motivation to seek a job abroad. Nevertheless, the percentage markedly changed when participants were asked about educational (72.9%) and professional reasons (72.5%) for moving abroad and being admitted to a residency programme. Further, moving to a foreign country as a specialist was a good alternative for most respondents (68.1%). Assessing the duration of living abroad after graduation, less than one year and a maximum of 2 years were considered convenient timeframes to attend the residency programme abroad (66.8% and 68.6%, respectively). Few participants would remain abroad after a speciality degree or even for a lifetime (34.3% vs 17.3%).

Significant associations with the primary outcome ("willingness of moving abroad after graduation") resulted for being single, having earlier experiences abroad during high school and/or college, and being uncertain about the choice of specialty after graduation. Pushing factors such as personal, educational, and professional reasons were positively associated with the intention to migrate abroad after graduation. Exploring peculiar aspects highlighted that quality of life abroad, family support, professional engagement, team building, and failing the national exam to access any residency programme were considered appropriate reasons for seeking a job abroad. Language proficiency, separation from family and friends, and getting used to an unknown work environment (colleagues, workplace, and tasks) were perceived as the main difficulties for moving abroad (see Table 2).

Knowledge about the organization and quality of residency programmes and information sources were investigated. The relative results are shown in supplementary tables (S1, S2). Almost 80% of participants stated low knowledge about the application and medical specialties programmes abroad, and about 70% were not informed about remuneration and quality training. More than 40% of students found information about residency admission, programme, quality of training, and remuneration mainly from relatives and friends, social networks, and websites. Medical associations were consulted by less than 30%, whereas other information sources were scarcely considered.

Multivariable regression models

Multivariable regression of primary outcome highlighted that medical students were more likely to move abroad and seek a job as residents for personal and professional reasons and return to their country of origin. Those who had experiences abroad during high school or college tended to move abroad after graduation. Finally, knowledge about applying for a residency programme was associated positively with

Table 1 - Characteristics of participants and relation with the primary outcome

Characteristics			Willingness of migrating	
	Overall **N** n=307	**No** **n (%)** n=146	**Yes** **n (%)** n=161	p-value
Age	**Median** 24	**IQR** 23-25		**0.022**
Gender				
Male	98 (32.0)	44 (30.3)	54 (33.5)	0.550
Female	208 (68.0)	101 (69.7)	107 (66.5)	
Nationality				
Italian	294 (96.1)	141 (97.2)	153 (95.0)	0.320
Foreign	12 (3.9)	4 (2.8)	8 (5.0)	
Socio-economic status				
Very high-high	261 (85.0)	127 (88.2)	134 (83.2)	0.218
Medium-low	46 (15.0)	17 (11.8)	27 (16.8)	
Marital status				
Single	136 (44.3)	55 (33.2)	81 (50.3)	**0.034**
Engaged-married	171 (55.7)	89 (61.8)	80 (49.7)	
Academic year				
4th	57 (18.7)	22 (15.3)	35 (21.7)	0.231
5th	74 (24.3)	32 (22.2)	42 (26.1)	
6th	103 (33.8)	56 (38.9)	47 (29.2)	
over	71 (23.3)	34 (23.6)	37 (23.0)	
Education				
High school	298 (97.4)	.	.	
College	8 (2.6)	.	.	
Willing to medical speciality				
Yes	307 (100.0)	.	.	
No	0 (0)	.	.	
Residency of choice				
Family medicine	20 (6.5)	10 (6.8)	10 (6.2)	0.821
Clinical service	154 (50.2)	80 (54.8)	74 (45.0)	0.122
Surgery	84 (27.4)	38 (26.0)	46 (28.6)	0.618
Others	22 (7.2)	9 (6.2)	13 (8.1)	0.517
Uncertain	40 (13.0)	13 (8.9)	27 (16.8)	**0.041**
Reasons for residency of choice*				
Doctor-patient relationship	222 (72.3)	.	.	
No doctor-patient relationship	18 (5.9)	.	.	
Social esteem	33 (10.7)	.	.	
Intensive workload	51 (16.6)	.	.	
Flexible work time	114 (37.1)	.	.	
Income	78 (25.4)	.	.	
Favourable supply/demand	56 (18.29)	.	.	
Multifaceted discipline	193 (62.9)	.	.	
Experiences abroad				
Yes	125 (40.8)	48 (32.9)	77 (48.1)	**0.007**
During High school	95 (76.0)	.	.	
During College	38 (30.4)	.	.	

Note: *Multi select multiple choice question; p-value<0.05; IQR – Interquartile Range

Table 2 - Pushing factors and barriers for moving abroad and association with primary outcome

Characteristic			Willingness of migrating	
	Overall N n=307	**No n (%)** n=146	**Yes n (%)** n=161	**p-value**
Pushing factors				
Personal reason				
No	141 (46.1)	110 (75.3)	31 (19.4)	**<0.001**
Yes	165 (53.9)	36 (24.7)	129 (80.6)	
Quality of life				
No	54 (17.6)	36 (24.7)	18 (11.2)	**0.002**
Yes	253 (82.4)	110 (75.3)	143 (82.8)	
Social condition				
No	48 (15.6)	29 (19.9)	19 (11.8)	0.052
Yes	259 (84.7)	117 (80.1)	142 (88.2)	
Family support				
No	115 (37.5)	66 (45.2)	49 (30.4)	**0.008**
Yes	192 (62.5)	80 (54.8)	112 (69.6)	
Reunion (with family, friends, partner)				
No	128 (42.1)	57 (39.3)	71 (44.6)	0.346
Yes	176 (57.9)	88 (60.7)	88 (55.3)	
Coming back to country of origin				
No	190 (62.5)	77 (53.1)	113 (71.0)	**0.001**
Yes	114 (37.5)	48 (46.9)	46 (28.9)	
Educational reason				
No	83 (27.1)	71 (48.6)	75 (51.4)	**<0.001**
Yes	223 (72.9)	12 (7.5)	148 (92.5)	
High quality programme				
No	27 (8.8)	14 (9.6)	13 (8.0)	0.640
Yes	280 (91.2)	132 (90.4)	148 (91.9)	
Good chance to get into residency programme				
No	96 (31.4)	53 (36.5)	43 (26.7)	0.064
Yes	210 (68.6)	92 (63.4)	118 (73.3)	
Failed exams in Italy				
No	155 (50.5)	65 (44.5)	90 (55.9)	**0.046**
Yes	152 (49.5)	81 (55.5)	71 (44.1)	
Professional reason				
No	84 (27.4)	80 (54.8)	4 (2.5)	**<0.001**
Yes	222 (72.5)	66 (45.2)	156 (97.5)	
Acceptable workload				
No	65 (21.6)	33 (23.1)	32 (20.2)	0.552
Yes	236 (78.4)	110 (76.9)	126 (79.7)	
High professional involvement and appreciation				
No	35 (11.5)	24 (16.7)	11 (6.9)	**0.008**
Yes	268 (88.4)	120 (83.3)	148 (93.1)	
Career opportunities				
No	43 (14.2)	26 (18.1)	17 (10.7)	0.067
Yes	260 (85.1)	118 (81.9)	142 (89.3)	
Research opportunities				
No	74 (24.5)	37 (25.9)	37 (23.3)	
Yes	228 (75.5)	106 (74.1)	122 (76.7)	
Organization of health care delivery				
No	133 (44.0)	70 (48.9)	63 (39.6)	0.103
Yes	169 (56.0)	73 (51.0)	96 (60.4)	

Centre of excellence				
No	81 (26.8)	42 (29.49	39 (24.5)	0.343
Yes	221 (73.2)	101 (70.6)	120 (75.5)	
Income				
No	25 (8.3)	19 (13.29	6 (3.8)	**0.003**
Yes	277 (91.7)	125 (86.8)	152 (96.2)	
Migration as trained specialist				
No	98 (32.0)	82 (56.2)	16 (10.0)	**<0.001**
Yes	208 (68.0)	64 (43.9)	144 (90.0)	
Barriers				
Bureaucratic procedures				
No	79 (25.7)	42 (28.8)	37 (23.0)	0.247
Yes	228 (74.3)	104 (71.2)	124 (77.0)	
Language barriers				
No	131 (43.7)	49 (34.5)	82 (51.9)	**0.002**
Yes	169 856.3)	93 (65.5)	76 (48.1)	
Family-friends separation				
No	72 824.2)	20 (14.2)	52 (33.1)	**<0.001**
Yes	226 (75.8)	121 (85.8)	105 (66.9)	
Colleagues relationships				
No	205 (69.0)	87 (62.6)	118 (74.7)	**0.025**
Yes	92 (31.0)	52 (37.4)	40 (25.3)	
Workload and work time				
No	233 (77.9)	109 (77.3)		0.807
Yes	66 (22.1)	32 (22.7)	34 (21.5)	
Methods and procedures at work				
No	184 (61.5)	78 (55.3)	106 (67.1)	**0.037**
Yes	115 (38.5)	63 (44.7)	52 (32.9)	
Weather conditions				
No	202 (67.6)	88 (62.4)	114 (72.1)	0.073
Yes	97 (32.4)	53 (37.6)	44 (27.8)	

Note: p-value<0.05

the primary outcome, albeit bureaucratic procedures were significantly perceived as a barrier to emigration (see Table 3).

Multivariable models for secondary outcomes suggested exciting results, mainly related to sources of information. Perceived knowledge about the application for the residency programme was higher among medical students who had experiences abroad during college or high school and among those who sought information online and from medical associations. More profound knowledge about the residency programme resulted in medical students interested in surgery and among those who sought information on blogs and forums, as well as from medical associations. Moreover, students who had experience abroad also knew about better residency programmes.

Our results showed that female students were less informed about the residency programme quality, whereas those fascinated with surgery showed better knowledge about it. Medical students who gathered information on social networks, blogs, and forums were better informed. In addition, seeking information from family and friends, as well as from medical associations, was positively related to a higher knowledge about the quality of the residency programme. Finally, higher foreign language proficiency was linked to higher knowledge. Regarding economic remuneration, students who showed higher knowledge sought information on websites and through medical associations (see Table 4).

Discussion

The WHO reported that 15% of HCWs currently work outside their country of origin, and such migration flow is emphasised among LMICs. As a

Table 3 - Multiple regression model for primary outcome and socio-demographic characteristics

Willingness of migrating	adjOR	p-value	95% CI
Age	0.9	0.112	0.8 -1.0
Gender	0.9	0.674	0.5 - 1.5
Clinical service for the residency programme	0.7	0.25	0.5 -1.2
Experiences abroad	1.9	**0.008**	1.1 -3.1
Socio-economic status	0.6	0.15	0.3 - 1.1
Marital status	0.6	0.052	0.4 - 1.0
Perceived barriers and facilitators	adjOR	p-value	95% CI
Personal reasons	8.1	**0.000**	3.6 - 18.3
Educational reasons	2.8	0.073	0.9-8.7
Professional reasons	8.3	**0.007**	1.8 - 38.2
Emigration as specialist	2.6	0.102	0.8 - 8.2
Quality of life	1.6	0.477	0.4 - 6.0
Social conditions	0.8	0.713	0.2 - 3.2
Family support	1.4	0.390	0.5 - 3.4
Coming back to the country of origin	0.2	**0.001**	0.1 - 0.5
Reunion with family or friends	2.6	0.086	0.9 - 7.9
Good chance to get into a residency programme	1.3	0.572	0.5-3.6
Failed exams in Italy	0.6	0.182	0.2-1.3
High professional involvement and appreciation	1.6	0.549	0.3-7.5
Career opportunities	0.6	0.512	0.1-2.7
Organisation of health care delivery	0.8	0.590	0.3-1.8
Income	1.2	0.836	0.1-11.1
Bureaucratic procedures	3.4	**0.012**	1.3-8.8
Language barriers	0.6	0.232	0.3-1.4
Family-friends separation	0.6	0.275	0.2-1.5
Colleagues relationships	0.6	0.218	0.2-1.4
Methods and procedures at work	0.5	0.068	0.2-1.0
Weather conditions	0.5	0.143	0.2-1.2
Knowledge about getting into a residency programme	14.5	**0.002**	2.7-78.8
Knowledge about the residency programme	0.7	0.606	0.2-2.9
Knowledge about the quality of the residency programme	0.9	0.933	0.3-2.9
Knowledge about income as a medical resident	1.2	0.650	0.5-3.3

Note: adjOR – adjusted Odds Ratio; p-value<0.05; CI – Confidence Interval

consequence of such phenomenon, countries of birth of migrating doctors and nurses have to face significant financial losses from their education and training investment before graduation (12).

Overall, the United States, the United Kingdom and Germany are the most popular OECD countries among migrating HCWs for numerous reasons, such as higher salaries, high-quality training and better career opportunities, besides socio-economic and political stability and safety (6,22).

The current survey can be considered the first Italian study to investigate medical students' opinions about migrating after graduation and assess their level of information about post-graduate residency programmes outside Italy. The literature reports the main findings from projects carried out in LMCIs, which significantly differ from HICs in terms of economic and political situations. Analyses about the brain drain phenomenon focus mainly on qualified HCWs such as physicians and nurses. Therefore, the opinions and intentions of medical students can be influenced by several factors, such as gossip, others' experiences, and mass media, excluding direct, first-hand involvement in the healthcare world of work.

According to our analysis, more than half of the surveyed students intended to move abroad after graduation. Similar results were obtained from cross-sectional research in Croatia (13). In contrast, almost 70% of Turkish medical students and more than 80% of Irish, Serbian and Romanian medical students stated they want to pursue their careers abroad (14-17). A multicentre research conducted in five Polish medical

Table 4 - Multiple regression model for secondary outcomes and sociodemographic characteristics

Knowledge about:	Access to the residency programme			Quality of training		
	Adj OR	p-value	IC (95%)	Adj OR	p-value	IC (95%)
Age	1.0	0.997	0.9 ; 1.1	0.9	0.495	0.8 ; 1.1
Gender	0.6	0.214	0.3 ; 1.3	0.3	**0.001**	0.2 ; 0.6
Socio-economical status	0.6	0.246	0.2 ; 1.4	0.7	0.420	0.3 ; 1.7
Experience abroad	2.6	**0.008**	1.3 ; 5.4	1.5	0.239	0.8 ; 2.8
Level of language proficiency	2.4	0.067	0.9 ; 6.4	2.4	**0.044**	1.1 ; 5.5
Residency of choice						
Family medicine	1.3	0.714	0.3 ; 5.2	3.1	0.070	0.9 ; 10.3
Surgery	1.4	0.342	0.6 ; 3.1	2.7	**0.006**	1.3 ; 5.5
Others	1.7	0.454	0.4 ; 7.0	0.7	0.570	0.2 ; 2.7
Source of Information						
Relatives and friends	1.3	0.454	0.6 ; 2.7	2.0	**0.040**	1.1 ; 3.8
Social Networks	0.8	0.613	0.4 ; 1.7	2.3	**0.014**	1.2 ; 4.7
Blogs and forums	4.0	**0.002**	1.6 ; 10.2	2.8	**0.025**	1.1 ; 6.8
Websites	2.5	**0.011**	1.2 ; 5.3	1.8	**0.009**	1.2 ; 5.1
Medical associations	5.0	**<0.001**	2.4 ; 10.5	2.5	**0.009**	1.2 ; 5.1
Knowledge about:	Residency programme			Compensation		
	Adj OR	p-value	IC (95%)	Adj OR	p-value	IC (95%)
Age	0.9	0.910	0.9 ; 1.1	0.99	0.971	0.9 ; 1.1
Gender	0.5	0.060	0.2 ; 1.1	0.7	0.344	0.4, 1.3
Socio-economical status	0.7	0.428	0.2 ; 1.7	0.7	0.320	0.3 ; 3.3
Experience abroad	2.8	**0.003**	1.4 ; 5.7	2.0	**0.014**	1.1 ; 3.6
Level of language proficiency	2.8	0.034	1.1 ; 7.5	0.7	0.275	0.3 ; 1.3
Residency of choice						
Family medicine	1.1	0.935	0.2 ; 4.4	0.3	0.102	0.1 ; 1.2
Surgery	2.4	0.190	0.6 ; 9.5	1.3	0.379	0.7 ; 2.5
Others	2.5	0.190	0.6 ; 9.5	1.1	0.987	0.3, 3.3
Source of Information						
Relatives and friends	1.6	0.175	0.8 ; 3.3	1.5	0.177	0.8 ; 2.6
Social Networks	1.2	0.559	0.6, 2.6	1.6	0.140	0.9 ; 2.8
Blogs and forums	3.0	**0.016**	1.2 ; 7.5	1.3	0.550	0.6 ; 2.9
Websites	1.6	0.187	0.8 ; 3.2	2.4	**0.002**	1.4 ; 4.4
Medical associations	3.3	**0.001**	1.6 ; 6.9	2.8	**0.002**	1.5 ; 5.3

Note: adjOR – adjusted Odds Ratio; p-value<0.05; CI – Confidence Interval

schools reported that 62% of respondents planned to continue their professional training abroad (18).

The comparability among these data reflects a widespread sense of dissatisfaction and uncertainty about the prospect of living in one's own home country in the future. Since Italy belongs, according to the World Bank, to the category of HICs (23), the willingness to migrate among Italian medical students represents a paradoxical situation compared with other countries. A similar situation was observed in Ireland, where previous studies highlighted emigration intentions comparable to those of students from LMICs, such as in India, Lebanon, and Pakistan. According to Gouda et al., these similarities could be ascribed to limited postgraduate training positions and scarce career advancement possibilities (19). Indeed, the Chi-Square test (i.e. not confirmed by the regression model) associated migration intent with failing the national exam to get into a residency programme. Similarly, in a national-wide survey carried out among Portuguese junior doctors, the score of the National Medical Exam was identified as a convincing reason to work abroad (20).

In Italy, an increase of 21% of job positions in residency programmes was registered from 2019 to 2021 (11). Limiting access to the residency programme so

strictly over the past years may have exacerbated the frustration among freshly graduated physicians who experience high-stress levels due to limited specialization opportunities (24). Consequently, the limited access may have induced some of them to consider finding a job abroad. However, such relevant changes in the number of medical training positions and the automatic recognition of professional qualification after graduation (25) were probably the result of political choices driven by the serious difficulties reported by HCWs regarding the severe personnel shortage that emerged during the COVID-19 pandemic. Plausibly, these policies will have to handle criticism from medical categories for lacking and inadequate planning strategies and supply of healthcare resources.

Focussing on pushing factors of emigration, the multivariable regression model highlighted that personal reasons, such as returning to the country of origin, and professional ones, were significantly associated with migration intent. In addition, past experiences abroad were positively associated with emigration intentions. A case study on Serbian medical students highlighted that having been abroad before might be considered a potential predictor; gender and age did not seem to relate to willingness to migrate, as confirmed by our analyses (16).

A previous experience abroad during high school and medical studies has positive effects, enhancing language proficiency and prompting self-efficacy beliefs (26). Accordingly, international mobility is highly fostered within the EU area by reducing barriers by recognizing qualifications and active recruitment strategies in some medical schools to attract international students (7). For instance, participation in the Erasmus+ Programme represents a life-changing opportunity to develop skills and knowledge that effectively help tackle our society's challenges. In recent years, Italian participants in this project have notably increased in developing European cooperation projects (27). Hence, having experienced a period abroad can effectively enhance the attitude to pursue medical speciality training in other countries, supported by a higher level of self-confidence in language skills and a more robust adaptability to enjoy living and work-life abroad.

About peculiarities of personal motivation, the Chi-Square test identified as a predictor of migrating intentions a better quality of life in the country of destination, the concurrent familiar and social support to move abroad, and the possibility of being professionally appreciated and engaged at work, including a higher income. However, regression analysis did not confirm any significance for these items and generally considered personal and professional reasons can be hardly analyzed and discussed as predictors of migration.

Regarding economic compensation, financial dissatisfaction does not represent a pushing factor among Italian students, probably due to the financial support offered by their parents and the lack of economic and other obligations. On the contrary, financial factors were relevant for medical students from Ireland, Croatia, and Lithuania (13,19,28).

Among the barriers to migration intentions, bureaucratic obstacles outweigh other personal factors, such as separation from family and friends. Despite the equipollence of the medical degree throughout the EU and the automatic recognition of the basic medical training for general practitioner and specialist qualifications, working abroad as a HCW requires collecting broad documentation and obtaining a high-level language certification, besides eventually the recognition of the professional qualification. Once these steps are completed, the fulfilment of other selection criteria is necessary to find a suitable job position.

Indeed, solid incentives and determination, along with substantial economic and time investments, are crucial to start such procedures, especially after completing an already demanding study programme.

Further research should better analyze both predictors and barriers of migration intentions among medical students. Accordingly, evaluating specific determinants of the brain drain phenomenon since the beginning of one's medical career could help plan targeted strategies and implement retention policies.

The current study showed some limitations, such as the small sample. In addition, the questionnaire was not validated and a pilot study for testing it was not performed. However, all students who attended the vaccination campaign agreed to participate. Generalising the current findings is arduous since the sample included only students from the medical school of Turin. In addition, social and mobility restrictions experienced during the pandemic and the different organisation of clinical internships over the past years could represent a relevant bias about the current opinion of moving abroad after graduation.

Notwithstanding, this is the first Italian investigation into medical students' opinions and intentions about their next postgraduate training, aiming to early identify needs and problems affecting the future medical workforce. Further analyses involving a higher number of participants and potentially more medical schools could provide a prompt warning for upcoming migration trends.

Previous considerations from Italian research about the impact of medical migration on the Italian National Health Service explored the challenges faced by the Italian medical workforce. Every year, 1000 medical doctors leave Italy to seek employment abroad; this phenomenon substantially affects the medical workforce shortage, in addition to the impending massive retirement of Italian doctors expected over the last decade. Economic and residential factors such as obtaining appropriate wages and housing and professional requirements were perceived barriers, whereas a significant motivator was the long career and professional advancement duration (29). Therefore, the drivers of moving abroad among medical students and doctors seem similar before graduation and after beginning their professional careers. It is reasonable to consider them as concrete factors influencing HCWs' migration. These findings match Maslow's theory of motivation, which identified financial safety needs, self-actualisation, and professional and educational development as significant contributors to migration. Retention in the country of origin can be encouraged by creating desirable employment opportunities via local and international partnerships. When financial needs are met, interventions should increase education and professional opportunities (3).

Conclusion

Current and future political decisions should urgently address the needs and requirements of the medical workforce by allocating financial resources to make the offer from the Italian National Health System competitive and attractive. Investments should involve infrastructures, technologies, human resources, and national collective agreement. Innovative reforms should finally embrace undergraduate and postgraduate training to improve physicians' skills and competencies. Efforts must be agreed between multiple stakeholders, involving politicians, academics and even medical associations, which often gain acceptance from students and specialists.

Riassunto

Indagine trasversale sui determinanti e sui pareri degli studenti di medicina circa lo svolgimento all'estero della professione medica

Background. La carenza di professionisti in ambito sanitario e la loro tendenza a migrare all'estero rappresentano alcuni dei problemi cruciali dei sistemi sanitari in molti paesi del mondo. Lo scopo di questo studio è la valutazione delle intenzioni di un campione di studenti di medicina italiani a proseguire la propria formazione professionale all'estero, analizzando i fattori favorenti e bloccanti di tale fenomeno.

Disegno dello studio e metodi. È stato condotto uno studio osservazionale cross-sectional tramite la somministrazione di un questionario ad un campione di studenti iscritti al secondo triennio e fuori corso del corso di laurea in Medicina e Chirurgia dell'Università di Torino. Sono state valutate le intenzioni di emigrare in seguito alla laurea come outcome primario. Il livello di conoscenza in merito ai programmi di specializzazione, alle modalità di iscrizione, alla qualità del percorso formativo e alla remunerazione economica è stato considerato come outcome secondario. È stata condotta un'analisi descrittiva per tutte le variabili, e sono stati elaborati dei modelli di regressione univariabile e multivariabile per la valutazione degli outcome primario e secondario.

Risultati. In totale, sono stati raccolti 307 questionari. Più della metà del campione ha dichiarato di voler migrare all'estero dopo la laurea, principalmente alla ricerca di un percorso di formazione di alta qualità. Il modello di regressione ha evidenziato un'associazione significativa tra l'outcome primario e le motivazioni personale e professionale. Una precedente esperienza all'estero (Erasmus, lavorativa o altro) è risultata associata ad una maggiore intenzione di emigrare, mentre le difficoltà burocratiche sono state considerate come principale ostacolo alla realizzazione di un percorso professionale all'estero. Una migliore conoscenza rispetto a caratteristiche e qualità dei programmi di specializzazione è risultata per coloro che si sono informati online su siti web, forum e blog e tra coloro che hanno consultato delle associazioni dedicate.

Conclusioni. Risulta fondamentale l'attuazione di politiche che incitino le future generazioni di medici a rimanere nel proprio paese di origine, finalizzando interventi e strategie mirate ad offrire percorsi formative di alta qualità e prospettive di carriera accattivanti, insieme ad una remunerazione economica appropriata e competitiva rispetto a paesi esteri meta di giovani professionisti.

References

1. Adovor E, Czaika M, Docquier F, Moullan Y. Medical brain drain: How many, where and why? J Health Econ. 2021 Mar;**76**:102409. doi: 10.1016/j.jhealeco.2020.102409. Epub 2020 Dec 30. PMID: 33465558.
2. Bourassa Forcier M, Simoens S, Giuffrida A. Impact, regulation and health policy implications of physician migration in OECD countries. Hum Resour Health. 2004 Jul 16;**2**(1):12. doi: 10.1186/1478-4491-2-12. PMID: 15257752.
3. Dohlman L, DiMeglio M, Hajj J, Laudanski K. Global Brain Drain: How Can the Maslow Theory of Motivation Improve Our Understanding of Physician Migration? Int J Environ Res Public Health. 2019 Apr 2;**16**(7):1182. doi: 10.3390/ijerph16071182. PMID: 30986972.
4. World Health Organization (WHO). WHO health workforce support and safeguards list 2023. World Health Organization; 2023. Available from: https://www.who.int/publications-detail-redirect/9789240069787 [Last accessed: 2024 May 12].
5. World Health Organization (WHO). Decommissioning

medical devices. Geneve; 2019. Available from: https://www.who.int/publications/i/item/9789241517041 [Last accessed: 2024 May 12].
6. Kamarulzaman A, Ramnarayan K, Mocumbi AO. Plugging the medical brain drain. Lancet. 2022 Oct;**400**(10362):1492–4. doi: 10.1016/S0140-6736(22)02087-6. PMID: 36522198.
7. Socha-Dietrich K, Dumont JC. International migration and movement of doctors to and within OECD countries – 2000 to 2018: Developments in countries of destination and impact on countries of origin. OECD Health Working Papers. 2021 Feb;126. https://dx.doi.org/10.1787/7ca8643e-en. Available from: https://www.oecd.org/health/international-migration-and-movement-of-doctors-to-and-within-oecd-countries-2000-to-2018-7ca8643e-en.htm [Last accessed: 2024 May 12].
8. Frenk J, Chen LC, Chandran L, Groff EOH, King R, Meleis A, et al. Challenges and opportunities for educating health professionals after the COVID-19 pandemic. Lancet. 2022 Oct;**400**(10362):1539–56. doi: 10.1016/S0140-6736-(22)02092-X. PMID: 36522209.
9. Dussault G, Fronteira I, Cabral J. Migration of health personnel in the WHO European Region. WHO Europe. 2009;1–41. Available from: https://iris.who.int/handle/10665/349664 [Last accessed: 2024 May 12].
10. Eurostat Data Browser. 2022. 2022. Health personnel (excluding nursing and caring professionals) - historical data (1980-2021). Available from: https://ec.europa.eu/eurostat/databrowser/view/HLTH_RS_PRS1/default/table?lang=en [Last accessed: 2024 May 12].
11. Palermo C, Ragazzo F, Montemurro D, D'Arienzo M. Il fabbisogno di personale medico nel SSN dal 2016 al 2030. La relazione tra pensionamenti, accessi alle scuole di Medicina e Chirurgia e formazione post-laurea. Available from: https://www.anaao.it/public/aaa_9717107_programmazione_2016_versione_finale.pdf [Last accessed: 2024 May 12].
12. Chen L, Evans T, Anand S, Boufford JI, Brown H, Chowdhury M, et al. Human resources for health: overcoming the crisis. Lancet. 2004 Nov;**364**(9449):1984–90. doi: 10.1016/S0140-6736(04)17482-5. PMID: 15567015.
13. Bojanic A, Bojanic K, Likic R. Brain drain: final year medical students' intentions of training abroad. Postgrad Med J. 2015 Jun 1;**91**(1076):315–21. doi: 10.1136/postgradmedj-2014-132908. Epub 2015 May 20. PMID: 25995369.
14. Gouda P, Kitt K, Evans DS, Goggin D, McGrath D, Last J, et al. Ireland's medical brain drain: migration intentions of Irish medical students. Hum Resour Health. 2015 Dec 12;**13**:11. doi: 10.1186/s12960-015-0003-9. PMID: 25889783.
15. Suciu ȘM, Popescu CA, Ciumageanu MD, Buzoianu AD. Physician migration at its roots: a study on the emigration preferences and plans among medical students in Romania. Hum Resour Health. 2017 Dec 19;**15**(1):6. doi: 10.1186/s12960-017-0181-8. PMID: 28103939.
16. Santric-Milicevic MM, Terzic-Supic ZJ, Matejic BR, Vasic V, Ricketts TC. First- and fifth-year medical students' intention for emigration and practice abroad: A case study of Serbia. Health Policy. 2014 Nov;**118**(2):173–83. doi: 10.1016/j.healthpol.2014.09.018. Epub 2014 Oct 7. PMID: 25458972.
17. Sancak B, Selek SN, Sarı E. Depression, anxiety, stress levels and five-factor personality traits as predictors of clinical medical students' migration intention: A cross-sectional study of brain drain. Int J Health Plann Manage. 2023 Jul;**38**(4):1015-1031. doi: 10.1002/hpm.3646. Epub 2023 Apr 16. PMID: 37062888.
18. Krajewski-Siuda K, Szromek A, Romaniuk P, Gericke CA, Szpak A, Kaczmarek K. Emigration preferences and plans among medical students in Poland. Hum Resour Health. 2012 Apr 30;**10**(1):8. doi: 10.1186/1478-4491-10-8. PMID: 22546006.
19. Gouda P, Kitt K, Evans DS, Goggin D, McGrath D, Last J, et al. Push and stay factors affecting Irish medical student migration intentions. Irish J Med Sci (1971 -). 2017 Feb 9;**186**(1):25–31. doi: 10.1007/s11845-015-1388-0. Epub 2015 Dec 9. PMID: 26650751.Ramos P, Alves H. Migration intentions among Portuguese junior doctors: Results from a survey. Health Policy. 2017 Dec;**121**(12):1208–14. doi: 10.1016/j.healthpol.2017.09.016. Epub 2017 Sep 28. PMID: 28987457.
20. Ramos P, Alves H. Migration intentions among Portuguese junior doctors: Results from a survey. Health Policy. 2017 Dec;**121**(12):1208–14. doi: 10.1016/j.healthpol.2017.09.016. Epub 2017 Sep 28. PMID: 28987457.
21. Hosmer DW, Jr, Lemeshow S, Sturdivant RX. Applied logistic regression. 3rd ed. John Wiley & Sons, Inc; 2013 (Wiley Series in Probability and Statistics). doi: 10.1002/978111854
22. Recent Trends in International Migration of Doctors, Nurses and Medical Students. OECD; 2019. https://doi.org/10.1787/5571ef48-en.
23. World Bank Group. High-income countries [Internet]. 2024. Available from: https://data.worldbank.org/income-level/high-income [Last accessed: 2024 May 12].
24. Leombruni P, Corradi A, Lo Moro G, Acampora A, Agodi A, Celotto D, et al. Stress in Medical Students: PRIMES, an Italian, Multicenter Cross-Sectional Study. Int J Environ Res Public Health. 2022 Apr 20;**19**(9):5010. doi: 10.3390/ijerph19095010. PMID: 35564409.
25. DECRETO-LEGGE 17 marzo 2020, n. 18 Misure di potenziamento del Servizio sanitario nazionale e di sostegno economico per famiglie, lavoratori e imprese connesse all'emergenza epidemiologica da COVID-19. (20G00034) (GU Serie Generale n.70 del 17-03-2020)
26. Kim HI, Cha KA. Effects of Experience Abroad and Language Proficiency on Self-Efficacy Beliefs in Language Learning. Psychol Rep. 2017 Aug 4;**120**(4):670–94. doi: 10.1177/0033294117697088. Epub 2017 Apr 4. PMID: 28558539.
27. Istituto Nazionale di Documentazione I e RE. INDIREinforma. 2022. Erasmus+: nel 2022 cresce la partecipazione italiana al Programma. Available from: https://www.indire.it/2022/12/23/erasmus-nel-2022-cresce-la-partecipazione-italiana-al-programma/ [Last accessed: 2024 May 12].
28. Goštautaitė B, Bučiūnienė I, Milašauskienė Ž, Bareikis

K, Bertašiūtė E, Mikelionienė G. Migration intentions of Lithuanian physicians, nurses, residents and medical students. Health Policy. 2018 Oct;**122**(10):1126–31. doi: 10.1016/j.healthpol.2018.07.001. Epub 2018 Jul 6. PMID: 30006085.

29. Riccò M, Vezzosi L, Balzarini F. Challenges faced by the Italian medical workforce. Lancet. 2020 Mar 28;**395**(10229):e55–6. doi: 10.1016/S0140-6736-(19)33003-X. PMID: 32222194.

Corresponding Author: Dott.ssa Giuseppina Lo Moro, Department of Public Health Sciences and Paediatrics, University of Turin, Via Santena 5bis, 10126 Torino, Italy
e-mail: giuseppina.lomoro@unito.it

Ann Ig. 2025 Jan-Feb; 37(1): 97-127 doi: 10.7416/ai.2024.2646. Epub 2024 Jul 18.

