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Contents

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Migration and infectious disease risk: knowledge and perception among university students in two European countries

Domitilla Marconi[1,2], Virginia Casigliani[1], Sara Mazzilli[1], Lara Tavoschi[1], Pier Luigi Lopalco[3]

Keywords: Migrants; communicable diseases; stigma; healthcare students; professional education
Parole chiave: Malattie infettive; salute dei migranti; stigma; determinante di salute; percezione del rischio infettivo; studenti di area sanitaria

Abstract

Background. *In the past years, migration has increasingly affected the European continent. The concerns of the local population about infection spread by migrants may increase as an unjustified stigma. Our study aimed to assess the knowledge and risk perception of infectious disease associated with migration among university students.*
Methods. *Between January and February 2020, we conducted an online survey in Italian and Spanish University students. We collected data on demographics, perception, and knowledge of infectious diseases associated with migration. We performed descriptive and risk factors analysis to assess the association among selected variables.*
Results. *We collected 1,397 answers, 73.16% from Italian students and 26.84% from Spanish students, 34.54% and 38.67% enrolled in healthcare degrees, respectively. We found a statistically significant correlation between the knowledge of infectious diseases and the perception of the infectious risk associated with migration, not confirmed for the area of study. Healthcare students had the best levels of knowledge and perception of the migratory phenomenon, but the higher perception of infectious risk. Exposure to the media coverage about migration was associated with the worst perception of the migratory phenomenon and infectious risk.*
Conclusion. *Our study showed that, despite healthcare students had the best levels of knowledge, they had the highest risk perception of infectious diseases associated with migration. The inclusion of courses on migration medicine in current healthcare curricula and the increase of practical training could help to avoid the development of biased approaches towards migrants among healthcare professionals.*

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Introduction

Europe, particularly the European Union (EU), represents one of the most historically sought-after destinations for migrants. In recent years, the migration phenomenon has gained increasing significance, with estimates indicating that by 2017, the immigration rate had surpassed the emigration rate in the EU (1). Nowadays, migrants constitute at least 10% of the EU population (2).

Southern Europe, notably Italy and Spain, is significantly impacted by irregular migration via sea and land routes, a topic widely debated in public discussions and extensively covered by national media outlets (3). Media coverage often perpetuates prejudices against migrants, contributing to the increasing concerns regarding the potential transmission of infectious diseases (4). Refugees and migrants frequently find themselves ending their journeys in marginalised urban areas, where they are perceived as a matter of emotional security (4,5). They are commonly viewed as competing with citizens for employment opportunities and social services, thus exacerbating xenophobic sentiments and anti-migrant attitudes. This current situation has influenced migrant health policies, which typically prioritise the health of the resident population and aim to prevent the importation of infectious diseases from abroad, neglecting the health needs of migrants (5).

However, literature indicates that infections in migrants have marginal public health implications for European countries' populations. Indeed, the unprecedented arrival of a considerable number of refugees and migrants in the last decade has not been associated with significant outbreaks of infectious diseases (6).

This is partly due to the limited interaction between migrants and the host population. On the contrary, data suggest that an increase in disease transmission is often observed among refugees and migrants, who often suffer from low vaccination coverage (7-9).

Available data indicate that foreign individuals often arrive in a state of good health, sometimes surpassing that of the host population, a phenomenon defined in literature as the "healthy migrant effect" (10). Their health tends to decline after their arrival in the destination country, referred to as the "exhausted healthy migrant effect", due to poor living conditions and suboptimal social integration. In particular, the limited integration into the host country leads to a state of loneliness and isolation, which inevitably affects the health of migrants (8-11): the stigma towards this population represents a negative health determinant and discrimination is a fundamental cause of negative health outcomes, exacerbating inequalities (12-13). These disparities persist regardless of socioeconomic status, even when adjusting for the latter, indicating that differences in health outcomes remain, primarily attributable to ethnic/racial inequalities (13,14).

Perceived discrimination negatively impacts healthcare-seeking and adherence behaviours among migrants (15-18). On the other hand, health professionals may have unconscious biases towards minorities, affecting the quality of care, doctor-patient communication and professional performance (15, 19-21).

Only recently migrant health emerged as a key issue. Prevention services and access to care by refugees and migrants are recognised as fundamental human rights (22) and prioritising vulnerable populations and at high risk groups in societies is increasingly considered the appropriate public health strategy to achieve global health goals (23).

This study aimed to investigate the perception of the infectious disease risk associated with the migrant population among the university student population residing in Italy and Spain. Secondly, we focused on the perception of risk among students enrolled in healthcare degrees, as they represent the future healthcare workforce.

Methods

1. Data collection and participants

This study is based on two national cross-sectional surveys conducted between January and February 2020. The survey was administered to two cohorts of university students in Italy and Spain, recruited through convenience sampling. The questionnaire was distributed via various online platforms, including undergraduate students' Facebook groups, QRcode posted on the noticeboards within university premises, and via the mailing list of the University of Murcia. The students were invited to participate in an online survey conducted using Google Forms®. The survey included a detailed explanation regarding the purpose and the voluntary nature of the study and clarified that respondents' anonymity was guaranteed.

2. Measurements

The questionnaire development was informed by a narrative synthesis of existing literature on migrants' health and infections, in particular, we referred to the

study by Visalli et al (24) and by Istituto Cattaneo (25). The questionnaire (available in Annex 1) consisted of five parts.

The first part of the questionnaire collected the students' personal information (age, gender, geographical area, field of study). The second and third parts respectively investigated the attitude towards the migrant population and knowledge about the migratory phenomenon. The fourth part explored the knowledge regarding the risks associated with acquiring and/or transmitting infectious diseases by migrants, while the fifth and final part investigated the participants' risk perception.

The survey comprised categorical responses and a 5-point Likert scale (2 levels of agreement, 1 neutral choice, 2 levels of disagreement).

Three questions were designed to investigate the perception of the migratory phenomenon, two with a scoring range of0 to 2 and one with a scoring range of 1 to 3. The total score ranges from 1 to 7, where the higher scores indicate a more negative perception of the migratory phenomenon.

Four questions were designed to assess the perception of the infectious risk associated with migration. Among these, three were scored items on a 5-point Likert scale, while one was a yes/no question. The median of the Likert scale responses was calculated, and an additional point was attributed for a negative answer to the yes/no question. The total score ranges from 1 to 6, where the higher scores indicate a more negative perception of the infectious risk.

A Likert question was included to test the knowledge and perception of infectious risk concerning 6 selected infectious diseases, tuberculosis, meningitis, malaria, HIV/AIDS, tetanus, and scabies. The question stated: "Some infectious diseases have re-emerged in the last ten years due to migration".

Two additional questions were designed to investigate the knowledge of infectious diseases. The total knowledge score ranges from 1 to 7 points, where a higher score corresponds to a worse knowledge of infectious diseases.

The questions used in the scores are reported in the table below (Table 1).

A pilot study was conducted with 10 Italian students purposively selected among researchers' acquaintances. The questionnaire was revised based on their feedback and suggestions.

Data analysis was carried out using the software Stata (version 13.0). We excluded participants who met the following criteria: a) people older than 32 yo; b) people who were not currently enrolled in a university course; c) people who didn't answer the question about the area of study (missing data). We categorised the variable "area of study" into four groups. Following the guidelines of the University of Pisa, we identified "healthcare area", "scientific-non-healthcare area", "non-scientific area" and "other" to include all those respondents who had not indicated the exact course of study.

A descriptive analysis of the main characteristics of the sample was performed. A bivariate analysis was carried out to explore the association between each independent variable and the different outcomes of interest using Wilcoxon-Mann-Whitney or Kruskal-Wallis tests. Then, a univariate analysis was carried out to explore the association between each independent variable and the different outcomes of interest using linear regression. Independent variables, with an association with a p-value less than 0.05 during the univariate analyses, were included in the multivariate linear regression. Lastly, a multivariate linear regression model was constructed to identify factors significantly and independently associated with the following binary outcome variable: "perception of the migratory phenomenon", "perception of the infectious risk associated with the migratory phenomenon" and "knowledge of infectious diseases".

To build multivariate models a manual stepwise variables' selection procedure was used to assess confounding and effect modification. To select the variables included in the models, the Likelihood-ratio test was used. All reported values are two-sided, and a value of $p \leq 0.05$ was used as a threshold for statistical significance for all analyses.

During the study planning period, we checked the requirements of the competent Ethics Committee of the University of Pisa. In accordance with the Ethics Committee's guidelines, the study did not require approval as it did not require the involvement of patients, medical interventions of any sort, or experiments on animals. However, we complied with the principles of informed consent and anonymization: we obtained consent from each respondent following the written explanation of the study's aims and objectives.

Results

1. Sample characteristics

We collected 1,469 (1,086 from Italy and 383 from Spain) answers. After applying the exclusion criteria, we included 1,397 responders in the study: 1,022

Table 1 - Questions used to elaborate the scores "knowledge of infectious diseases", "perception of the migratory phenomenon" and "perception of the infectious risk associated with migration"

Questions used for building the score evaluating the knowledge of infectious diseases		1-7
Have infectious diseases increased over the past 10 years?	Yes, No, I don't know	0-2
Tuberculosis is contagious in all its forms.	Likert scale	1-5
Questions used for building the score evaluating the perception of the migratory phenomenon		1-7
Do immigrants represent a security problem in your country?	Yes, No, I don't know	0-2
Do immigrants affect the unemployment in your country?	Yes, No, I don't know	0-2
How many foreigners do you think are resident on average in your country?	<3%, 3-6%, 6-9%, 9-12%, 12-25%, 25-50%, >50%	1-3
Questions used for building the score evaluating the perception of the infectious risk associated with migration		1-6
Migrations cause the spread of new diseases that were not present in your country before	Likert scale	1-5
Some infectious diseases have re-emerged in the last ten years due to migration: tuberculosis	Likert scale	1-5
Some infectious diseases have re-emerged in the last ten years due to migration: meningitis	Likert scale	1-5
Some infectious diseases have re-emerged in the last ten years due to migration: malaria	Likert scale	1-5
Some infectious diseases have re-emerged in the last ten years due to migration: HIV	Likert scale	1-5
Some infectious diseases have re-emerged in the last ten years due to migration: tetanus	Likert scale	1-5
Some infectious diseases have re-emerged in the last ten years due to migration: scabies	Likert scale	1-5
Serious and contagious diseases are more common in the foreign population than in the resident population (1-5)	Likert scale	1-5
Can migrants living in our city spread diseases and represent a danger to our health?	Yes, No	(+1)

a. Likert scale: 1. Strongly disagree 2. Disagree 3. Neither agree nor disagree 4. Agree 5. Strongly agree.

Table 2 - Frequency distribution (absolute number and percentage) of on Likert scale for each item.

Questions	Strongly disagree		Disagree		Neither agree nor disagree		Agree		Strongly agree		Total	Missing data	
	n	%	n	%	n	%	n	%	n	%	n	n	%
Tuberculosis is contagious in all its forms	406	29.06	324	23.19	454	32.50	152	10.88	61	4.37	1397	0	0
Migrations are the cause of new diseases that were not present in your country before	275	19.69	331	23.69	340	24.34	294	21.05	157	11.24	1397	0	0
Some infectious diseases have re-emerged in the last ten years due to migration: tuberculosis	382	27.36	321	22.99	424	30.37	186	13.32	83	5.95	1396	1	0.07
Some infectious diseases have re-emerged in the last ten years due to migration: meningitis	602	43.19	323	23.17	319	22.88	117	8.39	33	2.37	1394	3	0.21
Some infectious diseases have re-emerged in the last ten years due to migration: malaria	388	27.81	304	21.79	369	26.45	231	16.56	103	7.38	1395	2	0.14
Some infectious diseases have re-emerged in the last ten years due to migration: HIV	670	47.99	286	20.49	289	20.70	102	7.31	49	3.51	1396	1	0.07
Some infectious diseases have re-emerged in the last ten years due to migration: tetanus	802	57.45	242	17.34	278	19.91	53	3.80	21	1.50	1396	1	0.07
Some infectious diseases have re-emerged in the last ten years due to migration: scabies	437	31.33	312	22.37	393	28.17	178	12.76	75	5.38	1395	2	0.14
The health of foreigners improves after they arrive in your country	73	5.23	183	13.11	506	36.25	471	33.74	163	11.68	1396	1	0.07
Serious and contagious diseases are more common in the foreign population than in the population of your country	189	13.54	323	23.14	470	33.67	297	21.28	117	8.38	1396	1	0.07

(73.16%) were Italian (F: 668/1,022, M: 341/1,022, others: 13/1,022) and 375 (26.84%) Spanish (F: 253/375, M: 119/375, others: 3/375). The median age was 24 for Italy and 22 for Spain (range 18 to 32). In Italy, 34.54% of students were pursuing healthcare degrees, 30.92% studied scientific subjects, 34.15% studied non-scientific subjects, and 0.39% did not specify their field of study. In Spain, these percentages were 38.67%, 19.73%, 28.80%, and 12.80%, respectively. The sample included students from various regions of Italy, with 59% from central regions, 27% from southern regions and 14% from northern regions. In Spain, most respondents (73%) came from the region of Murcia, in the South.