Vaccine Literacy and Hesitancy on routine and travelers' vaccines: a preliminary online survey

Luigi Roberto Biasio[1], Chiara Lorini[2], Sergio Pecorelli[1]

Key words: Vaccine Literacy; Vaccine Hesitancy; Routine Vaccines; Travelers' Vaccines
Parole chiave: Alfabetizzazione Vaccinale; Esitazione Vaccinale; Vaccini di routine; Vaccini del viaggiatore

Abstract

Background. *The vast amount of conflicting information during the COVID-19 pandemic might have had a detrimental effect on people's opinions about vaccinations, including groups like travelers. This study aimed at assessing Vaccine Literacy in a sample of the general Italian population, together with antecedents of Vaccine Hesitancy, such as confidence, complacency, and convenience, the so-called "3Cs", and their effects on accepting routine and travelers' vaccines.*
Study Design. *A specifically designed anonymous questionnaire was created by using Google forms and validated through a face validity process. Subsequently, it was employed in an online cross-sectional survey.*
Methods. *The assessment Vaccine Literacy scale used in this survey was similar to that employed in earlier surveys. In addition to demographic data and information sources used by participants, the questionnaire was composed, in total, of nine multiple choice questions on Vaccine Literacy, and six questions on the 3Cs. Considered outcomes were self-reported participants' beliefs, attitudes, behaviors and intentions toward recommended routinary adulthoods vaccines and arboviral vaccines for travelers. A section of the questionnaire focused on chikungunya awareness, taken as an example of arboviral disease that has caused outbreaks in Italy, but not yet vaccine-preventable at the time of the investigation.*
Results. *After cleaning the database, 357 responses were suitable for analysis. Vaccine Literacy mean functional score was 2.81 ± 0.74 (lower than in an earlier survey, $p = 0.012$), while the interactive-critical (score 3.41 ± 0.50) was higher ($p<0.001$). Vaccine literacy was confirmed to be associated with attitudes and behaviors towards vaccination, with the 3Cs often acting as a mediator. However, interactive Vaccine Literacy was misaligned with respect to functional and critical ones, as if looking for information sources or discussing about vaccination was less relevant than amidst the pandemic. Also, there was an increase in Vaccine Hesitancy, particularly with regard to travel vaccinations, with 10-17% of individuals refusing to be vaccinated if travelling in areas at risk. The main limitation of the study was the unbalance in demographic variables, in particular the education level.*
Conclusions. *The study highlights the risks associated with current travel, including those related to climate change and the spread of vector-borne infections. It underscores the importance of raising awareness about arboviral diseases and the vaccines available to prevent them. As with all online surveys that employ convenience sampling, this study might not have provided a comprehensive representation of the entire population. Nevertheless, a dedicated analysis has been conducted to reduce biases and make data interpretation easier. Despite the need for further research, the findings indicate potential new approaches for assessing Vaccine Literacy and Vaccine Hesitancy, to ease the development of new communication strategies to enhance routine and travel vaccinations.*

1 Giovanni Lorenzini Foundation, Milan, Italy
2 Department of Health Sciences, University of Florence, Florence, Italy

Annali di Igiene : Medicina Preventiva e di Comunità (Ann Ig)
ISSN (print) 1120-9135 ISSN (online) 3035-5559

https://www.annali-igiene.it

Introduction

Sustaining vaccine acceptance is extremely important for public health, particularly given the impact of the COVID-19 infodemic. The abundance of contradictory information may have negatively influenced people's views on vaccinations, including specific populations such as travelers (1). The field of travel medicine is always developing, and the importance of vaccinations before traveling is becoming more significant. In fact, vaccinations are important not only for protecting travelers from specific diseases but also for preventing the spread of infections (2, 3).

Environmental factors influencing risks while traveling include the destination, the duration and purpose of travel, as well as the regional climate(4). Tropical and subtropical areas present an elevated risk of vector-borne infections, such as those caused by arboviruses. Additionally, shifts in global climate can amplify the danger. Higher temperatures and rainfall are known to boost virus replication and spread rates (4, 5), as happened for the Japanese encephalitis outbreak in Australia (6).

Traveler's health and their actions while overseas play a crucial role in the level of risk they face from diseases linked to travel. To minimize these threats, effective methods include proper self-care and vaccination. While personal safety practices like using bed nets, screens, and insect repellents do offer some protection, immunization is the most reliable form of defense against vaccine-preventable infectious diseases (2).

Despite evidence of effectiveness and safety of modern vaccines, vaccine hesitancy (VH) has increased, leading to delayed vaccination or refusal even when vaccines are readily available. The rise in skepticism and reluctance to vaccinate escalated during the COVID-19 pandemic with the spread of misinformation through different sources, mainly social media platforms (7). VH stems from a complex decision-making process influenced by various often latent factors encompassed in the "3Cs" model (8) including complacency, confidence, and convenience. The 3Cs represent the main psychological antecedents of vaccination, i.e. beliefs and attitudes people have towards vaccines.

On the other hand, Vaccine Literacy (VL) is defined as the sum of knowledge, motivation, and competencies to find, understand, and judge immunization-related information to make appropriate decisions about vaccination (9). VL is linked to Health Literacy (HL), but the two realms only partially overlap. In fact, competencies and knowledge about vaccines are unique: even individuals with higher levels of HL may lack the necessary skills about vaccination. VL is also a process of improving information about vaccination, building communication, and increasing people's engagement on vaccines (community VL). VL is also organizational, including the different degrees of complexity within a health organization focused on communication and immunization practice (9). Different tools (psychometric tests) have been developed to assess individual and population VL (10, 11) as well as VH levels (12, 13). The results of such investigations are useful to health institutions, as they serve as a basis for developing targeted communication strategies and health education campaigns.

Limited VL has been identified as a potential contributing factor to VH and low vaccine uptake in several studies, despite not all of them have confirmed this association(10). VL has received growing attention through research during the pandemic: emerging literature has proposed different online measures to explore population and individual VL skills, in addition to attitudes and behaviors about coronavirus and vaccine acceptance. Based on the existing literature showing that functional and interactive-critical VL are directly and negatively associated with VH, it has been shown that during the COVID-19 pandemic the 3Cs played a significant role in mediating VL with VH (14).

Therefore, this survey was prompted by the resurgence of international travel after the pandemic, the increased research on travelers' related diseases, as well as the development of novel vaccines against arboviruses. At the same time, climate changes make countries with an environmentally temperate climate suitable for the development of endemic outbreaks of arboviruses, as already happened in Southern Europe for dengue (15) and chikungunya (16). Understanding travelers' VL and VH and their role towards vaccination outcomes is important for a better communication, as well as development and implementation of effective strategies to prevent infectious risk.

Study objectives

This online cross-sectional survey aimed to assess the VL levels in a sample of the Italian general population, and to confirm the proportion of individuals with limited VL, in comparison with previous similar studies.

Additional objectives were to assess people's beliefs, attitudes, and behaviors related to routine

vaccines and those recommended for international travel, and to confirm the negative association between VL and VH intended as intention (willingness) to get vaccinated, and the actual receipt of vaccines (vaccine uptake).

We aimed also to confirm if the psychological antecedents of vaccination (the 3Cs), could act as a mediator between VL and VH, taking into account the influence of demographic determinants.

Methods

An anonymous online questionnaire was used, with a similar VL scale to that employed in earlier cross-sectional surveys. The questionnaire had been adapted to the scope of the study following changes proposed by an expert panel before it was finalized and distributed. The purpose of this face validation was to evaluate: a) the reliability of the questionnaire (how the questions included in the test appeared to be suitable to measure its theoretical construct, considering the Italian socio-cultural situations), b) its comprehensibility (how the questions seemed understandable to the adult population >18 years of age), c) the sensitivity (how the questions appeared to be able to identify variations in the measures under investigation), d) the efficiency (how efficient the questions appeared in detecting the aspects related to the test construct). The same validation process was performed also for items related to the psychological antecedents of VH. The VL and VH items' definitions are reported in the following sections.

After face validity, the questionnaire was distributed to a broad audience via Google Forms, a platform that specializes in creating and administering web-based surveys. A survey URL was created, to be embedded in email messages and web pages. This allowed respondents to access the survey and submit their responses. For its distribution, a convenient, non-probabilistic sampling method has been adopted, as for many similar published surveys (10). The URL – together with a QR code - was forwarded during the second week of February 2024 (a reminder was sent two weeks later) to about 50 addressees selected from the mailing list of Giovanni Lorenzini Foundation (Milan, Italy). This list included general population, in addition to representatives of citizen, scientific Societies (including the Italian Society of Travel Medicine), patient and healthcare workers associations. Recipients were free to fill in the questionnaire and were asked to forward the link to others, without communicating back their list of addresses. No incentives were offered to respondents, and no targeted replies were purchased. The survey was aimed at Italian adult individuals, aged 18 y and older, interested in looking for information about travelers' vaccines, as well as routine vaccines. No other exclusion criteria were applied. The questionnaire was composed, in total, of nine multiple choice questions on VL, and six questions on the 3Cs.

The questionnaire included main demographic data - age group (four age classes, for consistency with earlier surveys), sex, native language, educational levels (four groups), occupational status, area of residence - together with sources of information, intention / planning to travel during the current year, and possible destinations, according to different climate areas. A small amount of information was asked to respect most respondents' anonymity, focusing on the essential demographic variables relevant to the research questions. The first page of the questionnaire provided participants with information about the rationale and scope of the survey. Participants were asked to give honest answers and were informed that they were not given any incentives, that could reply only once to the survey, and that continuing to the following pages of the survey and forwarding the filled questionnaire constituted consent. Participants were free to send answers via PC, tablet, or smartphone. The study has been performed following the Declaration of Helsinki as revised in 2013, and according to the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) guidelines (17).

VL measures

The questions assessing VL levels were adapted from a self-reported questionnaire for adulthood vaccination derived from the Ishikawa test for chronic non-communicable diseases (18), which had already been validated for content and construct (19). Nine items of the questionnaire aimed at assessing functional, interactive (also said communicative) and critical VL, according to Nutbeam's definition (20). From the psychometric point of view, functional VL questions are mainly about language, involving the semantic system and referring to 'crystallized' knowledge, while the interactive and critical questions focus on 'procedural' knowledge and 'fluid' cognitive efforts, such as problem-solving and decision-making. Each response is rated with a forced four-point Likert scale (4 – never, 3 – rarely, 2 – sometimes, 1 – often, for the functional questions; 1 – never, 2 – rarely, 3 – sometimes, 4 – often, for the interactive and critical

subscale). The score is obtained from the mean value of the answers to each sub-scale (range 1 to 4), with a higher value corresponding to a higher VL level. In this survey, a composite VL score was also adopted, comprehensive of all VL subscales, as well as a mean score of interactive plus critical VL (interactive-critical VL).

Despite rated on an ordinal scale, these variables have been treated as numerical, as in previous studies where similar instruments were employed, showing a high overlap of results both when tested using parametric and non-parametric tests (10). A nominal metric has also been used in this study, dividing the scores in tertiles, and considering as limited VL the scores in the bottom tertile.

3Cs measures

Determinants of VH were elicited using participants' level of agreement to six "negative" statements based on the "the 3Cs" psychological antecedents of vaccination. Specifically, the statements refer to the three dimensions of the 3C model, namely "confidence" (two items), "complacency" (two items) and "convenience" (two items). Answers to each question were evaluated using a four-point Likert scale, for consistency with the VL scale. Higher scores indicate higher levels of confidence, complacency, and convenience toward vaccination (scores: 1= completely agree with the negative statements; 2=partially agree; 3=partially disagree; 4=completely disagree) and evaluated as continuous variable. Each of the 3Cs was evaluated separately, but an average score was also adopted to summarize all the 3Cs subscales. "Vaccine acceptance" was intended as a positive attitude towards vaccination (i.e. the opposite of VH).

Outcomes

Considered outcomes were the self-reported participants' behaviors and intentions (intended as precursor of behaviors) toward recommended routinary adulthoods vaccines and arboviral vaccines for travelers. Vaccine uptake reported by participants was calculated by considering the total number of vaccinations received from that listed in the questionnaire, ("routine vaccine uptake", or "vaccines received"), corresponding to those recommended for adults in the Italian National Vaccination Plan (21): influenza, COVID-19, Herpes Zoster, Pneumo, dTaP (diphteria-tetanus-pertussis) booster.

Additionally, we determined the number of people who reported receiving each specific vaccine through a nominal yes/no scale. Last seasonal flu Vaccine uptake was taken as a main outcome regarding single vaccine immunization status, considering it as a reference for adults' vaccination, while willingness to receive next seasonal flu vaccine was taken to evaluate the intention to be vaccinated. For the travelers' vaccines, the most administered one in the Italian practice (i.e. yellow fever) was used as the reference for the outcome "travelers' vaccine uptake".

Awareness about chikungunya

In line with recent definitions (9), knowledge about vaccines and related diseases has been considered as part of VL, which also includes motivation and skills. Thus, a specific section of the survey was focused on chikungunya to evaluate the respondents' awareness of a travelers' preventable communicable disease, also causing local outbreaks Italy (22).

The reason for this choice was that, unlike other arboviral infections (dengue, yellow fever, tick-borne, and Japanese encephalitis), chikungunya was not vaccine-preventable at the time of the survey, likely making participants less familiar and find it more challenging to respond. Knowledge about chikungunya was assessed through a summative score, namely the sum of correct responses (true/false) to seven questions (score between 0 and 7).

Control questions

Control questions were included to identify inconsistent or unreliable responses, such as being vaccinated with non-existent vaccines at the time of the survey. Also, we examined how information sources used by the participants correlated with responses to the VL questions and 3Cs statements, and how the number of received travelers' vaccines against arboviruses were associated with planning travels to tropical and subtropical areas.

Statistical analysis

Data from a study conducted in 2020 was considered as reference for power calculation (23). Taking as criterion for defining the sample size an expected prevalence of 37% of individuals with limited VL levels (score in the lower tertile of the study population), 359 subjects were to be enrolled, at 95% confidence, and 5% margin of error.

Analysis was carried out using SPSS v27 (24), and NCSS (25) v23.0.2 software, along with the open source software Jamovi v2.4.11 to complement analyses with additional tests like the mediation model using the jAMM module (26). This package

allows estimation of the direct and indirect effects of independent variables on the dependent variables, by also examining all paths of the mediation model components, including moderating effects. Mediation and moderation were also explored through the Hayes' process module v4.2 included in SPSS. The use of more software also allowed us to verify the consistency between findings.

Descriptive analysis showed percentages, means, standard deviations, confidence intervals, medians, percentiles. The internal consistency of the psychometric questions (VL and VH scales) was assessed through Cronbach's alpha and MacDonald's omega coefficients. Non-parametric tests were mainly used for describing comparisons, due to the non-normal distribution of data. Kruskal-Wallis, Wilcoxon, Mann–Whitney, ROC curves, and χ^2 tests were employed.

Simple and multiple logistic and linear regression analyses were performed to determine demographic and psychological factors associated with outcomes. The variables significantly associated with the outcomes (i.e., with p-values < 0.05) at the simple regression were identified as candidates for multiple logistic regression models. Mediation analysis was performed to understand the pathway through which VL affected outcomes via the 3Cs (taken as mediators), also considering a possible moderating role of different levels of education, classes of age, gender, and healthcare worker status. Spearman's rho correlation coefficient was calculated to determine the relationships between the VL, the VH scales, and outcomes. Principal Component Analysis (PCA) was conducted to investigate latent factors and how the questions of the VL subscales, and those of the 3Cs scale, were related to one another, as well as the loading of each item on the different components of the model.

Results

Data was gathered beginning in the second week of February through to the first week of April 2024. A total of 367 responses were obtained. However, seven participants were excluded from analysis because of inconsistent responses (claiming to be vaccinated with non-existing vaccines), and the first three, because sent by the investigators for testing the questionnaire. As a result, 357 responses were suitable for analysis.

Demographics

As for gender, 62% of participants were female (Table 1). The most represented age group was between 31 and 50 years of age (41%), while the least represented was between 18 and 30 years (8%). Almost all participants were Italian-speaking, 54% lived in central Italy, 30% in northern Italy, the remaining in the south and islands. Regarding occupation, about 30% of participants were healthcare workers. Most participants (64%) planned to travel during the year in temperate climate areas, while 18% intended to travel in subtropical and tropical zones, and 15% had no travel plans.

Education and age were the main causes of unbalance of the sample, with 71% of participants holding a master's degree, while only 8% were in the younger age class. However, excluding from the analysis healthcare workers, the difference in education level was not significant across age classes ($\chi 2$, p=0.183).

Data reliability

Reliability of the items related to VL together with the psychological antecedents of VH revealed an acceptable internal consistency, as Cronbach's α and McDonald's ω values were 0.720 and 0.768, respectively. In addition, other checks have been

Table 1 – Demographics

Age class (years)	**18 - 30**	**31 - 50**	**50 - 65**	**>65**
	8.2%	41.1%	32.4%	18.3%
Sex	F 62%		M 38%	
Education level	**Primary, other**	**High, vocational school**	**Bachelor's degree**	**Master's degree**
	4.3%	15,3%	9%	71.4%
Area of residence	**Northern Italy**	**Central Italy**	**Southern Italy & Larger Islands**	
	28,6%	53.5%	17,9%	
Occupation (most represented)	**HCW**	**Employee, Officer**	**Self-employed**	**Retired**
	29.7%	33%	13.9%	12.8%

performed to control the consistency of the study sample, such as the correlation of participants declaring to be vaccinated against yellow fever and those planning trips to tropical and subtropical areas (Spearman r= 0.411, P< 0.001), as well as between respondents stating to use more than one information sources and responses to question #3 ("…have consulted more than one source of information...") (r=0.251, P< 0.001), and between those who declared to get information from the doctors and the responses to question #4 ("...you discussed with the doctor or others what you understood about vaccinations...") (r=0.278, P< 0.001).

Six outliers (lowest values) have been identified in the critical VL subscale (Rosner test P<0.05). However, they have been maintained in the analysis, as, considering the limited variability of the dataset (range used: 1 to 4), the exclusion of lower values could have had an impact on the assessment of participants with limited VL. At the end, excluding the outliers didn't change significantly in terms of means and correlation between VL variables.

VL and 3Cs scores

The functional VL score was 2.81 ± 0.74 (median= 3), the interactive score was 3.22 ± 0.71 (median= 3.50), while the critical one was 3.59 ± 0.60 (median= 4) (Table 2). The overall VL score was 3.21 ± 0.42 (Median 3.33), while a mixed interactive-critical one was 3.41 ± 0.50 (median= 3.50). Higher VL subscales were associated with healthcare worker status, except interactive (Kruskal-Wallis P=0.436) and interactive-critical VL (P=0.073) (Table 3). Higher interactive and interactive-critical VL were observed for females (P= 0.007, and P= 0.020, respectively). VL scores in Northern Italy were generally higher compared to other regions.

VL scores have been compared with those reported in an earlier survey, conducted using similar methods and measures during the COVID-19 pandemic (23). In mid-2020 functional VL score was higher with respect to this study (2.92 ± 0.70, p = 0.012, Mann-Whitney test independent samples, two-tailed probability), while an interactive-critical score was lower (3.27 ± 0.54, p<0.001).

We also calculated the proportion of participants with "limited" VL, identified as those in the lower tertile of the study population score. They were 42% for functional VL, 43% for interactive-critical VL, while for total VL was 36.2% (N=357), very similar to the limited total VL proportion observed in 2020 (36.6%, N=885) (23) (Mann-Whitney P= 0.948) which was used for power calculation of this study. Post-hoc margin of error was = 4.99.

Table 4 displays the 3Cs' scores related to people's psychological attitudes towards vaccination. These scores are based on how much participants agreed with statements about vaccines reported in the table. Higher scores indicate more confidence, complacency, and convenience related to vaccination, suggesting less consequent VH. Yet, these values are not as high as those seen in an earlier study (23). For example, when measuring "confidence" with a nearly identical question, in 2020, the score was 3.77 ± 0.55, whereas in current survey it was 3.51 ± 0.75, showing a significant difference (Mann-Whitney P<0.001).

However, positive correlations were observed between outcomes and each of the 3Cs, all of them being significant predictors of seasonal flu vaccination status and intention to receive the forthcoming flu vaccine.

Values of all psychological antecedents observed in HCWs were significantly higher respect to the rest of participants (Kruskal-Wallis P= between < 0.001 and 0.013), except for the convenience statement: 'I do not get vaccinated because going to the vaccination clinic is complicated' (P= 0.692).

Correlation between psychological variables and outcomes

A significant positive correlation between each of the 3Cs and the different VL subscales emerged, except for interactive VL. Routine vaccines uptake and knowledge about chikungunya were always positively correlated with the 3Cs, while having received travel vaccines was correlated only with complacency and convenience (Table 5).

Notably, interactive VL was negatively correlated with functional VL and positively with critical VL (gray boxes in Table 5). On the contrary, analysis of the same items from the 2020 survey showed that interactive VL was always positively correlated with the other VL subscales and the 3Cs.

In addition, applying Kruskal-Wallis test on variables assessed through nominal scales (factor codes: yes/no), a significant association was shown between seasonal flu vaccine uptake and both functional and critical VL (P< 0.001), while the association was not significant for interactive VL (P= 0.564). Also, the association was significant between intention to be vaccinated against next seasonal influenza for functional (P< 0.001) and critical VL (P= 0.002), while it was not for interactive VL (P=0.228).

Table 2 - Descriptive analysis of VL score (mean scores of functional, interactive, critical, interactive-critical subscales, and overall)

	Functional VL	Interactive VL	Critical VL	Interactive-critical VL	Overall VL
Mean	2.81	3.22	3.59	3.41	3.21
SD	0.74	0.71	0.60	0.50	0.42
Median	3.00	3.50	4.00	3.50	3.33
25 - 75 Percentile	2.00 to 3.00	2.88 to 4.00	3.00 to 4.00	3.00 to 3.75	3.00 to 3.50

Table 3 - Descriptive analysis of VL score by job (healthcare workers -HCW- vs. others – non-HCW): mean scores of functional, interactive, critical, interactive critical, and overall VL. Associations tested by Kruskal-Wallis test (K-W)

		Functional VL	K-W P	Interactive VL	K-W P	Critical VL	K-W P	Interactive-critical VL	K-W P	Overall	K-W P
Mean	Non-HCW	2.69	<0.001	3.20	0.436	3.56	0.057	3.38	0.073	3.15	<0.001
	HCW	3.10		3.26		3.67		3.47		3.35	
SD	Non-HCW	0.70		0.71		0.61		0.49		0.41	
	HCW	0.73		0.70		0.57		0.51		0.41	

Table 4 - Descriptives of psychological antecedents of VH (the 3Cs), assessed through agreement to negative statements on vaccines through a four-point scale: 1=completely agree; 2=partially agree; 3=partially disagree; 4=completely disagree). The higher the score, more positive beliefs and attitudes towards vaccination are, and less VH exists

3Cs⇒	Confidence		Complacency		Convenience	
Statements⇒	'I do not trust the quality of vaccines'	'I do not trust doctors'	'I'm fine, so I don't have to get vaccinated'	'Climate change will not increase the risk of infection'	'I do not get vaccinated as going to the vaccination clinic is complicated'	'I won't pay out of my own pocket to be vaccinated'
Mean	3.51	3.52	3.65	3.50	3.62	3.12
SD	0.75	0.70	0.67	0.77	0.69	1.00
Median	4.00	4.00	4.00	4.00	4.00	3.00
25 - 75 Percentile	3.00 to 4.00	3.00 to 4.00	3.00 to 4.00	3.00 to 4.00	3.00 to 4.00	2.00 to 4.00

Table 5 - Correlation table between VL, 3Cs and outcome variables (Spearman's rho = * p < 0.05, ** p < 0.01, *** p < 0.001, °p>=0.05)

Variables		VL			3Cs			Outcomes	
		Functional VL	Interactive VL	Critical VL	Confidence	Complacency	Convenience	Routine vaccines uptake	Travel vaccines uptake
VL	Functional VL	—							
	Interactive VL	-0.187***	—						
	Critical VL	0.331***	0.133**	—					
3Cs	Confidence	0.399***	0.024°	0.384***	—				
	Complacency	0.293***	0.048°	0.259***	0.533***	—			
	Convenience	0.270***	0.028°	0.376***	0.482***	0.466***	—		
Outcomes	Routine vaccines uptake	0.148**	-0.054°	0.149**	0.285***	0.239***	0.279***	—	
	Travel vaccines uptake	0.082°	0.054°	0.049°	0.090°	0.144**	0.124*	0.129*	—
	Knowledge on chikungunya	0.384***	0.000°	0.167**	0.254***	0.236***	0.162**	0.232***	0.060°

Table 6 - Principal Component Analysis: VL and 3Cs items' loading on four components, after Varimax rotation. Values for each variable correspond to the factor for which the squared cosine is the largest. Lower uniqueness values indicate higher correlation with other variables included in the PCA

VL	Items	Components (factors)				
Functional VL	***When you listen, or read about vaccines...***	1	2	3	4	Uniqueness
	1...find words or expressions you don't know...			0.863		0.195
	2...you find what you hear or read hard to understand...			0.814		0.227
Interactive VL	***When you looked for information about vaccines...***					
	3...you have consulted more than one source of information...				0.802	0.333
	4...you discussed with the doctor or others what you understood about vaccinations...				0.736	0.432
Critical VL	5...you found the information you were looking for…		0.886			0.151
	6...you have found useful information to decide whether to vaccinate you and/or your children...		0.880			0.150
3Cs	***Describe agreement with each of the statements below***					
Confidence	'I do not trust the quality of vaccines'	0.785				0.289
	'I don't trust doctors'	0.774				0.362
Complacency	I'm healthy, so I don't have to vaccinate'	0.772				0.349
	'Climate change will not increase the risk of infection'	0.664				0.420
Convenience	'I do not get vaccinated because going to the vaccination clinic is complicated'	0.630				0.455
	'I won't pay out of my own pocket to be vaccinated'	0.619				0.542

Principal Component Analysis on VL and 3Cs items

PCA was applied on the psychological variables, namely VL questions and 3Cs statements. Based on four components, analysis showed that VL and 3Cs items loaded on separate factors, similarly to what had been observed in the 2020 (23), with 48% of the total variance explained by the first two components (Bartlett's Test of Sphericity P<0.001, KMO = 0.783) (Table 6). After Varimax rotation, visualizing three components, the 2020 survey had shown interactive items - round dots in Figure 1 - situated between the functional and critical items. This implied a consistent

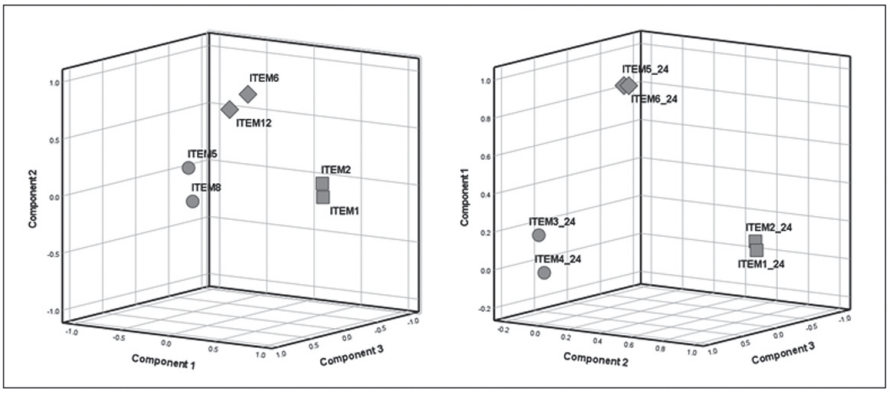


Figure 1 - PCA plots: VL items' loading on three components after Varimax rotation in 2020 (left graph) and current (2024) survey (right graph). Square= functional items – Round= interactive items – Diamond= critical items. Differently than in 2020, In the 2024 survey interactive items appeared misaligned with respect to functional and critical items.

relationship among all the elements of VL, which appeared to move conjointly, a trend not seen in the present study where interactive items were not aligned, particularly with the other VL subscales (ref. to supplementary Material S1 and S2 for more detail).

Regression and mediation analyses

Relationships between demographic predictors, intermediate variables (VL and the 3Cs), and outcomes were assessed using simple and multiple logistic and linear regression, as well as through a multi-mediation model (26). The latter was performed to evaluate the mediating effect of the 3Cs in the relationship between VL and outcomes and determine whether demographic factors like education and age - which appeared unbalanced - might have affected the results, when entered in the model as moderators.

When examining the factors influencing the uptake of routine vaccines, taking the seasonal flu vaccine as reference, simple logistic regression was shown to be significant (z-test, $p<0.05$) for all variables, except gender ($p=0.636$) which was therefore not included in the multiple regression model. This last indicated that age and healthcare worker status ($p<0.001$), along with the 3Cs ($p=0.010$), were still important factors in predicting flu vaccine uptake. However, education level ($p=0.704$) and VL score ($p=0.503$) did not maintain significance after adjusting for the other variables in the model (overall model test χ^2, $p< 0.001$). Predictive values of these variables are shown in Figure 2).

These patterns held true for overall routine vaccine uptake and intention to receive the next seasonal flu vaccine, with age and healthcare worker status being significant factors in both models ($p< 0.001$). On the other hand, the decision to get travel vaccines appeared to be independent of the factors examined. However, it's important to consider that this finding is based on a small number of participants who actually received vaccinations for their travels. Additionally, it should be noted that the most commonly administered vaccine (yellow fever) is mandatory for travelers entering and/or leaving certain countries. This requirement could potentially influence any correlation between variables.

We applied the same demographic variables to the multiple mediation model to examine their moderating effect on the relationship between VL (taken as a predictor) and the 3Cs (acting as mediator), in relation to the outcomes. Without introducing any moderator into the model, the 3Cs' mediating effect between VL and flu vaccination status explained 42% of the total effect ($p= 0.003$), while VL confirmed a non-significant direct effect ($p=0.056$) (Supplementary Material S4).

Including "education" in the model, it appeared to have no significant direct (Education → flu vaccine uptake, $p= 0.180$) or mediated effect (Education → 3CS → flu vaccine uptake, $p= 0.085$). However, during conditional mediation, taking "education"

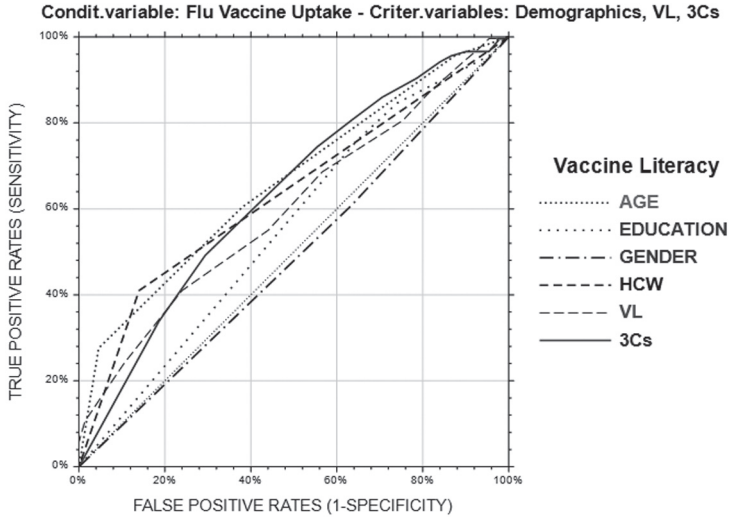


Figure 2 – Receiver Operating Characteristic (ROC) analysis of the demographic variables (predictive value, Area Under the Curve - AUC) of conditioned variable "flu vaccine received". AUC Age= 0.662 (p=0.000), Education=0.558 (p=0.010), Female Gender=0.488 (p=0.682), Healthcare Workers=0.636 (p=0.000), VL=0.602 (p=0.000), 3Cs=0.635 (p=0.000) (Supplementary Material S3)

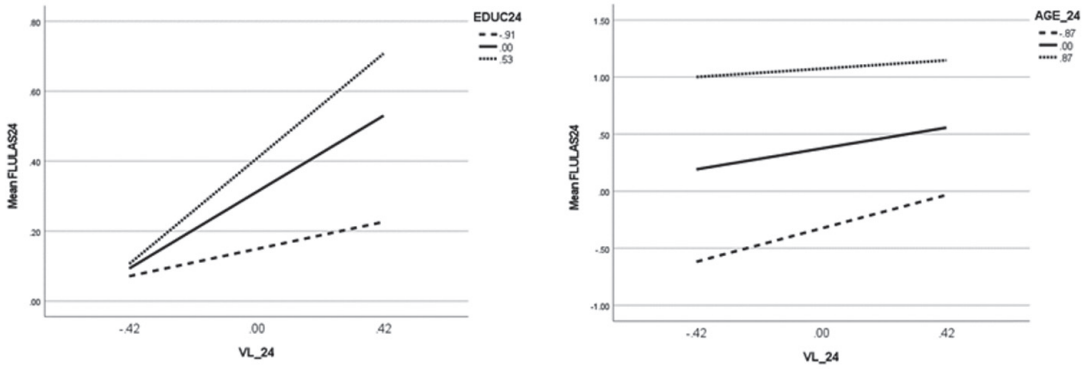


Figure 3 - Moderating effect of education (left) and age (right) on the relationship between VL and last flu vaccine received

as moderator at its low level (-1 SD) the effect on flu vaccine uptake was 56%, while it was 43% at the average level, and 33% at its high level (+1 SD). It implies that the impact of education acting as moderator on flu vaccination was partial, and more influential for individuals with lower education, although values observed at its various levels were quite close each other and all significant ($p< 0.05$) (Figure 3).

When "age" was included in the mediation model, it showed a significant direct effect on flu vaccine received ($p< 0.001$), whereas the indirect effect was not. In the conditional mediation analysis with "age" acting as the moderator, the effect on flu vaccine uptake was 47% at the low level (-1 SD), 51% at the average level, and 48% at the high level (+1 SD) of age. These percentages are close to each other, indicating that the variable "age" played a partial and similar moderating role on flu vaccine uptake at all age classes (Figure 3). As a moderator, healthcare worker status had a significant effect on flu vaccine uptake (93% at -1 SD). This effect lessened to 31% at the average level and further dropped to 9% at +1 SD, proving the direct influence that healthcare worker status has on vaccine acceptance. Similar results to those seen with the outcome "flu vaccine received" were seen when the outcomes "routine vaccines uptake", or "intention to receive the next seasonal flu vaccine", were included in the model.

Routine vaccines intention and behaviors

Correlation of routine vaccine uptake – i.e. the total number (sum) of routine vaccines received with VL - and psychological antecedents of vaccination are reported in Table 5. Fifty-eight percent of people reported they had received flu vaccine, 98% COVID-19 vaccine,15% shingles, 37% pneumococcal vaccine, and 80% dTaP booster. This latter percentage appears to be excessively high in comparison to the actual number of booster vaccinations in the adult Italian population. It is possible that some respondents misunderstood the question and thought it referred to the dose administered during adolescence, not to the 10-year dTaP booster. In support, the coverage for this vaccine to Italian adolescents in 2022 was 71% (27). Due to this inconsistency, dTaP was not included in the outcome "routine vaccines uptake".

Travelers' vaccines intention and behaviors

As mentioned, the questionnaire was intended for the general population but was also distributed to travelers. Of all participants, 15% did not plan to travel during the year, while 18% planned to visit tropical or subtropical areas.

Regarding arboviral vaccines, coverage rate was 3% for dengue and tick-borne disease, 1% for Japanese encephalitis, and 18% for yellow fever. The correlation between planning trips to endemic areas and vaccines received was significant only for yellow fever (χ^2 Tests 57.3, $p <0.001$). Intention to be vaccinated was similar for all arboviral diseases, with about 50% of responses, while willing to be vaccinated against dengue was higher (66%) (Friedman test, $p< 0.001$). Refusal to be vaccinated accounted between 11% and 17% for the different diseases. As expected, sum of refused vaccinations were negatively correlated with each of the 3Cs (Spearman's rho between 0.192 and 0.224, $p< 0.001$).

Awareness about chikungunya

Participants' average knowledge score about chikungunya was 5.4 on a scale of 1 to 7. Healthcare

workers scored higher with an average of 6 compared to 5.1. The knowledge score had a positive correlation with functional and critical VL skills, as well as with the 3Cs, as shown in Table 5. However, these relatively high scores were mainly linked to the knowledge of disease's characteristics (causes, symptoms), while only 66% of participants correctly identified that there are no effective treatments for chikungunya, and only 60% knew that there wasn't a preventive vaccine available in Italy at the time of the survey.

As expected, healthcare workers had a significantly higher percentage of correct responses for both knowledge of treatments against chikungunya (Kruskal-Wallis: p= 0.035) and about vaccine's availability (p= 0.003). Also, there were significant correlations with higher vaccine literacy (p= 0.027 and p= 0.026, respectively), education level (p= 0.005 and p= 0.030, respectively), and having experience of vaccinations against arboviral diseases (yellow fever) (p= 0.009).

Discussion

VL is defined as the sum of knowledge, motivation and competencies to find, understand and judge immunization-related information to make appropriate decisions about vaccination. It is also a process of improving vaccine communication and increasing people's engagement about vaccines (9). VL assessment is critical to public health strategies aimed at increasing vaccine coverage, countering VH, and ensuring that communities are informed, prepared, and protected against vaccine-preventable illnesses. Assessing VL helps public health and healthcare providers identify gaps in public knowledge and misunderstandings about vaccines, also revealing disparities across different groups of the population. All this is crucial for developing communication strategies that address specific concerns and provide clear and accessible information.

Different tools (psychometric tests) have been developed to assess individual and population VL skills (10), in addition to VH levels (12, 13). To the best of our knowledge, this survey is the first to focus on travelers' VL using a dedicated assessment tool. We think this study is important because it evaluates the VL levels in a sample of the Italian general population shortly after the pandemic. It also examines psychological factors linked to VH, like beliefs and attitudes regarding confidence, complacency, and convenience about vaccinations, known as the 3Cs. We also studied how the 3Cs relate to VL, and their impact on the uptake of routine and travel vaccines, along with the intent to get vaccinated, giving a detailed evaluation of all the factors affecting outcomes.

Study population

The survey was conducted among the general population in Italy to gather – among others - initial insights about travelers' vaccination. This was done before conducting more extensive surveys focusing on selected groups of travelers. Therefore, we consider this survey representing a first step toward the evaluation of VL in specific areas of medicine. Unlike HL – for which there is a huge proliferation of measures (28) - the number of tools to assess VL is relatively limited. Therefore, as for HL tools developed for several specific contexts and populations outside of pandemic emergencies, we started adopting a similar approach for VL in the specific area of travel and migration medicine.

The number of participants in our sample was lower than initially expected, although we do not consider it a limitation as the intended target sample size was achieved. Still, it is important to highlight the reasons behind this lower number, as they may provide insights into people's attitudes and behaviors toward vaccinations in the post-pandemic period. During the early stage of the COVID-19 outbreak, we carried out a similar online survey, using similar tools, methods, and distribution channels. That survey had a significantly higher level of participation, with 885 people enrolled within a shorter timeframe (23).

We think this happened because more people became interested in vaccines during that period. There was also a feeling of hope and confidence that a SARS-CoV-2 vaccine would be available soon since many were still being developed in the middle of 2020. Additionally, during that survey, there were isolation measures in place, making people more available for web consultations, also taking part in the many online surveys performed amidst the pandemic (29). Interest in vaccines seems now to have decreased (30), probably due to a decline in confidence, and an increase in complacency, as also shown in this study. We think these are the reasons why fewer people have participated in this survey. Additionally, the topic of travel vaccines may not be as attractive as the COVID-19 vaccine, unless respondents had plans for international travel, which represents a limitation (self-selection bias) as it will be detailed later.

VL framework and assessment tool used

To accomplish the objectives of the study, we made

reference to the Health Literacy Skills Framework by Squiers et al(31), which we adapted to VL (10) (Figure 4).

Looking at this framework, we used an assessment VL scale which was similar to the one used in previous surveys, although with a reduced number of items. For the mediators, we utilized a scale assessing the 3Cs derived from that used by Lu et al (14). We found it interesting to combine these two assessment tools since their construct follows a similar and complementary conceptual approach. Consequently, the methods employed in this study represent an effort to advance in the development of tools for assessing VL and its associated variables.

Using the above tool, we evaluated how the factors mentioned influence the outcomes of two categories of vaccines: routine adult vaccines and those specifically recommended for travelers visiting high-risk areas where vector-borne diseases are present. This is relevant, as today it also entails the additional challenge of a local risk associated with climate change, which could pose a significant threat to public health.

VL and 3Cs roles

Findings from this survey align with results of previous studies and reviews, which mostly indicate that VL skills can predict health outcomes, like intention to be vaccinated, or vaccines received(10, 11, 36). However, not all studies have confirmed these findings, A recent meta-analysis regarding the association between VL and vaccine intention and uptake (37), has indicated that VL significantly influenced vaccination intentions, although its correlation with vaccination status was weaker in comparison.

However, most studies have overlooked the indirect role that VL may play, as well as the mediating impact of beliefs and attitudes towards behaviors. Some researchers have examined the mediating role of VL and of the psychological factors influencing VH (14, 38, 39), although these aspects remain largely unexplored. We have tried to reduce this gap, by performing mediation and moderation analyses, which confirmed that VL can have direct effects on outcomes, but its effects can be also mediated by the psychological antecedents of vaccination. The mediated effects we have observed were partial, similar to Shon's et al (38) who, using a VL single-item nominal tool demonstrated the mediating effects of health beliefs between flu VL and flu vaccine acceptance in students, although the literacy of influenza vaccines improved the vaccination behavior also directly. Conversely, Lu et al showed a completely mediated effect by the 3Cs, between VL and outcomes (14). Also Collini et al (39) found that vaccine confidence completely mediated the relationship between interactive-critical VL (assessed through the HLVa tool)l (19) and the intention of nursing home personnel to get vaccinated

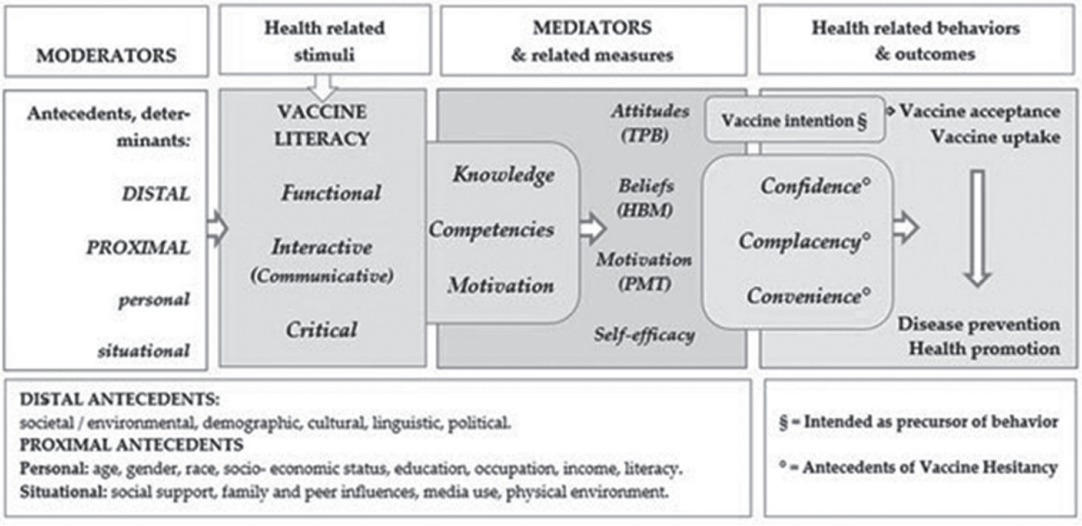


Figure 4 - VL theoretical framework(10): VL is placed between background (moderators) and mediators and partially overlaps these last, explaining its mediating and mediated role toward attitudes, behaviors and health outcomes. Adapted from Squiers' Health Literacy Skills Framework) (31) and Paasche-Orlow (32). HBM = Health Belief Model (33), TPB = Theory of Planned Behavior (34), PMT = Protection Motivation Theory (35).

against influenza. These differences may be linked to methods and tools used, cultural differences between populations, and in mediation tests employed. In fact, mediation models vary significantly from one another, making it challenging to interpret the results. Nevertheless, current literature – despite limited so far – shows that the 3Cs play a mediating role, either partially or fully, between VL and outcomes. Our findings confirm that VL showed a non-significant direct effect on flu vaccination status and intention to be vaccinated on regression and multi mediation models, while the effect mediated by the 3Cs was significant, this confirming the validity of the framework.

Interactive vs functional and critical VL

COVID-related infodemic had a negative impact on individuals because of the abundance of contradictory information (7). However, it also provided opportunities to improve people's discernment of vaccine information. Research has shown that higher VL was associated with higher COVID-19 vaccine acceptance (40). The VL levels were similar in most of the populations studied, with the VL functional score often lower than the interactive-critical one, as if the latter was stimulated by the infodemic to search and try to understand more information, while the functional VL was challenged by the technicality of the information(40). This has been confirmed in the current survey, where functional VL was even lower than in an earlier survey conducted on the same population (23), while interactive and critical VL were higher, as reported in Results.

Despite the high interactive score value, at the PCA, the interactive items were placed in a misaligned position with respect to the other VL items, as if finding information (interactive), understanding (functional), interpreting and using it (critical VL), were no longer actions integrated in a continuous process, but disconnected from each other. Furthermore, while functional and critical VL showed a significant predictive role toward seasonal flu vaccine uptake, interactive VL was not predictive. These findings were also supported by the mediation analysis. This showed that the interactive VL had no significant direct effect on receiving the flu vaccine, nor indirect effects through the 3Cs. Similar findings have been seen for the other outcomes, namely intention to receive the forthcoming flu vaccine, and sum of routine vaccines received. Notably, these observations apply to the entire study population, as well as to selected groups, such as healthcare workers, female and male genders. Moreover, as mentioned, we assessed the impact of consulting multiple information sources by comparing this approach with interactive VL and finding a significant positive correlation. However, this correlation did not extend to the other VL subscales. This finding points again to the limited role of communicative VL. Consulting more information sources seemed to have little influence on the decision on vaccination, as evidenced by the non-significant correlation with critical VL.

The findings support the idea of persisting effects of the pandemic on people's attitudes and behaviors. It seems that searching for information about vaccines and discussing it doesn't catch people's interest as much as it did before, causing their acquired opinions and attitudes to solidify further, leading to decisions being made based on set beliefs and crystallized knowledge. Ongoing discourse about COVID-19 informed, but also induced fatigue (41), causing individuals to avoid new information and further entrench their existing opinions (42). This risk to lead away people from empowerment rather than bringing them closer. Therefore, understanding these dynamics is crucial for crafting strategies that effectively engage individuals in consulting more information sources and having meaningful conversations about vaccination.

As for the VL scores, the analysis showed that they were quite similar to those of previous datasets (40), and the proportion of participants with limited VL was very similar (about 37%). Findings about VL skills were also consistent with factors analyses performed earlier (40). Although a reduced number of items was included, the scale we used can be considered a composite tool, as it contains elements related to the psychological factors influencing VL, as well as knowledge questions about mosquito borne disease (chikungunya being taken as an example). At the same time, the instrument encompasses questions about the psychological antecedents of vaccination, also exploring the behavior of individuals on routine and travelers' vaccines.

Using such tools in the future will help in the standardization of results and enable easier comparison across settings. If composite instruments become widely used, it would likely be feasible to calculate a "composite score". In our context, this could consist of an average of scores for VL, education, and knowledge, according to most recent definition of VL (9). It is important to point out that in this survey knowledge about chikungunya was significantly correlated with education (Spearman's

rho P<0.01). This also supports the inclusion of education as part of the composite score as an indicator of competencies(10).

Outcomes: intention to be vaccinated and vaccine uptake

Some Authors reported that acceptance of routine vaccines like flu seems to be higher after the pandemic (43). However, this is not in agreement with other studies. For example, in a survey conducted in Poland more than half of moderate vaccine supporters declared that their vaccine confidence was weakened during the COVID-19 pandemic (44). Notably, in our study the intention to be vaccinated against flu was similar (68%) to that reported in the 2020 survey (66%) (23). In fact, although we found an increase in negative beliefs and attitudes towards vaccination for all the 3Cs, these variables remained correlated with routine vaccine uptake.

In the 2020 survey only 41% of respondents reported receiving the previous seasonal flu shot (23), whereas this was 58% in the current survey. The lower vaccination rate in that period might be attributed to the younger proportion of survey participants, also considering that flu vaccination rates in the general adult population in Italy were notably low just before the Covid-19 outbreak (45). As reported by some Authors, one potentially positive effect during the pandemic was the increase in flu vaccine uptake (46).

Regarding travelers' vaccinations, these can be categorized as routinary, recommended, and required, according to the destination region. Vaccine acceptance and uptake by travelers is influenced by a variety of factors, such as the accessibility to vaccination clinics, individuals' information sources and knowledge about the risks related to the trip, as well as their antecedents, knowledge, attitudes and behaviors toward vaccination in general. Travelers', and also healthcare professionals' knowledge and perception of trips' infectious risk are important factors, as some diseases may be considered irrelevant due to the low incidence reported, but may be important to be prevented due to their potential severity (47).

The number of respondents declaring to be vaccinated against arboviral diseases was limited: as this survey was dedicated to the general population, only few planning to travel to at risk areas. In addition, not all arboviral infections are preventable by immunization. Also, travelers' vaccines are not reimbursed in Italy, which may contribute to a scarce behavior. In addition, a low perception of the risk among travelers may exists due to VH and other reasons (48). Three percent of the participants declared to be vaccinated against dengue and tick-borne disease, and < 1% against Japanese encephalitis. The seven participants who declared to be vaccinated against Zika and chikungunya were excluded from the analysis, as vaccines were not available (chikungunya vaccine was only licensed in the USA for a few months, at the time of this survey). In fact, these questions were included to check data quality.

As mentioned, the relative high percentage of participants vaccinated against yellow fever (18.5%) may be explained by the fact that vaccination against this disease is mandatory when traveling to several countries, together with the fact that the survey questionnaire was also disseminated through newsletters of public health and travel medicine scientific societies. The low percentage of participants vaccinated against dengue can be explained by the fact that approval and availability of the vaccine was very recent at the time of this survey. Many participants intended to get vaccinated against arboviruses before traveling to tropical and subtropical regions. However, a percentage up to 17%, expressed refusal to get vaccinated. As predicted, the rate of vaccination refusal was inversely related to VL and the 3Cs (Spearman's p<0.05 and p< 0.001, respectively). This aligns with other findings, highlighting VH's considerable influence in the field of travel medicine (48).

Awareness about travelers' infectious risk: the example of chikungunya

Among Italian travelers a low attitude to get vaccinated before a trip seems to exist whether for business or pleasure, unlike other European populations, despite the similar proportion of journeys each year (49). Limited medical communication, challenging access to travel clinics, and vaccine costs may also contribute to this issue, aligning with the convenience aspect of the 3Cs model. Unlike most routine vaccinations in Italy, travelers' vaccines are not reimbursed, even though the spread of infections by travelers has the potential to cause serious problems among residents and significantly affect public health.

Chikungunya virus, spread by vectors such as mosquitoes, poses a threat to travelers and carries the potential for wider spread due to climate change, similar to other arboviruses. Participants' knowledge on it was chosen to be assessed in this study because, unlike other tropical diseases preventable by vaccines and used in Italy, no vaccine for chikungunya existed

at the time of the survey. Thus, it was hypothesized that the general public might be less familiar with chikungunya than with other vaccine-preventable diseases, making it a more discriminating measure of their knowledge on traveler's vaccination.

An average knowledge score about chikungunya of 5.4 was obtained from the participants, from a range between 1 and 7. The score was higher in healthcare workers and was positively correlated with VL skills and with the 3Cs antecedents of vaccination. However, despite a quite high average score, only 66% of participants responded correctly to the question related to the availability of effective treatments against chikungunya, and 60% responded correctly regarding that of the existence of a preventive vaccine in Italy. Here also, the percentage of participants who responded correctly was higher among healthcare workers.

We think the high rate of mistakes concerning the availability of effective treatments and vaccines for chikungunya stems from the public's limited awareness of arboviral infections. This is especially true for non-traveling people who may mix up the "exotic" names of different diseases. This is confirmed by the significant correlation of correct responses with yellow fever vaccine received ($p<0.01$), and the non-significant correlation with routine vaccine uptake. This remains a hypothesis, though, that suggests a potential reason for the mistakes. Regardless of the cause, this unawareness must be considered in communication to the public about chikungunya, and in continuing medical education. These factors are important given the growing risk of arboviral diseases, which regards not only travelers but local populations in Italy as well, as evidenced by the recent chikungunya (22) and dengue outbreaks (50).

Study limitations

We addressed the known restraints of cross-sectional studies, such as limitation in demonstrating causality, using statistical techniques like regression and mediation models to mitigate this problem to some extent. However, while these statistical measures can help strengthen the evidence for causal relationships, they cannot completely overcome the limitations of cross-sectional design.

In particular, a specific limitation was the unbalance in demographic variables, which was more pronounced compared to a similar earlier survey (23), despite the same methods were followed, including sampling. Convenience sampling can offer benefits. It is a quick and cost-effective method. Additionally, it can sometimes provide insights into specific population segments - like international travelers - that may be harder to reach through probabilistic sampling methods. However, convenience sampling has several limitations. Since participation is based on accessibility, the resulting sample may not accurately represent the broader population, allowing individuals with strong opinions on the topic to be more likely to take part (self-selection bias). Furthermore, despite participants are invited to provide honest answers, the risk of a social desirability bias exists.

Despite the unbalanced educational backgrounds, with most respondents holding higher education degrees, excluding healthcare workers dropped the average education level significantly (Mann-Whitney $p=0.003$). In online surveys education unbalance is a common limitation. Indeed, individuals with low level of education are less likely to participate than individuals with high level (51). For example, while only 21% of respondents by mail to a survey completed college, 57% of the web respondents were graduated (52). In our study, statistical analysis has shown that education did not have a significant effect at the multiple regression model, and it only showed a limited moderating effect between VL and outcomes at its lower level. Regarding unbalance in age, regression analysis showed a significant effect on outcomes, but the moderation model demonstrated the effect was equally balanced between the different age classes. Regarding gender unbalance, females tended to respond more than males like in other online surveys (53, 54), and the higher interactive-critical VL skills we observed in female population was similar to what was already observed for HL (55, 56).

Notably, in addition to the reliability tests and controls executed on collected data, VL skills were consistent with earlier datasets (40) although there were expectable score variations due to differences in demographic variables and historic periods. However, the proportion of participants with limited VL skills was very similar, around 37%, which we believe confirm the validity of the assessment tool used and reliability of results.

Conclusions

The ongoing presence of VH after the pandemic, combined with the resumption of international travel and climate changes, raises concerns on the potential for spreading vector-borne diseases. This aroused our interest in conducting this preliminary research which aimed to assess VL by using a composite scale

for both routine and travel vaccinations. The results revealed VL levels among the Italian population that partially varied from previous findings, with lower functional, and higher interactive-critical skills, while positive beliefs toward vaccination were reduced, despite the association between higher VL and vaccine acceptance was maintained, as well as the proportion of individuals with limited VL. The study also found a mismatch in the relationship between interactive (communicative) VL and other VL subscales, which should be further investigated. It has been confirmed that psychological factors—known as the 3Cs—affect vaccination decisions, frequently acting as mediators between VL and outcomes, influencing both the intention to get vaccinated and the actual uptake of vaccines, whether for routine or travel purposes. Public health efforts need to continuously find effective ways to combat VH and promote vaccine acceptance within communities and in the context of international travel. Despite its limitations, this survey provides a basis for further research aimed at better understanding the interaction between VL and VH among travelers. A deeper insight into this complex relationship can lead to improved communication and innovative strategies for prevention of community and travelers' infectious diseases.

Author Contributions: Conceptualization, Methodology, Data extraction, Analysis, Writing L.R.B.; Review and Editing C.L. and S.P..; Validation, L.R.B., C.L. and S.P. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Conflicts of Interest: Authors declare no conflicts of interests related to the subject of the research; L.R.B. provides scientific advice to companies in the field of routine and travelers' vaccination.

Riassunto

Alfabetizzazione ed esitazione vaccinale riguardo i vaccini di routine e dei viaggiatori: indagine online preliminare

Background. L'enorme quantità di informazioni contrastanti circolate durante la pandemia COVID-19 potrebbe aver avuto un effetto negativo sulle opinioni della popolazione riguardo le vaccinazioni, comprese categorie come quella dei viaggiatori. Questa indagine aveva l'obiettivo di valutare i livelli di alfabetizzazione vaccinale nella popolazione italiana, e degli antecedenti dell'esitazione vaccinale, quali fiducia (confidenza), compiacimento e convenienza (le cosiddette "3C"), e i loro effetti sull'accettazione dei vaccini di routine e dei viaggiatori.

Disegno dello Studio. Uno specifico questionario anonimo è stato sviluppato su Google forms, validato attraverso un processo di "face validity" ed impiegato in uno studio cross-sectional online.

Metodi. La scala di valutazione dell'alfabetizzazione vaccinale utilizzata in questa indagine era simile a quella usata in precedenti indagini. Oltre ai dati demografici ed alle fonti di informazione utilizzate dai partecipanti, il questionario era composto, in totale, da nove domande a risposta multipla sull'alfabetizzazione vaccinale e da sei domande sulle 3C. I risultati (outcomes) considerati erano le convinzioni, i comportamenti e le intenzioni dichiarate dai partecipanti nei confronti delle vaccinazioni di routine raccomandate per gli adulti e quelle contro gli arbovirus per i viaggiatori. Una parte del questionario era dedicata al livello di conoscenza della chikungunya, presa quale esempio di malattia da arbovirus che ha già causato focolai autoctoni in Italia, ma non ancora vaccino-prevenibile al momento dell'indagine.

Risultati. Dopo aver ripulito il database, 357 risposte sono risultate utili per l'analisi statistica. Il punteggio medio dell'alfabetizzazione vaccinale funzionale era 2.81 ± 0.74, inferiore rispetto a studi precedenti, mentre quello dell'interattivo-critica (punteggio 3.41 ± 0.50) era più elevato ($p<0.001$). È stata confermata l'associazione dell'alfabetizzazione vaccinale con gli atteggiamenti e comportamenti vaccinali, e con le 3Cs che spesso agivano quali mediatori tra l'alfabetizzazione vaccinale e gli outcomes. L'alfabetizzazione vaccinale interattiva appariva disallineata rispetto a quella funzionale e critica, come se la ricerca di più fonti di informazione o le continue discussioni sulle vaccinazioni fossero meno rilevanti rispetto al periodo pandemico. Inoltre, è stato riscontrato un aumento dell'esitazione vaccinale, in particolare per quanto riguarda le vaccinazioni dei viaggiatori, con il 10-17% di individui che rifiutavano di essere vaccinati prima di viaggi verso aree a rischio. Il principale limite dello studio era lo squilibrio nelle variabili demografiche, in particolare l'istruzione.

Conclusioni. Lo studio evidenzia il rischio di viaggiare verso aree a rischio, anche con riferimento ai cambiamenti climatici e alla diffusione di infezioni trasmesse da vettori. Indica altresì la necessità di aumentare la consapevolezza sulle malattie da arbovirus ed i relativi vaccini. Come per tutti i sondaggi condotti con campionamento di convenienza, questo studio potrebbe non rappresentare completamente la popolazione. L'analisi statistica ha però permesso di minimizzare questi limiti, facilitando l'interpretazione dei dati. Nonostante la necessità di ulteriori ricerche, i risultati dell'indagine suggeriscono nuovi approcci per la valutazione dell'alfabetizzazione ed esitazione vaccinale per facilitare lo sviluppo di nuove strategie si comunicazione per sostenere le vaccinazioni di routine e per i viaggiatori.

References

1. Leong WY. COVID-19's impact on travel medicine surpasses that of all other emerging viral diseases. J Travel Med. 2020;**27**(8). doi: 10.1093/jtm/taaa221. PubMed PMID: 33247591; PubMed Central PMCID: PMC7798941.
2. Rogers B, Bunn WB, Connor BA. An Update on Travel Vaccines and Issues in Travel and International Medicine. Workplace Health Saf. 2016;**64**(10):462-8. Epub 20160928. doi: 10.1177/2165079916633478. PubMed PMID: 27555602.
3. Steffen R. Travel vaccine preventable diseases-updated logarithmic scale with monthly incidence rates. J Travel Med. 2018;**25**(1). doi: 10.1093/jtm/tay046. PubMed PMID: 30016468.
4. Tian HY, Bi P, Cazelles B, Zhou S, Huang SQ, Yang J, et

al. How environmental conditions impact mosquito ecology and Japanese encephalitis: an eco-epidemiological approach. Environ Int. 2015;**79**:17-24. Epub 20150311. doi: 10.1016/j.envint.2015.03.002. PubMed PMID: 25771078.
5. Kilpatrick AM, Meola MA, Moudy RM, Kramer LD. Temperature, viral genetics, and the transmission of West Nile virus by Culex pipiens mosquitoes. PLoS Pathog. 2008;**4**(6):e1000092. Epub 20080627. doi: 10.1371/journal.ppat.1000092. PubMed PMID: 18584026; PubMed Central PMCID: PMC2430533.
6. Wadman M. Rude awakening. Science. 2023 Nov 24;**382**(6673):872-877. doi: 10.1126/science.adn0008. Epub 2023 Nov 23. PMID: 37995232.
7. Larson HJ, Gakidou E, Murray CJL. The Vaccine-Hesitant Moment. N Engl J Med. 2022;**387**(1):58-65. Epub 20220629. doi: 10.1056/NEJMra2106441. PubMed PMID: 35767527; PubMed Central PMCID: PMC9258752.
8. MacDonald NE, Hesitancy SWGoV. Vaccine hesitancy: Definition, scope and determinants. Vaccine. 2015;**33**(34):4161-4. Epub 20150417. doi: 10.1016/j.vaccine.2015.04.036. PubMed PMID: 25896383.
9. Lorini C, Del Riccio M, Zanobini P, Biasio RL, Bonanni P, Giorgetti D, et al. Vaccination as a social practice: towards a definition of personal, community, population, and organizational vaccine literacy. BMC Public Health. 2023;**23**(1):1501. Epub 20230808. doi: 10.1186/s12889-023-16437-6. PubMed PMID: 37553624; PubMed Central PMCID: PMC10408168.
10. Biasio LR, Zanobini P, Lorini C, Bonaccorsi G. Perspectives in the Development of Tools to Assess Vaccine Literacy. Vaccines. 2024;**12**(4). doi: 10.3390/vaccines12040422.
11. Zhang E, Dai Z, Wang S, Wang X, Zhang X, Fang Q. Vaccine Literacy and Vaccination: A Systematic Review. Int J Public Health. 2023;**68**:1605606. Epub 20230214. doi: 10.3389/ijph.2023.1605606. PubMed PMID: 36866001; PubMed Central PMCID: PMC9970990.
12. Larson HJ, Jarrett C, Schulz WS, Chaudhuri M, Zhou Y, Dube E, et al. Measuring vaccine hesitancy: The development of a survey tool. Vaccine. 2015;**33**(34):4165-75. Epub 20150418. doi: 10.1016/j.vaccine.2015.04.037. PubMed PMID: 25896384.
13. Betsch C, Schmid P, Heinemeier D, Korn L, Holtmann C, Bohm R. Beyond confidence: Development of a measure assessing the 5C psychological antecedents of vaccination. PLoS One. 2018;**13**(12):e0208601. Epub 20181207. doi: 10.1371/journal.pone.0208601. PubMed PMID: 30532274; PubMed Central PMCID: PMC6285469.
14. Lu Y, Wang Q, Zhu S, Xu S, Kadirhaz M, Zhang Y, et al. Lessons learned from COVID-19 vaccination implementation: How psychological antecedents of vaccinations mediate the relationship between vaccine literacy and vaccine hesitancy. Soc Sci Med. 2023;**336**:116270. Epub 20230926. doi: 10.1016/j.socscimed.2023.116270. PubMed PMID: 37778145.
15. European Centre for Disease Prevention and Control (ECDC). Autochthonous vectorial transmission of dengue virus in mainland EU/EEA, 2010-present. Available from: https://www.ecdc.europa.eu/en/all-topics-z/dengue/surveillance-and-disease-data/autochthonous-transmission-dengue-virus-eueea [Last accessed: 2024 Jun 16].
16. European Centre for Disease Prevention and Control (ECDC). Autochthonous transmission of chikungunya virus in mainland EU/EEA, 2007–present. Available from: https://www.ecdc.europa.eu/en/infectious-disease-topics/z-disease-list/chikungunya-virus-disease/surveillance-threats-and [Last accessed: 2024 Jun 16].
17. Eysenbach G. Improving the quality of Web surveys: the Checklist for Reporting Results of Internet E-Surveys (CHERRIES). J Med Internet Res. 2004;**6**(3):e34. Epub 20040929. doi: 10.2196/jmir.6.3.e34. PubMed PMID: 15471760; PubMed Central PMCID: PMC1550605.
18. Ishikawa H, Takeuchi T, Yano E. Measuring functional, communicative, and critical health literacy among diabetic patients. Diabetes Care. 2008;**31**(5):874-9. Epub 20080225. doi: 10.2337/dc07-1932. PubMed PMID: 18299446.
19. Health Literacy Tools Shed. Health Literacy about Vaccination of adults in ITalian - HLVa-IT. 2023. Available from: https://healthliteracy.bu.edu/hlva-it. [Last accessed: 2024 Jun 16].
20. Nutbeam D. Health literacy as a public health goal: a challenge for contemporary health education and communication strategies into the 21st century. Health Promotion International. 2000 Sep;**15**(3):259-67. https://doi.org/10.1093/heapro/15.3.259.
21. Ministry of Health, Italy. Piano nazionale di prevenzione vaccinale (PNPV) 2023-2025 2023. Available from: https://www.trovanorme.salute.gov.it/norme/dettaglioAtto?id=95963&completo=true [Last accessed: 2024 Jun 16].
22. Rezza G. chikungunya is back in Italy: 2007-2017. J Travel Med. 2018;**25**(1). doi: 10.1093/jtm/tay004. PubMed PMID: 29669058.
23. Biasio LR, Bonaccorsi G, Lorini C, Pecorelli S. Assessing COVID-19 vaccine literacy: a preliminary online survey. Hum Vaccin Immunother. 2021;**17**(5):1304-12. Epub 20201029. doi: 10.1080/21645515.2020.1829315. PubMed PMID: 33118868; PubMed Central PMCID: PMC8078752.
24. IBM. Software IBM SPSS 2024. Available from: https://www.ibm.com/it-it/spss. [Last accessed: 2024 Jun 16].
25. NCSS. Statistical, Graphics, and Sample Size Software 2024. Available from: https://www.ncss.com/ [Last accessed: 2024 Jun 16].
26. Gallucci M. jAMM: jamovi Advanced Mediation Models. [jamovi module] 2020. Available from: https://jamovi-amm.github.io/ [Last accessed: 2024 Jun 16].
27. Ministry of Health, Italy. Vaccinazioni dell'età pediatrica e dell'adolescenza - Coperture vaccinali 2024. Available from: https://www.salute.gov.it/portale/documentazione/p6_2_8_3_1.jsp?lingua=italiano&id=20 [Last accesse: 2024 Jun 16].
28. Nguyen TH, Paasche-Orlow MK, McCormack LA. The state of the science of health literacy measurement. Information Services & Use. 2017;**37**(2):189-203. doi: 10.3233/isu-170827.