Approximately 45% of the sample agreed or strongly agreed that migrants' health improves after r they arrive in Italy or Spain. However, a significant proportion of the sample either did not know if they agreed or gave a neutral answer (36%).

Additionally, almost half of the sample (52.15%) referred exposure to media coverage on infectious diseases among migrant population.

The answers to Likert-scale questions are reported in Table 2.

2. Perception of the migratory phenomenon

In both countries there was a non-negative perception of the migratory phenomenon: approximately 80% of the Italian sample and 77% of the Spanish one had a score lower than or equal to 3/7.

Regarding the area of study, we observed that the students pursuing a healthcare degree had the best perception of the migratory phenomenon. Descriptive data are reported in Table 1 in Annex 2.

The multivariate linear regression analysis showed that female students (Coef. 0.19, p< 0.01), Spanish students (Coef. 0.25, p< 0.01) and students from scientific and non-scientific areas (Respectively Coef. 0.30 and 0.33, p< 0.01) had a worse perception of the migratory phenomenon. Moreover, students with a worse perception of the infectious risk associated with migration also exhibited a worse perception of the migratory phenomenon (Coef. 2.38, p<0.01). Exposure to media coverage related to infectious diseases in the migrant population was associated with a worse perception of the migratory phenomenon (Coef. 0.16, p< 0.01).

3. Perception of the infectious risk associated with migration

Almost half of the sample exhibited a low perception of the infectious risk (47.8%, score 1-2/6). When considering the country, Italian students had a lower risk perception (52.1%) than Spanish students (35.9%).

The perception of infectious risk was highest among healthcare students (48.29%, score 1-2/6).

The multivariate linear regression analysis showed that Spanish students (Coef. 0.16, p < 0.04) had a higher perception of the infectious risk associated with migration. Students from scientific and non-scientific degrees (Respectively Coef. -0.28 and -0.65, p<0.01) had a lower perception of the infectious risk associated with migration when compared with students enrolled in healthcare degrees. A lower level of knowledge of infectious diseases was associated with a higher perception of the infectious risk associated with migration. Students with worse perception of the migratory phenomenon had a higher perception of the infectious risk associated with migration. In addition, exposure to news related to infectious diseases in the migrant population is associated with a higher perception of the infectious risk associated with migration (Coef. 0.31, p < 0,01).

4. Knowledge of infectious diseases

The level of knowledge, as determined by our scoring system, was considered good in almost half of the respondents (51.2% scoring between 1-3/7). Healthcare students had the highest level of knowledge of infectious diseases.

The multivariate linear regression analysis showed that students aged 23-25 years (Coef. -0.28, p< 0.01) had a better knowledge of infectious diseases, while students from scientific and non-scientific areas (Respectively Coef. 0.89 and -0.84, p<0.01) had a worse knowledge of infectious diseases when compared with students who were pursuing a healthcare degree.

Discussion

This study aimed to investigate the perception of the migratory phenomenon and the perception of the infectious risk associated with migration among Italian and Spanish university students.

Existing literature reports that stigma and prejudice negatively affect both the mental and physical health of migrants. Numerous studies have demonstrated the association between perceived discrimination and depression, anxiety, and psychological distress (26), as well as chronic conditions; stigma has been linked to increased mortality rates too (27). In our study,

we found that the majority of the students (79%) had a positive perception of migration (score <4, score 1-7). Additionally, we observed that students with a worse perception of migration had also a higher perception of the infectious risk related to migration. This finding aligns with previous studies reporting an association between perceived infectious risk and stigma (28-29).

This correlation appears particularly strong during infectious disease outbreaks. For instance, during the Ebola outbreak in 2014-2015, an increase in discrimination and stigmatisation episodes against African immigrants (30) was documented in the US.

Data collection for our study took place from January to mid-February 2020, in the very early phase of the COVID-19 pandemic. Although there were no autochthonous cases reported in Italy nor in Spain in that period, the high media coverage may have influenced the risk perception of the study participants. In the first phase of the pandemic, an increase in stigmatizing and discriminating behaviours towards Chinese and Asian-looking individuals was observed (31). However, the survey referenced specific infectious diseases, such as tuberculosis and malaria, which may have limited the impact.

Both a worse perception of migration and a higher perception of the infectious risk associated with migration were found to be associated with exposure to media coverage about infectious diseases in the migrant population. It is now established that the media plays a relevant role in influencing the public opinion towards immigration (32). In addition, social media platforms can exacerbate stigma towards migration, as it happened during the Ebola outbreak, when sensationalized reports spread fast on online platforms and increased fear among the population (30). Several studies have corroborated that social media influences public opinion on the matter of infectious diseases (33).

Around 45% of our sample agreed or strongly agreed that the migrants' health improves after their arrival in Italy or Spain. However, this response was not correlated to the perception of the migratory phenomenon, while it was directly correlated with the risk perception of infectious diseases. This finding may reveal the lack of knowledge of the barriers to access to health services that migrants can experience, such as stigma, legal obstacles, administrative and financial hurdles, low health literacy, language and cultural barriers, and even fear of detention and deportation for irregular migration. The migrant population is heterogeneous, and as a result risks and vulnerabilities often vary among groups of people. Some groups (e.g. refugees) are more vulnerable or marginalized because of their history which affects all aspects of their health. Migratory status is an important determinant of health and a determinant of access to health services that contribute to health outcomes (5).

Almost half of the sample (51.2%) had a good knowledge of infectious diseases (score < 3). As expected, students pursuing a healthcare degree had a higher score than the rest of the respondents. This finding is relevant due to the observed correlation between level of knowledge and risk perception of infectious diseases related to migration, highlighting the importance of fostering knowledge on communicable diseases also among students enrolled in other degrees.

According to a recent study analyzing the health conditions of migrants who landed in Sicily and the perception of the resident population (24), the level of education influences the perception of infectious disease risk associated with migration. In that study, 42.7% of responders believed that migrants represented a danger for their health, whereas in our study only 28.34% of students expressed the same wrong concern. The disproportion among the two studies may be related to the different population sampled, as in the Sicilian study respondents were mainly males, older and few had a university degree. The findings are congruent with the correlation we found between the risk perception and the level of knowledge.

Interestingly, students in the healthcare field, despite having a higher level of knowledge, reported an increased risk perception of infectious diseases associated with migration than students in other fields, however, this heightened risk perception did not translate into a similar perception regarding the migratory phenomenon itself. This may be explained by the fact that their future profession will expose them to a higher risk of acquiring infectious diseases compared with the general population.

Studies investigating knowledge, attitude and perception among medical students toward patients living with HIV or HCV have shown that students with higher knowledge about the disease tend to have a better attitude toward visiting patients. It is evident that there is a need to increase education on infectious diseases in order to reduce the stigma and negative attitudes (34,35).

Furthermore, a study conducted among Polish medical students in the fifth grade showed that a period

of training with HIV patients reduced the fear of being infected and improved the confidence in relationships with patients (36).

The planning of targeting training activities is crucial to reduce the risk perception and to establish a better doctor-patient relationship (36). This is particularly relevant to assure equity in healthcare. According to the literature, preconceived ideas based on prejudice and stereotypes among healthcare workers may affect their behaviours towards migrants with consequences on diagnostic services and care access (20, 37-39).

Among Spanish students we observed a poorer perception of the migratory phenomenon and higher perception of risk towards infectious disease. The socio-cultural context may have contributed to these results, however further studies need to be carried out to thoroughly understand these differences.

A limitation of our study is the uneven number of respondents across the two countries, preventing more detailed analysis of convergences and differences between the two populations. Furthermore, because of the snowball sampling method used, a selection bias is present, and the sample could not be representative of the national populations. In addition, despite the exclusion criteria adopted, we cannot completely exclude the presence of individuals of the same age group who are not enrolled in university. Despite conducting an extensive literature review, we were unable to identify a validated questionnaire that adequately addressed the specific needs and objectives of our study. Consequently, we developed our own questionnaire.

To the best of our knowledge, this is the first study to investigate the perception of the risk of infectious diseases associated with migration among undergraduates. Of particular interest is the perception and attitude of healthcare students, for whom it is necessary to plan tailor-made educational interventions.

Conclusions

In conclusion, our study showed that university students generally have a positive perception of the migration phenomenon. A higher risk perception of infectious diseases was observed among students pursuing a healthcare degree, despite their higher level of knowledge of infectious diseases. To address the gap between knowledge and perception, we believe it is necessary to introduce changes in the educational curriculum of the health areas, incorporating education about human rights, equity, sensitivity to diversity and reflecting on the inclusiveness of the health services. Other university courses could also benefit from including these topics in their curricula. Furthermore, as demonstrated in previous studies, increasing the time that healthcare areas' students dedicate to practical training in hospital and social services, such as outpatient services for people in vulnerable situations, could help reduce their heightened perception of risk regarding the transmission of infectious diseases.

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Riassunto

Fenomeni migratori e rischio infettivo: percezione, attitudini e conoscenze in due coorti di studenti universitari italiani e spagnoli

Introduzione. Negli ultimi anni il fenomeno migratorio ha interessato sempre più il continente europeo. Lo stigma nei confronti di questa minoranza e la xenofobia hanno alimentano le preoccupazioni della popolazione residente circa il rischio di trasmissione di malattie infettive dai migranti ai residenti. I migranti, tuttavia, solitamente arrivano in Europa in uno stato di buona salute. Lo stigma nei loro confronti è assimilabile ad un determinante di salute.

Metodi. Tra gennaio e febbraio 2020 abbiamo condotto un sondaggio online in due coorti di studenti universitari in Italia e Spagna. Abbiamo raccolto dati circa caratteristiche demografiche, percezione e conoscenza di trasmissione di malattie infettive dalla popolazione migrante alla popolazione residente in questi due Paesi. Per studiare le nostre variabili abbiamo eseguito analisi descrittive e analisi multivariate. Il livello di significatività stabilito è $p < 0,05$.

Risultati. Abbiamo raccolto 1397 risposte, il 73,16% da studenti italiani e il 26,84% da studenti spagnoli, rispettivamente il 34,54% e il 38,67% iscritti a lauree sanitarie. Abbiamo trovato una correlazione statisticamente significativa tra la conoscenza delle malattie infettive e la percezione del rischio infettivo associato alla migrazione, non confermata per l'area di studio. Gli studenti del settore sanitario avevano i migliori livelli di conoscenza e percezione del fenomeno migratorio, ma la percezione del rischio infettivo era più elevata. L'esposizione alla copertura mediatica sulla migrazione è stata associata alla peggiore percezione del fenomeno migratorio e del rischio infettivo.

Conclusioni. Il nostro studio ha dimostrato che gli studenti di

medicina, pur avendo i migliori livelli di conoscenza, hanno la più alta percezione del rischio di malattie infettive associate alla migrazione. L'inclusione di corsi sulla medicina delle migrazioni negli attuali curricula sanitari e l'aumento della formazione pratica potrebbero contribuire a evitare lo sviluppo di approcci stigmatizzanti nei confronti dei migranti tra gli operatori sanitari.

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Annex 1.

Survey

FIRST SECTION

Welcome, below you will be asked to answer a few short questions about the perception of transmission of infectious diseases. The survey is anonymous.

1. Gender: M, F, other

2. Age: 18-22, 23-25, >26

3. University course

4. Region of residence

5. Have infectious diseases increased over the past 10 years? Yes, No, I don't know

SECOND SECTION

Here are some multiple-choice questions with the possibility of marking a single answer. We remind you that the survey is anonymous.

6. Do you feel uncomfortable shaking hands with a person from an African country? Yes, No, I don't know

7. You are in public transport, such as a bus, and the person seated in front of you is a foreigner and coughs. How do you react? I move, it annoys me, I put something to cover my nose and mouth, I don't care

8. Do immigrants represent a security problem in your country? Yes, No, I don't know

9. Do immigrants affect the unemployment in your country? Yes, No, I don't know

THIRD SECTION

10. How many foreigners do you think are living on average in your country?

<3%, 3-6%, 6-9%, 9-12%, 12-25%, 25-50%, >50%

In the next questions, we ask you to give your opinion on a series of affirmations.

Please indicate 1 when you are not agreeing at all with the affirmation and 5 when you are strongly in agreement. Select number 3 when you neither agree nor disagree.

11. Tuberculosis is contagious in all its forms (1-5)

12. Migrations are the cause of new diseases that were not present in your country before (1-5)

13. Some infectious diseases have re-emerged in the last ten years due to migration:

Tuberculosis (1-5)

Meningitis (1-5)

Malaria (1-5)

HIV (1-5)

Tetanus (1-5)

Scabies (1-5)

14. The health of foreigners improves after they arrive in your country (1-5)

15. Serious and contagious diseases are more common in the foreign population than in the resident population (1-5)

16. Can migrants living in our city spread diseases and represent a danger to our health? Yes, No

17. In the last year, have you heard or read any news on media about infectious diseases in the migrant population? Yes, No

Thank you for answering to our survey.