29. De Man J, Campbell L, Tabana H, Wouters E. The pandemic of online research in times of COVID-19. BMJ Open. 2021;**11**(2):e043866. Epub 20210223. doi: 10.1136/bmjopen-2020-043866. PubMed PMID: 33622948; PubMed Central PMCID: PMC7907624.
30. Altman JD, Miner DS, Lee AA, Asay AE, Nielson BU, Rose AM, et al. Factors Affecting Vaccine Attitudes Influenced by the COVID-19 Pandemic. Vaccines (Basel). 2023;**11**(3). Epub 20230223. doi: 10.3390/vaccines11030516. PubMed PMID: 36992100; PubMed Central PMCID: PMC10057947.
31. Squiers L, Peinado S, Berkman N, Boudewyns V, McCormack L. The health literacy skills framework. J Health Commun. 2012;**17** Suppl 3:30-54. doi: 10.1080/10810730.2012.713442. PubMed PMID: 23030560.
32. Paasche-Orlow MK, Wolf MS. The Causal Pathways Linking Health Literacy to Health Outcomes. Am J Health Behav. 2007 Sep-Oct;**31** Suppl 1:S19-26. doi: 10.5555/ajhb.2007.31.supp.S19. PMID: 17931132.
33. Carpenter CJ. A meta-analysis of the effectiveness of health belief model variables in predicting behavior. Health Commun. 2010;**25**(8):661-9. doi: 10.1080/10410236.2010.521906. PubMed PMID: 21153982.
34. Ajzen I. The Theory of Planned Behavior. In: Lange PAM, Kruglanski W, Higgins ET, eds. Handbook of Theories of Social Psychology: Vol. 1. London: Sage; 2012: 438-59. doi: 10.4135/9781446249215.n22.
35. Kowalski RM, Deas N, Britt N, Richardson E, Finnell S, Evans K, et al. Protection Motivation Theory and Intentions to Receive the COVID-19 Vaccine. Health Promot Pract. 2023;**24**(3):465-70. Epub 20220208. doi: 10.1177/15248399211070807. PubMed PMID: 35130748; PubMed Central PMCID: PMC10159786.
36. Fenta ET, Tiruneh MG, Delie AM, Kidie AA, Ayal BG, Limenh LW, et al. Health literacy and COVID-19 vaccine acceptance worldwide: A systematic review. SAGE Open Med. 2023;11:20503121231197869. Epub 20231009. doi: 10.1177/20503121231197869. PubMed PMID: 37823070; PubMed Central PMCID: PMC10563502.
37. Isonne C, Iera J, Sciurti A, Renzi E, De Blasiis MR, Marzuillo C, et al. How well does vaccine literacy predict intention to vaccinate and vaccination status? A systematic review and meta-analysis. Hum Vaccin Immunother. 2024;**20**(1):2300848. Epub 20240104. doi: 10.1080/21645515.2023.2300848. PubMed PMID: 38174706; PubMed Central PMCID: PMC10773666.
38. Shon EJ, Lee L. Effects of Vaccine Literacy, Health Beliefs, and Flu Vaccination on Perceived Physical Health Status among Under/Graduate Students. Vaccines (Basel). 2023;**11**(4). Epub 20230330. doi: 10.3390/vaccines11040765. PubMed PMID: 37112677; PubMed Central PMCID: PMC10141033.
39. Collini F, Bonaccorsi G, Del Riccio M, Bruschi M, Forni S, Galletti G, et al. Does Vaccine Confidence Mediate the Relationship between Vaccine Literacy and Influenza Vaccination? Exploring Determinants of Vaccination among Staff Members of Nursing Homes in Tuscany, Italy, during the COVID-19 Pandemic. Vaccines (Basel). 2023;**11**(8). Epub 20230817. doi: 10.3390/vaccines11081375. PubMed PMID: 37631943; PubMed Central PMCID: PMC10458978.
40. Biasio LR, Zanobini P, Lorini C, Monaci P, Fanfani A, Gallinoro V, et al. COVID-19 vaccine literacy: A scoping review. Hum Vaccin Immunother. 2023;**19**(1):2176083. Epub 20230215. doi: 10.1080/21645515.2023.2176083. PubMed PMID: 36794338; PubMed Central PMCID: PMC10026896.
41. Qin C, Deng J, Du M, Liu Q, Wang Y, Yan W, et al. Pandemic Fatigue and Vaccine Hesitancy among People Who Have Recovered from COVID-19 Infection in the Post-Pandemic Era: Cross-Sectional Study in China. Vaccines (Basel). 2023;**11**(10). Epub 20231005. doi: 10.3390/vaccines11101570. PubMed PMID: 37896973; PubMed Central PMCID: PMC10610579.
42. Lewandowsky S, Ecker UK, Seifert CM, Schwarz N, Cook J. Misinformation and Its Correction: Continued Influence and Successful Debiasing. Psychol Sci Public Interest. 2012;**13**(3):106-31. doi: 10.1177/1529100612451018. PubMed PMID: 26173286.
43. Caserotti M, Girardi P, Rubaltelli E, Tasso A, Lotto L, Gavaruzzi T. Associations of COVID-19 risk perception with vaccine hesitancy over time for Italian residents. Soc Sci Med. 2021;**272**:113688. Epub 20210107. doi: 10.1016/j.socscimed.2021.113688. PubMed PMID: 33485215; PubMed Central PMCID: PMC7788320.
44. Sobierajski T, Rzymski P, Wanke-Rytt M. Impact of the COVID-19 Pandemic on Attitudes toward Vaccination: Representative Study of Polish Society. Vaccines (Basel). 2023;**11**(6). Epub 20230606. doi: 10.3390/vaccines11061069. PubMed PMID: 37376458; PubMed Central PMCID: PMC10303243.
45. Ministry of Health, Italy. Dati coperture vaccinali Influenza 2024. Available from: https://www.salute.gov.it/portale/influenza/dettaglioContenutiInfluenza.jsp?lingua=italiano&id=679&area=influenza&menu=vuoto [Last accessed: 2024 Jun 16].
46. Kong G, Lim NA, Chin YH, Ng YPM, Amin Z. Effect of COVID-19 Pandemic on Influenza Vaccination Intention: A Meta-Analysis and Systematic Review. Vaccines (Basel). 2022;**10**(4). Epub 20220413. doi: 10.3390/vaccines10040606. PubMed PMID: 35455354; PubMed Central PMCID: PMC9026798.
47. Steffen R, Chen LH, Leggat PA. Travel vaccines-priorities determined by incidence and impact. J Travel Med. 2023;**30**(7). doi: 10.1093/jtm/taad085. PubMed PMID: 37341307.
48. Milionis C, Ilias I, Tselebis A, Pachi A. Psychological and Social Aspects of Vaccination Hesitancy-Implications for Travel Medicine in the Aftermath of the COVID-19 Crisis: A Narrative Review. Medicina (Kaunas). 2023;**59**(10). Epub 20230928. doi: 10.3390/medicina59101744. PubMed PMID: 37893462; PubMed Central PMCID: PMC10608755.
49. Banca d'Italia. Indagine sul turismo internazionale 2016. Available from: www.bancaditalia.it/statistiche [Last accessed: 2024 Jun 16].

50. Barzon L, Gobbi F, Capelli G, Montarsi F, Martini S, Riccetti S, et al. Autochthonous dengue outbreak in Italy 2020: clinical, virological and entomological findings. J Travel Med. 2021;**28**(8). doi: 10.1093/jtm/taab130. PubMed PMID: 34409443; PubMed Central PMCID: PMC8499737.
51. Reinikainen J, Tolonen H, Borodulin K, Harkanen T, Jousilahti P, Karvanen J, et al. Participation rates by educational levels have diverged during 25 years in Finnish health examination surveys. Eur J Public Health. 2018;**28**(2):237-43. doi: 10.1093/eurpub/ckx151. PubMed PMID: 29036286.
52. Keeter S. Coverage Error in Internet Surveys: Pew_Research_Center; 2015. Available from: https://www.pewresearch.org/methods/2015/09/22/coverage-error-in-internet-surveys/ [Last accessed: 2024 Jun 16].
53. Royall K. A woman's perspective – a look at gender and survey participation 2020. Available from: https://culturecounts.cc/blog/a-womans-perspective-a-look-at-gender-and-survey-participation [Last accessed: 2024 Jun 16].
54. Wu M-J, Zhao K, Fils-Aime F. Response rates of online surveys in published research: A meta-analysis. Computers in Human Behavior Reports. 2022;7. doi: 10.1016/j.chbr.2022.100206.
55. Lee HY, Lee J, Kim NK. Gender Differences in Health Literacy Among Korean Adults: Do Women Have a Higher Level of Health Literacy Than Men? Am J Mens Health. 2015;**9**(5):370-9. Epub 20140813. doi: 10.1177/1557988314545485. PubMed PMID: 25122719.
56. Bonaccorsi G, Gallinoro V, Guida A, Morittu C, Ferro Allodola V, Lastrucci V, et al. Digital Health Literacy and Information-Seeking in the Era of COVID-19: Gender Differences Emerged from a Florentine University Experience. Int J Environ Res Public Health. 2023 Jan 21;**20**(3):2611. Epub 20230131. doi: 10.3390/ijerph20032611. PubMed PMID: 36767976; PubMed Central PMCID: PMC9915269.

SUPPLEMENTARY MATERIAL

SUPPLEMENTARY MATERIAL S1 - SPSS Principal Component Analysis

Variables Created	FAC1_1	Component score 1
	FAC2_1	Component score 2
	FAC3_1	Component score 3

[DataSet1]

Descriptive Statistics

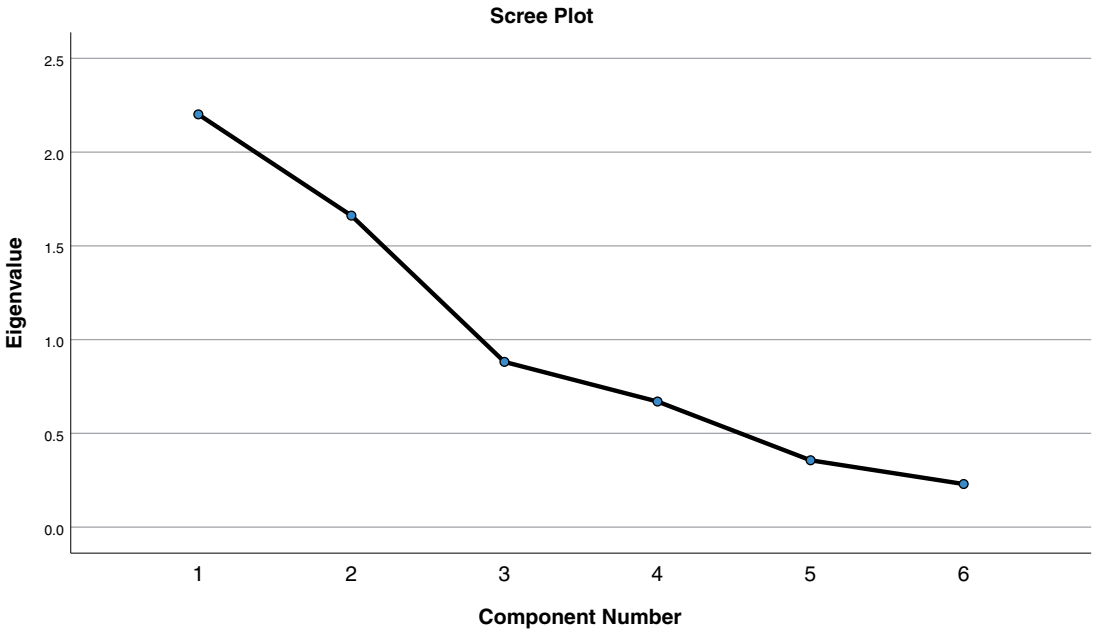
	Mean	Std. Deviation[a]	Analysis N[a]	
ITEM1_24	2.74	.833	357	0
ITEM2_24	2.88	.786	357	0
ITEM3_24	3.47	.744	357	0
ITEM4_24	2.97	.991	357	0
ITEM5_24	3.59	.620	357	0
ITEM6_24	3.60	.661	357	0

a. For each variable, missing values are replaced with the variable mean.

Correlation Matrix[a]

		ITEM1_24	ITEM2_24	ITEM3_24	ITEM4_24	ITEM5_24	ITEM6_24
Correlation	ITEM1_24	1.000	.646	-.153	-.155	.229	.231
	ITEM2_24	.646	1.000	-.143	-.170	.278	.237
	ITEM3_24	-.153	-.143	1.000	.323	.150	.162
	ITEM4_24	-.155	-.170	.323	1.000	.068	.090
	ITEM5_24	.229	.278	.150	.068	1.000	.766
	ITEM6_24	.231	.237	.162	.090	.766	1.000
Sig. (1-tailed)	ITEM1_24		.000	.002	.002	.000	.000
	ITEM2_24	.000		.003	.001	.000	.000
	ITEM3_24	.002	.003		.000	.002	.001
	ITEM4_24	.002	.001	.000		.100	.045
	ITEM5_24	.000	.000	.002	.100		.000
	ITEM6_24	.000	.000	.001	.045	.000	

a. Determinant = .177



Component Matrix[a]

	Component		
	1	2	3
ITEM1_24	.693	-.433	.400
ITEM2_24	.717	-.418	.358
ITEM3_24	.004	.712	.341
ITEM4_24	-.088	.658	.527
ITEM5_24	.782	.410	-.317
ITEM6_24	.767	.437	-.314

Extraction Method: Principal Component Analysis.

a. 3 components extracted.

Rotated Component Matrix[a]

	Component		
	1	2	3
ITEM1_24	.116	.897	-.096
ITEM2_24	.161	.882	-.113
ITEM3_24	.166	-.129	.761
ITEM4_24	-.017	-.059	.846
ITEM5_24	.923	.153	.069
ITEM6_24	.923	.132	.092

Extraction Method: Principal Component Analysis.
Rotation Method: Varimax with Kaiser Normalization.[a]

a. Rotation converged in 5 iterations.

Component Transformation Matrix

Component	1	2	3
1	.739	.672	-.043
2	.464	-.462	.756
3	-.488	.578	.654

Extraction Method: Principal Component Analysis.
Rotation Method: Varimax with Kaiser Normalization.

Notes

Variables Created	FAC1_2	Component score 1
	FAC2_2	Component score 2
	FAC3_2	Component score 3

Descriptive Statistics

	Mean	Std. Deviation[a]	Analysis N[a]	Missing N
ITEM1	2.75	.829	885	0
ITEM2	2.92	.787	885	0
ITEM5	3.38	.855	885	0
ITEM12	3.27	.954	885	0
ITEM6	3.22	.750	885	0
ITEM8	2.87	1.064	885	0

a. For each variable, missing values are replaced with the variable mean.

Correlation Matrix[a]

		ITEM1	ITEM2	ITEM5	ITEM12	ITEM6	ITEM8
Correlation	ITEM1	1.000	.591	.025	.124	.136	.065
	ITEM2	.591	1.000	.030	.175	.212	.090
	ITEM5	.025	.030	1.000	.310	.243	.303
	ITEM12	.124	.175	.310	1.000	.429	.276
	ITEM6	.136	.212	.243	.429	1.000	.195
	ITEM8	.065	.090	.303	.276	.195	1.000
Sig. (1-tailed)	ITEM1		.000	.233	.000	.000	.026
	ITEM2	.000		.184	.000	.000	.004
	ITEM5	.233	.184		.000	.000	.000
	ITEM12	.000	.000	.000		.000	.000
	ITEM6	.000	.000	.000	.000		.000
	ITEM8	.026	.004	.000	.000	.000	

a. Determinant = .386

KMO and Bartlett's Test

Kaiser-Meyer-Olkin Measure of Sampling Adequacy.		.626
Bartlett's Test of Sphericity	Approx. Chi-Square	838.047
	df	15
	Sig.	.000

Communalities

	Initial	Extraction
ITEM1	1.000	.799
ITEM2	1.000	.791
ITEM5	1.000	.579
ITEM12	1.000	.667
ITEM6	1.000	.763
ITEM8	1.000	.755

Extraction Method: Principal Component Analysis.

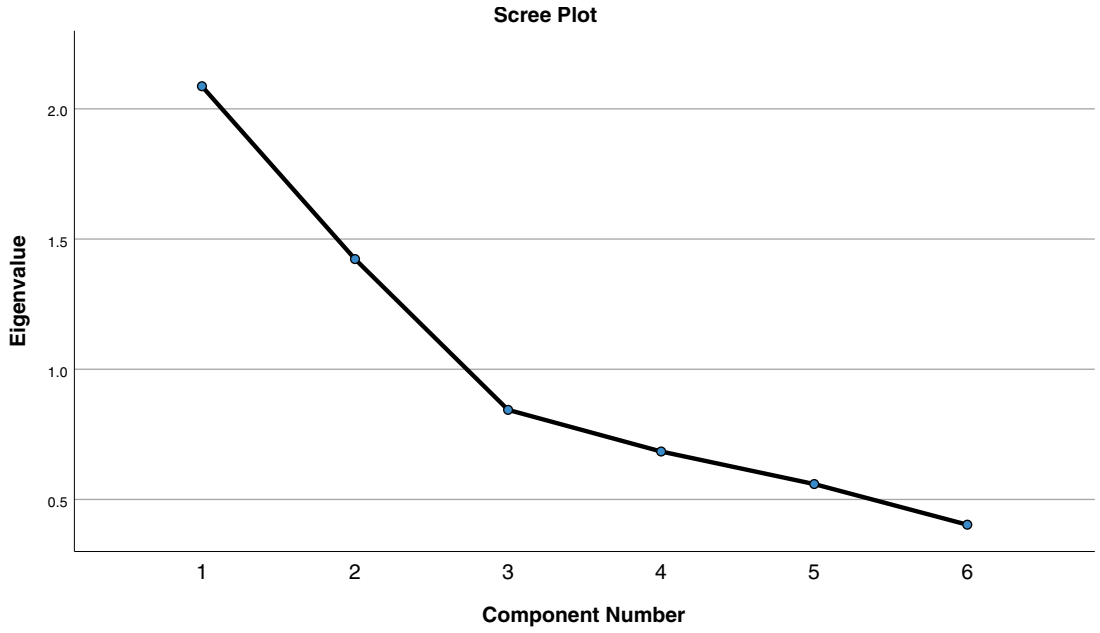
Total Variance Explained

	Initial Eigenvalues			Extraction Sums of Squared Loadings		
Component	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	2.087	34.780	34.780	2.087	34.780	34.780
2	1.423	23.717	58.497	1.423	23.717	58.497
3	.844	14.066	72.563	.844	14.066	72.563
4	.684	11.401	83.964			
5	.559	9.319	93.283			
6	.403	6.717	100.000			

Total Variance Explained

	Rotation Sums of Squared Loadings		
Component	Total	% of Variance	Cumulative %
1	1.597	26.621	26.621
2	1.439	23.988	50.610
3	1.317	21.954	72.563
4			
5			
6			

Extraction Method: Principal Component Analysis.



Component Matrix[a]

	Component		
	1	2	3
ITEM1	.524	.706	.164
ITEM2	.585	.666	.070
ITEM5	.521	-.484	.271
ITEM12	.697	-.288	-.313
ITEM6	.665	-.175	-.540
ITEM8	.522	-.365	.591

Extraction Method: Principal Component Analysis.

a. 3 components extracted.

Rotated Component Matrix[a]

	Component		
	1	2	3
ITEM1	.893	.037	.029
ITEM2	.876	.154	.015
ITEM5	-.062	.294	.699
ITEM12	.083	.761	.284
ITEM6	.115	.864	.053
ITEM8	.096	.040	.863

Extraction Method: Principal Component Analysis.
Rotation Method: Varimax with Kaiser Normalization.[a]

a. Rotation converged in 5 iterations.

Component Transformation Matrix

Component	1	2	3
1	.542	.665	.514
2	.819	-.280	-.501
3	.190	-.692	.696

Extraction Method: Principal Component Analysis.
Rotation Method: Varimax with Kaiser Normalization.

SUPPLEMENTARY MATERIAL S2 - jamovi Principal Component Analysis

	Component Loadings				
	1	2	3	4	Uniqueness
ITEM1_24			0.863		0.195
ITEM2_24			0.814		0.227
ITEM3_24				0.802	0.333
ITEM4_24				0.736	0.432
ITEM5_24		0.886			0.151
ITEM6_24		0.880			0.150
CONF1_24	0.785				0.289
CONF2_24	0.774				0.362
COMPL1_24	0.772				0.349
COMPL2_24	0.664				0.420
CONV1_24	0.630				0.455
CONV2_24	0.619				0.542

Note. 'varimax' rotation was used

Component Statistics

Summary

Component	SS Loadings	% of Variance	Cumulative %
1	3.19	26.6	26.6
2	1.84	15.4	42.0
3	1.68	14.0	56.0
4	1.38	11.5	67.5

Bartlett's Test of Sphericity

χ^2	df	p
1511	66	< .001

KMO Measure of Sampling Adequacy

	MSA
Overall	0.786
ITEM1_24	0.726
ITEM2_24	0.747
ITEM3_24	0.601
ITEM4_24	0.606
ITEM5_24	0.675
ITEM6_24	0.685
CONF1_24	0.809
CONF2_24	0.807
COMPL1_24	0.884
COMPL2_24	0.882
CONV1_24	0.880
CONV2_24	0.920

Eigenvalues

Initial Eigenvalues

Component	Eigenvalue	% of Variance	Cumulative %
1	4.099	34.16	34.2
2	1.670	13.92	48.1
3	1.386	11.55	59.6
4	0.940	7.84	67.5
5	0.757	6.31	73.8
6	0.707	5.89	79.7
7	0.648	5.40	85.1
8	0.556	4.64	89.7
9	0.433	3.61	93.3
10	0.337	2.81	96.1
11	0.251	2.09	98.2
12	0.214	1.79	100.0

Supplementary Material S3 - NCSS ROC

Dataset C:\Users\lrbia\Desktop\Databases survey FGL travelers\
DATABASE SURVEYs 2020_2021_2024.NCSS
Condition Variable FLULAST_24

Area Under Curve Analysis (Empirical Estimation)

Estimated Prevalence = 207 / 357 = 0.5798
Estimated Prevalence is the proportion of the sample with a positive condition of 1. The estimated prevalence should only be used as a valid estimate of the population prevalence when the entire sample is a random sample of the population.

Criterion	Count	AUC	Standard Error	Z-Value to Test AUC ≠ 0.5	2-Sided P-Value	95% Confidence Limits Lower	Upper
AGE_24	357	0.6618	0.0265	6.099	0.0000	0.6066	0.7106
EDUCAT_24	357	0.5579	0.0250	2.314	0.0207	0.5069	0.6051
F1M0_24	357	0.4877	0.0261	-0.473	0.6363	0.4350	0.5371
HCW_24	357	0.6353	0.0223	6.078	0.0000	0.5896	0.6769
VL_24	357	0.6019	0.0295	3.449	0.0006	0.5408	0.6566
X3CS_24	357	0.6345	0.0294	4.572	0.0000	0.5733	0.6887

Definitions:

Criterion	The Criterion Variable containing the scores of the individuals.
Count	The number of the individuals used in the analysis.
AUC	The area under the ROC curve using the empirical (trapezoidal) approach.
Standard Error	The standard error of the AUC estimate.
Z-Value	The Z-score for testing the designated hypothesis test.
P-Value	The probability level associated with the Z-Value.
Lower and Upper Confidence Limits	Form the confidence interval for AUC.

Dataset C:\Users\lrbia\Desktop\Databases survey FGL travelers\
DATABASE SURVEYs 2020_2021_2024.NCSS
Condition Variable FLULAST_24

Area Under Curve Analysis (Binormal Estimation)

Estimated Prevalence = 207 / 357 = 0.5798
Estimated Prevalence is the proportion of the sample with a positive condition of 1. The estimated prevalence should only be used as a valid estimate of the population prevalence when the entire sample is a random sample of the population.

Criterion	Count	AUC	Standard Error	Z-Value to Test AUC ≠ 0.5	2-Sided P-Value	95% Confidence Limits Lower	Upper
AGE_24	357	0.6783	0.0275	6.476	0.0000	0.6206	0.7287
EDUCAT_24	357	0.5677	0.0302	2.241	0.0250	0.5056	0.6240
F1M0_24	357	0.4857	0.0302	-0.473	0.6362	0.4243	0.5427
HCW_24	357	0.6730	0.0273	6.334	0.0000	0.6159	0.7231
VL_24	357	0.6065	0.0294	3.624	0.0003	0.5457	0.6609
X3CS_24	357	0.6280	0.0296	4.331	0.0000	0.5666	0.6825

Definitions:

Criterion	The Criterion Variable containing the scores of the individuals.
Count	The number of the individuals used in the analysis.
AUC	The area under the ROC curve using the Binormal estimation approach.
Standard Error	The standard error of the AUC estimate.
Z-Value	The Z-score for testing the designated hypothesis test.
P-Value	The probability level associated with the Z-Value.
Lower and Upper Confidence Limits	Form the confidence interval for AUC.

Dataset C:\Users\lrbia\Desktop\Databases survey FGL travelers\
DATABASE SURVEYs 2020_2021_2024.NCSS
Condition Variable FLULAST_24

Area Under Curve Analysis (Empirical Estimation)

Estimated Prevalence = 207 / 357 = 0.5798
Estimated Prevalence is the proportion of the sample with a positive condition of 1. The estimated prevalence should only be used as a valid estimate of the population prevalence when the entire sample is a random sample of the population.

Criterion	Count	AUC	Standard Error	Z-Value to Test AUC ≠ 0.5	2-Sided P-Value	95% Confidence Limits Lower	Upper
FUNCTIONAL_VL	357	0.6427	0.0282	5.059	0.0000	0.5841	0.6947
INTERACTIVE_VL	357	0.4617	0.0301	-1.273	0.2031	0.4006	0.5186
CRITICAL_VL	357	0.5857	0.0272	3.157	0.0016	0.5300	0.6364

Definitions:
Criterion The Criterion Variable containing the scores of the individuals.
Count The number of the individuals used in the analysis.
AUC The area under the ROC curve using the empirical (trapezoidal) approach.
Standard Error The standard error of the AUC estimate.
Z-Value The Z-score for testing the designated hypothesis test.
P-Value The probability level associated with the Z-Value.
Lower and Upper Confidence Limits Form the confidence interval for AUC.

Area Under Curve Analysis (Binormal Estimation)

Estimated Prevalence = 207 / 357 = 0.5798
Estimated Prevalence is the proportion of the sample with a positive condition of 1. The estimated prevalence should only be used as a valid estimate of the population prevalence when the entire sample is a random sample of the population.

Criterion	Count	AUC	Standard Error	Z-Value to Test AUC ≠ 0.5	2-Sided P-Value	95% Confidence Limits Lower	Upper
FUNCTIONAL_VL	357	0.6429	0.0284	5.031	0.0000	0.5838	0.6952
INTERACTIVE_VL	357	0.4620	0.0301	-1.264	0.2061	0.4010	0.5189
CRITICAL_VL	357	0.5921	0.0302	3.052	0.0023	0.5298	0.6481

Definitions:
Criterion The Criterion Variable containing the scores of the individuals.
Count The number of the individuals used in the analysis.
AUC The area under the ROC curve using the Binormal estimation approach.
Standard Error The standard error of the AUC estimate.
Z-Value The Z-score for testing the designated hypothesis test.
P-Value The probability level associated with the Z-Value.
Lower and Upper Confidence Limits Form the confidence interval for AUC.

Supplementary Material S4
jamovi MEDIATION AND MODERATION

LAST FLU VACCINE UPTAKE Indirect and Total Effects

				95% C.I. (a)				
Type	Effect	Estimate	SE	Lower	Upper	β	z	p
Indirect	FUVL_24 ⇒ CONFID_24 ⇒ FLULAST_24	0.03218	0.01599	8.39E-04	0.06353	0.04783	2.0124	0.044
	FUVL_24 ⇒ COMPLAC_24 ⇒ FLULAST_24	-0.00123	0.01355	-0.02779	0.02533	-0.00183	-0.0907	0.928
	FUVL_24 ⇒ CONVEN_24 ⇒ FLULAST_24	0.00345	0.00867	-0.01354	0.02043	0.00512	0.3976	0.691
	INTVL_24 ⇒ CONFID_24 ⇒ FLULAST_24	0.00411	0.00544	-0.00656	0.01478	0.0059	0.7555	0.45
	INTVL_24 ⇒ COMPLAC_24 ⇒ FLULAST_24	-4.02e−4	0.00443	-0.00909	0.00829	-5.76e−4	-0.0906	0.928
	INTVL_24 ⇒ CONVEN_24 ⇒ FLULAST_24	3.04E-04	0.00117	-0.002	0.0026	4.36E-04	0.2592	0.795
	CRVL_24 ⇒ CONFID_24 ⇒ FLULAST_24	0.02854	0.01477	-4.19e−4	0.05749	0.03475	1.9316	0.053
	CRVL_24 ⇒ COMPLAC_24 ⇒ FLULAST_24	-7.78e−4	0.00857	-0.01758	0.01603	-9.47e−4	-0.0907	0.928
	CRVL_24 ⇒ CONVEN_24 ⇒ FLULAST_24	0.00594	0.0149	-0.02326	0.03515	0.00723	0.3987	0.69
Component	FUVL_24 ⇒ CONFID_24	0.29778	0.0469	0.20587	0.3897	0.32461	6.3498	< .001
	CONFID_24 ⇒ FLULAST_24	0.10808	0.05094	0.00824	0.20791	0.14735	2.1218	0.034
	FUVL_24 ⇒ COMPLAC_24	0.24986	0.0447	0.16225	0.33747	0.29704	5.5895	< .001
	COMPLAC_24 ⇒ FLULAST_24	-0.00492	0.05422	-0.11119	0.10135	-0.00615	-0.0907	0.928
	FUVL_24 ⇒ CONVEN_24	0.19358	0.05	0.09557	0.29158	0.20351	3.8711	< .001
	CONVEN_24 ⇒ FLULAST_24	0.0178	0.04453	-0.06948	0.10508	0.02516	0.3998	0.689
	INTVL_24 ⇒ CONFID_24	0.03806	0.04707	-0.0542	0.13032	0.04005	0.8085	0.419
	INTVL_24 ⇒ COMPLAC_24	0.08165	0.04487	-0.0063	0.16959	0.0937	1.8197	0.069
	INTVL_24 ⇒ CONVEN_24	0.01709	0.05019	-0.08129	0.11547	0.01734	0.3405	0.733
	CRVL_24 ⇒ CONFID_24	0.26403	0.05656	0.15317	0.37489	0.23581	4.6681	< .001
	CRVL_24 ⇒ COMPLAC_24	0.15804	0.05391	0.05237	0.26371	0.15393	2.9313	0.003
	CRVL_24 ⇒ CONVEN_24	0.33375	0.06031	0.21554	0.45195	0.28747	5.5339	< .001
Direct	FUVL_24 ⇒ FLULAST_24	0.10378	0.0391	0.02714	0.18042	0.15423	2.6539	0.008
	INTVL_24 ⇒ FLULAST_24	-0.03157	0.03708	-0.10424	0.04109	-0.0453	-0.8516	0.394
	CRVL_24 ⇒ FLULAST_24	0.05767	0.04662	-0.0337	0.14905	0.07023	1.2371	0.216
Total	FUVL_24 ⇒ FLULAST_24	0.13818	0.03719	0.06528	0.21108	0.20536	3.715	< .001
	INTVL_24 ⇒ FLULAST_24	-0.02756	0.03733	-0.10073	0.04562	-0.03954	-0.7381	0.46
	CRVL_24 ⇒ FLULAST_24	0.09137	0.04486	0.00345	0.1793	0.11126	2.0369	0.042

FORTHCOMING FLU VACCINE INTENTION Indirect and Total Effects

				95% C.I.				
Type	Effect	(a) Estimate	SE	Lower	Upper	β	z	p
Indirect	FUVL_24 ⇒ CONFID_24 ⇒ FLUNEXT_24	0.03557	0.01507	0.00603	0.0651	0.05596	2.36	0.018
	FUVL_24 ⇒ COMPLAC_24 ⇒ FLUNEXT_24	0.01276	0.0127	-0.01214	0.03765	0.02007	1.004	0.315
	FUVL_24 ⇒ CONVEN_24 ⇒ FLUNEXT_24	0.00749	0.00818	-0.00854	0.02353	0.01179	0.916	0.36
	INTVL_24 ⇒ CONFID_24 ⇒ FLUNEXT_24	0.00455	0.0059	-0.00702	0.01611	0.0069	0.77	0.441
	INTVL_24 ⇒ COMPLAC_24 ⇒ FLUNEXT_24	0.00417	0.00468	-0.00501	0.01334	0.00633	0.89	0.373
	INTVL_24 ⇒ CONVEN_24 ⇒ FLUNEXT_24	6.62E-04	0.00207	-0.00339	0.00471	0.001	0.32	0.749
	CRVL_24 ⇒ CONFID_24 ⇒ FLUNEXT_24	0.03154	0.01412	0.00385	0.05922	0.04065	2.233	0.026
	CRVL_24 ⇒ COMPLAC_24 ⇒ FLUNEXT_24	0.00807	0.00837	-0.00834	0.02447	0.0104	0.964	0.335
	CRVL_24 ⇒ CONVEN_24 ⇒ FLUNEXT_24	0.01292	0.0139	-0.01433	0.04017	0.01665	0.929	0.353
Component	FUVL_24 ⇒ CONFID_24	0.29778	0.0469	0.20587	0.3897	0.32461	6.35	< .001
	CONFID_24 ⇒ FLUNEXT_24	0.11944	0.04698	0.02736	0.21152	0.1724	2.542	0.011
	FUVL_24 ⇒ COMPLAC_24	0.24986	0.0447	0.16225	0.33747	0.29704	5.589	< .001
	COMPLAC_24 ⇒ FLUNEXT_24	0.05105	0.05001	-0.04697	0.14907	0.06757	1.021	0.307
	FUVL_24 ⇒ CONVEN_24	0.19358	0.05	0.09557	0.29158	0.20351	3.871	< .001
	CONVEN_24 ⇒ FLUNEXT_24	0.03871	0.04107	-0.04179	0.11921	0.05794	0.943	0.346
	INTVL_24 ⇒ CONFID_24	0.03806	0.04707	-0.0542	0.13032	0.04005	0.808	0.419
	INTVL_24 ⇒ COMPLAC_24	0.08165	0.04487	-0.0063	0.16959	0.0937	1.82	0.069
	INTVL_24 ⇒ CONVEN_24	0.01709	0.05019	-0.08129	0.11547	0.01734	0.34	0.733
	CRVL_24 ⇒ CONFID_24	0.26403	0.05656	0.15317	0.37489	0.23581	4.668	< .001
	CRVL_24 ⇒ COMPLAC_24	0.15804	0.05391	0.05237	0.26371	0.15393	2.931	0.003
	CRVL_24 ⇒ CONVEN_24	0.33375	0.06031	0.21554	0.45195	0.28747	5.534	< .001
Direct	FUVL_24 ⇒ FLUNEXT_24	0.09996	0.03607	0.02928	0.17065	0.15729	2.772	0.006
	INTVL_24 ⇒ FLUNEXT_24	0.02202	0.0342	-0.045	0.08904	0.03344	0.644	0.52
	CRVL_24 ⇒ FLUNEXT_24	0.02392	0.043	-0.06036	0.1082	0.03083	0.556	0.578
Total	FUVL_24 ⇒ FLUNEXT_24	0.15578	0.03492	0.08733	0.22423	0.24511	4.461	< .001
	INTVL_24 ⇒ FLUNEXT_24	0.03139	0.03505	-0.03731	0.1001	0.04768	0.896	0.371
	CRVL_24 ⇒ FLUNEXT_24	0.07644	0.04212	-0.00611	0.159	0.09854	1.815	0.07

Indirect and Total Effects

				95% C.I. (a)				
Type	Effect	Estimate	SE	Lower	Upper	β	z	p
Indirect	FUVL_24 ⇒ 3CS_24 ⇒ FLULAST_24	0.03018	0.01354	0.00365	0.0567	0.04486	2.229	0.026
	INTVL_24 ➡ 3CS_24 ➡ FLULAST_24	0.00557	0.0052	-0.00463	0.0158	0.00799	1.07	0.284
	CRVL_24 ⇒ 3CS_24 ⇒ FLULAST_24	0.03078	0.01412	0.00309	0.0585	0.03748	2.179	0.029
Component	FUVL_24 ⇒ 3CS_24	0.24707	0.03787	0.17285	0.3213	0.32729	6.524	< .001
	3CS_24 ⇒ FLULAST_24	0.12216	0.0515	0.02122	0.2231	0.13706	2.372	0.018
	INTVL_24 ⇒ 3CS_24	0.0456	0.03801	-0.02891	0.1201	0.05831	1.2	0.23
	CRVL_24 ⇒ 3CS_24	0.25194	0.04568	0.16241	0.3415	0.27343	5.516	< .001
Direct	FUVL_24 ⇒ FLULAST_24	0.10799	0.03899	0.03158	0.1844	0.1605	2.77	0.006
	INTVL_24 ➡ FLULAST_24	-0.03313	0.03707	-0.10578	0.0395	-0.04753	-0.894	0.371
	CRVL_24 ⇒ FLULAST_24	0.0606	0.0463	-0.03016	0.1513	0.07378	1.309	0.191
Total	FUVL_24 ⇒ FLULAST_24	0.13818	0.03719	0.06528	0.2111	0.20536	3.715	< .001
	INTVL_24 ➡ FLULAST_24	-0.02756	0.03733	-0.10073	0.0456	-0.03954	-0.738	0.46
	CRVL_24 ⇒ FLULAST_24	0.09137	0.04486	0.00345	0.1793	0.11126	2.037	0.042