Annex 2.

Table 1 - Perception of migratory phenomenon

	1		2		3		4		5		6		7		
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	N
Country															1,397
Italy	200	19.57	343	33.56	270	26.42	117	11.45	61	5.97	17	1.66	14	1.37	1,022
Spain	10	2.67	123	32.80	158	42.13	34	9.07	31	8.27	13	3.47	6	1.60	375
Gender															1,397
F	114	12.38	288	31.27	313	33.98	107	11.62	62	6.73	21	2.28	16	1.74	921
M	92	20.00	172	37.39	110	23.91	44	9.57	30	6.52	9	1.96	3	0.65	460
other	4	25.00	6	37.50	5	31.25	0	0.00	0	0.00	0	0.00	1	6.25	16
Age															1,397
18-22	69	11.64	199	33.56	198	33.39	67	11.30	36	6.07	14	2.36	10	1.69	593
23-25	85	15.92	181	33.90	158	29.59	59	11.05	37	6.93	9	1.69	5	0.94	534
>26	56	20.74	86	31.85	72	26.67	25	9.26	19	7.04	7	2.59	5	1.85	270
Area of study															1,397
Health care area	96	19.28	179	35.94	124	24.90	51	10.24	31	6.22	10	2.01	7	1.41	498
Non-scientific area	61	13.35	138	30.20	158	34.57	53	11.60	33	7.22	8	1.75	6	1.31	457
Scientific area	52	13.33	132	33.85	126	32.31	40	10.26	24	6.15	9	2.31	7	1.79	390
Others area	1	1.92	17	32.69	20	38.46	7	13.46	4	7.69	3	5.77	0	0.00	52
Knowledge of infectious diseases															1,397
1	34	20.73	72	43.90	35	21.34	14	8.54	6	3.66	2	1.22	1	0.61	164
2	36	21.30	56	33.14	49	28.99	18	10.65	8	4.73	0	0.00	2	1.18	169
3	61	15.93	137	35.77	99	25.85	47	12.27	26	6.79	11	2.87	2	0.52	383
4	53	13.77	130	33.77	123	31.95	44	11.43	28	7.27	3	0.78	4	1.04	385
5	15	8.11	46	24.86	84	45.41	17	9.19	14	7.57	5	2.70	4	2.16	185
6	7	8.86	18	22.78	25	31.65	11	13.92	8	10.13	6	7.59	4	5.06	79
7	4	12.50	7	21.88	13	40.63	0	0.00	2	6.25	3	9.38	3	9.38	32
Perception of infectious risk associated with migration															1,395
1	65	20.44	147	46.23	85	26.73	14	4.40	5	1.57	2	0.63	0	0.00	318
2	84	24.07	125	35.82	100	28.65	26	7.45	8	2.29	4	1.15	2	0.57	349
3	39	10.08	128	33.07	127	32.82	52	13.44	29	7.49	7	1.81	5	1.29	387
4	17	8.46	43	21.39	74	36.82	33	16.42	25	12.44	4	1.99	5	2.49	201
5	5	4.42	19	16.81	35	30.97	22	19.47	20	17.70	11	9.73	1	0.88	113
6	0	0.00	3	11.11	6	22.22	4	14.81	5	18.52	2	7.41	7	25.93	27
Health improvement after arrival															1,396
1	8	10.96	26	35.62	24	32.88	4	5.48	10	13.70	0	0.00	1	1.37	73
2	21	11.48	53	28.96	62	33.88	27	14.75	13	7.10	6	3.28	1	0.55	183
3	82	16.21	158	31.23	167	33.00	54	10.67	30	5.93	10	1.98	5	0.99	506
4	78	16.56	182	38.64	132	28.03	44	9.34	22	4.67	7	1.49	6	1.27	471
5	21	12.88	47	28.83	42	25.77	22	13.50	17	10.43	7	4.29	7	4.29	163
News about infectious diseases in the migrant population															1,396
No	116	17.39	233	34.93	211	31.63	64	9.60	35	5.25	5	0.75	3	0.45	667
Sì	94	12.89	233	31.96	216	29.63	87	11.93	57	7.82	25	3.43	17	2.33	729
Foreigners living in your country															1,397
<6%	210	78.95	28	10.53	21	7.89	2	0.75	5	1.88	0	0.00	0	0.00	266
6-12%	0	0.00	438	72.52	75	12.42	75	12.42	6	0.99	10	1.66	0	0.00	604
>12%	0	0.00	0	0.00	332	63.00	74	14.04	81	15.37	20	3.80	20	3.80	527

Tab 2. Perception of infectious risk associated with migration

	1		2		3		4		5		6		
	n	%	n	%	n	%	n	%	n	%	n	%	N
Country													1,395
Italy	250	24.46	283	27.69	261	25.54	138	13.50	73	7.14	17	1.66	1022
Spain	68	18.23	66	17.69	126	33.78	63	16.89	40	10.72	10	2.68	373
Gender													1,395
F	195	21.2	223	24.24	257	27.93	141	15.33	86	9.35	18	1.96	920
M	119	25.93	124	27.02	124	27.02	58	12.64	26	5.66	8	1.74	459
other	4	25	2	12.5	6	37.5	2	12.5	1	6.25	1	6.25	16
Age													1,395
18-22	120	20.27	146	24.66	180	30.41	86	14.53	47	7.94	13	2.2	592
23-25	119	22.33	137	25.7	139	26.08	83	15.57	47	8.82	8	1.5	533
>26	79	29.26	66	24.44	68	25.19	32	11.85	19	7.04	6	2.22	270
Area of study													1,395
Healthcare area	95	19.11	145	29.18	111	22.33	74	14.89	55	11.07	17	3.42	497
Non-scientific area	130	28.45	102	22.32	132	28.88	63	13.79	26	5.69	4	0.88	457
Scientific area	83	21.34	93	23.91	122	31.36	58	14.91	28	7.20	5	1.29	389
Others area	10	19.23	9	17.31	22	42.31	6	11.54	4	7.69	1	1.92	52
Knowledge of infectious diseases													1,395
1	53	32.32	53	32.32	32	19.51	13	7.93	7	4.27	6	3.66	164
2	61	36.09	43	25.44	36	21.3	15	8.88	14	8.28	0	0	169
3	90	23.56	116	30.37	87	22.77	52	13.61	32	8.38	5	1.31	382
4	71	18.49	81	21.09	140	36.46	69	17.97	22	5.73	1	0.26	384
5	26	14.05	35	18.92	72	38.92	29	15.68	16	8.65	7	3.78	185
6	10	12.66	16	20.25	18	22.78	15	18.99	17	21.52	3	3.8	79
7	7	21.88	5	15.63	2	6.25	8	25	5	15.63	5	15.63	32

Tab 3. Knowledge of infectious disease

	1		2		3		4		5		6		7		
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	N
Country															1,397
Italy	124	12.13	134	13.11	277	27.10	296	28.96	123	12.04	47	4.60	21	2.05	1,022
Spain	40	10.67	35	9.33	106	28.27	89	23.73	62	16.53	32	8.53	11	2.93	375
Gender															1,397
F	106	11.51	109	11.83	246	26.71	244	26.49	130	14.12	62	6.73	24	2.61	921
M	55	11.96	58	12.61	135	29.35	136	29.57	53	11.52	16	3.48	7	1.52	460
other	3	18.75	2	12.50	2	12.50	5	31.25	2	12.50	1	6.25	1	6.25	16
Age															1,397
18-22	51	8.60	66	11.13	156	26.31	169	28.50	97	16.36	41	6.91	13	2.19	593
23-25	83	15.54	69	12.92	147	27.53	142	26.59	56	10.49	27	5.06	10	1.87	534
>26	30	11.11	34	12.59	80	29.63	74	27.41	32	11.85	11	4.07	9	3.33	270
Area of study															1,397
Healthcare area	123	24.70	77	15.46	147	29.52	80	16.06	36	7.23	20	4.02	15	3.01	498
Non-scientific area	19	4.16	54	11.82	119	26.04	146	31.95	84	18.38	29	6.35	6	1.31	457
Scientific area	15	3.85	36	9.23	99	25.38	149	38.21	57	14.62	24	6.15	10	2.56	390
others area	7	13.46	2	3.85	18	34.62	10	19.23	8	15.38	6	11.54	1	1.92	52
Perception of the migratory phenomenon															1,397
1	34	16.19	36	17.14	61	29.05	53	25.24	15	7.14	7	3.33	4	1.90	210
2	72	15.45	56	12.02	137	29.40	130	27.90	46	9.87	18	3.86	7	1.50	466
3	35	8.18	49	11.45	99	23.13	123	28.74	84	19.63	25	5.84	13	3.04	428
4	14	9.27	18	11.92	47	31.13	44	29.14	17	11.26	11	7.28	0	0.00	151
5	6	6.52	8	8.70	26	28.26	28	30.43	14	15.22	8	8.70	2	2.17	92
6	2	6.67	0	0.00	11	36.67	3	10.00	5	16.67	6	20.00	3	10.00	30
7	1	5.00	2	10.00	2	10.00	4	20.00	4	20.00	4	20.00	3	15.00	20
Perception of the infectious risk associated with migration															1,395
1	53	16.67	61	19.18	90	28.30	71	22.33	26	8.18	10	3.14	7	2.20	318
2	53	15.19	43	12.32	116	33.24	81	23.21	35	10.03	16	4.58	5	1.43	349
3	32	8.27	36	9.30	87	22.48	140	36.18	72	18.60	18	4.65	2	0.52	387
4	13	6.47	15	7.46	52	25.87	69	34.33	29	14.43	15	7.46	8	3.98	201
5	7	6.19	14	12.39	32	28.32	22	19.47	16	14.16	17	15.04	5	4.42	113
6	6	22.22	0	0.00	5	18.52	1	3.70	7	25.93	3	11.11	5	18.52	27

Health improvement after arrival														1,396
1	16	21.92	14	19.18	15	20.55	19	26.03	4	5.48	1	1.37	4	5.48	73
2	21	11.48	25	13.66	43	23.50	46	25.14	34	18.58	12	6.56	2	1.09	183
3	53	10.47	62	12.25	146	28.85	149	29.45	59	11.66	30	5.93	7	1.38	506
4	50	10.62	50	10.62	128	27.18	143	30.36	70	14.86	20	4.25	10	2.12	471
5	24	14.72	18	11.04	50	30.67	28	17.18	18	11.04	16	9.82	9	5.52	163
News about infectious diseases in the migrant population															1,396
No	61	9.15	86	12.89	175	26.24	215	32.23	90	13.49	28	4.20	12	1.80	667
Sì	103	14.13	83	11.39	207	28.40	170	23.32	95	13.03	51	7.00	20	2.74	729
Foreigners living in your country															1,397
<6%	40	15.04	45	16.92	79	29.70	71	26.69	20	7.52	7	2.63	4	1.50	266
6-12%	85	14.07	76	12.58	178	29.47	162	26.82	70	11.59	21	3.48	12	1.99	604
>12%	39	7.40	48	9.11	126	23.91	152	28.84	95	18.03	51	9.68	16	3.04	527

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Quality information and fake news on Covid-19 and immunization among adolescents: a qualitative analysis in school settings

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Keywords: Fake news; Covid-19; immunization; adolescents
Parole chiave: Fake news; Covid-19; immunizzazione; adolescenti

Abstract

Background. *Correct information is an essential tool to guide thoughts, attitudes, daily choices or more important decisions such as those regarding health. Today, a huge amount of information sources and media is available. Increasing possibilities of obtaining data also require understanding and positioning skills, particularly the ability to navigate the ocean of information and to choose what is best without becoming overwhelmed.*
Objective. *In the present study, focus group methodology has been used as a survey instrument in a school setting in order to study the knowledge, preconceptions, and attitudes of students toward vaccination practice, to promote favourable and knowledgeable attitudes about vaccination and counteract the spread of fake news.*
Material and methods. *In an educational institution in Apulia in March 2023, 2 focus group sessions were conducted with students as part of an educational project. The selected sample of 23 students was divided into two groups consisting of 12 and 11 participants each, respectively, chosen through the probabilistic method. The knowledge and attitude baseline was assessed through a structured questionnaire at the start of the day. Then, before the focus group sessions, the first group (A) was exposed to an informative video conducted by an expert on the topic of vaccination and fake news, while the second group (B) attended a frontal lesson on the same issues. The guiding questions that the moderators considered in both groups for the topic of vaccination investigated the importance, the usefulness of vaccines, and the trust in political authorities.*
Results. *The responses to the initial questionnaire revealed high variability among the two groups, although they were randomly selected. Transcripts of the dialogues were categorized by ATLAS.ti into 204 total codes and 87 categories, then combined to form increasingly generic categories that were united by related themes. It was developed in a specific model of favouring and hindering factors divided into 4 thematic domains specially adapted to the school context: perception of disease risk, emotional aspects, beliefs about the vaccine, and attitudes toward fake news.*
Discussion. *The category "Fake News" with 97 mentions turns out to be the most discussed by students within all the explored domains. Adolescents have a greater attitude to be overcome by conspiracy theories, probably because they are more exposed to online news. We could detect a generalised sense of confusion with respect to the communication of the pandemic period that emphasised, in many of them, prior perplexities. Public health policies, criticised by the participants, led them to develop a sceptical and conspiratorial attitude toward the authorities, claiming economic interests behind some management choices. "Emotions," with 63 quotes, confirmed the strong impact of the emotional sphere, multifaceted and diverse, on adolescents' personal experience during the pandemic.*
Conclusions. *The results suggest that a single intervention (video or lesson) is not able to change attitudes and thinking tendencies of the adolescents examined. In addition, the leader figure present in both groups, was found to influence, in both study conditions (group A and group B), students' opinions, especially on the issue of fake news, more than a short-term intervention.*

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Introduction

Correct information is an essential tool to guide our thoughts, attitudes, everyday choices or more important decisions such as those that protect our health.

Today, we have within reach a vast number of information sources and means of communication, which greatly increase the possibility of obtaining data but also require understanding and positioning skills, in particular the ability to navigate the ocean of information and choose what is best without becoming overwhelmed. Such an aptitude may be easier to develop in the presence of specific expertise in a subject matter. On the other hand, it may prove alienating in front of an uncritical attitude on what the net conveys.

In fact, most of the content circulating on the Internet is approximate, if not false. These are the so-called hoaxes or fake news, which are often deviant and spread exponentially through the net, shifting public opinion towards the goals of partisan interests, and not always to the protection of the community (1).

This is the case with information on the COVID-19 pandemic and vaccinations, complex topics that involve people's emotional state and economic impact and thus can be the target of manipulation efforts by specific groups with vested interests. For this reason, field studies can be useful to identify current information gaps, ideas, health literacy levels, habits, concerns and motivations within local target groups.

In school settings, it is important to provide tools and content to correctly communicate the importance of vaccinations and counteract fake news.

In the present study, focus group (FG) methodology was chosen as an instrument useful to observe knowledge, preconceptions and attitudes towards vaccination practice among students, to promote a favourable and aware attitude towards vaccination and to counteract the spread of fake news.

The FG methodology was chosen precisely because of its characteristics, since it is based on the social interaction of the participants and considers the group as a vehicle for the transmission of information, role awareness and cultural growth. Within each group, in fact, personal opinions are not solely the result of individual reflections but derive from collective discussion and comparison with other group members (2).

FG research is a type of qualitative data collection study designed to gather information beyond the scope of quantitative analysis. In this type of technique the social actors are not considered as mere sources of information, but as protagonists of the research, able to jointly elaborate a vision of the phenomenon under investigation.

This crucial aspect represents the first important feature of the method and, for this reason, differs from traditional group interviews where interaction takes place from time to time between the participants and the moderator.

FGs can be applied to different research contexts, especially those with a low degree of structuration, and their conduct can be useful to detect complex opinions, delve into the positive and negative aspects of a phenomenon and explore attitudes, opinions and expectations.

It is a particularly useful method for exploring in depth the opinions, attitudes or behaviour of a community and examining the attitudes underlying human thought and behaviour (3).

Starting from the assumption that the acceptance of infectious disease prevention methods is influenced by proper communication, the aim of this work was to detect, by means of FG analysis, the effects of a short informational-scientific, technological (video) or traditional (lecture) intervention on the opinion of a class of students with respect to the topics of 'vaccination' and 'fake news'.

Materials and methods

In a school in Apulia in March 2023, two FG sessions were conducted with students belonging to the same class. The FG sessions were part of an educational project performed by the school teachers and approved by the School Council and involved a class group recruited on voluntary basis among the classes of the 5th grade. Before the start, all student were informed about the content of the project by their teachers. In addition, before each FG session, all participants were provided with a written form containing a detailed description of the method and information on the use of personal data. The signed form were given back and saved by the teachers. No personal data were collected and analysed by the researchers.

The selected sample of 23 students was randomly divided, by the means of a simple draw system, into two groups, group A of 12 (including 3 males) and group B of 11 (including 4 females) participants. A standard, close-ended questionnaire was distributed to the students in order to collect the overall attitude of

the students regarding vaccines and fake news.

Each FG included the presence of a moderator supported by an observer with the task of ensuring legitimate outcomes and reducing bias in the discussions. Group A was conducted at the end of the exposure to an informative video conducted by an expert on the topic of vaccinations and fake news. Group B attended a short lecture by the teacher followed by a discussion on the same topics.

The guiding questions that the moderator considered in both groups for the topic of vaccinations investigated the importance and usefulness of vaccines and trust in political authorities (Are vaccines important? Are vaccines useless or dangerous? Do you suspect that they do not tell us the whole truth about vaccines?).

The total duration of the focus groups, during which the students were able to freely discuss the various topics proposed at the table, was respectively 1 hour and 20 minutes for group A and 1 hour and 10 minutes for group B.

A self-administered questionnaire was distributed to each participant after the FG sessions in order to evaluate the perceived quality and collect feedback on the FG experience. Collected information were only relevant for the quality improvement process of the researchers and are not analysed and reported in this paper.

As per standard procedure, all focus group sessions were recorded and transcribed in full, indicating the discussion domain and marking each participant's intervention with an identification number from 1 to 12 for group A and from 1 to 11 for group B.

The transcribed texts were then imported into the ATLAS.ti software which, exploiting artificial intelligence (AI) technology, performed qualitative content analysis. In ATLAS.ti, categories can be renamed, deleted, grouped and joined together by the experimenters (4).

Data were analysed using inductive thematic analysis (5), which benefits from theoretical flexibility and the ability to categorise, organise and describe students' experiences through the identification of key themes and sub-themes. The transcribed texts were imported into ATLAS.ti software, which also exploited artificial intelligence (AI) technology to perform qualitative content analysis. In ATLAS.ti, categories can be renamed, deleted, grouped and joined together by the experimenters (6). Two researchers independently examined the coding of the texts and further refined it after discussion and consensus. Codes and sub-codes were grouped into themes, ensuring that these were consistent, clear and distinct.

Results

The responses to the initial questionnaire revealed high variability between the groups, although they were randomly selected (Tables 1 and 2).

Transcripts of the dialogues were categorised by ATLAS.ti into 204 total codes and 87 categories, which were then combined to form more and more generic categories with related themes. Ultimately, within the themes, the following 6 macro-categories were identified and analysed:

1. Communication;
2. Emotions;
3. Beliefs;
4. Health Perception;

Table 1 - Results of initial evaluation questionnaire on vaccines (1 = Absolutely not; 10 = Absolutely yes)

How do you evaluate the following statements: We list some hotly debated topics on vaccines, can you give us your opinion?	Average of responses Group A	Average of responses Group B
Vaccines expose you to the risk of even serious side effects	2.75	3.92
Vaccines are important for your health	9.58	9.82
Vaccines are effective	9.33	9.18
Serious side effects from vaccines are often kept hidden	3,75	5,00
Children are given too many vaccinations at once	2.58	3.64
Vaccines protect against little or no serious diseases	6.33	4.91
You feel anxious about getting vaccinated	2.82	1.91
You support the introduction of compulsory vaccination to attend school	6.67	6.45
Achieving full vaccination coverage of the population (over 95%) is necessary to protect the youngest children and the weakest people who cannot be vaccinated	9.8	9.73
Vaccines are above all an economic business for pharmaceutical companies	2.50	3.55

Table 2 - Results of the initial evaluation questionnaire on fake news (1 = Absolutely not; 10 = Absolutely yes)

How do you evaluate the following statements: We list some statements on the topic of fake news, can you give us your opinion?	Average of responses Group A	Average of responses Group B
Fake news poses a health risk	7.83	8.36
Fake news is a problem for democracy	8.25	7.00
Fake news is actually an opportunity to spread opinions that are often kept hidden	2.50	3.36
Fake news poses no risk because it is easy to identify them and not fall into the trap	333	3.73
I think I am not particularly inclined to believe in fake news	7.92	7.91
In my group of friends and acquaintances I often receive news that I later discover is fake news	5.25	5
I have, even unintentionally, spread fake news	2.42	2.18
Governments are the first to take advantage of fake news to cover up inconvenient truths	5.08	3.18
It is difficult to label news as fake news because there are no absolute truths	3.83	4.27
Every time I read something that has to do with my health I check what the source of the information is	9.67	8.73

5. Digital Literacy;
6. Personal experiences.

The knowledge, preconceptions and attitudes towards vaccination practice and fake news of the 23 secondary school students included in the study were framed in a model of favourable and hindering factors divided into 4 thematic domains specifically adapted to the school context (Table 3). The questions and topics addressed during the discussion sessions have been summarised in Table 4.

1. Beliefs about vaccines

With the questions inherent to this domain, the personal attitudes and prior knowledge with regard to vaccinations were investigated in the two groups of adolescents.

The analysis of the FG transcripts revealed concordant views between the two groups with respect to the experience of each participant:

"Yes, also because of the demonstration that diseases, i.e. vaccines, have improved and changed with time; so if, for example, it took five years to test the vaccine regarding smallpox, as technology improves, the time decreases and the effectiveness of this vaccine also improves, reducing the effects..." (Student 4, group A)

"As was the case with smallpox, it is possible to eradicate the disease. You have to take into account that vaccines have been created for a hundred years, maybe even less. It's right to think of a long-term effect, i.e. the possibility of eliminating certain diseases that are a serious problem at the moment but that may become solutions in the future. That is, there may be a solution to them"(Student 8, Group B).

Table 3 - Tables and Domains

	Domain
1	Perception of disease risk
2	Emotional aspects
3	Beliefs about vaccines
4	Attitudes towards fake news

2. Perception of risk

In relation to the perceived risk of disease, students discussed the importance of prevention in order to reduce the spread of the virus. In particular, within the 'perception of risk' domain, two main themes emerged relating to the perception of the current severity of Covid-19 in the community at large and in the family.

2.1 Perception of the current severity of COVID19 in the community at large

"It is important to get vaccinated in the first place to protect our health and the health of the most fragile people because maybe not everyone has the possibility to get vaccinated for medical reasons. If you go for vaccination, you protect yourself but also the more delicate and fragile people" (Student 8, group B)

2.2 Perception of the current severity of COVID19 in the family

"*If a friend of mine did not want to get vaccinated,*

Table 4 - Discussion Topics

Domain	Question	Discussion points
Beliefs about vaccines	How would you explain the importance of vaccination to a non-present partner? What beliefs have adolescents developed about vaccines?	You consider vaccines important for your health; Vaccines serve to protect the population and especially the weakest.
Perception of disease risk Perception of current severity of COVID19 in the general community and family	What beliefs have adolescents developed with respect to vaccines?	Severity of COVID19 (lethality, severity of illness, impact on absence from school or work) Perception of the current severity of COVID19 in frail individuals; Perception of the importance of diagnosis for setting specific therapy for COVID19.
Emotional aspects	Are vaccines useless or dangerous? What emotions do you feel at the idea of vaccinating yourself?	Children are given too many vaccinations at once; Vaccines protect against diseases that are not serious or have almost disappeared; Fake news poses a health risk; Fake news poses a problem for democracy
Attitude towards fake news What role does fake news play in communication? Do you think you are prone to fall for fake news or have you fallen into the trap of fake news? When you hear statements such as 'they are hiding something from us, who knows what they are injecting us with instead of vaccines', what do you think?	Attitude towards fake news What role does fake news play in communication? Do you think you are prone to fall for fake news or have you fallen into the trap of fake news? When you hear statements such as 'they are hiding something from us, who knows what they are injecting us with instead of vaccines', what do you think?	Fake news poses no risk because it is easy to identify it and not to fall into the trap; Fake news is actually an opportunity to spread opinions that are often kept hidden; Governments are the first to benefit from fake news to cover up inconvenient truths; I believe that I am not particularly inclined to believe in fake news; In my group of friends and acquaintances, I often receive news that I later discover to be fake news.; I have, even unintentionally, spread fake news; It is difficult to label a piece of news as fake news because there are no absolute truths; Whenever I read something that has to do with my health I check what the source of the information is; Serious side effects from vaccines are often kept hidden; Vaccines are primarily an economic business for pharmaceutical companies.

I would tell him to do it to protect not only ourselves, but also the elderly people in our family; for example, our grandparents, who may already have diseases. So our not getting vaccinated could first of all circulate the virus and then attack them as well who could be affected more, because it could also be lethal" (Student 12, Group A).