Indirect and Total Effects

				95% C.I. (a)				
Type	Effect	Estimate	SE	Lower	Upper	β	z	p
Indirect	VL_24 ➡ 3CS_24 ➡ FLULAST_24	0.0915	0.0306	0.0315	0.151	0.0771	2.99	0.003
Component	VL_24 ⇒ 3CS_24	0.5701	0.0637	0.44531	0.695	0.4282	8.95	< .001
	3CS_24 ⇒ FLULAST_24	0.1604	0.0506	0.06129	0.26	0.18	3.17	0.002
Direct	VL_24 ⇒ FLULAST_24	0.1286	0.0673	-0.00343	0.261	0.1084	1.91	0.056
Total	VL_24 ⇒ FLULAST_24	0.22	0.0618	0.09892	0.341	0.1854	3.56	< .001

Indirect and Total Effects

				95% C.I. (a)				
Type	Effect	Estimate	SE	Lower	Upper	β	z	p
Indirect	FUVL_24 ⇒ 3CS_24 ⇒ FLUNEXT_24	0.05164	0.01415	0.02391	0.0794	0.0812	3.65	< .001
	INTVL_24 ⇒ 3CS_24 ⇒ FLUNEXT_24	0.00953	0.00823	-0.00661	0.0257	0.0145	1.157	0.247
	CRVL_24 ⇒ 3CS_24 ⇒ FLUNEXT_24	0.05265	0.0153	0.02266	0.0826	0.0679	3.441	< .001
Component	FUVL_24 ⇒ 3CS_24	0.24707	0.03787	0.17285	0.3213	0.3273	6.524	< .001
	3CS_24 ⇒ FLUNEXT_24	0.209	0.04746	0.11597	0.302	0.2482	4.403	< .001
	INTVL_24 ⇒ 3CS_24	0.0456	0.03801	-0.02891	0.1201	0.0583	1.2	0.23
	CRVL_24 ⇒ 3CS_24	0.25194	0.04568	0.16241	0.3415	0.2734	5.516	< .001
Direct	FUVL_24 ⇒ FLUNEXT_24	0.10414	0.03593	0.03372	0.1746	0.1639	2.898	0.004
	INTVL_24 ⇒ FLUNEXT_24	0.02186	0.03416	-0.04509	0.0888	0.0332	0.64	0.522
	CRVL_24 ⇒ FLUNEXT_24	0.02379	0.04267	-0.05985	0.1074	0.0307	0.557	0.577
Total	FUVL_24 ⇒ FLUNEXT_24	0.15578	0.03492	0.08733	0.2242	0.2451	4.461	< .001
	INTVL_24 ⇒ FLUNEXT_24	0.03139	0.03505	-0.03731	0.1001	0.0477	0.896	0.371
	CRVL_24 ⇒ FLUNEXT_24	0.07644	0.04212	-0.00611	0.159	0.0985	1.815	0.07

Indirect and Total Effects

				95% C.I. (a)				
Type	Effect	Estimate	SE	Lower	Upper	β	z	p
Indirect	VL_24 ⇒ 3CS_24 ⇒ FLUNEXT_24	0.129	0.0301	0.0705	0.188	0.115	4.3	< .001
Component	VL_24 ⇒ 3CS_24	0.57	0.0637	0.4453	0.695	0.428	8.95	< .001
	3CS_24 ⇒ FLUNEXT_24	0.227	0.0463	0.1363	0.318	0.27	4.91	< .001
Direct	VL_24 ⇒ FLUNEXT_24	0.145	0.0616	0.0245	0.266	0.13	2.36	0.018
Total	VL_24 ⇒ FLUNEXT_24	0.275	0.0576	0.1617	0.387	0.245	4.77	< .001

ROUTINE VACCINES UPTAKE Indirect and Total Effects

Type	Effect	Estimate	SE	95% C.I. (a) Lower	95% C.I. (a) Upper	β	z	p
Indirect	FUVL_24 ⇒ CONFID_24 ⇒ ROUVUPTK_24	0.09922	0.03651	0.02766	0.1708	0.067	2.717	0.007
	FUVL_24 ⇒ COMPLAC_24 ⇒ ROUVUPTK_24	0.0096	0.02952	-0.04826	0.0675	0.00648	0.325	0.745
	FUVL_24 ⇒ CONVEN_24 ⇒ ROUVUPTK_24	0.03855	0.02123	-0.00307	0.0802	0.02603	1.815	0.069
	INTVL_24 ⇒ CONFID_24 ⇒ ROUVUPTK_24	0.01268	0.01624	-0.01915	0.0445	0.00827	0.781	0.435
	INTVL_24 ⇒ COMPLAC_24 ⇒ ROUVUPTK_24	0.00314	0.00978	-0.01604	0.0223	0.00205	0.321	0.748
	INTVL_24 ⇒ CONVEN_24 ⇒ ROUVUPTK_24	0.0034	0.01013	-0.01645	0.0233	0.00222	0.336	0.737
	CRVL_24 ⇒ CONFID_24 ⇒ ROUVUPTK_24	0.08797	0.0348	0.01976	0.1562	0.04867	2.528	0.011
	CRVL_24 ⇒ COMPLAC_24 ⇒ ROUVUPTK_24	0.00607	0.01876	-0.03069	0.0428	0.00336	0.324	0.746
	CRVL_24 ⇒ CONVEN_24 ⇒ ROUVUPTK_24	0.06646	0.03449	-0.00115	0.1341	0.03677	1.927	0.054
Component	FUVL_24 ⇒ CONFID_24	0.29778	0.0469	0.20587	0.3897	0.32461	6.35	< .001
	CONFID_24 ⇒ ROUVUPTK_24	0.3332	0.11082	0.116	0.5504	0.2064	3.007	0.003
	FUVL_24 ⇒ COMPLAC_24	0.24986	0.0447	0.16225	0.3375	0.29704	5.589	< .001
	COMPLAC_24 ⇒ ROUVUPTK_24	0.03844	0.11797	-0.19277	0.2696	0.02183	0.326	0.745
	FUVL_24 ⇒ CONVEN_24	0.19358	0.05	0.09557	0.2916	0.20351	3.871	< .001
	CONVEN_24 ⇒ ROUVUPTK_24	0.19912	0.09688	0.00924	0.389	0.12789	2.055	0.04
	INTVL_24 ⇒ CONFID_24	0.03806	0.04707	-0.0542	0.1303	0.04005	0.808	0.419
	INTVL_24 ⇒ COMPLAC_24	0.08165	0.04487	-0.0063	0.1696	0.0937	1.82	0.069
	INTVL_24 ⇒ CONVEN_24	0.01709	0.05019	-0.08129	0.1155	0.01734	0.34	0.733
	CRVL_24 ⇒ CONFID_24	0.26403	0.05656	0.15317	0.3749	0.23581	4.668	< .001
	CRVL_24 ⇒ COMPLAC_24	0.15804	0.05391	0.05237	0.2637	0.15393	2.931	0.003
	CRVL_24 ⇒ CONVEN_24	0.33375	0.06031	0.21554	0.452	0.28747	5.534	< .001
Direct	FUVL_24 ⇒ ROUVUPTK_24	-0.02302	0.08507	-0.18976	0.1437	-0.01554	-0.271	0.787
	INTVL_24 ⇒ ROUVUPTK_24	-0.10413	0.08066	-0.26223	0.054	-0.06788	-1.291	0.197
	CRVL_24 ⇒ ROUVUPTK_24	0.11068	0.10143	-0.08812	0.3095	0.06123	1.091	0.275
Total	FUVL_24 ⇒ ROUVUPTK_24	0.12435	0.08326	-0.03884	0.2875	0.08397	1.494	0.135
	INTVL_24 ⇒ ROUVUPTK_24	-0.08491	0.08357	-0.24871	0.0789	-0.05535	-1.016	0.31
	CRVL_24 ⇒ ROUVUPTK_24	0.27119	0.10042	0.07437	0.468	0.15003	2.701	0.007

Indirect and Total Effects

Type	Effect	Estimate	SE	95% C.I. (a) Lower	95% C.I. (a) Upper	β	z	p
Indirect	FUVL_24 ⇒ 3CS_24 ⇒ ROUVUPTK_24	0.1427	0.0353	0.0735	0.2119	0.0964	4.043	< .001
	INTVL_24 ⇒ 3CS_24 ⇒ ROUVUPTK_24	0.0263	0.0225	-0.0178	0.0705	0.0172	1.168	0.243
	CRVL_24 ⇒ 3CS_24 ⇒ ROUVUPTK_24	0.1455	0.0386	0.0698	0.2212	0.0805	3.765	< .001
Component	FUVL_24 ⇒ 3CS_24	0.2471	0.0379	0.1728	0.3213	0.3273	6.524	< .001
	3CS_24 ⇒ ROUVUPTK_24	0.5775	0.1121	0.3578	0.7972	0.2944	5.152	< .001
	INTVL_24 ⇒ 3CS_24	0.0456	0.038	-0.0289	0.1201	0.0583	1.2	0.23
	CRVL_24 ⇒ 3CS_24	0.2519	0.0457	0.1624	0.3415	0.2734	5.516	< .001
Direct	FUVL_24 ⇒ ROUVUPTK_24	-0.0183	0.0849	-0.1847	0.148	-0.0124	-0.216	0.829
	INTVL_24 ⇒ ROUVUPTK_24	-0.1112	0.0807	-0.2694	0.0469	-0.0725	-1.379	0.168
	CRVL_24 ⇒ ROUVUPTK_24	0.1257	0.1008	-0.0718	0.3232	0.0695	1.247	0.212
Total	FUVL_24 ⇒ ROUVUPTK_24	0.1243	0.0833	-0.0388	0.2875	0.084	1.494	0.135
	INTVL_24 ⇒ ROUVUPTK_24	-0.0849	0.0836	-0.2487	0.0789	-0.0553	-1.016	0.31
	CRVL_24 ⇒ ROUVUPTK_24	0.2712	0.1004	0.0744	0.468	0.15	2.701	0.007

Type	Effect	Estimate	SE	Lower	Upper	β	z	p
Indirect	VL_24 ⇒ 3CS_24 ⇒ ROUVUPTK_24	0.35182	0.0736	0.2076	0.496	0.13471	4.7819	< .001
Component	VL_24 ⇒ 3CS_24	0.5701	0.0637	0.4453	0.695	0.42824	8.9541	< .001
	3CS_24 ⇒ ROUVUPTK_24	0.61711	0.1091	0.4033	0.831	0.31457	5.6561	< .001
Direct	VL_24 ⇒ ROUVUPTK_24	-0.00655	0.1452	-0.2912	0.278	-0.00251	-0.0451	0.964
Total	VL_24 ⇒ ROUVUPTK_24	0.34526	0.1372	0.0764	0.614	0.1322	2.5165	0.012

Indirect and Total Effects

Type	Effect	Estimate	SE	95% C.I. (a) Lower	95% C.I. (a) Upper	β	z	p
Indirect	VL_24 ⇒ 3CS_24 ⇒ FLULAST_24	0.09475	0.02948	0.037	0.15253	0.07985	3.214	0.001
	AGE_24 ➡ 3CS_24 ➡ FLULAST_24	-0.00176	0.00509	-0.0117	0.00823	-0.00309	-0.345	0.73
Component	VL_24 ⇒ 3CS_24	0.57139	0.06377	0.4464	0.69637	0.42921	8.961	< .001
	3CS_24 ⇒ FLULAST_24	0.16583	0.04816	0.0714	0.26021	0.18605	3.444	< .001
	AGE_24 ⇒ 3CS_24	-0.0106	0.03056	-0.0705	0.04931	-0.01661	-0.347	0.729
Direct	VL_24 ⇒ FLULAST_24	0.10498	0.06421	-0.0209	0.23084	0.08847	1.635	0.102
	AGE_24 ⇒ FLULAST_24	0.1695	0.02781	0.115	0.22402	0.29803	6.094	< .001
Total	VL_24 ⇒ FLULAST_24	0.19973	0.05906	0.084	0.31548	0.16832	3.382	< .001
	AGE_24 ⇒ FLULAST_24	0.16774	0.02831	0.1123	0.22323	0.29494	5.926	< .001

Indirect and Total Effects

Type	Effect	Estimate	SE	95% C.I. (a) Lower	95% C.I. (a) Upper	β	z	p
Indirect	VL_24 ⇒ 3CS_24 ⇒ FLULAST_24	0.08327	0.02935	0.02574	0.1408	0.0702	2.84	0.005
	EDUCAT_24 ➡ 3CS_24 ➡ FLULAST_24	0.00946	0.0055	-0.00131	0.0202	0.0174	1.72	0.085
Component	VL_24 ⇒ 3CS_24	0.54451	0.06445	0.41819	0.6708	0.409	8.45	< .001
	3CS_24 ⇒ FLULAST_24	0.15293	0.05077	0.05341	0.2524	0.1716	3.01	0.003
	EDUCAT_24 ⇒ 3CS_24	0.06189	0.0295	0.00407	0.1197	0.1016	2.1	0.036
Direct	VL_24 ⇒ FLULAST_24	0.11706	0.06773	-0.01568	0.2498	0.0987	1.73	0.084
	EDUCAT_24 ⇒ FLULAST_24	0.03818	0.02847	-0.01762	0.094	0.0703	1.34	0.18
Total	VL_24 ⇒ FLULAST_24	0.20033	0.06269	0.07746	0.3232	0.1688	3.2	0.001
	EDUCAT_24 ⇒ FLULAST_24	0.04764	0.02869	-0.0086	0.1039	0.0877	1.66	0.097

Conditional Mediation

Moderator levels	Type	Effect	Estimate	SE	95% C.I. (a) Lower	95% C.I. (a) Upper	β	z	p
AGE									
Mean-1-SD	Indirect	VL ⇒ 3Cs ⇒ FLULAST	0.113	0.0307	0.05274	0.173	0.0939	3.676	< .001
Mean-1-SD	Component	VL ⇒ 3Cs	0.4909	0.0855	0.32342	0.658	0.3688	5.744	< .001
Mean-1-SD		3Cs ⇒ FLULAST	0.2301	0.0481	0.13583	0.324	0.2545	4.783	< .001
Mean-1-SD	Direct	VL ⇒ FLULAST	0.1294	0.0812	-0.02972	0.289	0.1076	1.594	0.111
Mean-1-SD	Total	VL ⇒ FLULAST	0.2406	0.0793	0.08524	0.396	0.2028	3.035	0.002
Mean	Indirect	VL ⇒ 3Cs ⇒ FLULAST	0.0993	0.0299	0.04071	0.158	0.0836	3.323	< .001
Mean	Component	VL ⇒ 3Cs	0.5776	0.0639	0.4524	0.703	0.4339	9.045	< .001
Mean		3Cs ⇒ FLULAST	0.1719	0.0481	0.07758	0.266	0.1927	3.572	< .001
Mean	Direct	VL ⇒ FLULAST	0.1012	0.0645	-0.02516	0.228	0.0852	1.57	0.116
Mean	Total	VL ⇒ FLULAST	0.196	0.0592	0.07993	0.312	0.1652	3.309	< .001
Mean+1-SD	Indirect	VL ⇒ 3Cs ⇒ FLULAST	0.0755	0.0337	0.0095	0.141	0.064	2.242	0.025
Mean+1-SD	Component	VL ⇒ 3Cs	0.6642	0.0931	0.48171	0.847	0.499	7.134	< .001
Mean+1-SD		3Cs ⇒ FLULAST	0.1136	0.0481	0.01933	0.208	0.1283	2.362	0.018
Mean+1-SD	Direct	VL ⇒ FLULAST	0.073	0.0905	-0.10436	0.25	0.0619	0.807	0.42
Mean+1-SD	Total	VL ⇒ FLULAST	0.1514	0.0864	-0.01784	0.321	0.1276	1.753	0.08

Conditional Mediation

Moderator levels	Type	Effect	Estimate	SE	95% C.I. (a) Lower	95% C.I. (a) Upper	β	z	p
EDUCAT									
Mean-1-SD	Indirect	VL ⇒ 3Cs ⇒ FLULAST	0.0799	0.0339	0.01358	0.146	0.0676	2.361	0.018
Mean-1-SD	Component	VL ⇒ 3Cs	0.6292	0.0883	0.45617	0.802	0.4727	7.127	< .001
Mean-1-SD		3Cs ⇒ FLULAST	0.127	0.0508	0.02753	0.227	0.143	2.502	0.012
Mean-1-SD	Direct	VL ⇒ FLULAST	0.0664	0.0906	-0.11118	0.244	0.0561	0.733	0.464
Mean-1-SD	Total	VL ⇒ FLULAST	0.1428	0.086	-0.02574	0.311	0.1203	1.661	0.097
Mean	Indirect	VL ⇒ 3Cs ⇒ FLULAST	0.0866	0.0292	0.02939	0.144	0.0729	2.967	0.003
Mean	Component	VL ⇒ 3Cs	0.5376	0.0644	0.41141	0.664	0.4039	8.348	< .001
Mean		3Cs ⇒ FLULAST	0.1611	0.0508	0.06162	0.261	0.1806	3.174	0.002
Mean	Direct	VL ⇒ FLULAST	0.1203	0.0676	-0.01225	0.253	0.1013	1.779	0.075
Mean	Total	VL ⇒ FLULAST	0.2043	0.0627	0.08138	0.327	0.1722	3.257	0.001
Mean+1-SD	Indirect	VL ⇒ 3Cs ⇒ FLULAST	0.0871	0.0291	0.03	0.144	0.0728	2.99	0.003
Mean+1-SD	Component	VL ⇒ 3Cs	0.4461	0.0938	0.26222	0.63	0.3351	4.756	< .001
Mean+1-SD		3Cs ⇒ FLULAST	0.1962	0.0508	0.0957	0.295	0.2173	3.845	< .001
Mean+1-SD	Direct	VL ⇒ FLULAST	0.1743	0.0929	-0.00774	0.356	0.1458	1.877	0.061
Mean+1-SD	Total	VL ⇒ FLULAST	0.2659	0.0914	0.08682	0.445	0.224	2.91	0.004

Note. Confidence intervals computed with method: Standard (Delta method)

Note. Betas are completely standardized effect sizes

jamovi linear regression

Model Coefficients - ROUVUPTK_24

Predictor	Estimate	SE	t	p
Intercept [a]	1.4161	0.4764	2.972	0.003
VL_24	-0.1111	0.1211	-0.917	0.360
3CS_24	0.3730	0.0912	4.089	< .001
AGE_24:				
2 – 1	-0.1615	0.1753	-0.921	0.357
3 – 1	-0.0705	0.1785	-0.395	0.693
4 – 1	0.7233	0.1933	3.742	< .001
EDUCAT_24:				
2 – 1	-0.3638	0.2388	-1.524	0.129
3 – 1	-0.5297	0.2573	-2.058	0.040
4 – 1	-0.3722	0.2154	-1.728	0.085
F1M0_24:				
1 – 0	-0.1364	0.0926	-1.473	0.142
HCW_24:				
1 – 0	0.4241	0.1033	4.106	< .001

[a] Represents reference level

jamovi logistic regression

Model Coefficients - FLULAST_24

Predictor	Estimate	SE	Z	p
Intercept	-3.698	1.365	-2.709	0.007
AGE_24:				
2 – 1	0.820	0.494	1.659	0.097
3 – 1	1.260	0.504	2.502	0.012
4 – 1	3.354	0.629	5.332	< .001
EDUCAT_24:				
2 – 1	-0.623	0.654	-0.952	0.341
3 – 1	-0.146	0.696	-0.210	0.833
4 – 1	-0.255	0.583	-0.438	0.662
F1M0_24:				
1 – 0	-0.189	0.262	-0.718	0.473
HCW_24:				
1 – 0	1.594	0.309	5.157	< .001
VL_24	0.263	0.338	0.779	0.436
3CS_24	0.549	0.258	2.123	0.034

Note. Estimates represent the log odds of "FLULAST_24 = 1" vs. "FLULAST_24 = 0"

Model Coefficients - FLUNEXT_24

Predictor	Estimate	SE	Z	p
Intercept	-6.7677	1.488	-4.5489	< .001
AGE_24:				
2 – 1	1.0127	0.482	2.1013	0.036
3 – 1	1.8972	0.507	3.7409	< .001
4 – 1	3.5633	0.681	5.2336	< .001
EDUCAT_24:				
2 – 1	-0.0422	0.690	-0.0612	0.951
3 – 1	0.2965	0.742	0.3996	0.689
4 – 1	0.1295	0.622	0.2081	0.835
F1M0_24:				
1 – 0	0.2634	0.279	0.9452	0.345
HCW_24:				
1 – 0	1.2695	0.349	3.6337	< .001
VL_24	0.4322	0.358	1.2083	0.227
3CS_24	1.1801	0.279	4.2279	< .001

Note. Estimates represent the log odds of "FLUNEXT_24 = 1" vs. "FLUNEXT_24 = 0"

Model Coefficients - YFVAC_24

Predictor	Estimate	SE	Z	p
Intercept	-5.781	1.951	-2.963	0.003
AGE_24:				
2 – 1	2.199	1.058	2.080	0.038
3 – 1	1.753	1.064	1.647	0.100
4 – 1	1.268	1.102	1.151	0.250
EDUCAT_24:				
2 – 1	-1.493	0.712	-2.098	0.036
3 – 1	-2.060	0.929	-2.217	0.027
4 – 1	-1.059	0.578	-1.834	0.067
F1M0_24:				
1 – 0	-0.640	0.297	-2.154	0.031
HCW_24:				
1 – 0	-0.205	0.332	-0.617	0.537
VL_24	0.316	0.413	0.765	0.444
3CS_24	0.843	0.374	2.254	0.024

Note. Estimates represent the log odds of "YFVAC_24 = 1" vs. "YFVAC_24 = 0"

Corresponding author: Luigi Roberto Biasio, Giovanni Lorenzini Foundation, Viale Piave 35, 20129 Milan, Italy
e-mail: lrbiasio@gmail.com

Ann Ig. 2025 Jan-Feb; 37(1): 128-140 doi: 10.7416/ai.2024.2644. Epub 2024 Jul 11.

Machine learning *vs*. regression models to predict the risk of *Legionella* contamination in a hospital water network

Osvalda De Giglio[1], Fabrizio Fasano[1], Giusy Diella[1], Valentina Spagnuolo[1,2], Francesco Triggiano[1], Marco Lopuzzo[1,2], Francesca Apollonio[1], Carla Maria Leone[3], Maria Teresa Montagna[1]

Keywords: Legionella; Machine learning; Water network; Hospital; Artificial Intelligence
Parole chiave: Legionella; Machine Learning; Rete idrica; Ospedale; Intelligenza artificiale

Abstract

Introduction. *The periodic monitoring of Legionella in hospital water networks allows preventive measures to be taken to avoid the risk of legionellosis to patients and healthcare workers.*
Study design. *The aim of the study is to standardize a method for predicting the risk of Legionella contamination in the water supply of a hospital facility, by comparing Machine Learning, conventional and combined models.*
Methods. *During the period July 2021– October 2022, water sampling for Legionella detection was performed in the rooms of an Italian hospital pavilion (89.9% of the total number of rooms). Fifty-eight parameters regarding the structural and environmental characteristics of the water network were collected. Models were built on 70% of the dataset and tested on the remaining 30% to evaluate accuracy, sensitivity, and specificity.*
Results*. A total of 1,053 water samples were analyzed and 57 (5.4%) were positive for Legionella. Of the Machine Learning models tested, the most efficient had an input layer (56 neurons), hidden layer (30 neurons), and output layer (two neurons). Accuracy was 93.4%, sensitivity was 43.8%, and specificity was 96%. The regression model had an accuracy of 82.9%, sensitivity of 20.3%, and specificity of 97.3%. The combination of the models achieved an accuracy of 82.3%, sensitivity of 22.4%, and specificity of 98.4%. The most important parameters that influenced the model results were the type of water network (hot/cold), the replacement of filter valves, and atmospheric temperature. Among the models tested, Machine Learning obtained the best results in terms of accuracy and sensitivity.*
Conclusions. *Future studies are required to improve these predictive models by expanding the dataset using other parameters and other pavilions of the same hospital.*

[1] *Interdisciplinary Department of Medicine, Hygiene Section, University of Bari Aldo Moro, Bari, Italy*
[2] *Department of Precision and Regenerative Medicine and Ionian Area (DiMePre-J), University of Bari Aldo Moro, Bari, Italy*
[3] *Azienda Ospedaliero Universitaria Policlinico di Bari, Hygiene Section, Bari, Italy*

Annali di Igiene : Medicina Preventiva e di Comunità (Ann Ig)
ISSN (print) 1120-9135 ISSN (online) 3035-5559

https://www.annali-igiene.it

Introduction

Legionella are Gram-negative bacteria that can colonize natural (e.g., rivers, lakes, and ponds) and artificial aquatic environments (e.g., drinking water systems, taps, faucets, showers, cooling towers, and fountains) (1). After individuals inhale contaminated aerosols, they can develop various clinical forms of legionellosis, such as a flu-like illness (Pontiac fever) or severe pneumonia known as Legionnaires' disease (LD) (2). The disease can be of community or nosocomial origin. In recent years, nosocomial legionellosis has attracted particular attention because of the complexity of hospital water systems and the vulnerability of hospitalized patients, which can lead to serious consequences with a high mortality rate (3).

The World Health Organization proposed the Water Safety Plan (WSP) in 2004 and revised it in subsequent years to both organize and systematize drinking water management practices and ensure the applicability of these practices to drinking water quality management (4,5). Additionally, according to the new European Drinking Water Directive (6) transposed in Italy on 18 February 2023 (7), *Legionella* is a microbiological parameter to be detected in the water supply of health and community facilities.

In recent years, LD cases have increased overall, probably because of the systematic surveillance developed in many countries and improved testing in microbiology laboratories (8-10). The Centers for Disease Control and Prevention (CDC) has estimated that 90% of outbreaks could be prevented through safe water management programs (11).

The ability to colonize various natural and artificial ecosystems makes the eradication of these microorganisms difficult (12). Several factors favor the proliferation of *Legionella*, including a water temperature between 20°C and 50°C (13) and the stagnation of water inside pipes (14). Moreover, *Legionella* can parasitize freshwater protozoa and persist in biofilm, thereby allowing for greater resistance to environmental factors and remediation treatments (12). Some authors (15) have highlighted the importance of chemical parameters (hardness, free chlorine concentration, pH, and trace element concentrations) and the material of water system pipes. For example, copper pipes reduce the risk of water colonization because of the natural antimicrobial effect of copper (16). More recently, competition with *Pseudomonas aeruginosa* has also been considered. Indeed, some researchers have reported that the presence of *P. aeruginosa* in the water supply is inversely correlated with the presence of *Legionella* (17).

Water is not free from microorganisms and poorly managed water networks can be particularly vulnerable to *Legionella* (18). In healthcare facilities, the management of construction activities is particularly complicated because of the complexity and variability of the buildings (age and size, time since the last renovation, number of floors, and number of rooms and water points/floors), which are often outdated and no longer suitable for current organizational and healthcare practices (19).

To date, conventional statistical methods and models for *Legionella* risk in water networks have been limited and often difficult to implement in practice (20-22).

In recent years, innovative artificial intelligence (AI) models, such as machine learning (ML)/deep learning (DL), have achieved tremendous success worldwide in various fields (23,24); however, there is still little scientific evidence on their application to risk caused by *Legionella* (25-27).

The term "artificial intelligence" was coined in the 1950s and describes a machine's capacity, particularly computer systems, to conduct operations that ordinarily require human intellect (e.g., visual perception, speech recognition, and decision-making) (28,29). ML is a branch of AI that uses algorithms to give machines the ability to learn from data (input) and improve over time without human help. DL is a subfield of ML and AI that uses artificial neural networks to simulate the cellular behavior of the human brain and learns from its experience. However, a massive volume of data needs to be provided at input (30).

The aim of the present study is to standardize a method for predicting the risk of *Legionella* contamination in the water supply of a hospital facility, by comparing ML, conventional models, and combined models.

Methods

Study design

The study was conducted in an Italian hospital, structured into several pavilions, which has implemented a WSP since October 2020. For this purpose, a systematic and organized water network monitoring process was planned, with associated differentiated maintenance interventions, derived from the analysis of the risk of water contamination by microorganisms, including *Legionella*.

For this study, a seven-floor pavilion (12,800 m^2) organized into two wings (north and south) was considered because of the plant scenario and the related maintenance interventions. One of the wings underwent a complete renovation of the network in the period March–June 2021, whereas the other wing did not undergo any extraordinary maintenance interventions. The pavilion had 396 rooms equipped with taps, showers, and bidets. The water network developed into five lines and 33 risers, characterized by a very varied structure in terms of installations (e.g., some sections were underground and others above ground, the presence of dead-end branches) and the characteristics of the water pipes (e.g., type of material, presence of filters, mixers). Technical data provided by the hospital's technical equipment and microbiological data were collected and analyzed to build predictive models of *Legionella* contamination in the water supply.

Legionella survey

Between July 2021 and October 2022, 356 of the 396 rooms (89.9%) present in the pavilion (99% confidence level, 2.2% confidence interval) were monitored for *Legionella* detection. A total of 1,053 water samples were analyzed (all samples for the wing of the pavilion under renovation were taken after the extraordinary maintenance intervention).

Water samples (1 L) were collected in sterile dark containers containing sodium thiosulphate pentahydrate (0.01%, w/v) to neutralize the chloride present in the water, transported to room temperature in isothermal bags, and analyzed within 24 hours according to current regulations (31,32). The water was filtered through a polycarbonate membrane with 0.2-µm pores and a diameter of 47 mm (Millipore Corporation, Bedford, MA, USA), and then suspended in 10 mL of the same water sample and vortexed. Subsequently, 200 µL of each sample was seeded on plates containing *Legionella* selective agar (GVPC, Biolife Italiana Srl, Milan, Italy) and incubated at 36°C ± 2°C for 7–10 days in a humid environment. Quantitative evaluation was expressed in colony-forming units/liter (cfu/L). Suspect colonies were subcultured on two *Legionella* BCYE agars (Biolife Italiana Srl, Milan, Italy) with and without L-cysteine. Colonies grown only on BCYE cysteine agar plates were considered to belong to the genus *Legionella* and were identified for confirmation in latex agglutination tests with polyvalent (Biolife Italiana Srl, Milan, Italy) and monovalent (Biogenetics Srl, Tokyo, Japan) antisera.

Water samples containing < 50 cfu/L were considered negative (hereafter referred to as 0 cfu/L).

Data collection

A total of 58 parameters relating to the structural and environmental characteristics of the water network and pavilion were studied, and are listed schematically below:

- structural parameters of the pavilion: floor and wings;
- infrastructural parameters of the water network up to the point of supply: length, location (underground and above ground), material of tube pipes (copper, steel, and multi-layer), diameters of tube pipes measured in mm (63.5, 50.8, 38.1, 31.75, 25.4, 19.05, 12.7, 10.16, 8.128, 6.604, 5.08, 4.572, 4.064, 3.556, 3.302, and 3.048), average pipe diameter, number of diameter changes along the water mains route, number of network lines, number of risers, type of network (hot/cold), presence of dead-end branches, and presence of corners along the water mains route (both total and partial);
- parameters of the water supply points in the rooms: number of water supply points used and not used, and type (tap, shower, and bidet);
- parameters of water network maintenance: total network renovation (Yes/No), days since renovation, replacement of filter valves (Yes/No) and days since the last replacement, replacement of aerator filters (Yes/No) and days since the last replacement, replacement of mixers (Yes/No) and days since the last replacement, replacement of shower heads (Yes/No) and days since the last replacement, replacement of flexible hoses (Yes/No) and days since the last replacement, disinfection of the network with sodium hypochlorite for two days (Yes/No) and days since the last disinfection, and presence of an absolute filter at the distribution point (Yes/No) and days since the installation of the absolute filter;
- water sampling parameters: water temperature at the time of sampling, pre- or post-flush sampling method, and detection (positive/negative) and load (cfu/L) of *Legionella*.
- climatic parameters: month of sampling, average air temperature on the day of sampling, and temperature range recorded on the day of sampling (33).

Statistical analysis

The development of the models involved the following steps:

• To make the descriptive parameters comparable with the alphanumeric parameters and include them in the analysis, the ordinal coding technique was used (34).

• The data obtained from the 1,053 water samples analyzed were pre-randomized.

• The independent parameters were normalized to a single comparable unit of measurement (range 0–1) using the following formula (35):

$$Xn = (Xnn - Min(X))/Max(X) - Min(X),$$

where:

Xn is the normalized value of each variable for record n
Xnn is the non-normalized value of each variable for record n
Max(X) is the maximum value of each variable
Min(X) is the minimum value of each variable.

The entire dataset was divided into two parts: 70% to train the model and 30% to evaluate the quality of the model (testing phase) (36). Furthermore, to test the robustness of the model another partition of the dataset was used: 50% for training and 50% for testing (37).

Development of predictive models

A useful glossary table consisting of commonly used terms in predictive modeling can be found in Table 1 (38-44).

Several ML/DL models were tested to predict the risk of *Legionella* contamination in the water network. All ML/DL models were developed considering the training dataset (70% and 50%). The number of hidden layers, number of neurons within each layer, and model training parameters (model training epochs, batch size, and validation split) were modified.

The purpose of these models was to understand which independent variables (n = 57) influence the dependent variable "*Legionella* detection (positive/negative)".

Each ML/DL model was supervised and adapted to solve classification problems (prediction of the *Legionella* sampling results, positive or negative). A bias neuron was added to each layer of the models to increase their effectiveness. The activation function for each layer was ReLU (Rectified Linear Unit); for the last level, which was a classification problem, softmax was considered (45,46).

For each model, the confusion matrix was calculated on 30% and 50% of the test dataset, which allowed us to understand how correctly the model was able to predict the sampling results compared with the real data present in the dataset. Through these confusion matrices, it was possible to define both the accuracy of the model, and its sensitivity and specificity (47).