"It is important to vaccinate in the first place to protect our health and the health of the most fragile people because maybe not everyone has the possibility to vaccinate for medical reasons. If you go for vaccination, you protect yourself but also the more delicate and fragile people. We heard, with regard to the fake news earlier, the talk about the rubella vaccine and everything that happened in the 1990s with regard to the fake news of the autism vaccine, and frankly knowing and having the knowledge about vaccines and perhaps being aware of the vaccine one is going to have, gives us a way to go towards solutions" (Student 8, group B).

Vaccinations therefore represent, for the participants in the two FGs, a benefit not only for the individual but also for the whole community.

3. Emotional aspects

Within the domain under investigation for both groups, mixed feelings of fear of side effects and trust in science predominated.

The emotional impact was multifaceted and diverse with some students reacting to the vaccination practice with proactive and proactive attitudes, while others experienced deleterious effects on their psyche, with anxiety, frustration, inadequacy and loneliness prevailing.

3.1 Fear of the side effects of vaccines

"Vaccines have side effects, so maybe a person can have an important pathology and it can interfere and they might get sick or, even on a genetic level, you might inherit a disease from relatives and, if it hasn't manifested itself yet, one thinks about it more; maybe the vaccine doesn't do anything to me now and later it will, if it's related to a chronic or inherited pathology" (Student 1, Group B).

"Eh look, actually when I did the COVID vaccine, when I went the first time I had to do the first dose, I was fainting before I even went in, because I was afraid...It can happen to one person out of a thousand people, out of billions...maybe I'm just the person, I don't want to!" (Student 9, group A).

3.2 Trust in science

"*I have always done vaccines quietly, without being afraid of anything*" (Student 8, group A).

"In my opinion, we live in a society that is now used to the idea of the vaccine. We know well or badly what side effects we can have. So to me it conveys confidence to get the vaccine because we now know what the side effects can be, which are quite mild" (Student 10, group B).

4 Attitudes towards fake news

This domain explored participants' attitudes towards sources of information (institutional and non-institutional) and views on the government's handling of communication during the Covid-19 pandemic, revealing conspiracy theories and a low sense of trust towards political and health authorities.

The students reported a generalised sense of confusion regarding communication during the pandemic period, which emphasised, in many of them, previous perplexities.

4.1 Possible conspiracy theories

"In my opinion there is always something going on, because you don't know the whole truth anyway..." (Student 6, group A)

"But it was in the first year of the pandemic, but I can say COVID like other viruses. I think we were sort of used to it in that respect anyway. I take the first summer of covid and I take football into consideration; I noticed in the summer that they hid the number of infections within the team, within the club and within the stadiums, in order to restart the league, in order to restart something that would be financially profitable for the clubs" (Student 4 - group A).

"I see it from the other side of the coin, in the sense that they have pushed so much on the seriousness of the virus, on the fact of the deaths, on the fact of the many contagions; you could hear very high numbers on television when Conte was on, talking about the new decrees. In my opinion, they really pushed people to vaccinate to try to reduce the severity". (Student 7, group A).

"Instead, I always wondered, when the quarantine period began, I went to the statistics, to the graph of COVID patients and I saw that from the March period to the June period there were about three thousand deaths a day; when the summer came, they dropped dramatically and we're talking about thirty, forty deaths a day. For me it was a strange thing, because they hid the deaths in order to revive the summer economy, tourism and everything" (Student 2, Group B).

"But they did! In the sense that at the beginning, when they said all those contagions, they said that the disease COVID was many things...They did psychological terrorism.From that moment on they started to hide the contagions, as happened this Christmas, that at the beginning of January all the infected started to come out again and during the Christmas holidays, although they said everyone was positive they didn't hear that there was a definite infected" (Student 5, group B).

4.2 Trust placed in political and health authorities

The qualitative analysis revealed the students' critical attitude towards the governmental system that led the battle against Covid-19 and disagreement with some of the political choices made regarding compulsory vaccination:

"But I disagree with one thing: the moment they put the obligation, we are no longer in a democratic country because so many people who remained consistent with their thinking, stayed at home and lost their jobs. In my point of view, they were wrong, because you can't force a person to do something they don't want to do because otherwise…" (Student 9 group A).

"But they told you: 'do you want to go to dinner? you have to do it', 'do you want to go to the stadium? you have to do it'". (Student 3, Group B).

4.3 Searching for official sources of information

Analysis of the FG transcripts explored different attitudes of the participants in relation to searching for information on the pandemic, with some students making their personal judgements based on comparison with non-institutional sources (such as

family members) and others preferring to search for information on official sources.

"I have an experience on the contrary, always something related to my father, to the army; he told me that the American army was provided with all this material, while the Italian army was not. The State did not pass them on because they thought it was not harmful. This is unimportant fake news, more so, but contrary to what you are saying...if I think that a son lost a father because of fake news…" (Student 1, group A).

"I had the first COVID vaccination around the time the second one was coming out, so I went quite quiet, because my father, my mother and my brother had already had it, so I thought: 'If nothing happened to them, why should something happen to me?" (Student 5, group B).

Although both group A and group B expressed that they researched information through the use of non-institutional sources, only a few students in group B emphasised the importance of official sources as a means of defence against fake news.

"If I read something, in anything, I don't just rely on an article; I go and do some research. I rewrite the same thing on the search bar and I compare who's talking about it, if I'm talking about, for example, certified newspapers or newspapers that are actually scientific, OK, maybe I start relying on those... but if the sites are all absurd sites, with strange names or with something that doesn't fit, I realise there's something I can't rely on". (Student 8, group B).

Discussion

The COVID-19 virus has emerged and spread globally culminating in a worldwide pandemic; mysterious emergence and speed of dissemination has generated a proliferation of spurious information and a plethora of misinformation and conspiracy theories. Hoaxes and misinformation are very dangerous when they concern health and it is often not easy to distinguish between millions of pieces of information (7). In particular, for children and adolescents it is difficult to assess the truthfulness of the content of texts, images, and videos. The present study intends to present the results of a qualitative investigation that was carried out by means of FGs on a class of adolescents, in order to explore in depth their opinions, attitudes or behaviour towards vaccination practices, to promote informed peer discussion on vaccination and to counteract the spread of fake news.

The qualitative analysis revealed singular insights and the FG method allowed for spontaneous and stimulating conversations, highlighting the young participants' keen critical sense and lively interest in the topics under discussion.

The "Fake News" category, with 97 mentions, was the most discussed by the students within all the domains explored. A specific reflection on the use of digital technology during the pandemic is needed. In fact, the limitation of physical interaction in daily life increases the possibility of entering the spiral of conspiracy, with the difference that, in a situation of isolation as in the pandemic phase, spreading false information touches the deeper and more complex process of sharing social representations and consensus-building mechanisms. Adolescents were more likely to be overwhelmed by conspiracy theories, precisely because they were more exposed to online news.

An analysis of the discussions that emerged among the teenagers revealed a high level of sensitivity and interest in the topic; there was a generalised sense of confusion about the communication of the pandemic period that emphasised, in many of them, previous perplexities. This result confirms a recent study which revealed that four out of ten adolescents cannot distinguish between real and fake news (8). Greškovičová et al suggests that although adolescents are frequent Internet users, most are unable to clearly identify fake news, the only exception being click-bait headlines, which evidently arouse adolescents' distrust (8).

In fact, adolescents are a 'vulnerable' group, precisely because of the developmental stage they are in, they are the age group most sensitive to information from the digital world, which is often misleading. Although about 71% of teenagers use the Internet, many are not able to 'filter' health information (9). Misinformation, and in particular misinformation about health issues, is a serious public health concern, with an increased prevalence of fake health news on social media platforms in recent years. Previous research has shown that online health messages are mostly incomplete and inaccurate and contain potentially harmful health information (10-14).

As far as trust in political and health authorities is concerned, our study group showed a general tendency of distrust; public health policies, criticised by the participants, led to the development of a sceptical and conspiratorial attitude towards the authorities, claiming economic interests behind certain management choices. The lack of trust in the institutions was

fostered by the lack of clear media communication in agreement with the most up-to-date scientific content, leaving room for the rooting of personal convictions that were not always scientifically grounded.

In relation to the category 'Emotions', the groups mentioned the emotional sphere 63 times, confirming the importance of emotions on the personal experience of adolescents during the pandemic. The emotional impact was multifaceted and diversified with some students reacting to the vaccination practice by showing proactive and proactive attitudes, while others experienced deleterious effects on their psyche, with anxiety, frustration, inadequacy and loneliness prevailing.

Vaccination scepticism, noted in the previous category, has, in fact, leveraged states of fear, uncertainty, and misinformation, as well as finding fertile ground in the operational algorithms of social media. In the discussions, scepticism gave way to hesitancy with respect to vaccination adherence, in line with recently published research showing that belief in conspiracy is correlated with negative attitudes of fear and anxiety towards vaccination (15, 16).

Many students also expressed concern about the consequences of the spread of the virus among family members and in the community at large; the discussions that emerged in this regard suggest a good ability on the part of adolescents to correctly perceive the risk of the disease, even if thoughts of bewilderment and confusion caused by fake news and the infodemic about vaccines and Covid prevail.

High perceived risk, as described by the 'risk as feelings' model published in Social Science & Medicine, correlates directly with the frequency of the hazardous event (17). Risks are perceived as more dangerous when they are infrequent, unclear to science, and characterised by a catastrophic nature, as is the case with Covid-19, which correlates with high risk perception (18, 19). The high perception of risk discussed by the students can, therefore, be explained by the fact that the topic of discussion focused on a new disease, unknown until recently to both scientists and citizens, of a catastrophic nature and with an unpredictable outcome.

The peculiar characteristic of the participants to express their thoughts in the discussion sessions with anecdotes and personal experiences, underlined a sense of strong participation and emotional involvement towards all the topics addressed in the focus groups. Observation of the group dynamics revealed the figure of the leader who influenced, in both study conditions (group A and group B), the students' opinions, particularly on the subject of fake news. In a situation of confusion or scarce information, individuals' cognitive processes 'latch on' to information derived from the opinions of others, especially if the sources are considered authoritative, as in the case of the opinion leader (20). A line of research on intragroup regulation processes, i.e. those processes that concern the functioning and conduct of social life in groups, has shown how the moral dimension is central to the definition of the self both individually and socially, thus influencing the choice and evaluation of the groups to which one wishes to belong (21).

Media literacy seems to be more important for adolescents in relation to risk behaviour and deciding what to avoid than for promoting healthy disease prevention behaviour. The low level of trust placed in institutions by FG participants is favoured by the lack of effective media communication, which has left room for the spread of personal beliefs that are, more often than not, wrong. Institutions and schools should therefore focus on disseminating clear and targeted messages to help combat misinformation and non-compliant behaviour.

The ingroup to which the students belonged acquired, during the FG, great power in defining their opinion on vaccinations; during the discussions, the leader's presence modified the students' thoughts and prompted them to shape their beliefs according to the group's prototypical characteristics, i.e. those characteristics that consensually defined the group's essence. On the basis of the above, one member of Group A and one of Group B were able to represent the fundamental characteristics of the two groups, and to influence the members to a greater extent than the training interventions, proposed on video or through the frontal lecture, since they were perceived as less representative in the short term.

As far as the experimental conditions used in the following study are concerned, watching the video or the frontal lecture did not have a different effect on the students' opinion; the starting questionnaire identified differences in attitude between the two groups already at the beginning. It does not therefore seem possible to stimulate a certain mentality or attitude to vaccinations at least with the presentation of a single stimulus for a short time. Further studies could curb this limitation and show different results if a real educational programme on public health issues, structured over several meetings, is presented to the class group. However, it is possible to discuss the data concerning the analysis of the conspiracy beliefs of the group that

emerged where the leader's opinion influenced that of the participants more; it is likely that, in a period like the pandemic where physical distance was felt very strongly, the communicative exchange between the young people works more than the information video. Media hype about vaccination, as well as distrust of traditional sources of information, may further contribute to confusion or misunderstanding. When information is more confusing, the opinion of a leader is more likely to influence the thoughts of the group.

Finally, the choice of the FG as a research technique, in accordance with what was suggested by Di Nubila (22), responded to the need to address increasingly complex and topical issues such as that of vaccines, with multiple possibilities of interpretation and food for thought in order to better address current public health situations.

The study presented some limitations. Even if the two groups were randomly selected, a significant difference in the knowledge and attitude towards vaccines and fake news was revealed before the intervention. Dishomogeneity may be due to the small sample size. In addition, the research has been conducted in one school in a Southern Italian province, hence the results cannot not be inferred to the whole Italian students' population. On the other hand, the in depth analysis allowed by the FG method allows the collection of relevant insights notwithstanding the paucity of observations and the limited generability of the results.

Conclusions

The analysis of the FGs revealed several interesting points of reflection, which shed light on peculiar elements for taking actions aimed at reducing young people's mistrust and distrust of vaccinations and improving their ability to discern health information coming from the web.

In conclusion, the results of the present study suggest that, in the context of qualitative analysis, the FG method proves to be a useful tool to detect knowledge, preconceptions and attitudes towards vaccination practice. As far as educational tools are concerned, however, it would seem that using video or giving a frontal lecture on infectious diseases and vaccines does not induce any kind of change in the thinking tendencies of the adolescents surveyed. Since in the world of health, videos can play an important role as tools for information, prevention, and building shared communities around health issues, it would be interesting to extend the study to a larger number of young people to refute the results.

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Riassunto

Informazioni di qualità e fake news su Covid-19 ed immunizzazione fra gli adolescenti: un'analisi qualitativa in ambiente scolastico

Introduzione. La corretta informazione è uno strumento essenziale per indirizzare pensieri, attitudimi, e le decisioni quotidiane su questioni important su temi riguardanti la salute. Oggi è disponibile una vasta quantità di mezzi e fonti di informazione. Le aumentate possibilità di ottenere dati però richiede abilità di comprensione e posizionamento, con particolare riferimento alla capacità di navigare nell'oceano di informazioni per poter operare scelte senza il rischio di esserne sopraffatti.

Obiettivo. Nel presente studio è stata usata la metodologia del focus group come strumento di indagine in ambiente scolastico per studiare conoscenze, preconcetti e attitudini degli studenti nei confronti della pratica vaccinale, per promuovere atteggiamenti favorevoli e consapevolisulla vaccinazione e contrastare la diffusione di fake news.

Materiali e Metodi. In un istituto scolastico in Puglia, nel marzo 2023, sono state condotte due sessioni di focus group con studenti arruolati su base volontaria in un progetto educativo deliberato dal Consiglio di Istituto. Il campione selezionato di 23 studenti è stato distribuito casualmente in due gruppi composti rispettivamente da 12 e 11 partecipanti. La conoscenza e l'atteggiamento di base sono stati valutati tramite un questionario strutturato all'inizio della giornata. Successivamente, prima delle sessioni di FG, al primo gruppo (A) è stato proiettato un video informativo condotto da un esperto sul tema della vaccinazione e delle fake news, mentre il secondo gruppo (B) ha partecipato a una lezione frontale sugli stessi argomenti. Le domande guida che i moderatori hanno considerato in entrambi i gruppi per il tema della vaccinazione hanno riguardato l'importanza, l'utilità dei vaccini e la fiducia nelle autorità politiche.

Risultati. Le risposte al questionario iniziale hanno rivelato una grande variabilità tra i gruppi, sebbene fossero stati selezionati casualmente. Le trascrizioni dei dialoghi sono state categorizzate da ATLAS.ti in 204 codici totali e 87 categorie, quindi combinate per formare categorie sempre più generiche unite da temi correlati. È stato sviluppato un modello specifico di fattori favorenti e ostacolanti diviso in 4 domini tematici appositamente adattati al contesto scolastico: percezione del rischio di malattia, aspetti emotivi, credenze sul vaccino e atteggiamenti verso le fake news.

Discussione. La categoria "Fake News" con 97 menzioni risulta essere la più discussa dagli studenti in tutti i domini esplorati. Gli

adolescenti hanno una maggiore propensione a essere sopraffatti dalle teorie del complotto, probabilmente perché sono più esposti alle notizie online. Abbiamo potuto rilevare un senso generalizzato di confusione rispetto alla comunicazione del periodo pandemico che ha amplificato, in molti di loro, perplessità pregresse. Le politiche di sanità pubblica, criticate dai partecipanti, li hanno portati a sviluppare un atteggiamento scettico e complottista verso le autorità, sostenendo interessi economici dietro alcune scelte di gestione. La categoria "Emozioni", con 63 citazioni, ha confermato il forte impatto della sfera emotiva, sfaccettata e diversificata, sull'esperienza personale degli adolescenti durante la pandemia.

Conclusioni. I risultati suggeriscono che un singolo intervento (video o lezione) non è in grado di cambiare atteggiamenti e tendenze di pensiero degli adolescenti esaminati. Inoltre, si è scoperto che la figura del leader presente in entrambi i gruppi influenzava, in entrambe le condizioni di studio (gruppo A e gruppo B), le opinioni degli studenti, soprattutto sul tema delle fake news, più di un intervento a breve termine.

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Firearm ownership and suicide: Has the time come to discuss uniformity of health and social assessments in aid of regulation? Reflection from a retrospective study on a forensic case series

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Keywords: Suicide; firearm; license; forensic medicine; regulation; health prevention
Parole Chiave: Suicidio; arma da fuoco; licenza; medicina forense; regolamentazione; medicina preventiva

Abstract

Background. *Firearm-related deaths are an issue of ongoing public interest, from a health and economic perspective. Worldwide, firearm prevalence in suicides varies widely, depending on multiple factors including the availability of weapons in each country. Although several studies have shown that national laws about gun ownership, reducing legal access to guns, decrease the risk of suicide by firearm, the current situation clashes with widely differing legislations.*
Study design. *Retrospective study on a forensic case series.*
Methods. *Autopsy reports assessed at the Section of Legal Medicine of Milan (Italy) from January 2014 to December 2023 were retrospectively documented. Only firearm suicides were considered. For each case, a close analysis of the criminal offence reports has been performed to obtain information about the gender and age of the victim, as well as the legal possession of firearms, psychiatric disorders, alcohol, and illicit drug abuse.*
Results. *Among all the 1,164 suicides assessed at the Section of Legal Medicine of Milan over a 10-year-period, 101 cases (8.7%) were firearm-related. The male to female ratio was therefore about 13:1. No seasonal trends were observed. Most of the individuals owned the firearm license. Of the entire dataset, 35.6% suffered from psychiatric disorders, 4% of alcohol abuse and 2% of drug addiction. Among the owners of a firearm license, 42.3% had psychiatric disorders.*
Conclusions. *Knowledge about firearm suicide and its relation to firearm legal possession is limited and current preventive laws should be reconsidered. Present administrative and clinical examinations required to obtain a firearm license in Italy and in some European territories are dealt with. The evaluation of the firearm-related risk of abuse is an essential but complex procedure, which requires not only clinic-anamnestic data but also in-deep psychiatric information. There is a need to develop and reinvigorate a debate that currently presents very heterogeneous solutions, but which would probably benefit from a common vision of the prevention strategies that can be implemented and enacted for the benefit of the entire community.*

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Introduction

Suicide is a significant public health issue worldwide and its prevention is crucial for healthcare and the community (1). A recent (2023) review by Favril et al. (2) reported that mood disorders and psychotic disorders had the largest effect sizes within the psychiatric domain, and previous suicide attempts or self-harm were the strongest risk factor overall (2). Interestingly, this finding is consistent with previous research on suicides in the Milan metropolitan area, where psychiatric diseases have always been considered as significant risk factors (3-5). In this regard, Favril et al. (2) reported that dementia was the only mental condition not associated with suicidal behavior. By contrast, sociodemographic factors such age, sex or marital status were moderately associated with suicide mortality. Worldwide, firearm prevalence in suicides varies widely, depending also on the acceptance and availability of firearms in each country (6). The use of firearms in suicides ranges from less than 5% in Japan to 50.5% in the U.S., where it is the most common method of suicide (7). Several studies have demonstrated that national laws, which reduce the access to guns at a population level, decrease the risk of suicide by firearms (8-11). Indeed, fewer people die from suicide overall in places with stricter laws regulating the purchase, trading and use of firearms. Suicide risk increases when firearms are more available. Knowledge about firearm suicide and its relation to firearm legality in the European setting is limited and studies are scarce (12-13). A reflection on this issue is proposed, starting from the analysis of the trend of firearm-related suicides over a 10-year period in an area of interest in Italy, consisting of the Milan metropolitan area.

In Italy, the possession of weapons is extensively regulated: there are different types of licenses which follow specific administrative and clinical trials in relation to firearms and their use (14-15).

Rifle license for skeet. The license is issued by the central police station; it also authorizes the transport of the gun for the shooting range. The validity is set up to 5 years and can be revoked for public safety reasons.

Rifle license for hunting. The license is issued by the central police station; it also authorizes the transport of the gun. The validity is set up to 6 years and can be revoked for public safety reasons.

Handgun license for personal defense. The license is issued by the prefecture only in selected cases with mandatory justifications: the decision is purely discretional. The license also authorizes the transport of the gun. The validity is set up to 5 years but with annual renewal.

Rifle license for personal defense. The license is issued by the central police station only in selected cases with mandatory justifications: the decision is purely discretional. The police commissioner can reject the license request if the candidate has been convicted for violent crimes. The license also authorizes the use of handguns and the transport of the firearms. The validity is set up to 5 years but with annual renewal.

Handgun license for security guards. The license is issued by the prefecture upon the request of the employer. The license also authorizes the use for personal defense and the transport of the gun. The validity is set up to 6 years but with biannual renewal.

License for firearms detention only. The license can be issued to anyone who provides the medical certificates for firearm detention. The validity of the medical certificate is set up to 5 years.

Every firearm license before being issued requires medical certifications. In the first place, the candidate must exhibit the anamnestic certificate which is compiled by the general practitioner. This examination aims to certificate the absence of psychiatric disorders, alcohol or illicit drug abuse, neurologic diseases, epilepsy, or mental disability (14). Of course, the presence of only one of such conditions rules out the possibility to obtain the license. In the second place, the candidate must exhibit a second certificate which is issued by a medicolegal consultant belonging to the Local Health Authority or by an Army physician. These experts assess the visual acuity and the hearing threshold; as for the general practitioner, they also certificate the absence of neuropsychiatric disorders based on anamnestic data. Other tests such as toxicological or biochemical examinations are facultative and requested occasionally by the medicolegal consultant.

Therefore, the present study sought to analyze whether the suicide victim population in the Milan metropolitan area included individuals in legal possession of weapons, as well as the presence of psychiatric disorders, alcohol, or illicit drug abuse conditions. Furthermore, the authors discuss the administrative and clinical examinations which are needed to obtain a gun license in Europe, with a focus on potential prevention strategies and regulations to reduce firearm-related suicides which are potentially applicable worldwide.

Methods

6,661 autopsy reports assessed at the Section of Legal Medicine of Milan (Italy) from January 2014 to December 2023 were retrospectively documented. A total number of 1,164 suicides were collected, and then reported per year. The list of analyzed cases was based on internal database search; among them, only firearm suicides were considered. For each case, we performed a close analysis of the criminal offence reports which could provide information about the gender and age of the victims. The reports were also informative on the legal detention of the firearms (license) that were used for suicides. Further data were collected by interviewing the victims' relatives before the autopsy examination as well as by analyzing the clinical documentation that was still available. Therefore, we examined the personal medical history of the victims with a specific focus on psychiatric disorders, conditions of alcohol or illicit drug abuse. For statistical analyses and graphics SPSS Statistics 29.0.1.0 has been used.

Results

Among all the 1164 suicides assessed at the Institute of Legal Medicine of Milan over a 10-year-period, 101 cases (8.7%) of firearm-related suicides occurred. There were 94 males (93.1%) and 7 females (6.9%); the male to female ratio was therefore about 13:1. By dividing all cases into groups of 20 years, there were only 12 victims (11.9%) under 40 years of age, 36 victims (35.6%) between 41 and 60 years old, 36 (35.6%) victims between 61 and 80 years old, and 17 victims (16.8%) over 81 years of age. No seasonal trends were observed. Fig. 1 and Fig. 2 show the temporal trend of firearm-related suicides. Almost all the deceased were Italian (97%), with only 3 cases of foreigners observed (one German, one Chilean and one from the Czech Republic). Fig. 3 shows the distribution of work activities in the analyzed dataset: most of the subjects were retired, but among those in employment the most represented included law enforcement personnel (17.8%), of whom 94.4% were male.

Regarding the detention of the firearm used, in 10 reports there was no information about its legal possession. Out of the remaining reports, 79 individuals (86.8%) owned the firearm license, which means that they were considered suitable for the possession and/or use of the firearm; in 4 cases the weapon was held by a family member (4.4%) and in 8 cases (8.8%) the weapon was held illegally.

Furthermore, 38 cases (37.6%) suffered from at least one of a) psychiatric disorders (36 cases, 35.6%), b) alcohol abuse (4 cases, 4.0%), and c) drug addiction (2 cases, 2.0%). Specifically with regard to those suffering from psychiatric disorders, 75% had a history of major depression and 11.1% of anxiety disorder. Among those who owned a firearm license, 42.3% were found to have a psychiatric disorder, of whom depression accounted for 72.7% of cases.

Applying the chi-square test, no significant associations were found between the variables analyzed (possession of firearm license, psychiatric disorders, drinking habits and drug addiction).