Additionally, the R package Variable Importance Plots (VIP), which is a permutation based VI scoring method, was used to evaluate which factors most influenced the dependent variables within each model (44).

Poisson regression model

To estimate which parameters can predict water contamination by *Legionella*, the inferential statistical model was tested on the dependent variable "*Legionella* load (cfu/L)" and the independent variables (n = 57) according to the methods used by other authors (48-50). The *Poisson* regression

Table 1 - Glossary summary of common terminology in predictive modeling.

Term	Definition
Neuron	The basic element of a neural network, which connects toother neurons through transmitting data to each other (38)
Neural network	It consists of many simple, connected processors called neurons, each producing a sequence of real-valued activations (39)
Bias neuron	A weight parameter for an extra input whose activation is permanently set to +1 (40)
Hidden layer	In an artificial neural network, this is defined as the layer between the input and output layers, where the result of their action cannot be directly observed (38)
epochs of learning	Each repeated entry of the full set of training patterns (40)
batch size	Hyperparameter of deep learning that controls the number of the training samples that are "fed" into the neural network before internal model parameters are updated (41)
validation split	A set of data used to test the performance of the network during training, but not used for modifying the weights of the network (40)
Rectified Linear Input (ReLU)	The activation function most frequently used followed by SoftMax for classification problems (42, 43)
permutation based VI scoring method	It is a method to measure variable importance scores for the predictors in a model (44).

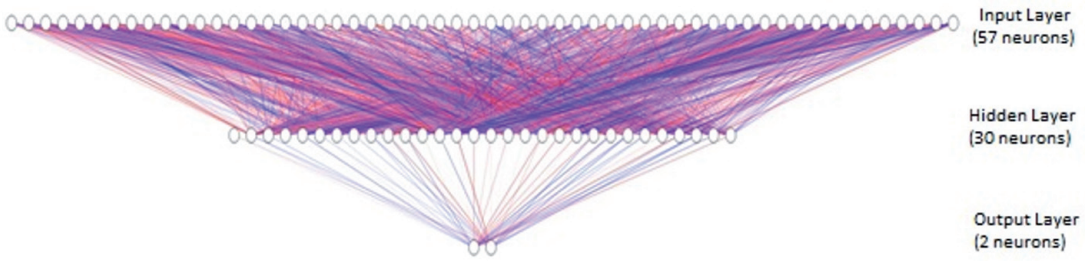


Figure 1 - Machine learning model architecture for Legionella results.

model was developed (70% and 50% of the dataset) and tested (30% and 50% of the dataset) on the *Legionella* load detected in the samples (0 cfu/L in the case of a negative result). Subsequently, only those parameters/risk factors with a p-value < 0.05 were considered to be statistically significant and included in the final model.

Predictions from the final *Poisson* regression model for each parameter analyzed in this study were used to calculate an overall risk score for *Legionella* positive outcomes using the following formula (50):

$$e^{(\alpha+\beta 1X1+\beta 2X2+...+\beta kXk),}$$

where:

α = intercept of the model;
β = coefficient of the regression model for each risk factor;
X = score of each risk factor.

ROC curve

The ROC curve was applied to the maintenance interventions of the water systems that were particularly relevant for the purposes of the forecasting models to determine the cut-off of days within which to perform subsequent maintenance interventions. R version 3.6.1 was used to perform all statistical tests.

Results

Of the 1,053 water samples analyzed for *Legionella*, 57 (5.4%) tested positive, of which 49 (86%) were for *Legionella pneumophila* (Lpn) serogroup (sg) 1, seven (12.3%) for Lpn sg 6, and one (1.7%) for Lpn sg 1+6. Regarding the detected concentration, 42 (73.7%) samples had a load < 1,000 cfu/L, 14 (24.6%) between 1,000 and 10,000 cfu/L, and one (1.7%) > 10,000 cfu/L.

When randomized and divided between the training (70%, 737/1,053) and testing (30%, 316/1,053) datasets, the positive samples were fairly evenly distributed (5.2%, 38/737 vs 6%, 19/316 water samples respectively). Similarly, for the algorithms created and tested with a 50%-50% split between the training and testing datasets, the positive water samples were distributed with 5.7% (30/527) in the training and 5.1% in the testing dataset (27/526).

Machine learning model

Of all the models tested, the ML model with 70% of dataset for training and 30% for testing, proved to be the most efficient model for predicting *Legionella* sample results (positive/negative) (Figure 1) (51). It started with 57 input benchmarks (input layer) and had a single hidden layer of 30 neurons and an output layer of two neurons (one for positive sample results and one for negative sample results). All layers had a bias neuron to increase their effectiveness.

The model was trained on the 737 samples of the train dataset (70%) with the following parameters: epochs of learning = 200, batch size = 4, and validation split = 0.6. The trained model, checked on 316 samples of the test dataset (30%), yielded the results in the confusion matrix shown in Table 2.

Table 2 - Confusion matrix for the machine learning model for *Legionella* detection

	Predictive results: positive	Predictive results: negative	Total real results
Real results: positive	**7**	12	19
Real results: negative	9	**288**	297
Total predictive results	16	300	**316**

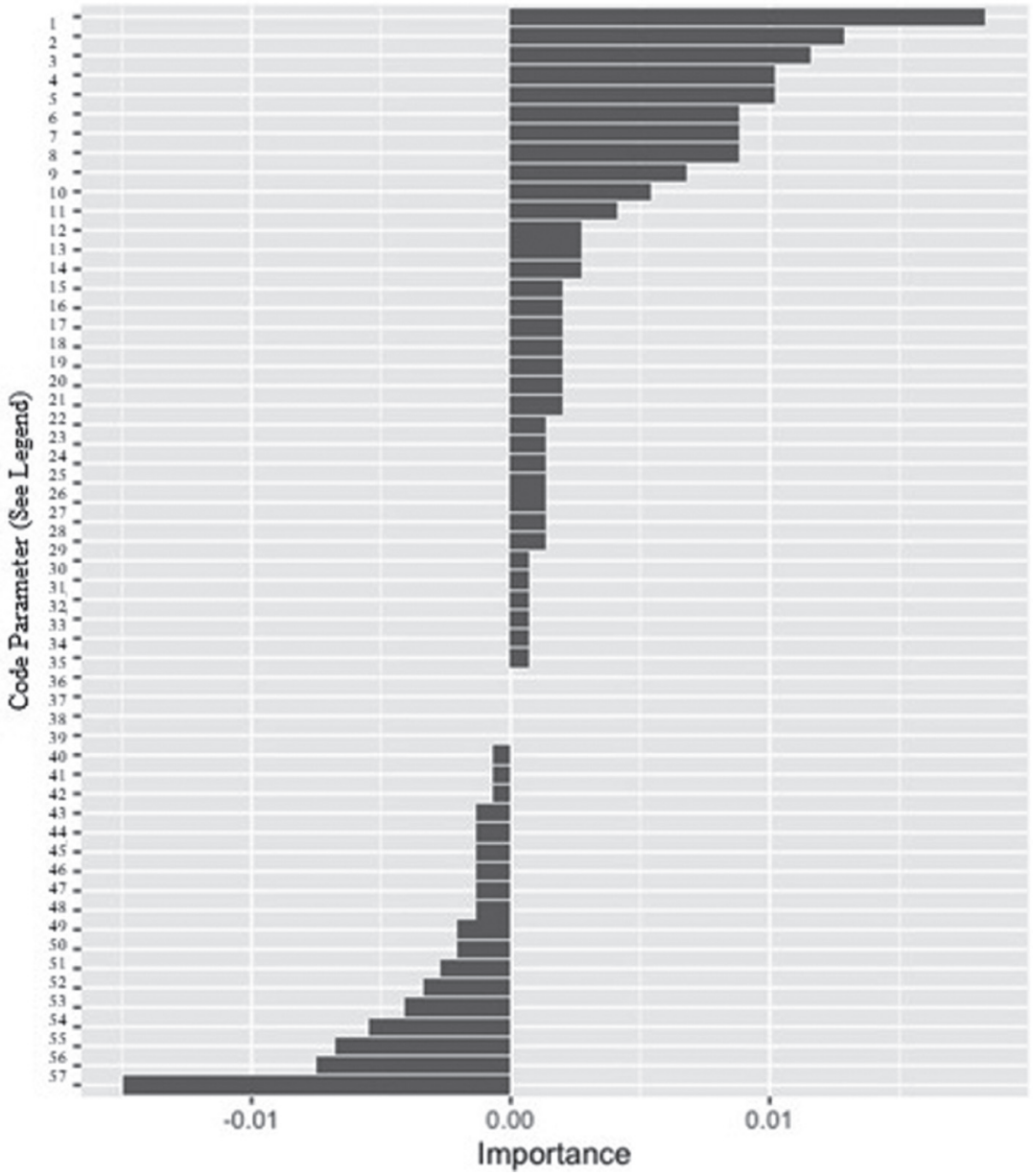


Figure 2 - Graphical representation of the importance of each parameter examined in the accuracy of the machine learning model.

Legend: 1. Type of water network (hot/cold), 2. water temperature at the time of sampling, 3. percentage of the water network with a 6.604 mm pipe diameter, 4. percentage of the underground water network, 5. number of days from the last filter valve replacement to the day of sampling, 6. aerator filter replacement (Yes/No), 7. number of days since the last disinfection of the water network with sodium hypochlorite for two days, 8. percentage of the water network with a 31.75 mm pipe diameter, 9. days since the last replacement of flexible hoses, 10. percentage of the above ground network, 11. replacement of flexible hoses (Yes/No), 12. length of the water network, 13. Total restructuring of the water network (Yes/No), 14. number of dead legs along the route, 15. total number of corners of the water network along the way , 16. replacement of filter valves (Yes/No), 17. days since the last shower head replacement to the day of sampling, 18. number of days since the total water network renovation, 19. mean atmospheric temperature on the day of sampling, 20. average tube pipe diameter, 21. percentage of the network with a 8.128 mm pipe diameter, 22. mixer replacement (Yes/No), 23. days since the last mixer replacement, 24. floor, 25. month of water sampling, 26. presence of an absolute filter at the point of use (Yes/No), 27. percentage of the water network with a 63.5 mm pipe diameter, 28. type of point of use (tap, shower, and bidet), 29. number of days since the last replacement of aerator filters to the day of sampling, 30. replacement of shower heads (Yes/No), 31. number of water delivery points in the room, 32. number of days since the installation of the absolute filter to the day of sampling, 33. percentage of the water network with a 12.7 mm pipe diameter, 34. percentage of the water network with a 3.556 mm pipe diameter, 35. number of unusable water delivery points in the room, 36. temperature range registered on the day of sampling, 37. percentage of the water network with a 4.572 mm pipe diameter, 38. percentage of the water system with 3.302 mm pipes, 39. percentage of the water system with 4.064 mm pipes, 40. sampling methods pre- or post-flushing, 41. percentage of the water system with 5.08 mm pipes, 42. wing, 43. percentage of the copper network, 44. percentage of the steel network, 45. number of water network risers, 46. percentage of the water mains with a 38.1 mm pipe diameter, 47. percentage of the water mains with a 3.048 mm pipe diameter, 48. number of diameter changes along the way, 49. percentage of multi-layer water pipes, 50. percentage of the water mains with a 19.05 mm pipe diameter, 51.number of corners along the water mains route (partial) 52. water network line, 53. percentage of the water system with 5.08 mm pipes, 54. percentage of the water system with 25.4 mm pipes, 55. percentage of the water system with 50.8 mm pipes, 56. percentage of the water system with 10.16 mm pipes, 57. disinfection of the network with sodium hypochlorite (continuous hyperchlorination) for two days (Yes/No).

Table 3 - Poisson regression model applied to the *Legionella* load (cfu/L).

	β	(eβ−1) = RR (%)	p-value
Intercept	-0.10230		< 0.0001*
Floor of the pavilion	0.13358	14.3	< 0.0001*
Hot/cold water network	0.10323	10.9	< 0.0001*
Mean atmospheric temperature on the day of sampling	0.09117	9.5	< 0.0001*
Atmospheric temperature range on the day of sampling	-0.12797	-12.0	< 0.0001*
Days since the last replacement of the filter valves	0.12782	13.6	< 0.0001*

*p < 0.05 statistically significant

Table 4 - Confusion matrix for the Poisson regression model.

	Predictive results: positive	Predictive results: negative	Total real Results
Real results: positive	**12**	7	19
Real results: negative	47	**250**	297
Total predictive results	59	257	**316**

Table 5 - Confusion matrix for the machine learning model + Poisson regression model.

	Predictive results: positive	Predictive results: negative	Total real Results
Real results: positive	**15**	4	19
Real results: negative	52	**245**	297
Total predictive results	67	249	**316**

The ML model had a prediction accuracy of 93.4% (295/316), with a sensitivity of 43.8% (7/16) and specificity of 96% (288/300).

The VIP package of R was applied to the model to determine which parameters had the greatest influence on the accuracy of the model. The results were shown in Figure 2.

From our data, it appears that some parameters, such as 1. type of water network, hot/cold, 2. water temperature at time of sampling, and 3. percentage of the water network with a 6.604 mm pipe diameter, had great importance in the model in a directly proportional sense (e.g., when the temperature of the water increased, the risk of *Legionella* contamination also increased). Other parameters, such as 55. percentage of the water system with 50.8 mm pipes, 56. percentage of the water system with 10.16 mm pipes, and 57. disinfection of the network with sodium hypochlorite for two days), were very important, but in an inversely proportional sense (e.g., as the percentage of pipes with a diameter of 10.16 mm or 50.8 mm that reached the point of supply increased, the risk of *Legionella* contamination decreased).

Poisson regression model

Table 3 shows the parameters that were statistically significant in influencing the best *Poisson regression* model applied to the *Legionella* load (training dataset 70%). Some parameters had a directly proportional influence, whereas others were inversely proportional (i.e., for each degree increase in the atmospheric temperature range on the day of sampling, the relative risk of *Legionella* contamination decreased by 12% in terms of the load).

Testing the model on the test dataset (30%) yielded the results shown in Table 4. The Poisson regression model had a prediction accuracy of 82.9% (262/316), with a sensitivity of 20.3% (12/59) and specificity of 97.3% (250/257).

The combination of the two models, where at least one of the two found positive predictions, obtained the results in Table 5. The combined model had a prediction accuracy of 82.3% (260/316), with a sensitivity of 22.4% (15/67) and specificity of 98.4% (245/249).

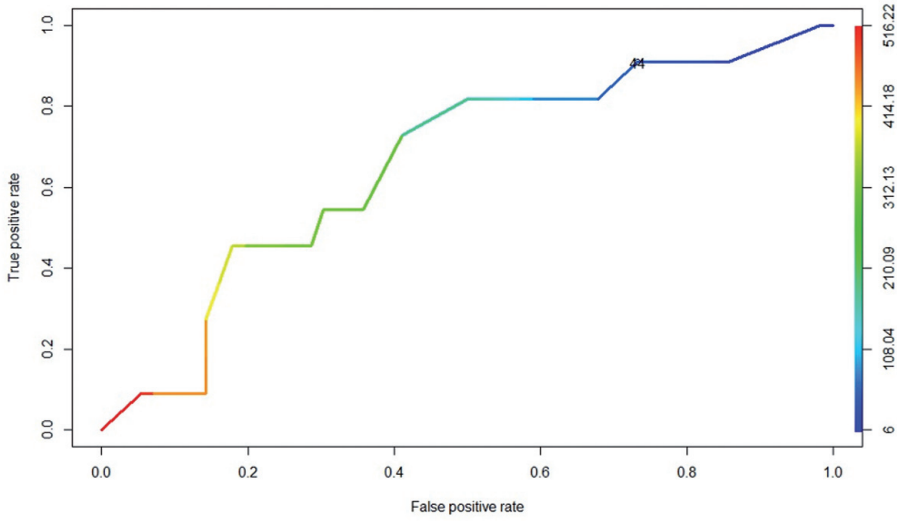


Figure 3 - ROC curves for the frequency of filter valve replacement and result of *Legionella* samples.

ROC curve

Considering the importance of the parameter "days since the last replacement of filter valves" by both models (Figure 2 and Table 2), the ROC curve (Figure 3) was applied to compare days from the last replacement with the result of *Legionella* in the sampling day.

The ROC curve showed that the ideal cut-off, beyond which 90% of the *Legionella* samples tested positive, was 44 days after the last maintenance intervention.

Discussion

Current AI tools are increasingly advancing, particularly ML and DL techniques, and have been applied in many areas of medicine, such as providing health information, making medical diagnoses, and predicting a patient's risk of future complications (52). Our study is one of the few in the field that analyzes a large number of parameters (n = 57) to predict *Legionella* contamination of a water supply. It is also the first to combine two types of statistical models (ML and Poisson regression).

Among the models tested (ML, Poisson regression, and ML combined with Poisson regression), ML obtained the best results both in terms of predictive accuracy (93.4%) and sensitivity (43.8%). Regarding specificity, the combination of the two models provided the best results (98.4%). The application of these innovative models ensured a more correct approach than traditional models for monitoring the water network, a factor that should not be overlooked when discussing healthcare facilities and vulnerable patients (53). Our results showed that these predictive models could be useful to improve the quality of management in complex hospital organizations, which represent a high-risk environment for LD transmission due to, for example, old plumbing systems, dead-end branches, lack of use of tap water (13).

The analysis of the factors that influence the prediction models yielded interesting results. By comparing the parameters that most influenced the presence (ML model) and load (*Poisson* Regression) of *Legionella*, a coincidence was found for some parameters: "type of water network (hot/cold water)" and "days from the last filter valve replacement to the day of sampling".

The "type of water network (hot/cold)" was the first factor in the order of importance according to the ML model and was statistically significant for the *Poisson* regression model. In particular, the *Poisson* regression analysis showed that the cold water network presented the risk of greater contamination than the hot water network. The role of the type of water network in influencing the presence of *Legionella* has been confirmed in the scientific literature (54) and it is not uncommon to find *Legionella* in cold water networks (>20°C) (47, 55-57). This aspect needs to be studied in depth because only hypotheses can explain these results at present: it is possible that

the temperature of the cold water network does not reach temperatures < 20°C for various reasons (e.g., systems that are too superficial); that users obtain hot water more frequently, which reduces the flow of cold water; or that some buildings are closed in emergency cases, which causes the stagnation of the network and consequently greater contamination by *Legionella* (6,58). All these situations should be avoided in the management of the water network to reduce the risk of Legionella contamination.

The other parameter in common that most influenced the two models was the maintenance intervention for filter valve replacement (days from the last replacement to the day of sampling). Our results indicate that the valve filter becomes contaminated before the expiry date established by the manufacturer (90 days), therefore it is necessary to microbiologically monitor the filter to establish the duration of its validity. According to the *Poisson* regression model, each additional day that the filter valve was not replaced corresponded to a 13.6% increase in the risk of *Legionella* contamination of the water network. This confirmed the importance of establishing an appropriate maintenance program regarding filter valve replacement (59).

The atmospheric temperature parameter analyzed in the predictive models was also particularly interesting. According to some authors (48,60,61), the ML model highlighted that, as the average daily atmospheric temperature increased, the presence of *Legionella* in the water network also increased. According to other authors (62,63), the *Poisson* regression model revealed that the average atmospheric temperature had a trend directly proportional to the risk of increased *Legionella* load.

The ML model highlighted how the diameter of the water pipes also influences the presence of *Legionella*: overall, as the diameter increased, the presence of *Legionella* decreased. Other authors (64-68) have shown that the diameter of the pipes (including the water flow) can influence the formation of biofilm, which is widely considered to be the ideal habitat for the proliferation of *Legionella*. Our results could be influenced by some limitations of this study. For example, we did not consider the extent, presence of biofilms and/or other competing microorganisms such as *Pseudomonas aeruginosa*. Furthermore, we found that continuous disinfection with sodium hypochlorite was a parameter associated with the presence of *Legionella* because it was performed when a high microbial load was present in the water samples. Therefore, we believe that the application of these predictive models can be improved by expanding the number of parameters to be studied.

In addition, the lack of sensitivity could probably be due to the low number of positive samples, which do not allow the algorithm to adapt perfectly to the variation in risk of *Legionella* contamination at each individual water supply point. For this reason, we intend to extend the study to other pavilions of the same hospital to increase the dataset. This would improve the performance of the ML/DL models on the one hand and increase the test sensitivity on the other (69). Another method to increase the sensitivity of the model may be to eliminate the independent variables that least influence the development of the model. These "pruning" techniques have been developed recently and several authors have shown that they often lead to improved model performance (70,71).

Conclusions

In this study, we have shown that the application of artificial intelligence methods to aqueous matrices can improve the modeling of water contamination compared to classical statistical analysis.

Some recommendations arising from the main findings are summarized below:

- check and maintain the cold water temperature <20°C, because it can present a greater risk of *Legionella* contamination than the hot water network;
- check the expiry date of the valve filter, as it may become contaminated before the expiry date;
- monitor the water network, especially during the hottest periods, as the average atmospheric temperature favors the risk of *Legionella* contamination.

In accordance with the new European directive 2020/2184, predictive models would allow a rational choice for the control and prevention of water contamination (e.g. remediation systems) and a better management of the risk of waterborne diseases in terms of time and cost.

Author Contributions: Conceptualization, O.D.G, F.F. and M.T.M; methodology, O.D.G, G.D, F.F, F.T, V.S. and M.L.; data curation, formal analysis, O.D.G, G.D, F.F. and F.T.; writing - original draft, O.D.G, F.F, G.D. and M.T.M; writing - review & editing, M.L.,V.S., F.A., F.T. and C.M.L; supervision, O.D.G, F.F. and M.T.M.
All authors have read and agreed to the present version of the manuscript.
Funding: This research did not receive any external funding. It was supported by university funds managed by Osvalda De Giglio.
Data Availability Statement: Not applicable.
Acknowledgments: We thank Edanz (https://www.edanz.com/ac)

for editing a draft of this manuscript.

Conflicts of Interest: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Riassunto

Machine Learning vs. modelli di regressione per prevedere il rischio di contaminazione da *Legionella* in una rete idrica ospedaliera

Introduzione. Il monitoraggio periodico per rilevare la presenza di *Legionella* nelle reti idriche ospedaliere consente di adottare misure preventive per evitare il rischio di legionellosi in pazienti e operatori sanitari.

Disegno dello studio. Scopo dello studio è standardizzare un metodo per prevedere il rischio di contaminazione da *Legionella* nella rete idrica di una struttura ospedaliera, confrontando modelli di *Machine Learning* con modelli convenzionali e combinati.

Metodi. Nel periodo luglio 2021 – ottobre 2022 la ricerca di *Legionella* è stata effettuata in campioni di acqua prelevati in 356 stanze presenti in un padiglione ospedaliero italiano. Sono stati esaminati cinquantotto parametri riguardanti le caratteristiche strutturali e ambientali della rete idrica. I modelli sono stati costruiti sul 70% del dataset e testati sul restante 30% per valutare l'accuratezza, la sensibilità e la specificità.

Risultati. Sono stati analizzati 1.053 campioni di acqua, di cui 57 (5,4%) positivi per *Legionella*. Dei modelli *Machine Learning* testati, il più efficiente aveva uno strato di *input* (56 neuroni), uno strato nascosto (30 neuroni) e uno strato di *output* (due neuroni). L'accuratezza è risultata pari al 93,4%, la sensibilità al 43,8% e la specificità al 96%. Il modello di regressione ha rilevato un'accuratezza dell'82,9%, una sensibilità del 20,3% e una specificità del 97,3%. La combinazione dei modelli ha raggiunto un'accuratezza dell'82,3%, una sensibilità del 22,4% e una specificità del 98,4%. I parametri più importanti che hanno influenzato i risultati del modello sono stati il tipo di rete idrica (acqua calda/fredda), la sostituzione delle valvole dei filtri e la temperatura atmosferica. Tra i modelli testati, *Machine Learning* ha ottenuto i migliori risultati in termini di accuratezza e sensibilità.

Conclusioni. Sono necessari ulteriori studi per migliorare questi modelli predittivi, ampliando il *dataset* con l'inserimento di altri parametri e di altri padiglioni dello stesso ospedale.

References

1. Fields BS, Benson RF, Besser RE. Legionella and Legionnaires' disease: 25 years of investigation. Clin Microbiol Rev. 2002 Jul;**15**(3):506-26. doi: 10.1128/CMR.15.3.506-526.2002. PMID: 12097254.
2. Iliadi V, Staykova J, Iliadis S, Konstantinidou I, Sivykh P, Romanidou G, et al. Legionella pneumophila: The Journey from the Environment to the Blood. J Clin Med. 2022 Oct 18;**11**(20):6126. doi: 10.3390/jcm11206126. PMID: 36294446.
3. Samuelsson J, Payne Hallström L, Marrone G, Gomes Dias. J. Legionnaires' disease in the EU/EEA*: increasing trend from 2017 to 2019. Euro. Surveill. 2023, **28**(11), 2200114. doi: 10.2807/1560-7917.ES.2023.28.11.2200114. PMID: 36927719.
4. Guidelines for drinking-water quality: Third edition. Geneva: World Health Organization; 2004.
5. Guidelines for drinking-water quality: Fourth edition incorporating the first and second addenda. Geneva: World Health Organization; 2022. Available from: https://www.who.int/publications/i/item/9789240045064 [Last accessed: 2024 May 20].
6. Direttiva (E.U.), 2020/2184 del. Parlamento Europeo e del Consiglio del 16 dicembre 2020 Concernente la Qualità delle Acque Destinate al Consumo Umano. G.U. dell'Unione Europea L 435/1 del 23 dicembre 2020. Available from: http://data.europa.eu/eli/dir/2020/2184/oj [Last accessed: 2024 May 20].
7. Legislative Decree 18 February 2023 concerning the implementation of Directive (EU) 2020/2184 of the European Parliament and of the Council of 16 December 2020 concerning the quality of water intended for human consumption. Available from: https://www.gazzettaufficiale.it/eli/id/2023/03/06/23G00025/SG [Last accessed: 2024 May 20].
8. European Centre for Disease Prevention and Control (ECDC). Legionnaires' Disease: Annual Epidemiological Report for 2019. Annual Epidemiological Report on Communicable Diseases in Europe. Stockholm: ECDC; 2021.
9. Fischer FB, Saucy A, Vienneau D, Hattendorf J, Fanderl J, de Hoogh K, et al. Impacts of weather and air pollution on Legionnaires' disease in Switzerland: A national case-crossover study. Environ Res. 2023 Sep 15; **233**:116327. doi: 10.1016/j.envres.2023.116327. Epub 2023 Jun 22. PMID: 37354934.
10. Graham FF, Harte D, Zhang J, Fyfe C, Baker MG. Increased Incidence of Legionellosis after Improved Diagnostic Methods, New Zealand, 2000-2020. Emerg Infect Dis. 2023 Jun;**29**(6):1173-1182. doi: 10.3201/eid2906.221598. PMID: 37209673.
11. Centers for Disease Control and Prevention Legionnaires' Disease: Use Water Management Programs in Buildings to Help Prevent Outbreaks, 2016. Available from: https://www.cdc.gov/vitalsigns/legionnaires/index.html [Last accessed: 2024 May 20].
12. Kanarek P, Bogiel T, Breza-Boruta B. Legionellosis risk-an overview of Legionella spp. habitats in Europe. Environ Sci Pollut Res Int. 2022 Nov;**29**(51):76532-76542. doi: 10.1007/s11356-022-22950-9. Epub 2022 Sep 26. PMID: 36161570.
13. De Giglio O, Diella G, Lopuzzo M, Triggiano F, Calia C, Pousis C, et al. Management of Microbiological Contamination of the Water Network of a Newly Built Hospital Pavilion. Pathogens. 2021 Jan 16;**10**(1),75. doi: 10.3390/pathogens10010075.
14. Ghaznavi C, Ishikane M, Yoneoka D, Tanoue Y, Kawashima T, Eguchi A, et al. Effect of the COVID-19 pandemic

and state of emergency declarations on the relative incidence of legionellosis and invasive pneumococcal disease in Japan. J Infect Chemother. 2023 Jan;**29**(1), 90-4. doi: 10.1016/j.jiac.2022.08.016. Epub 2022 Sep 16. PMID: 36116719.
15. Borella P, Montagna MT, Stampi S, Stancanelli G, Romano-Spica V, Triassi M, et al. Legionella contamination in hot water of Italian hotels. Appl Environ Microbiol. 2005 Oct;**71**(10):5805-13. doi: 10.1128/AEM.71.10.5805-5813.2005. PMID: 16204491.
16. Kyritsi MA, Mouchtouri VA, Katsioulis A, Kostara E, Nakoulas V, Hatzinikou M, et al. Legionella Colonization of Hotel Water Systems in Touristic Places of Greece: Association with System Characteristics and Physicochemical Parameters. Int J Environ Res Public Health. 2018 Nov 30; **15**(12):2707. doi: https://doi.org/10.3390/ijerph15122707. PMID: 30513698.
17. D'Alò GL, Messina A, Mozzetti C, Cicciarella Modica D, De Filippis P. Competitive colonization of Legionella and Pseudomonas aeruginosa in water systems of residential facilities hosting closed communities Legionella versus Pseudomonas aeruginosa in water systems of residential facilities. Ig Sanita Pubbl. 2022 Mar-Apr; **79**(2):92-110.
18. De Giglio O, Diella G, Lopuzzo M, Triggiano F, Calia C, Pousis C, et al. Impact of lockdown on the microbiological status of the hospital water network during COVID-19 pandemic. Environ Res. 2020 Dec;**191**:110231. doi: 10.1016/j.envres.2020.110231. Epub 2020 Sep 23. PMID: 32976823.
19. Gamage SD, Jinadatha C, Coppin JD, Kralovic SM, Bender A, Ambrose M, et al. Factors That Affect Legionella Positivity in Healthcare Building Water Systems from a Large, National Environmental Surveillance Initiative. Environ Sci Technol. 2022 Aug 16;56(16):11363-11373. doi: 10.1021/acs.est.2c02194. Epub 2022 Aug 5. PMID: 35929739
20. Federigi I, De Giglio O, Diella G, Triggiano F, Apollonio F, D'Ambrosio M, et al. Quantitative Microbial Risk Assessment Applied to *Legionella* Contamination on Long-Distance Public Transport. Int J Environ Res Public Health. 2022 Feb 10;**19**(4):1960. doi: 10.3390/ijerph19041960. PMID: 35206148.
21. De Giglio O, Napoli C, Diella G, Fasano F, Lopuzzo M, Apollonio F, et al. Integrated approach for legionellosis risk analysis in touristic-recreational facilities. Environ Res. 2021 Nov; **202**:111649. doi: 10.1016/j.envres.2021.111649. Epub 2021 Jul 9. PMID: 34252427.
22. Nagy DJ, Dziewulski DM, Codru N, Lauper UL. Understanding the distribution of positive Legionella samples in healthcare-premise water systems: Using statistical analysis to determine a distribution for Legionella and to support sample size recommendations. Infect Control Hosp Epidemiol. 2021 Jan;**42**(1):63-68. doi: 10.1017/ice.2020.384. Epub 2020 Oct 8. PMID: 33028429.
23. Fasano F, Addante AS, Valenzano B, Scannicchio G. Variables Influencing per Capita Production, Separate Collection, and Costs of Municipal Solid Waste in the Apulia Region (Italy): An Experience of Deep Learning. Int J Environ Res Public Health. 2021 Jan 17;**18**(2):752. doi: 10.3390/ijerph18020752. PMID: 33477308.
24. Alom MZ, Taha TM, Yakopcic C, Westberg S, Sidike P, Nasrin MS, et al. State-of-the-Art Survey on Deep Learning Theory and Architectures. Electronics. 2019; **8**(3):292. doi: https://doi.org/10.3390/electronics8030292.
25. Brunello A, Civilini M, De Martin S, Saccomanno M, Vitacolonna N. Machine learning-assisted environmental surveillance of *Legionella*: A retrospective observational study in Friuli-Venezia Giulia region of Italy in the period 2002–2019. Informatics in Medicine Unlocked.2022; **28**:100803. doi: https://doi.org/10.1016/j.imu.2021.100803.
26. Tata A, Marzoli F, Cordovana M, Zacometti C, Massaro A, Barco L, et al. A multi-center validation study on the discrimination of *Legionella pneumophila* sg.1, *Legionella pneumophila* sg. 2-15 and *Legionella* non-*pneumophila* isolates from water by FT-IR spectroscopy. Front Microbiol. 2023 Apr 13;**14**:1150942. doi: 10.3389/fmicb.2023.1150942. PMID: 37125166.
27. Sinčak P, Ondo J, Kaposztasova D, Virčkova M, Vranayova Z, Sabol J. Artificial intelligence in public health prevention of legionelosis in drinking water systems. Int J Environ Res Public Health. 2014 Aug 21;**11**(8):8597-611. doi: 10.3390/ijerph110808597. PMID: 25153475.
28. Russell S, Norvig P. Artificial Intelligence: A Modern Approach. Global Edition; 2021.
29. Soori M, Arezoo B, Dastres R. Artificial intelligence, machine learning and deep learning in advanced robotics, a review. Cognitive Robotics. 202; **3**:54-70. doi: https://doi.org/10.1016/j.cogr.2023.04.001.
30. Sharma N, Sharma R, Jindal N. Machine Learning and Deep Learning Applications-A Vision. Global Transitions Proceedings. 2021;**2**(1):24-28. doi:https://doi.org/10.1016/j.gltp.2021.01.004.
31. Guidelines for the Prevention and Control of Legionellosis, 2015. Available from: http://www.salute.gov.it/imgs/C_17_pubblicazioni_2362_allegato.pdf. [Last accessed: 2024 May 20].
32. ISO 11731:2017. Water Quality—Enumeration of Legionella; International Organization for Standardization: Geneva, Switzerland; 2017.
33. Civil Protection Department Apulia Region. Available from: https://protezionecivile.puglia.it/bollettini-meteorologici-regionali-mensili. [Last accessed: 2024 May 20].
34. Potdar K, Pardawala TS, Pai CDA. Comparative Study of Categorical Variable Encoding Techniques for Neural Network Classifiers. Int. J. Comput Appl. 2017;**175**:7-9. doi: 10.5120/ijca2017915495.
35. Patro S, Sahu KK. Normalization: A Preprocessing Stage. IARJSET. 2015;**2**(3):20-22. doi: 10.5120/ijca2017915495.
36. Xu Y, Goodacre R. On Splitting Training and Validation Set: A Comparative Study of Cross-Validation, Bootstrap and Systematic Sampling for Estimating the Generalization Performance of Supervised Learning. J Anal Test. 2018;**2**(3):249-262. doi: 10.1007/s41664-018-0068-2. Epub 2018 Oct 29. PMID: 30842888.