Discussion

Suicide is a global health burden which accounts for over 1 million deaths per year worldwide. In the U.S., the leading suicidal method is represented by firearms, which is typically committed by white males over 50 years of age (16-17). The firearm license is owned by the victims in the majority of cases. A recent study by Chao et al. highlighted a significative correlation between the density of federal firearm licenses in the U.S. and the firearm-related suicide rate in the same area, without any correlation for firearm-related homicides (18). Therefore, the authors reported that specific laws on the possession of firearms, which are based on the evaluation of previous crimes and psychiatric disorders, affect the total number of firearm-related suicides. Moreover, the study pointed out that the lowered number of firearm-related suicides is associated with a global decrease of the number of all suicides (18). Boggs et al. documented that among 2,674 adults during 2000-2013 who committed suicide in the U.S., more than half of them (54.7%) suffered from alcohol or illicit drug abuse or other psychiatric disorders, and 42.8% of them committed suicide by using firearms (19). These data support the evidence that people suffering from psychiatric conditions show higher risks of firearm-related suicides (20-21). Furthermore, the lethality rate of the firearm-related suicides is higher compared with other detrimental methods such as drowning, hanging, and poisoning (22-23). As a result of this, the restriction to own firearms may be a possible strategy to decrease firearm-related deaths. Notably, firearm-related suicides include deaths among law enforcement officers. These events have

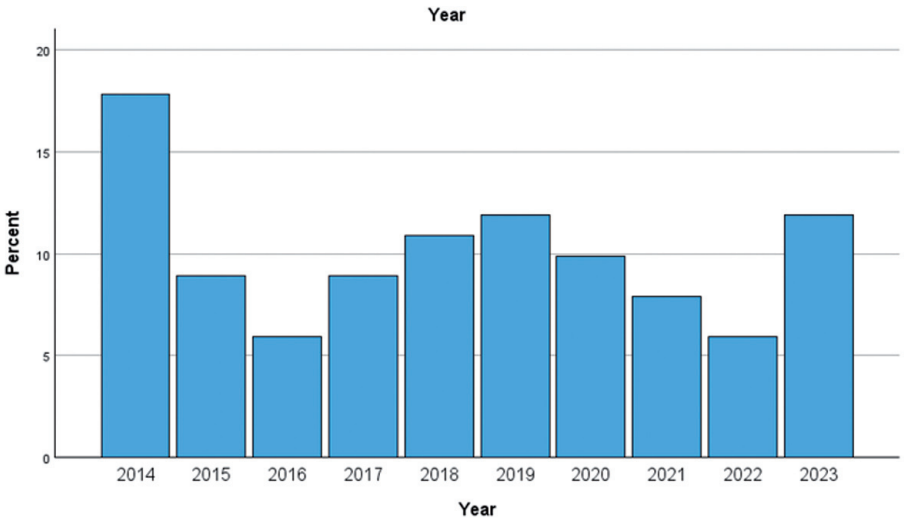

Figure 1 - Annual trend of firearm-related suicides in Milan from 2014 to 2023.

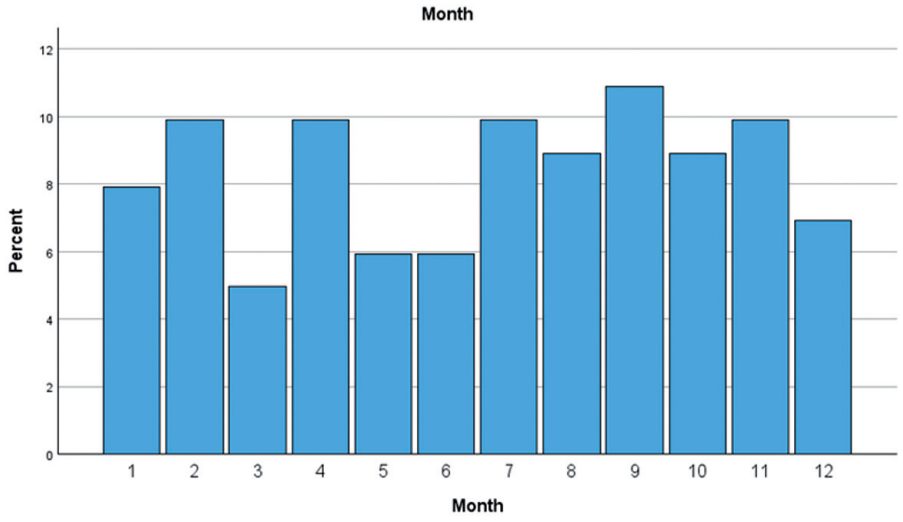

Figure 2 - seasonal trend of firearm-related suicides in Milan from 2014 to 2023.

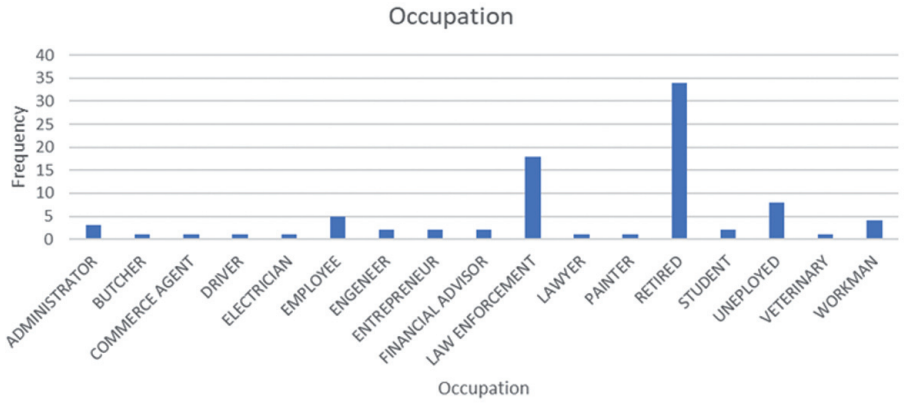

Figure 3 - distribution of work activities in the analyzed dataset.

been poorly studied but they have been reported all over the world and have raised important social issues. Police officers have been considered at increased risk of suicide (24): even though a study published by Marzuk et al. (2002) reported that the suicide rate from 1977 up to 1996 among New York City police officers was equal to, or even lower than, the suicide rate of the city's resident population (25). On the other hand, Grassi et al. (2019) reported that suicide rates among Italian police officers were significantly higher than those of the national resident population over a long and more recent observation period, i.e. from 1995 to 2017 (26). Similar results were assessed in a Portuguese study where the authors emphasized the widespread use of firearms to commit suicide (34 cases out of a total number of 39 victims) (27). These events should be observed less frequently than in the general population, given that police officers usually undergo psychological tests for the issuance of firearm license. However, it has also been underlined that these individuals can experience very stressful situations, emotional distress or other traumatic conditions which are less present in the majority of the rest of the population: in such circumstances, easy access to a firearm may be a relevant aspect (24). Therefore, a comprehensive psychological examination should be a crucial aspect of the recruitment process and be extended over a scheduled period among law enforcement officers. This procedure can detect potential suicidal behavior or psychological alterations, allowing for the therapeutic intervention and the temporary suspension of the firearm license if necessary.

In Europe and in other countries, male suicides by using firearms are less frequently reported than in the U.S. Therefore, several studies focused on the relationship between the availability of firearms and the suicide rates, highlighting that a more restrictive legislation on the possession and use of firearms can be considered as an efficient tool to decrease the number of suicides (28). For instance, no one in Japan may purchase a handgun or a rifle other than the police and the military. Hunters and target shooters may possess shotguns and airguns under strictly circumscribed conditions (29). Accordingly, the firearm-related suicide rate in Japan is estimated at 0.36 per million (30). Similar results have been observed in other countries such as Canada, United Kingdom, Austria, Australia, and New Zeeland and which have introduced stricter rules for the acquisition of the firearm license (31-35). Specifically, precautionary measures included the mandatory registration of all firearms and the exact indication of their use, the increase of the minimum age to obtain the license as well as of prohibited firearms, the reduction of the license temporal validity, and periodic meetings with the firearms' owners (36). The Austrian Government has increased the minimum age to 21 years and has introduced, since 1997, psychometric tests and periodic retrospective controls on the candidates. Birner demonstrated that this new Austrian legislation significantly decreased the number of firearm-related suicides among women between 20 and 65 years, and among all groups of men over 20 years (37). On the other hand, the firearm-related suicide rate in Switzerland can be considered high and it is estimated at 57.4 per million despite more regulation than the U.S. (13,38). This phenomenon has been explained by the fact that most adult men belong to the National Swiss Army and owns necessarily a firearm at home. However, as for Austria, Reisch et al. observed a reduction of suicide rates in Switzerland after firearm restriction resulting from the 2003 Army XXI reform (13). This reform included the discharge age from 43 to 33 and the reduction of manpower from 400,000 to about 200,000 personnel, with 120,000 receiving periodic military training and 80,000 reservists who have completed their total military training requirements. Furthermore, the reform established the necessity of a gun license and an increase in fee for soldiers who decide to purchase their gun after service.

A brief list of European countries including Italy whose firearm regulations are easily recoverable and clearly explained is presented in Table 1 (14,15,37,39-44), to indicate the non-uniformity of assessment.

Noteworthy, our research showed a clear predominance for male sex (94 out of 101 cases) and subjects over 40 years of age; these results are similar to what has been already observed in the U.S. and in other European countries (13,17,19,45-46). This research also showed that the majority of the victims (86.8%) has been judged as suitable for the possession and/or use of a firearm although suffering from psychiatric disorders (42.3%) or alcohol abuse (4%) at the moment of death. In one case, concerning a subject who suffered from depression, drug use was also detected. These results highlight a thorough revaluation of the effectiveness and appropriateness of the psychophysical standard before the issue of the license (47) as well as regular revaluations. Therefore, there are physical prerequisites such as the visual ability and the hearing threshold that can be measured objectively without any possibility of error. On the other hand, some psychiatric conditions such

Table 1 - European countries' firearm regulations (Italy is included).

Country	Requisites for firearms use	Level of restriction
Italy	Every firearm license before being issued requires medical certifications. Handgun and rifle licenses for self-defense can be issued to individuals of legal age; a second medicolegal assessment is necessary to evaluate the candidate. The final decision is discretional, and licenses need annual renewal. Licenses for skeet and hunting are issued after a medicolegal assessment and can be revoked anytime for safety public reasons. License for firearms detention only can be issued to anyone who provides the medical certificate with a validity of 5 years.	High (14,15)
Austria	All Austrian citizen over 18 can buy firearms from categories C without a permit after a three-day background check. They need to be registered six weeks after purchase. The law requires the owner to provide a good reason such as self-defense at home, hunting, sport shooting and collection, during registration. Purchase of category B weapons requires a firearm license. Authorities shall issue license to any non-prohibited citizen of European Economic Area over 21 who has a good reason. Category A requires further exceptions to be granted.	Medium (37)
France	All French citizen over 18 can purchase category D arms (black powder firearms designed before 1900 and compressed air arms). Category C firearms (e.g., shotguns, manual repeating rifles) can be obtained with a hunting license, or sport-shooting license with a medical certificate. Category B firearms are only available to sport-shooters licensed for at least 6 months, with a medical certificate, without felony convictions, and additionally requires at least three shooting sessions with an instructor each separated by 2 months. Category A special firearms (e.g., military arms) purchase not allowed.	High (39)
Germany	Weapon possession card and firearm license (to use or carry a loaded weapon). The license is issued by the police in selected cases: when the applicant can prove that they are in greater danger than the general public and that carrying a gun will keep them safer. A medical certificate for mental aptitude and no dependence from alcohol or illicit drugs is necessary if under 25 applying for their first gun license. A specialized knowledge of guns and a liability insurance for personal injury and property damage of at least €1 million is also required.	High (40)
Spain	A firearm license for rifles and shotguns may be obtained from the Guardia Civil after passing a police background check, a physiological and medical test, and a practical and theoretical exam. A sports license requires proof of sports activity of at least one competition each year. Police may inspect firearms at any time. A self-defense license is only available under special conditions.	Very high (41)
Sweden	Firearm licenses for hunting and sports shooting are issued by the police; it is also necessary to pass a hunting examination or membership in an approved sports shooting club for six months. Self-defense with firearms, as well as carry, is generally prohibited. Permits to carry firearms can be issued by the police under very special circumstances like an immediate and proven life threat.	Very high (42)
Switzerland	Purchase of firearms is allowed without permits. Some categories of arms are banned such as fully automatic guns.	Low (38,43)
United Kingdom	Firearm certificate for shotgun and sports rifles is issued from the local police force. Other firearms (e.g., handguns) require explicit permission from central government.	Very high (44)

as depression, anxiety and personality disorders may be difficult to be appreciated by general practitioners and medicolegal specialists (48). In such contexts, the candidates may dissimulate psychiatric disorders on purpose or may not realize that they suffer from these pathological conditions. Moreover, these diseases are still today considered as social stigma, and this situation further limits the possibility to make a correct diagnosis and treatment. These considerations provide the necessity to improve the clinical trial for the issue of firearm licenses; specifically, our results suggest integrating psychometric tests or psychiatric interviews. Of course, the aim of these diagnostic tools is to investigate the individual and familial psychopathological anamnesis, changes in the mood, emotions, or feelings, recent traumatic or stressful events, the personality of the individual, and situations of self-inflicted violence. Noteworthy, some Italian prefectures and central police stations have recently requested that the medicolegal practitioner obtains integrative evaluations for the firearm license, which included mandatory psychiatric interview as well as alcohol and drug tests.