37. Dobbin KK, Simon RM. Optimally splitting cases for training and testing high dimensional classifiers. BMC Med Genomics. 2011 Apr 8;**4**:31. doi: 10.1186/1755-8794-4-31. PMID: 21477282.
38. Kufel J, Bargieł-Łączek K, Kocot S, Kozlik M, Bartnikowska W, Janik M, et al. What Is Machine Learning, Artificial Neural Networks and Deep Learning?-Examples of Practical Applications in Medicine. Diagnostics (Basel). 2023 Aug 3;**13**(15):2582. doi: 10.3390/diagnostics13152582. PMID: 37568945.
39. Jürgen Schmidhuber. Deep learning in neural networks: An overview. Neural Networks. 2015;**61**:85-117. https://doi.org/10.1016/j.neunet.2014.09.003.
40. Stegemann J, Buenfeld N. A Glossary of Basic Neural Network Terminology for Regression Problems. Neural Comput. & Applic. 1999; **8**:290–6. https://doi.org/10.1007/s005210050034.
41. Xu C, Coen-Pirani P, Jiang X. Empirical Study of Overfitting in Deep Learning for Predicting Breast Cancer Metastasis. Cancers. 2023;**15**:1969. https://doi.org/10.3390/cancers15071969.
42. Bengio Y, Courville A, Vincent P. Representation Learning: A Review and New Perspectives. IEEE Transact Pattern Anal Machine Intell. 2013;**35**:1798-1828. doi: 10.1109/TPAMI.2013.50.
43. Deng L,Yu D. Deep Learning: Methods and Applications. Found. Trends Signal Process 2014;**7**:197-387. doi: 10.1561/2000000039.
44. Greenwell BM, Boehmke BC. Variable Importance Plots-An Introduction to the vip Package. R Journal 2020;**12(**1):343-366. https://doi.org/10.32614/RJ-2020-013.
45. Favorskaya MN, Andreev VV. The study of activation functions in deep learning for pedestrian detection and tracking. Int Arch Photogramm Remote Sens Spat Inf. Sci 2019; **XLII-2/W12**:53-9. doi: 10.5194/isprs-archives-XLII-2-W12-53-2019.
46. Eckle K, Shmidt-Hieber J. A comparison of deep networks with ReLU activation function and linear spline-type methods. Neural Netw**.** 2019;**110**:232–242. doi: 10.1016/j.neunet.2018.11.005.
47. Huang F, Zhang J, Zhou C, Wang Y, Huang J,Zhu L. A deep learning algorithm using a fully connected sparse autoencoder neural network for landslide susceptibility prediction. Landslides. 2020;**17**:217-229. doi: 10.1007/s10346-019-01274-9.
48. De Giglio O, Fasano F, Diella G, Lopuzzo M, Napoli C, Apollonio F, et al. Legionella and legionellosis in touristic-recreational facilities: Influence of climate factors and geostatistical analysis in Southern Italy (2001-2017). Environ Res. 2019;**178**:108721. doi: 10.1016/j.envres.2019.108721. Epub 2019 Sep 6. PMID: 31541805.
49. Conza L, Casati Pagani S, Gaia V. Influence of climate and geography on the occurrence of Legionella and amoebae in composting facilities. BMC Res Notes. 2014 Nov 24;**7**:831. doi: 10.1186/1756-0500-7-831. PMID: 25421541.
50. Cui Y, Kim DY, Zhu J. On the generalized poisson regression mixture model for mapping quantitative trait loci with count data. Genetics. 2006 Dec;**174**(4):2159-72. doi: 10.1534/genetics.106.061960. Epub 2006 Oct 8. PMID: 17028335.
51. Nguyen QH, Ly HB, Ho LS, Al-Ansari N, Le HV, Tran VQ, et al. Influence of Data Splitting on Performance of Machine Learning Models in Prediction of Shear Strength of Soil. Mathematical Problems in Engineering. 2021:1-15. doi: 10.1155/2021/4832864.
52. Singh P, Singh N, Singh KK, Singh A. Chapter 5 - Diagnosing of disease using machine learning. In: Singh KK, Elhoseny M, Singh A, Elngar AA, Eds. Machine Learning and the Internet of Medical Things in Healthcare. Academic Press; 2021:89-111. doi: https://doi.org/10.1016/B978-0-12-821229-5.00003-3.
53. Wilson AM, Canter K, Abney SE, Gerba CP, Myers ER, Hanlin J, et al. An application for relating Legionella shower water monitoring results to estimated health outcomes. Water Res. 2022 Aug 1;**221**:118812. doi: 10.1016/j.watres.2022.118812. Epub 2022 Jul 3. PMID: 35816914.
54. Marchesi I, Paduano S, Frezza G, Sircana L, Vecchi E, Zuccarello P, et al. Safety and Effectiveness of Monochloramine Treatment for Disinfecting Hospital Water Networks. Int J Environ Res Public Health. 2020 Aug 22;**17**(17):6116. doi: 10.3390/ijerph17176116. PMID: 32842654.
55. Papadakis A, Keramarou M, Chochlakis D, Sandalakis V, Mouchtouri VA, Psaroulaki A. *Legionella* spp. Colonization in Water Systems of Hotels Linked with Travel-Associated Legionnaires' Disease. **Water**. 2021;**13**(16):2243. https://doi.org/10.3390/w13162243.
56. Arvand M, Jungkind K, Hack A. Contamination of the cold water distribution system of health care facilities by Legionella pneumophila: do we know the true dimension? Euro Surveill. 2011 Apr 21;**16**(16):19844. PMID: 21527132.
57. Stout JE, Yu VL, Muraca P. Isolation of Legionella pneumophila from the cold water of hospital ice machines: implications for origin and transmission of the organism. Infect Control. 1985;**6**(4):141-6. doi: 10.1017/s0195941700062937. PMID: 3886578.
58. Istituto Superiore di Sanità 2020. Rapporto COVID-19, n. 21/2020. Guida per la prevenzione della contaminazione da Legionella negli impianti idrici di strutture turistico recettive, e altri edifici ad uso civile e industriale non utilizzati durante la pandemia COVID-19.
59. Sheffer PJ, Stout JE, Wagener MM, Muder RR. Efficacy of new point-of-use water filter for preventing exposure to Legionella and waterborne bacteria. Am J Infect Control. 2005;**33**(5 Suppl 1):S20-5. doi: 10.1016/j.ajic.2005.03.012. PMID: 15940113.
60. Walker JT. The influence of climate change on waterborne disease and Legionella: a review. Perspect Public Health. 2018 Sep;**138**(5):282-286. doi: 10.1177/1757913918791198. PMID: 30156484.
61. Fragou K, Kokkinos P, Gogos C, Alamanos Y, Vantarakis A. Prevalence of Legionella spp. in water systems of hospitals and hotels in South Western Greece. Int J Environ Health Res. 2012;**22**(4):340-54. doi: 10.1080/09603123.2011.643229.

Epub 2011 Dec 12. PMID: 22149148.
62. Montagna MT, Brigida S, Fasano F, Leone CM, D'Ambrosio M, Spagnuolo V, et al. The role of air temperature in Legionella water contamination and legionellosis incidence rates in southern Italy (2018-2023). Ann Ig. 2023 Nov-Dec;**35**(6):631-640. doi: 10.7416/ai.2023.2578. Epub 2023 Sep 20. PMID: 37724578.
63. Dupke S, Buchholz U, Fastner J, Förster C, Frank C, Lewin A, et al. Impact of climate change on waterborne infections and intoxications. J Health Monit. 2023 Jun 1;**8**(Suppl 3):62-77. doi: 10.25646/11402. PMID: 37342430; PMCID: PMC10278370.
64. Pavissich JP, Aybar M, Martin KJ, Nerenberg R. A methodology to assess the effects of biofilm roughness on substrate fluxes using image analysis, substrate profiling, and mathematical modelling. Water Sci Technol. 2014;**69**(9):1932-41. doi: 10.2166/wst.2014.103. PMID: 24804670.
65. Tierra G, Pavissich JP, Nerenberg R, Xu Z, Alber MS. Multicomponent model of deformation and detachment of a biofilm under fluid flow. J R Soc Interface. 2015 May 6;**12**(106):20150045. doi: 10.1098/rsif.2015.0045. PMID: 25808342.
66. Liu J, Chen H, Yao L, Wei Z, Lou L, Shan Y, et al.The spatial distribution of pollutants in pipe-scale of large-diameter pipelines in a drinking water distribution system. J Hazard Mater. 2016 Nov 5; **317**:27-35. doi: 10.1016/j.jhazmat.2016.05.048. Epub 2016 May 17. PMID: 27244696.
67. Shen Y, Monroy GL, Derlon N, Janjaroen D, Huang C, Morgenroth E, et al. Role of biofilm roughness and hydrodynamic conditions in *Legionella pneumophila* adhesion to and detachment from simulated drinking water biofilms. Environ Sci Technol. 2015;**49**(7):4274-82. doi: 10.1021/es505842v. Epub 2015 Mar 11. PMID: 25699403.
68. Lin H, Zhu X, Wang Y, Yu X. Effect of sodium hypochlorite on typical biofilms formed in drinking water distribution systems. J Water Health. 2017;**15**(2):218-227. doi: 10.2166/wh.2017.141. PMID: 28362303.
69. Hordri NF, Samar A, Yuhaniz SS, Shamsuddin SM. A systematic literature review on features of deep learning in big data analytics. Int J Adv Soft Comput Appl. 2017;**9**(1):32-49.
70. Vadera S, Ameen S. Methods for Pruning Deep Neural Networks. IEEE Access. 2022;**10**:63280-63300.
71. Ma YD, Zhao ZC, Liu D, He Z, Zhou W. OCAP: On-device Class-Aware Pruning for personalized edge DNN models. J Syst Architect. 2023;**142**:102956.

Corresponding author: Prof. Osvalda De Giglio, Interdisciplinary Department of Medicine, University of Bari Aldo Moro, Piazza Giulio Cesare 11, 70124 Bari, Italy
e-mail: osvalda.degiglio@uniba.it

Ann Ig. 2025 Jan Feb; 37(1): 141-153 doi: 10.7416/ai.2024.2655. Epub 2024 Oct 3

Sleep quality among Italian university students: the UnSleep multicenter study

Francesca Gallè[1], Fabiano Grassi[2], Federica Valeriani[3], Roberto Albertini[4], Silvia Angelillo[5], Giuseppina Caggiano[6], Annalisa Bargellini[7], Aida Bianco[5], Lavinia Bianco[2], Laura Dallolio[8], Giorgia Della Polla[9], Gabriella Di Giuseppe[9], Maria Eufemia Gioffrè[10], Pasqualina Laganà[11], Francesca Licata[5], Fabrizio Liguori[12], Giuseppina Lo Moro[13], Isabella Marchesi[7], Manuela Martella[13], Alice Masini[14], Maria Teresa Montagna[6], Christian Napoli[2], Stefania Oliva[2], Giovanni Battista Orsi[2], Stefania Paduano[7], Cesira Pasquarella[4], Concetta Paola Pelullo[1], Rossella Sacchetti[15], Roberta Siliquini[13,16], Francesco Triggiano[6], Licia Veronesi[4], Vincenzo Romano Spica[3], Matteo Vitali[2], Carmela Protano[2]

Keywords: Sleep; Undergraduates; Electronic Devices; Lifestyles
Parole chiave: Sonno; studenti universitari; dispositivi elettronici; stili di vita

Abstract

Background. *Scientific evidence demonstrates that poor sleep quality can lead to various health problems. This study aimed to investigate sleep patterns among Italian university students and identify several factors that may contribute to its quality.*
Study design. *Cross-sectional study.*
Methods. *An electronic questionnaire regarding sociodemographic characteristics, lifestyle, and sleep-related habits, including the Pittsburgh Sleep Quality Index (PSQI) questionnaire, was distributed between January 2022 and July 2023 among students belonging to 12 universities located in Northern, Central, and Southern Italy.*

[1] *Department of Medical, Movement and Wellbeing Sciences, University of Naples "Parthenope", Naples, Italy*
[2] *Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy*
[3] *Department of Movement, Human, and Health Sciences, University of Rome "Foro Italico", Rome, Italy*
[4] *Department of Medicine and Surgery, University of Parma, Parma, Italy*
[5] *Department of Health Sciences, School of Medicine, University of Catanzaro "Magna Græcia", Catanzaro, Italy*
[6] *Interdisciplinary Department of Medicine, University of Bari Aldo Moro, Bari, Italy*
[7] *Department of Biomedical, Metabolic and Neural Sciences, Section of Public Health, University of Modena and Reggio Emilia, Modena, Italy*
[8] *Department of Biomedical and Neuromotor Science Alma Mater Studiorum, University of Bologna, Bologna, Italy*
[9] *Department of Experimental Medicine, University of Campania "Luigi Vanvitelli", Naples, Italy*
[10] *Multispecialty Clinical Institute, Trauma Orthopedic Care, Messina, Italy*
[11] *Department of Biomedical and Dental Sciences and Morphofunctional Imaging, University of Messina, Messina, Italy*
[12] *Department of Economics and Legal Studies, University of Naples "Parthenope", Naples, Italy*
[13] *Department of Public Health Sciences and Pediatrics, University of Turin, Turin, Italy*
[14] *Department of Translational Medicine, Amedeo Avogadro University of Eastern Piedmont and Ospedale Maggiore della Carità, Novara, Italy*
[15] *Department of Education Studies "Giovanni Maria Bertin", University of Bologna, Bologna, Italy*
[16] *Hospital Medical Direction, A.O.U. City of Health and Science of Torino, Turin, Italy*

Annali di Igiene : Medicina Preventiva e di Comunità (Ann Ig)
ISSN (print) 1120-9135 ISSN (online) 3035-5559

https://www.annali-igiene.it

Results. *On a total of 1,674 questionnaires collected, the participants (mean age 24.06±4.56 years, 71.3% F) reported an average number of hours of nocturnal sleep equal to 6.89±1.28 hours. A total of 927 (54.6%) of respondents showed a poor sleep quality (PSQI >5). Regression analysis showed that better sleep quality is associated with lower age, attending universities in Northern Italy, less time spent on electronic devices during the day, not being used to study at night and not playing videogames before sleep.*
Conclusion. *From a public health perspective, our findings suggest that public health operators should raise the awareness of young adults about the importance of sleep quality for maintaining good health, as well as the impact that certain behaviors can have on sleep.*

Introduction

Sleep is a fundamental physiological process, and the importance of its quality for humans' health and well-being has been widely recognized (1). Although there is still no universally agreed-upon definition, sleep quality is understood as a combination of the individual's subjective satisfaction and certain quantitative components, such as duration, latency of onset, and sleep maintenance (2,3). Poor sleep quality, in the worst cases, can take on pathological characteristics such as insomnia, which is a sleep disorder characterized by repeated difficulties in the initiation, duration, maintenance, or quality of sleep. Numerous studies have demonstrated how poor sleep quality and actual sleep disorders negatively impact both the physical and mental health and the overall quality of life of individuals (4,5). The mutual relationship between sleep and mental health has been extensively researched and documented in various conditions, including post-traumatic stress disorder, and eating disorders, but also experiences on the psychosis spectrum, such as delusions and hallucinations (6). On the other hand, sleep disorders can represent either risk factors or consequences in other pathological conditions, such as cardiovascular and metabolic diseases, anxiety and depression, reduced cognitive functioning, which in turn can negatively affect daytime performances, both socially and professionally, and increase the risk of workplace and traffic accidents (4,7-10). It is evident, therefore, that conditions of severe and chronic poor sleep quality represent a public health issue and, consequently, the assessment of sleep quality is crucial for epidemiological and clinical studies (11). In contrast, complying with the sleep hygiene basics by handling sleep time and daily habits can improve sleep quality and duration (12).

Poor sleep quality, with varying levels of severity, appears to be particularly common in young adults, especially among university students: several studies conducted in different socio-cultural contexts have reported prevalence rates of poor sleep quality ranging from 50% to 70% (13-19). Some studies indicate that between 20% and 40% of university students sleep fewer than the 7 to 9 hours recommended for their age group, which is worrying considering that insufficient sleep can have negative effects on health such as obesity, hypertension, diabetes, and the development of conditions related with the onset of depression and anxiety symptoms, such as stress and burnout (13-15, 20-22). Additionally, it is known that the restrictions related to COVID-19 had an impact on sleep quality of university students (23): studies performed during that period reported an increase in sleep difficulties associated with high levels of depression, anxiety, and stress (23-25).

Numerous studies on this topic have been performed among students from different countries, including Jordan (26), United States (13), Mongolia (17), Ethiopia (14) and, in the European context, Germany (27) and Italy (28). However, the validity of the evidence coming from these investigations is often limited by the characteristics of the study samples, which are commonly represented by undergraduates enrolled in only one or few universities of each country. Many studies have also tried to identify factors related with sleep quality in university students, and their results appear heterogeneous, maybe due to the different cultural contexts examined (13,18,29,30). Furthermore, it should be considered that the cross-sectional design of these studies cannot allow to ascertain causal relationships between the investigated factors and sleep quality.

The multicenter study on University Students' Sleep (UnSleep) aimed at examining sleep quality in a sample of undergraduates enrolled across the whole Italian territory. Furthermore, possible associations between sleep quality and socio-demographic aspects, lifestyles and sleep-related habits of the Italian undergraduates were also examined.

Material and methods

Study design and population

This cross-sectional study was performed between January 2022 and July 2023 among students attending twelve Italian universities (University of Bari Aldo Moro, University of Bologna Alma Mater Studiorum, University of Campania "Luigi Vanvitelli", University of Catanzaro "Magna Græcia", University of Eastern Piedmont "Amedeo Avogadro", University of Messina, University of Modena and Reggio Emilia, University of Naples "Parthenope", University of Parma, University of Rome "Foro Italico", Sapienza University of Rome, University of Turin). Undergraduates were invited to participate during classes by a researcher who explained the aims of the investigation and guaranteed the respect of anonymity and privacy in data collection and elaboration. An electronic questionnaire was used to collect participants' information. A link to the questionnaire was provided to the students during the presentation of the study and they were also invited to spread the questionnaire among their colleagues who did not attend lessons. No incentives were provided to fill in the questionnaire. Participants were allowed to complete the questionnaire when they prefer, even out of classes. Universities were chosen by convenience. Considering a total population of 438,555 students in the involved Universities, a sample of at least 384 undergraduates would have been required assuming a 95% confidence level and a 50% response proportion. The study was carried out respecting the principles of the Declaration of Helsinki. The protocol of the study was approved by the Ethical Board of the University of Rome "Foro Italico" (CAR 140/2022).

In the first part of the questionnaire, students were asked to report their sociodemographic characteristics (age, gender, parents' educational level, university, residential status (residing in the university area, commuter, off-site), living conditions (alone, with familiars, with parents, with other non-familiar cohabitants), sentimental status (single, engaged but not married, married), occupational status (working or not, working frequency and main time slot). In the second section of the questionnaire information regarding lifestyle and sleep-related behaviors were collected: dietary habit (Mediterranean, vegetarian/vegan, weight loss diet, diet for a health condition, supplemented diet, no particular dietary regimen), weight and height for the body mass index (BMI) calculation, smoking habit (smoking or not, frequency of smoking, use of cigarettes/cut tobacco, heat tobacco devices, electronic cigarettes, more than one product), consumption of alcoholic beverages (consumption or not, frequency of consumption, type of beverages consumed, consumption during or out of meals), consumption of coffee, energy drinks, cannabis, cocaine, ecstasy, amphetamine, hallucinogens, opiates, non-psychoactive-drugs (NPDs), minutes per week of moderate-vigorous physical activity (MVPA), participation in sport (practicing or not, recreational or competitive level, individual or group sports), number of hours usually spent using electronic devices during the day, habit of studying during the night, reading paper or electronic books, watching films, studying on paper or electronic devices, videogaming, chatting or visiting social media, practicing other non-screen related recreational activities or physical activity before sleep. An additional question was posed to explore if the quantity/quality of their sleep changed in the course of the COVID-19 pandemic (no change, decreased, increased).

The third section of the questionnaire consisted in the Italian Version of the Pittsburgh Sleep Quality Index (PSQI) (31). The statistical software STATA was used to calculate the Cronbach's alpha index. A coefficient equal to 0.74 was obtained, indicating acceptable internal consistency.

A commitment statement was posed at the beginning of the questionnaire as attention check question. The mean time required to complete the questionnaire was 13 minutes. All the questions were mandatory. Therefore, only fully completed questionnaires were collected and used for the subsequent statistical analyses.

Statistical analyses

Continuous variables were expressed by mean and standard deviation (SD) or median and interquartile range (IQR) values on the basis of their distribution, while categorical variables were reported as number and percentage of respondents for each category. BMI was used to classify respondents' nutritional status (underweight, normal weight, overweight and obese), as recommended by the World Health Organization (https://www.who.int/europe/news-room/fact-sheets/item/a-healthy-lifestyle---who-recommendations). Participants were classified as "good quality sleepers" or "poor quality sleepers" on the basis of their PSQI score, considering the cut-off value of 5, as previously defined (31).

Depending on data distribution, the Student's t test for independent samples, the Wilcoxon rank sum test and the chi-squared test were used to highlight possible differences in the characteristics of the

respondents between participants grouped by PSQI score. In order to identify variables possibly related with sleep quality, a multiple logistic regression analysis was performed by including as independent those socio-demographic and behavioral variables that showed significant differences between sleep quality groups in the univariate analyses. To this aim, some answers were grouped to obtain dichotomous variables: diet (no particular regimen = 0, other regimens = 1); smoking frequency (non-smoker/quitter = 0, smoker = 1), type of smoking (cigarettes or tobacco = 0, electronic devices = 1), sport (no = 0, yes = 1). Age and MVPA/week values were classified as ≤ median value = 0 or > median value = 1.

The value of p = 0.05 was assumed as significance threshold. The statistical software IBM SPSS, version 28.0, was used for the analyses.

Results

A total of 1,674 complete questionnaires were collected. Table 1 shows the sociodemographic and behavioral characteristics of participants.

The sample was mainly composed by females, commuters, and students attending life science courses, living with relatives, and engaged in a relationship. The educational level of participants' parents was mainly high school. The majority of the sample did not work; about the half of workers was occupied mainly in the afternoon.

Table 1 - Characteristics of the sample

Variable	Values
Age (years)	
mean±SD	24.06±4.56
Gender *n(%)*	
female	1,193 (71.3)
male	468 (28.0)
other/no answer	13 (0.8)
Mother educational level *n(%)*	
mandatory	411 (24.6)
high-school	786 (47.0)
degree	477 (28.5)
Father educational level *n(%)*	
mandatory	475 (28.4)
high-school	787 (47.0)
degree	412 (24.6)
Geographical area *N (%)*	
North	527 (31.5)
Center	508 (30.3)
South	639 (38.2)
Study area *N (%)*	
life sciences	1,291 (77.1)
other	383 (22.9)
Residential status *N (%)*	
resident in the area	498 (29.7)
commuter	627 (37.5)
off-site	549 (32.8)
Living condition *N (%)*	
alone	96 (5.7)
with relatives	1,078 (64.4)
with partner	142 (8.5)
with cohabitants	358 (21.4)
Relationship status *N (%)*	
single	687 (41.0)
engaged, not married	936 (55.9)
married	51 (3.0)
Working activity *N (%)*	
none	907 (54.2)
<once a week	76 (4.5)
at least once a week	143 (8.5)
>once a week	260 (15.5)
every day	288 (17.2)
Main working time slot *N (%)*	
morning	247 (32.2)
afternoon	385 (50.2)
evening	89 (11.6)
night	46 (6.0)
Diet *N (%)*	
no particular regimen	780 (46.6)
Mediterranean diet	492 (29.4)
vegetarian or vegan	59 (3.5)
weight loss diet	179 (10.7)
diet for particular health condition	63 (3.8)
diet with temporary supplementation	101 (6.0)
BMI (kg/m^2)	
mean±SD	23.03±3.78
category n(%)	
underweight	95 (5.7)
normal weight	1,054 (63.0)
overweight	271 (16.2)
obese	254 (15.2)
Smoking *N (%)*	
no	1,011 (60.4)
yes, <3 times a week	123 (7.3)
yes, 4-6 times a week	48 (2.9)
yes, at least once a day	405 (24.2)
quitter	87 (5.2)
Smoking type *N (%)*	
cigarettes or cut tobacco	274 (16.4)
heat tobacco devices	184 (11.0)
electronic cigarettes	106 (6.3)
more than one product	94 (5.6)

Alcohol use *N (%)*	
no	288 (17.2)
yes, ≤once a month	397 (23.7)
yes, 2-4 times a month	606 (36.2)
yes, 2-3 times a week	284 (17.0)
yes, ≥times a week	28 (1.7)
yes, every day	71 (4.2)
Alcoholic beverage consumed *N (%)*	
wine	532 (38.7)
beer	525 (38.2)
spirits	318 (23.1)
Alcohol use time *N (%)*	
during meal	592 (42.7)
out of meal	794 (57.3)
MVPA/week (minutes)	
median (IQR)	120 (180)
Sport *N (%)*	
no	805 (48.1)
yes, recreational	733 (43.8)
yes, competitive	136 (8.1)
Sport category *N (%)*	
endurance	461 (54.9)
strength	378 (45.1)
Sport type *N (%)*	
individual	688 (80.4)
group	168 (19.6)
Night sleep (hours)	
mean±SD	6.89±1.28
PSQI (score)	
mean±SD	
N (%)	6.23±3.05
≤5	747 (45.4)
>5	927 (55.4)

As for the lifestyle, about the half of respondents did not follow particular diet regimens and the majority had a normal weight and were non-smokers; smokers preferred the use of traditional cigarettes or tobacco. Alcohol use was reported by the great majority of respondents: they consumed mainly wine and beer 2-4 times a month and out of the meals. The sample showed a weekly PA level lower than that recommended, and less than the half was engaged in sport. Recreational, endurance and individual sports were more commonly reported by those who exercised. As for sleep, the mean number of hours slept was lower than that recommended, and the mean PSQI was about 6 out of 21.

A total of 927 (54.6%) of participants showed a PSQI >5 and were identified as "poor quality sleepers". The univariate comparisons between respondents with poor and good sleep quality were reported in Table 2.

"Poor quality sleepers" showed higher age, greater proportions of females and students attending southern universities than "good quality sleepers". As for lifestyle, higher proportions of individuals who did not follow any dietary regimen, who commonly used energy drinks, cannabis, and hallucinogens, reporting lower levels of PA and sport practice, mainly individual sports, who smoked with a higher frequency and mainly traditional cigarettes or tobacco, were registered among "poor quality sleepers". As for the sleep-related behaviors, this group reported more time

Table 2 - Comparison of sociodemographic and behavioral characteristics between "poor quality sleepers" and "good quality sleepers" with related p values

Variable	Poor quality sleepers N=927	Good quality sleepers N=747	p value
Age mean±SD	24.2±4.7	23.8±4.3	0.008
Gender *n(%)*			
female	687 (74.1)	506 (67.7)	0.016
male	233 (25.1)	235 (31.5)	
other/no answer	7 (0.8)	6 (0.8)	
Mother's educational level *n(%)*			
mandatory	228 (24.6)	183 (24.5)	0.992
high-school	436 (47.0)	350 (46.9)	
degree	263 (28.4)	214 (28.6)	
Father's educational level *n(%)*			
mandatory	273 (29.4)	202 (27.0)	0.548
high-school	428 (46.2)	359 (48.1)	
degree	226 (24.4)	186 (24.9)	

Geographical area *n(%)*			
North	257 (27.7)	270 (36.1)	<0.001
Center	282 (30.4)	226 (30.3)	
South	388 (41.9)	251 (33.6)	
Study area *n(%)*			
life sciences	724 (78.1)	567 (75.9)	0.287
other	203 (21.8)	180 (24.0)	
Residential status *n(%)*			
resident in the area	263 (28.3)	235 (31.5)	0.349
commuter	358 (38.6)	269 (36.0)	
off-site	306 (33.1)	243 (32.5)	
Living condition *n(%)*			
alone	62 (6.7)	34 (4.5)	
with relatives	595 (64.2)	483 (64.7)	0.295
with partner	76 (8.2)	66 (8.8)	
with cohabitants	194 (20.9)	164 (22.0)	
Relationship status *n(%)*			
single	379 (40.9)	308 (41.2)	0.561
engaged, not married	516 (55.7)	420 (56.2)	
married	32 (3.4)	19 (25.4)	
Working activity *n(%)*			
none	499 (53.8)	408 (54.6)	
<once a week	37 (4.0)	39 (5.2)	0.577
at least once a week	76 (82.0)	67 (9.0)	
>once a week	152 (16.4)	108 (14.5)	
every day	163 (17.6)	125 (16.7)	
Main working time slot *n(%)*			
morning	149 (34.8)	98 (29.0)	
afternoon	196 (45.8)	189 (55.7)	0.105
evening	55 (12.8)	34 (10.0)	
night	28 (6.6)	18 (5.3)	
Diet *n(%)*			
no particular regimen	448 (48.3)	332 (44.4)	
Mediterranean diet	258 (27.8)	234 (31.3)	
vegetarian or vegan	33 (3.6)	26 (3.5)	0.003
weight loss diet	99 (10.7)	80 (10.7)	
diet for particular health condition	46 (5.0)	17 (2.3)	
diet with temporary supplementation	43 (4.6)	58 (7.8)	
BMI (kg/m^2)	23.1±3.8	22.9±3.6	
mean±SD underweight	59 (6.4)	36 (4.8)	0.066
normal weight	562 (60.6)	492 (65.9)	
overweight	167 (18.0)	104 (13.9)	0.049
obese	139 (15.0)	115 (15.4)	
Smoking *n(%)*			
no	510 (55.0)	501 (67.1)	
yes, <3 times a week	74 (8.0)	49 (6.6)	<0.001
yes, 4-6 times a week	30 (3.2)	18 (2.4)	
yes, at least once a day	254 (27.4)	151 (20.2)	
quitter	59 (6.4)	28 (3.7)	
Smoking type *n(%)*			
cigarettes or cut tobacco	175 (42.3)	99 (40.6)	
heat tobacco devices	108 (26.1)	76 (31.1)	<0.001
electronic cigarettes	63 (15.2)	43 (17.6)	
more than one product	68 (16.4)	26 (10.7)	

Alcohol use *n(%)*			
no	148 (16.0)	140 (18.7)	
yes, ≤once a month	222 (23.9)	175 (23.4)	
yes, 2-4 times a month	332 (35.8)	274 (37.0)	0.209
yes, 2-3 times a week	159 (17.2)	125 (16.7)	
yes, ≥times a week	19 (2.0)	9 (1.2)	
yes, every day	47 (5.1)	24 (3.2)	
Alcoholic beverage consumed *n(%)*			
wine	292 (37.8)	240 (39.9)	0.397
beer	297 (38.4)	228 (37.9)	
spirits	184 (23.8)	134 (22.2)	
Alcohol use time *n(%)*			
during meal	326 (41.9)	266 (43.8)	0.310
out of meal	452 (58.1)	342 (56.2)	
Coffee consumption *n(%)*			
no	139 (15.0)	111 (14.9)	0.939
yes	788 (85.0)	636 (85.1)	
Energy drink consumption *n(%)*			
no	726 (78.3)	619 (82.9)	0.020
yes	201 (21.7)	128 (17.1)	
Cannabis use *n(%)*			
no	806 (86.9)	674 (90.2)	0.037
yes	121 (13.1)	73 (9.8)	
Cocaine use *n(%)*			
no	920 (99.2)	744 (99.6)	0.351
yes	7 (0.8)	3 (0.4)	
Amphetamine use *n(%)*			
no	921 (99.3)	744 (99.6)	0.494
yes	6 (0.7)	3 (0.4)	
Hallucinogens use *n(%)*			
no	919 (99.1)	746 (99.9)	0.043
yes	8 (0.9)	1 (0.1)	
Ecstasy use *n(%)*			
no	923 (99.6)	745 (99.7)	0.806
yes	4 (0.4)	2 (0.3)	
Opiates use *n(%)*			
no	926 (99.9)	747 (100)	0.369
yes	1 (0.1)	0 (0.0)	
Non psychoactive drugs use *n(%)*			
no	926 (99.9)	747 (100)	0.369
yes	1 (0.1)	0 (0.0)	
MVPA/week (minutes)			
median (IQR)	100 (40)	120 (60)	<0.001
Sport *n(%)*			
no	472 (50.9)	333 (44.6)	0.002
yes, recreational	397 (42.8)	336 (45.0)	
yes, competitive	58 (6.3)	78 (10.4)	
Sport category *n(%)*			
endurance	237 (54.0)	224 (56.0)	0.558
strength	202 (46.0)	176 (44.0)	
Sport type *n(%)*			
individual	375 (83.5)	313 (76.9)	0.015
group	74 (16.5)	94 (23.1)	
Daily use of electronic devices			
≤2 hours	462 (49.8)	487 (65.2)	<0.001
>2 hours	465 (50.2)	260 (34.8)	

Studying in the night *n(%)*			
no	389 (42.0)	445 (59.6)	<0.001
yes	538 (58.0)	302 (40.4)	
Watching films before sleep *n(%)*			
no	184 (19.8)	139 (18.6)	0.522
yes	743 (80.2)	608 (81.4)	
Reading paper books before sleep *n(%)*			
no	608 (65.6)	490 (65.6)	0.997
yes	319 (34.4)	257 (34.4)	
Reading e-book before sleep *n(%)*			
no	838 (90.4)	680 (91.0)	0.659
yes	89 (9.6)	67 (0.9)	
Studying on paper before sleep *n(%)*			
no	587 (63.3)	542 (72.6)	<0.001
yes	340 (36.7)	205 (27.4)	
Studying with electronic devices before sleep *n(%)*			
no	604 (65.2)	551 (73.8)	<0.001
yes	323 (34.8)	196 (26.2)	
Playing videogames before sleep *n(%)*			
no	758 (81.8)	652 (87.3)	0.002
yes	169 (18.2)	95 (12.7)	
Other (non electronic) recreational activities *n(%)*			
no	738 (79.6)	620 (83.0)	0.078
yes	189 (20.4)	127 (17.0)	
Communication via chat before sleep *n(%)*			
no	88 (9.5)	99 (13.3)	0.015
yes	839 (90.5)	648 (86.7)	
Visit social network before sleep *n(%)*			
no	81 (8.7)	95 (12.7)	0.008
yes	846 (91.3)	652 (87.3)	
Physical activity before sleep *n(%)*			
no	845 (91.2)	674 (90.2)	0.516
yes	82 (8.8)	73 (9.8)	
Sleep quality after the pandemic *n(%)*			
no change	391 (42.2)	465 (62.2)	<0.001
decreased	392 (42.3)	158 (21.2)	
increased	144 (15.5)	124 (16.6)	

spent using electronic devices during the day and were more used to study by night than their counterparts; they showed higher proportions of those who study, both on paper and screen, play videogames and use chat or social media before sleep. A higher proportion of "poor quality sleepers" reported a decrease in sleep quality related to the pandemic respect to "good quality sleepers".

The results of the regression analysis are shown in Table 3. A better sleep quality seems to be associated with lower age, attending universities in Northern Italy, less time spent on electronic devices in the course of the day, and not being used to study at night.

Discussion

The results of this study highlight that more than half the sample analyzed showed poor sleep quality. The reason for this finding could be detected in the characteristics of the population studied. In fact, the student's transition to university is marked by changes in living conditions, increased responsibilities, and social obligations that can affect sleep (32,33). Furthermore, even though evidence on this issue is not consistent and comes mainly from correlational, and not experimental, studies, sleep can be influenced by numerous sociocultural factors, such as sleeping arrangements, evening mealtimes, and leisure

Table 3 - Results of the regression analysis performed considering good sleep quality as outcome.

Variable	Odds Ratio (CI95%)	p value
Age		
≤23 years	1.550 (1.139-2.108)	0.005
>23 years	*Reference*	
Gender		
female	0.110 (0.007-1.679)	0.112
male	0.202 (0.013-3.112)	0.251
other	*Reference*	
Geographical area		
North	2.386 (1.644-3.464)	<0.001
Center	1.223 (0.846-1.768)	0.285
South	*Reference*	
Diet		
no particular regimen	0.970 (0.715-1.314)	0.843
specific diet	*Reference*	
BMI		
underweight	0.702 (0.421-1.169)	0.174
normal weight	1.108 (0.829-1.481)	0.486
overweight	0.842 (0.583-1.217)	0.361
obese	*Reference*	
Energy drink use		
no	1.311 (0.904-1.902)	0.153
yes	*Reference*	
Cannabis use		
no	1.061 (0.657-1.712)	0.809
yes	*Reference*	
Hallucinogens use		
no	1.981 (0.135-29.099)	0.618
yes	*Reference*	
Smoking habit		
no	1.148 (0.799-1.648)	0.455
yes	*Reference*	
Smoking type		
traditional	0.705 (0.436-1.138)	0.152
other	*Reference*	
MVPA		
≤120 min/week	1.136 (0.831-1.555)	0.424
>120 min/week	*Reference*	
Sport		
no	0.789 (0.510-1.221)	0.288
yes	*Reference*	
Sport type		
individual	0.692 (0.466-1.027)	0.067
group	*Reference*	
Daily use of electronic devices		
≤2 hours	1.849 (1.352-2.529)	<0.001
>2 hours	*Reference*	
Studying in the night		
no	2.006 (1.436-2.802)	<0.001
yes	*Reference*	
Studying on paper before sleep		
no	1.281 (0.891-1.840)	0.181
yes	*Reference*	

Studying with electronic devices before sleep		
no	0.849 (0.601-1.199)	0.353
yes	*Reference*	
Playing videogames before sleep		
no	1.768 (1.161-2.692)	0.008
yes	*Reference*	
Communication via chat before sleep		
no	1.149 (0.687-1.921)	0.596
yes	*Reference*	
Visit social network before sleep		
no	1.138 (0.692-1.871)	0.611
yes	*Reference*	

activities, which can markedly change during the university years (34). In our study, "poor quality sleepers" showed higher proportions of individuals with unhealthy lifestyles, such as uncontrolled diet, low levels of physical activity and of sport participation, and use of tobacco and other substances. This is in line with previous studies suggesting that university students are more likely to engage in risky behaviors and this can negatively impact their sleep quality (16-18). However, the regression analysis confirmed only a few of these associations. In accordance with previous studies, a poorer sleep quality was found to be related with higher age, and then with aging processes, variations in hormones production, and life transitions (10, 35).

Furthermore, in our sample, students attending universities in Southern Italy showed a poorer sleep quality respect to those attending Northern Italian university. In continuity with studies performed on the Italian territory, our findings suggest that the socio-cultural differences existing between Northern and Southern Italy may also influence levels of the youth sleep and well-being, as previously reported in literature (36, 37).

Moreover, according to our research, poorer quality sleepers tend to spend more time using electronic devices during the day and are more likely to study and play videogames before bedtime compared to those who sleep well. Indeed, spending time on screens, particularly before going to bed, can result in various issues including less sleep time, low-quality sleep, and difficulty functioning during the day (38). When considering the relationship between electronic device usage and students' sleep, there are two important factors to keep in mind. The first is the time of device use before bedtime, and the second is the type of media being used. Studies have found that using electronic devices before bedtime can have a more significant impact on sleep quality than the total amount of time spent using them (38). Our study did not find any correlation between watching films or reading papers or e-books before sleep and a poorer sleep quality (39). However, correlations were found with the use of electronic devices for gaming and with the total daily screen time. Further research is necessary to determine how the different types of electronic devices can impact sleep quality. There are different theories regarding the relationship between screen use before bedtime and sleep. One theory is that the light emitted by electronic screens affects sleep, while another suggests that engaging in electronic entertainment before bed can impact sleep (40). Conversely, it should also be considered that students who struggle to sleep may use electronic devices to help them fall asleep at night (40). This could explain why some individuals opt to study using screens, play video games, or use chat or social media before going to bed, as observed in our population. Therefore, the use of electronic devices for recreational or work activities can have positive or negative effects on individual's sleep (38-40).

In order to improve long-term sleep quality and duration, sleep hygiene practices should be recommended, including achieving seven to nine hour of sleep, maintaining a consistent sleep/wake schedule and a regular bedtime routine, engaging in regular exercise, adopting a contemplative practice, avoiding caffeine, alcohol, heavy meals, and light exposure in the afternoon/evening which seem to be associated with fragmented poor-quality sleep (12).

Our study has both strengths and limitations. We believe it is the first of its kind in our country, as it has investigated sleep behaviors in a wide range of students from different degree courses at universities in Northern, Central, and Southern Italy. However, the universities were chosen by

convenience, not randomly, so the sample cannot be considered representative of the entire undergraduate population in Italy. Additionally, students were asked to participate during their classes, which means those who were absent may not have been informed about the study, although we asked participants to share the link among their peers. Even the high number of female participants in our sample (71.3%), which exceeds the proportion registered in the corresponding undergraduate population (58.5%), may be due to a higher participation in classes by female students. Therefore, the different gender distribution between sleep quality groups should be considered with caution, also because it did not find evidence in the regression analysis. Furthermore, the data were collected through an electronic questionnaire and self-reported, which may have resulted in some inaccuracies. Lastly, since the aim of this study was limited to ascertaining potential factors contributing to sleep quality, possible pathological profiles were not investigated in depth through specific scales as in previous experiences (28). Considering the relationship between sleep and mental health, this aspect should be investigated in future research.

A further consideration should be done regarding the COVID-19 pandemic. In the questionnaire, we asked participants to express their perception of possible changes that occurred in their sleep quality following the pandemic. The results are in line with other investigations performed in the same population and suggest the possible impact of changed behaviors on people's sleep habits (24,25,41). However, due to the cross-sectional design of the study and the need to contain the length of the questionnaire, it was not possible to perform a pre-post pandemic comparison and to study in depth these changes and their possible determinants. The effects of the COVID-19-related social and behavioral modifications on sleep quality should therefore be analyzed in the future.

Conclusions

In agreement with recent research, the results of this study suggest that sociocultural and behavioral factors are related with undergraduates' sleep quality. In particular, it appears that sleep quality of Italian undergraduates can be related with geographical area and use of electronic devices. However, due to the cross-sectional nature of our investigation, detailed experimental studies are needed to confirm or reject these associations. Anyway, the poor sleep quality shown by a great proportion of the sample highlights the opportunity to increase the students' awareness on the role of sleep quality in health maintenance and on the impact that some behaviors may have on sleep. In a public health perspective, this could lead individuals to improve their sleep quality and prevent possible associated disorders.

Riassunto

La qualità del sonno negli studenti universitari italiani: lo studio multicentrico UnSleep

Background. Le evidenze scientifiche dimostrano che una scarsa qualità del sonno può portare a diversi problemi di salute. Questo studio aveva lo scopo di indagare i patterns del sonno in un campione di studenti universitari italiani e a identificare fattori che potrebbero contribuire alla sua qualità.

Disegno dello studio. Studio trasversale.

Metodi. Un questionario elettronico riguardante caratteristiche socio-demografiche, stili di vita e abitudini legate al sonno, che includeva anche le domande del questionario Pittsburgh Sleep Quality Index (PSQI), è stato distribuito tra gennaio 2022 e luglio 2023 tra gli studenti appartenenti a 12 università situate nel nord, centro e sud Italia.

Risultati. Su un totale di 1674 questionari raccolti, i partecipanti (età media 24,06±4,56 anni, 71,3% F) hanno riportato un numero medio di ore di sonno notturno pari a 6,89±1,28 ore. 927 intervistati (54,6%) hanno mostrato una scarsa qualità del sonno (PSQI >5). L'analisi di regressione ha mostrato che una migliore qualità del sonno è associata ad un'età più bassa, alla frequenza delle università del Nord Italia, al minor tempo trascorso davanti ai dispositivi elettronici durante il giorno, al non essere abituati a studiare di notte e a non giocare ai videogiochi prima di dormire.

Conclusione. Dal punto di vista della salute pubblica, i risultati suggeriscono che gli operatori di sanità pubblica dovrebbero sensibilizzare i giovani sull'importanza della qualità del sonno per mantenere una buona salute, nonché sull'impatto che determinati comportamenti possono avere sul sonno.

References

1. Bin YS. Is Sleep Quality More Important Than Sleep Duration for Public Health?. Sleep. 2016 Sep;**39**(9):1629-1630. https://doi.org/10.5665/sleep.6078. Epub 2016 Aug 19. PMID: 27568809; PMCID: PMC4989250.
2. Krystal AD, Edinger JD. Measuring sleep quality. Sleep Med. 2008 Sep;**9**(Suppl 1):S10-7. doi: 10.1016/S1389-9457(08)70011-X. PMID: 18929313.
3. Ohayon M, Wickwire EM, Hirshkowitz M, Albert SM, Avidan A, Daly FJ, et al. National Sleep Foundation's sleep quality recommendations: first report. Sleep Health. 2017 Feb;**3**(1):6-19. https://doi.org/10.1016/j.sleh.2016.11.006. Epub 2016 Dec 23. PMID: 28346153.
4. Hertenstein E, Feige B, Gmeiner T, Kienzler C, Spiegelhalder K, Johann A, et al. Insomnia as a predictor of mental

disorders: A systematic review and meta-analysis. Sleep Med Rev. 2019 Feb;**43**:96-105. https://doi.org/10.1016/j.smrv.2018.10.006. Epub 2018 Nov 16. PMID: 30537570.
5. Sivertsen B, Hysing M, Harvey AG, Petrie KJ. The Epidemiology of Insomnia and Sleep Duration Across Mental and Physical Health: The SHoT Study. Front Psychol. 2021 Jun 14;**12**:662572. https://doi.org/10.3389/fpsyg.2021.662572. PMID: 34194368; PMCID: PMC8236531.
6. Scott AJ, Webb TL, Martyn-St James M, Rowse G, Weich S. Improving sleep quality leads to better mental health: A meta-analysis of randomised controlled trials. Sleep Med Rev. 2021 Dec;60:101556. doi: 10.1016/j.smrv.2021.101556. Epub 2021 Sep 23. PMID: 34607184; PMCID: PMC8651630.
7. Huang T, Mariani S, Redline S. Sleep Irregularity and Risk of Cardiovascular Events: The Multi-Ethnic Study of Atherosclerosis. J Am Coll Cardiol. 2020 Mar 10;**75**(9):991-999. https://doi.org/10.1016/j.jacc.2019.12.054. PMID: 32138974; PMCID: PMC7237955.
8. Knutson KL, Van Cauter E. Associations between sleep loss and increased risk of obesity and diabetes. Ann N Y Acad Sci. 2008;**1129**:287-304. https://doi.org/10.1196/annals.1417.033. PMID: 18591489; PMCID: PMC4394987.
9. Fang H, Tu S, Sheng J, Shao A. Depression in sleep disturbance: A review on a bidirectional relationship, mechanisms and treatment. J Cell Mol Med. 2019 Apr;**23**(4):2324-2332. https://doi.org/10.1111/jcmm.14170. Epub 2019 Feb 7. PMID: 30734486; PMCID: PMC6433686.
10. Léger D, Bayon V, Ohayon MM, Philip P, Ement P, Metlaine A, et al. Insomnia and accidents: cross-sectional study (EQUINOX) on sleep-related home, work and car accidents in 5293 subjects with insomnia from 10 countries. J Sleep Res. 2014 Apr;**23**(2):143-152. https://doi.org/10.1111/jsr.12104. Epub 2013 Nov 15. PMID: 24237855.
11. Morin CM, Drake CL, Harvey AG, Krystal AD, Manber R, Riemann D, et al. Insomnia disorder. Nat Rev Dis Primers 2015 Sep 3;**1**:15026. https://doi.org/10.1038/nrdp.2015.26. PMID: 27189779.
12. Baranwal N, Yu PK, Siegel NS. Sleep physiology, pathophysiology, and sleep hygiene. Prog Cardiovasc Dis. 2023 Mar-Apr;**77**:59-69. https://doi.org/10.1016/j.pcad.2023.02.005. Epub 2023 Feb 24. PMID: 36841492.
13. Becker SP, Jarrett MA, Luebbe AM, Garner AA, Burns GL, Kofler MJ. Sleep in a large, multi-university sample of college students: sleep problem prevalence, sex differences, and mental health correlates. Sleep Health. 2018 Apr;**4**(2):174-181. https://doi.org/10.1016/j.sleh.2018.01.001. Epub 2018 Feb 21. PMID: 29555131; PMCID: PMC5863586.
14. Lemma S, Gelaye B, Berhane Y, Worku A, Williams MA. Sleep quality and its psychological correlates among university students in Ethiopia: a cross-sectional study. BMC Psychiatry. 2012 Dec 28;**12**:237. https://doi.org/10.1186/1471-244X-12-237. PMID: 23270533; PMCID: PMC3554495.
15. Li W, Yin J, Cai X, Cheng X, Wang Y. Association between sleep duration and quality and depressive symptoms among university students: A cross-sectional study. PloS One. 2020 Sep 11;**15**(9):e0238811. https://doi.org/10.1371/journal.pone.0238811. PMID: 32915844; PMCID: PMC7485879.
16. Jahrami H, Dewald-Kaufmann J, Faris MAI, AlAnsari AMS, Taha M, AlAnsari N. Prevalence of sleep problems among medical students: a systematic review and meta-analysis. J Public Health (Berl.). 2020;**28**:605-622. https://doi.org/10.1007/s10389-019-01064-6.
17. Wang L, Qin P, Zhao Y, Duan S, Zhang Q, Liu Y, et al. Prevalence and risk factors of poor sleep quality among Inner Mongolia Medical University students: A cross-sectional survey. Psychiatry Res. 2016 Oct 30;**244**:243-248. https://doi.org/10.1016/j.psychres.2016.04.011. Epub 2016 Jul 19. PMID: 27500455.
18. Zhang L, Zheng H, Yi M, Zhang Y, Cai G, Li C, et al. Prediction of sleep quality among university students after analyzing lifestyles, sports habits, and mental health. Front Psychiatry. 2022 Aug 4;**13**:927619. https://doi.org/10.3389/fpsyt.2022.927619. PMID: 35990068; PMCID: PMC9385968.
19. Hirshkowitz M, Whiton K, Albert SM, Alessi C, Bruni O, DonCarlos L, et al. National Sleep Foundation's sleep time duration recommendations: methodology and results summary. Sleep Health. 2015 Mar;**1**(1):40-43. https://doi.org/10.1016/j.sleh.2014.12.010. Epub 2015 Jan 8. PMID: 29073412.
20. McMahon DM, Burch JB, Youngstedt SD, Wirth MD, Hardin JW, Hurley TG, et al. Relationships between chronotype, social jetlag, sleep, obesity and blood pressure in healthy young adults. Chronobiol Int. 2019 Apr;**36**(4):493-509. https://doi.org/10.1080/07420528.2018.1563094. Epub 2019 Jan 21. PMID: 30663440.
21. Cappuccio FP, D'Elia L, Strazzullo P, Miller MA. Quantity and quality of sleep and incidence of type 2 diabetes: a systematic review and meta-analysis. Diabetes Care. 2010 Feb;**33**(2):414-420. https://doi.org/10.2337/dc09-1124. Epub 2009 Nov 12. PMID: 19910503; PMCID: PMC2809295.
22. Zou P, Wang X, Sun L, Liu K, Hou G, Yang W, et al. Poorer sleep quality correlated with mental health problems in college students: A longitudinal observational study among 686 males. J Psychosom Res. 2020 Sep;**136**:110177. https://doi.org/10.1016/j.jpsychores.2020.110177. Epub 2020 Jun 27. PMID: 32623194.
23. Valenzuela RLG, Velasco RIB, Jorge MPPC, 2nd. Impact of COVID-19 pandemic on sleep of undergraduate students: A systematic literature review. Stress Health. 2023 Feb;**39**(1):4–34. https://doi.org/10.1002/smi.3171. Epub 2022 Jun 24. PMID: 35699687.
24. Franceschini C, Musetti A, Zenesini C, Palagini L, Scarpelli S, Quattropani MC, et al. Poor Sleep Quality and Its Consequences on Mental Health During the COVID-19 Lockdown in Italy. Front Psychology 2020 Nov 9;**11**:574475. https://doi.org/10.3389/fpsyg.2020.574475. PMID: 33304294; PMCID: PMC7693628.
25. Gualano MR, Lo Moro G, Voglino G, Bert F, Siliquini R. Effects of Covid-19 Lockdown on Mental Health and Sleep Disturbances in Italy. Int J Environ Res Public Health. 2020

Jul 2;**17**(13):4779. https://doi.org/10.3390/ijerph17134779. PMID: 32630821; PMCID: PMC7369943.
26. Alghwiri AA, Almomani F, Alghwiri AA, Whitney SL. Predictors of sleep quality among university students: the use of advanced machine learning techniques. Sleep Breath. 2021 Jun;**25**(2):1119-1126. https://doi.org/10.1007/s11325-020-02150-w. Epub 2020 Jul 23. PMID: 32700289.
27. Schmickler JM, Blaschkr S, Robbins R, Mess F. Determinants of Sleep Quality: A Cross-Sectional Study in University Students. Int J Environ Res Public Health. 2023 Jan 23;**20**(3):2019. https://doi.org/10.3390/ijerph20032019. PMID: 36767422; PMCID: PMC9915447.
28. Carpi M, Cianfarani C, Vestri A. Sleep Quality and Its Associations with Physical and Mental Health-Related Quality of Life among University Students: A Cross-Sectional Study. Int J Environ Res Public Health 2022 Mar 1;**19**(5):2874. https://doi.org/10.3390/ijerph19052874. PMID: 35270566; PMCID: PMC8910365.
29. Li Y, Bai W, Zhu B, Duan R, Yu X, Xu W, et al. Prevalence and correlates of poor sleep quality among college students: a cross-sectional survey. Health Qual Life Outcomes. 2020 Jul 1;**18**(1):210. https://doi.org/10.1186/s12955-020-01465-2. PMID: 32611434; PMCID: PMC7329462.
30. Peltzer K, Pengpid S. Nocturnal sleep problems among university students from 26 countries. Sleep Breath. 2015 May;**19**(2):499-508. https://doi.org/10.1007/s11325-014-1036-3. Epub 2014 Jul 14. PMID: 25017741.
31. Curcio G, Tempesta D, Scarlata S, Marzano C, Moroni F, Rossini PM, et al. Validity of the Italian version of the Pittsburgh Sleep Quality Index (PSQI). Neurol Sci. 2013 Apr;**34**(4):511-519. https://doi.org/10.1007/s10072-012-1085-y. Epub 2012 Apr 13. PMID: 22526760.
32. Foulkes L, McMillan D, Gregory AM. A bad night's sleep on campus: an interview study of first-year university students with poor sleep quality. Sleep Health. 2019 Jun;**5**(3):280-287. https://doi.org/10.1016/j.sleh.2019.01.003. Epub 2019 Mar 1. PMID: 31208711.
33. Deforche B, Van Dyck D, Deliens T, De Bourdeaudhuij I. Changes in weight, physical activity, sedentary behaviour and dietary intake during the transition to higher education: a prospective study. Int J Behav Nutr Phys Act. 2015 Feb 15;**12**:16. https://doi.org/10.1186/s12966-015-0173-9. PMID: 25881147; PMCID: PMC4332914.
34. Memon AR, Gupta CC, Crowther ME, Ferguson SA, Tuckwell GA, Vincent GE. Sleep and physical activity in university students: A systematic review and meta-analysis. Sleep Med Rev. 2021 Aug;**58**:101482. https://doi.org/10.1016/j.smrv.2021.101482. Epub 2021 Mar 20. PMID: 33864990.
35. Meers JM, Nowakowski S. Sleep, premenstrual mood disorder, and women's health. Curr Opin Psychol. 2020 Aug;**34**:43-49. https://doi.org/10.1016/j.copsyc.2019.09.003. Epub 2019 Sep 23. PMID: 31610482.
36. Breda M, Belli A, Esposito D, Di Pilla A, Melegari MG, DelRosso L, et al. Sleep habits and sleep disorders in Italian children and adolescents: a cross-sectional survey. J Clin Sleep Med. 2023 Apr 1;**19**(4):659-672. https://doi.org/10.5664/jcsm.10400. PMID: 36661089; PMCID: PMC10071380.
37. Scaioli G, Squillacioti G, Bersia M, Bellisario V, Borraccino A, Bono R, et al. The wellbeing of adolescents and the role of greenness: A cross-sectional study among Italian students. Front Public Health. 2023 Jan 18;**10**:1050533. https://doi.org/10.3389/fpubh.2022.1050533. PMID: 36743191; PMCID: PMC9889974.
38. Otsuka Y, Itani O, Nakajima S, Kaneko Y, Suzuki M, Kaneita Y. Impact of chronotype, insomnia symptoms, sleep duration, and electronic devices on nonrestorative sleep and daytime sleepiness among Japanese adolescents. Sleep Med 2023 Oct;**110**:36-43. https://doi.org/10.1016/j.sleep.2023.07.030. Epub 2023 Jul 29. PMID: 37531897.
39. Peltz JS, Bodenlos JS, Kingery JN, Rogge RD. The role of financial strain in college students' work hours, sleep, and mental health. J Am Coll Health 2019 Aug-Sep;**69**(6):577-584. https://doi.org/10.1080/07448481.2019.1705306. Epub 2020 Jan 15. PMID: 31940259.
40. Li TMH, Chan NY, Li CT, Chen J, Chan JWY, Liu Y, et al. The Associations of Electronic Media Use with Sleep and Circadian Problems, Social, Emotional and Behavioral Difficulties in Adolescents. Front Psychiatry 2022 Jun 9;**13**:892583. https://doi.org/10.3389/fpsyt.2022.892583. PMID: 35757219; PMCID: PMC9218337.
41. Gallè F, Sabella EA, Bianco L, Maninchedda M, Barchielli B, Liguori F, et al. How the COVID-19 Pandemic Has Impacted Daily Life? Assessing the Use of Web Resources for Recreational Activities in the Italian Adult Population. Int J Environ Rese Public Health. 2022 Nov 16;**19**(22):15136. https://doi.org/10.3390/ijerph192215136. PMID: 36429855; PMCID: PMC9690348.

Corresponding author: Federica Valeriani, Department of Movement, Human, and Health Sciences, University of Rome "Foro Italico", Piazza Lauro De Bosis 6, 00135 Rome, Italy
e-mail: federica.valeriani@uniroma4.it

Ann Ig. 2025 Jan-Feb; 37(1): 154-158 doi: 10.7416/ai.2024.2663.

Celebrating Public Health Lives
Marisa Cantarelli, *mater et magistra* of nursing discipline

Marisa Cantarelli, *mater et magistra* della disciplina infermieristica

Rosaria Alvaro[1], Maura Lusignani[2]

Prof. Marisa Cantarelli

[1] *MSN, FESC, FAAN, Full Professor of Nursing Sciences, Tor Vergata University, Rome, Italy*
President of the Italian Society of Nursing Sciences
[2] *MSN, Full Professor of Nursing Sciences, State University of Milan, Italy*

Annali di Igiene : Medicina Preventiva e di Comunità (Ann Ig)
ISSN (print) 1120-9135 ISSN (online) 3035-5559

https://www.annali-igiene.it

On October 5th, we lost Marisa Cantarelli, a Milanese woman, enlightened bourgeois, nurse, Vice Director of the Scuola Universitaria di Discipline Infermieristiche at the University of Milan, and a renowned Italian theorist in Nursing Science. For many of her young students at the University of Milan, she has been *a mater et magistra* of the nursing discipline, and her scientific contribution has spread nationally and internationally, continuing to guide us in the future.

We still remember her firm yet respectful character, when, in Via Sassi, in front of the Basilica of Santa Maria delle Grazie in Milan, she invited Maura to join the Scuola Universitaria di Discipline Infermieristiche. When the young nurse responded that she believed her skills were better suited for hospital management, Cantarelli did not get upset or discouraged, but smiled warmly and said, "Have faith in your abilities and give it a try." Thus a long period of synergy began, during which the student learned from the teacher nursing knowledge and strategies for professional development, in a period of great excitement. Not only did the teacher convey care for researchers and faculty dedicated to science, but she also promoted the values of courage, honesty, healthy ambition, and affection for the new generations in growth.

Cantarelli shared that she left her native city of Milan after World War II, choosing to become a nurse in Rome at the Italian Red Cross in 1950. Facing a challenging hospital environment with wards holding hundreds of patients and no other trained staff besides herself, she began to question how to improve nursing care in Italy.

The memory of the happiest period of her professional career, as Edoardo Manzoni wrote in his eulogy for Marisa Cantarelli, was when she returned to her city and began to catch a daily train to the provincial areas of the Adda region, where a bicycle awaited her. As a public health nurse, she rode through the countryside to care for people in what is now considered cutting-edge practice.

She also told us about her experience at the Nursing School at Magenta Hospital, which she reluctantly left later, to accept a position at the University of Milan, where she would spend the rest of her life. She became Vice Director of the Scuola Universitaria di Discipline Infermieristiche at the University of Milan, which she founded with Professor Giovanardi and managed from 1975 to 1999, collaborating closely with Professor Fara and Deans Professor Scala and Professor Coggi.

From that intense period, her writings remain, preserved in the books called Quaderni della Scuola Universitaria di Discipline Infermieristiche. In the early years of her leadership, Cantarelli distinguished herself in the scientific community by organizing the first Italian conference on the nursing discipline and presenting, for the first time in Italy, a theoretical model of nursing care.

While several Anglo-American theories and conceptual models were already present in the literature and taught at the Schools of Nursing in the 1980s, Italy lacked a theory derived from scientific research and the country's socio-health context. Cantarelli's "Theoretical Model of Nursing Performances" took shape through the studies and research of faculty and students under her guidance, based on the analysis of nursing activities in clinical practice conducted by nurses from various hospital and community settings.

Her idea of starting from clinical practice remains a fundamental aspect of nursing science today and forms the foundation of evidence-based practice. The result of this analysis led to the classification of nursing activities according to the type of nursing care needs. Different nursing care needs were identified in the Model, and coordinated

nursing care actions were established in response to these needs, resulting in specific nursing performances. The Model's application required clinical reasoning to diagnose the need and level of dependency of the person in need, make decisions about the nursing actions to be taken, and evaluate the outcome achieved for the person.

The Model, presented by Cantarelli at conferences and in publications, was adopted as a conceptual framework in the training of nursing degree courses at various Italian universities, where it is still in use today. In clinical practice, it has been implemented as a guide for nursing documentation in hospitals and as a framework for continuing education for nurses. In research, it has been used as a reference framework for identifying the health needs of the population. In nursing management, it has been adopted as a foundation for improving the quality of nursing care in hospitals and in the community. The Model was disseminated nationally and internationally through publications, texts, and conferences.

Cantarelli devoted herself with determination to the University School in Milan, focusing on developing nursing leadership and generating new conceptual frameworks for nursing care related to the functions of care, teaching, management, and research. The nursing leadership role at different levels of the health system was outlined according to the Mintzberg professional model, fostering the establishment of the nursing service in hospitals and the subsequent legislative recognition of its leadership role.

The educational function was realized in the preparation of faculty capable of designing and managing educational programs. However, Cantarelli focused primarily on the evidence from nursing research to demonstrate, within academia, the birth and development of the nursing scientific discipline and the need for its formal recognition among other disciplines. This goal was achieved, with the help of various synergies, through the legislative approval of the first scientific disciplinary sector for nursing sciences.

Cantarelli's students went on to hold significant roles in various areas of leadership, association, and academia. For several years, she frequently reunited them to align and update their knowledge and skills. As her students and faculty, we experienced Cantarelli's firmness, courage, and foresight as a promoter of the cultural and scientific development of the nursing profession, both in universities and national and international associations. Cantarelli dedicated years to research and teaching with an innovative vision always centered on the needs of the people being cared for.

She authoritatively expressed her divergent thinking when facing obstacles to the development of the discipline, posed by both internal and external forces. She was also a member of the Ethics Committee at the University of Milan.

She authored numerous publications and books on nursing sciences throughout her career and beyond. Her students, along with many nurses across our country, remember her university life and beyond with the greatest gratitude for the personal and professional growth she helped them achieve.

In recognition of her contributions, the University of Milan, together with other associations, proposed a prestigious recognition. In 2013, the Rector of the University of Milan awarded her an honorary degree in Nursing and Midwifery for her significant contributions to the field.

In December 2022, the City of Milan awarded her its highest honor, the "Ambrogino d'Oro", for her relentless dedication.

Marisa Cantarelli has left her student Maura, the nursing discipline at the University of Milan, and all nurses with a solid disciplinary, scientific, and cultural legacy, along with a professional life model of great value that will remain in our minds and hearts forever.

Corresponding author: Prof Rosaria Alvaro, Full Professor of Nursing Sciences, Tor Vergata University, Rome, Italy; President of the Italian Society of Nursing Sciences
e-mail: rosaria.alvaro@gmail.com

Addendum by the Editor In Chief of "Annali di Igiene, Medicina Preventiva e di Comunità"

While covering the role of Editor in Chief of this Journal since 1986, I will never forget that I spent quite a long period of my professional life at the State University of Milan, as a student from 1952 to 1958, and as a Faculty member, with growing roles, in the Medical School, from 1959 until 1986. After 1970, as "second Chair" of Hygiene, I helped my mentor, Prof Augusto Giovanardi, Director, and Marisa Cantarelli (Deputy Director) in the management of the "Special School in Nursing Disciplines", a teaching organization for nurses with the role of preparing the University to deliver the regular Degrees of first (3 years) and second (2 additional years) level. In 1974 I succeeded as Director, after my mentor's retirement, but always keeping in mind that the director of the school was necessarily a professor in Medicine only because, at that time, there were neither nurses holding a university degree nor a single nurse holding a full professorship: therefore, Cantarelli and myself collaborated very well together also because I left to her entirely – no exceptions - the specific choices regarding the profession. By the way, Cantarelli was not only an outstanding and authoritative nurse, but also a sophisticated mind, as the two authors of the above article, both now full professors of nursing, have explained in a convincing way.

To document the rich and multifaceted mind of Marisa Cantarelli, I remember that she was introduced to, and enthusiastically accepted by, the Soroptimist Club "Milano the Founder" (the first of its kind in Italy), a kind of Rotary Club reserved to Lady-professionals, where she became very active, served as President, and affirmed the professional role of nurses, including the ability of those well trained to manage complex sections of hospital organization, to do research and to offer teaching at university level.

After my move from the State University of Milan to the Sapienza University of Rome in 1986, my place was taken in sequence by two Deans of the Medical School, and their efforts in helping Marisa Cantarelli went on until a series of events took place, which made it really possible for a student to become a university-graduated nurse (University Diploma in 1991); in 2001 the diploma became a three-years university degree (in "nursing", sufficient to practice); and in 2004, adding two years

of advanced courses, opened the "magistral degree" in "nursing sciences", necessary for teaching, research and management and also a pre-requisite for competitions to start the Academic career as University Researcher.

Simultaneously, in the list of disciplined to be thought in the universities, three additional disciplines were added (Nursing science – general, clinical and pediatric: M/45; Nursing sciences in Obstetrics and Gynecology: M/47; Nursing and technical sciences in Neuro-psychiatry and Rehabilitation: M/48), and for owners of the the magistral degree the possibility to compete for the positions of Researcher, and later of Associate and Full Professor.

Therefore, at the opening of the new millennium, the "long march" of nurses reached the finish line, transforming them from passive executors of orders given by medical doctors, to independent professionals, with their own baggage of competencies, ready to cooperate with the medical components in the interest of the patients. Prepared until now in the Schools of Medicine (but where Specialization Courses, Masters and PhDs in Nursing already exist), we expect nurses to move to Schools of Nursing, where only Researchers, Associate and Full Professors of Nursing will be active, teaching not only in regular courses, but also in their Masters and PhDs. The biggest criticality, now, regards the number of such figures in the Italian Universities, that is still outrageously low: within MED/45, full professors are just 10, associate professors 32, Reserchers 40; for MED/47, respectively, 0, 2, 3; for MED/48: 8, 16, 23. Less than one specific teacher per course, in the whole Italy!

All of us are aware that a large part of the merit of the happy end goes to women like Marisa Cantarelli, who strongly believed in the theory and practice of nursing, who were successful in imposing their vision in the panorama of public health of our Country; but – irony of fate! – Marisa Cantarelli never obtained a University Degree in Nursing nor servede in the University as an Associate of Full Professor, because she retired due to age before such degrees were opened and the professorships in Nursing were established. Fortunately, this anomaly was cancelled by the Rector of the University of Milan, who in 2013 awarded Marisa Cantarelli an honorary degree.

At the end of this paper, we hope to have contributed to adequately celebrate the profile of Marisa, a great nurse and a woman of science, an example for all those who aspire to follow this noble profession.

As Saint Paul stated at the end of his life (2 Timothy 4:7), Marisa, at the end of yours, you can say that "you have fought - and won - the good fight, you have finished the race, and you have kept - intact - your faith".

Gaetano M Fara, MD, MPH, PhD
Professor Emeritus
School of Medicine, Sapienza University of Rome, Italy
e-mail: gaetanomaria.fara@uniroma1.it