Our results postulate another relevant consideration regarding the validity of the firearm license. Every license establishes a specific temporal validity which is age-independent and cannot be modified. However, the psychophysical prerequisites are subject to negative modifications which increase proportionately with aging; thus, a 5-years validity of a firearm license (e.g., rifle license for hunting) cannot be considered as suitable for the older population. Recently, the Friuli-Venezia Giulia Regional Administrative Tribunal (T.A.R.) has rejected the appeal of a citizen after that the central police station had declined the issue for a rifle license for hunting (49). Specifically, the medicolegal practitioner did not confirm the full validity of the medical certificate, lowering it up to 1 year with a mandatory reviewability, since the psychophysical prerequisites were not completely satisfied. The court stated that public safety is a right which is much more important than the individual possibility of detection/use of firearms; in fact, this faculty must be subordinated to the full and certain security of their use. Furthermore, our study observed that the most firearm-related suicides involved people over 61 years of age. As a consequence of this, these people would benefit from more extensive psychiatric examinations, which should also be more frequent over the years so as to detect organic modifications. A potential way to resolve this situation may come from the system in force for the driving license (50). In our country, the law establishes a normal validity of 10 years up to 50 years of age, then 5 years up to 70, 3 up to 80, and finally every 2 years over 80 years of age. The medicolegal practitioner can also reduce at any age the validity for specific pathological conditions. Mandatory possession of an insurance policy could be an additional element of social and protective interest. It might be useful to discuss the possibility of reporting the presence of a firearms license in health records accessible by the doctors treating the person, so that they have this information and can report any changes in health that might lead to the advisability or need for a review of the license.

Conclusion

In conclusion, the evaluation of the firearm-related risk of abuse is an essential but complex procedure, which requires not only clinic-anamnestic data but also deeper psychiatric information. Additionally, the European debate regarding the possession and use of firearms is quite poor, and it is worthy of more attention considering the results presented herein.

There are of course limitations in the present work. In the first place, the scarcity of available data, as it comes from a limited geographical area and therefore cannot be directly extended to the whole territory, an element that does not allow the observed data to be generalized. In addition, it was not possible to obtain further relevant elements, such as the presence of previous suicide attempts, unfavorable environmental and economic conditions, as well as the severity of any organic pathologies, which could have further emphasized the need for a more precise control of the subject. A national and supranational register on the topic would also be useful for the discussion on the diffusion of weapons in the population and its consequences.

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Riassunto

Possesso di armi da fuoco e suicidio: È giunto il momento di discutere sull'uniformità delle valutazioni sanitarie e sociali a sostegno della regolamentazione? Riflessione da uno studio retrospettivo su una serie di casi forensi

Premessa. I decessi correlati alle armi da fuoco sono un problema di interesse pubblico costante, sia dal punto di vista sanitario che economico. In tutto il mondo, la prevalenza delle armi da fuoco nei suicidi varia ampiamente, a seconda di molteplici fattori, tra cui vi è la disponibilità di armi sul territorio. Sebbene diversi studi abbiano dimostrato che le leggi nazionali sul possesso di armi, riducendone l'accesso, diminuiscano il rischio di suicidio con arma da fuoco, la situazione attuale vede legislazioni e regolamentazioni eterogenee.

Disegno dello studio. Ricerca originale.

Metodi. Sono state valutate retrospettivamente le risultanze di accertamenti autoptici della Sezione di Medicina Legale di Milano (Italia), nel periodo compreso tra gennaio 2014 e dicembre 2023. Sono stati inclusi unicamente i suicidi da arma da fuoco. Per ogni caso, è stata effettuata l'analisi delle informative delle Forze dell'Ordine per ottenere notizie sulla detenzione legale delle armi da fuoco nonché sul sesso, sull'età e sulla presenza di disturbi psichiatrici, abuso di alcol e di droghe delle vittime.

Risultati. Tra i 1.164 suicidi valutati presso la Sezione di Medicina Legale di Milano in un periodo di 10 anni, si sono verificati 101 casi (8,7%) di suicidi legati alle armi da fuoco. Il rapporto maschi/femmine è stato quindi di circa 13:1. Non sono state osservate tendenze stagionali. La maggior parte degli individui deteneva legalmente l'arma utilizzata. Dell'intera casistica, il 37,6% soffriva di disturbi psichiatrici, il 4% di abuso di alcol e il 2% di tossicodipendenza. Tra i possessori di porto d'armi, il 42,3% presentava disturbi psichiatrici.

Conclusioni. Poiché le conoscenze sul suicidio da arma da fuoco e sulla sua relazione con il possesso legale delle armi da fuoco sono limitate, è indicato discutere l'attuale legislazione preventiva. Partendo dai risultati di una *case series*, si illustrano gli esami amministrativi e clinici necessari per ottenere la licenza del porto d'armi in Italia e in alcuni territori europei. La valutazione del rischio di abuso delle armi da fuoco è una procedura essenziale ma complessa, che richiede non solo dati clinico-anamnestici ma anche informazioni psichiatriche approfondite. Occorre sviluppare e rinvigorire una discussione che ad oggi presenta soluzioni molto eterogenee, ma che probabilmente trarrebbe beneficio da una visione comune delle strategie di prevenzione che possono essere implementate e messe in atto a beneficio dell'intera comunità.

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The Italian version of the Nurses' Cancer Pain Management Competency Scale: a validation study

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Keywords: Nurses' Cancer Pain Management Competency Scale; reliability; validity; cancer pain
Parole chiave: Scala della competenza infermieristica, gestione del dolore da cancro; affidabilità; validità; dolore da cancro

Abstract

Background and aim. *The Nurses' Cancer Pain Management Competency Scale is a tool to explore nurses' competencies and subjective experiences in cancer pain management, and to help nurses understand their current shortcomings in cancer pain management. Furthermore, based on the scale's specific score, nurses can evaluate their lack of understanding about cancer pain management, advance research into this area, and enhance their capacity to control cancer pain while providing patient care. The scale is currently available only in English and in Chinese. The aim of this study was to translate the new scale and measure its reliability and validity in the Italian context.*
Study design. *Methodological research model.*
Methods. *The population of this methodological study included Italian nurses working in the oncology departments of 21 hospitals in Northern, Southern and Central Italy; the sample involved 243 nurses who met the inclusion criteria.*
Results. *Cronbach's alpha of the scale was 0.814. The Guttman half-reliability of the scale was 0.819. Nurses' cancer pain management competency includes four factors, which accounted for 71.43% of the cumulative variance: the context of pain management, pain assessment and measurement, management of pain, and multidimensional nature of pain. On a 4-point scale for total competency, the mean score was 2.65 ±0.89. The multidimensional nature of pain (2.88 ±0.76) was the factor that showed the highest mean score, whereas the management of pain factor was the lowest (2.52 ±0.73).*
Conclusion. *Nurses' cancer pain management competency can be assessed using the Italian version of the Nurses' Cancer Pain Management Competency Scale, which has strong validity and reliability.*

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Introduction

Pain is one of the most common symptoms experienced by cancer patients (1). In a recent review, a total of 52 studies were selected for the meta-analyses on pain and pain severity in the different stages of cancer disease (1). Pain prevalence rates were 39.3% after curative treatment, 55.0% during anticancer treatment and 66.4% in advanced, metastatic, or terminal disease. Moderate to severe pain was reported by 38.0% of all patients in studies that included all cancer stages (1). Cancer pain needs to be appropriately managed because pain interferes with patients' social and psychological wellbeing (2), and unrelieved pain causes negative clinical consequences (3).

Patients are greatly impacted by the physical and psychological suffering they experience as well as by fatigue and depression (4). As one of the most prevalent symptoms experienced by cancer patients, pain can impact a patient's life status, perceived quality of life, psychological well-being, and illness beliefs. In fact, patients with stage III and stage IV cancers generally report severe pain (5).

Pain is more prevalent (86%) among patients with stage III and IV cancer, who show anxiety (63%) and metastasis (76.4%) (5). Of the patients with cancer pain, 68%, 13%, and 19% experience mild, moderate, and severe pain, respectively. The highest proportion of cancer pain was seen in patients with gastrointestinal cancer (30%) followed by those with hematologic cancer (21%) (5).

Although currently no studies seem to describe well enough the association between pain and depression among cancer patients, cancer pain, if undertreated, worsens patients' psychological anguish and depressive feelings (6). It will also have a number of detrimental impacts, including the development of fear-avoidance beliefs, a drop in treatment compliance, and even an impact on patients' treatment and prognosis value (6).

An essential component of the pain management team are the oncology nurses, and as a result, managing cancer pain presents significant challenges for nurses (7). Assessing nurses' current cancer pain management competency and effectively developing personalized training programs are of great significance in improving nurses' cancer pain management competency and awareness (8). As of right now, the majority of cancer pain management research and investigation tools are patient-centered, and adequate instruments to assess nurses' cancer pain management proficiency are still lacking.

Oncology nurses should play a key role in optimal cancer pain management (9). Inadequately managed pain can lead to adverse physical and psychological patient outcomes for individual patients and their families. Of particular importance to nursing care, unrelieved pain reduces patient mobility, resulting in complications such as deep vein thrombosis, pulmonary embolus, and pneumonia. Complications related to inadequate pain management negatively affect the patient's welfare and the hospital performance because of extended lengths of stay and readmissions, both of which increase suffering and the cost of care (9).

Nurses' improper assessment and management of pain can lead to patient safety concerns and negative health outcomes. Knowledge of pain is influenced by specific work experience and training. In a recent Italian study (10), improved knowledge and attitudes were observed among nurses who attended a pain educational program in the last three years, providing further evidence of validity of a refresher course on pain. Participation in continuous professional development (in both formal and informal contexts) is an important component of clinical practice. However, nurses' cancer pain management competency is generally still insufficient (6).

Previous studies measured pain management competency using a self-assessed instrument focused on self-efficacy and knowledge (8). The Self-Perceived Pain Assessment Knowledge and Confidence Scale (Self-PAC) was developed based on several evidence-based clinical practice guidelines (11). The scale consists of three factors: pain assessment tool knowledge, pain assessment knowledge, and self-confidence. Findings support content validity, construct validity, good face validity, predictive validity, and internal consistency (11). However, it focuses solely on the domains of pain assessment capabilities rather than comprehensive pain management competency. The Knowledge and Attitudes Survey Regarding Pain (KASRP) is a self-administered test developed based on the existing standards of pain management and is one of the most widely used instruments to assess nurses' knowledge and attitudes toward pain management (10). The KASRP includes items regarding pain assessment, opioid dosing and route of administration, and side effects (10). However, the KASRP questionnaire has a limitation in that it focuses only on factual knowledge recall among the multifaceted attributes of pain competency.

The Nurses' Cancer Pain Management Competency Scale (NCPMCS) is a recently created new scale

to explore nurses' competencies and subjective experiences in cancer pain management, and to help nurses understand their current shortcomings in cancer pain management. Furthermore, based on the scale's specific score, nurses can evaluate their lack of understanding about cancer pain management, advance research into this area, and enhance their capacity to control cancer pain while providing patient care. The scale is currently available only in English and in Chinese (12,13).

Based on the previous premises, the aim of this study was to translate the new scale and measure its reliability and validity in the Italian context.

Methods

Study design

Before starting with the study, a quick bibliographic review was conducted by the first three authors to evaluate whether the NCPMCS had already been validated in Italian (12,13). The bibliographic review was conducted on Pubmed, Cinhal, Ilisi and on Google Scholar.

After bibliographic review and before starting with the validation study of the NCPMCS, authorization was requested via-email contact from the author of the questionnaire (doctor Young Sook Roh) (12).

Sample and setting

A convenience sample was chosen to test the instrument and carry out the study.

Registered Nurses or Charge Nurse from Northern, Central and Southern Italy accepted and participated in the survey. Convenience sampling was performed by sending a link to twenty-one Charge Nurses familiar with the lead authors. Potential sample of 430 questionnaires to be administered based on the staff who carried out clinical or managerial assistance activities in the selected oncology departments.

The inclusion criteria for participating and answering the questionnaire were as follows: 1. Be a Registered Nurse or Charge Nurse; 2. Having experience in nursing care of cancer patients or having worked in the oncology department during the period of employment in the hospital; 3. Volunteer participation in the study.

The exclusion criteria were: not having given consent to complete the online questionnaire and having no experience in oncology or pain management.

Data collection

Nurses were selected from different hospitals in Northern, Central and Southern Italy to complete the questionnaires and collect relevant data in May 2024.

With permission from the hospital administrations, the research teams distributed questionnaires via computerized software (google modules). The authors provided the department group admitting cancer patients with an electronic questionnaire with a link.

The group completed the questionnaire anonymously, after being informed of the pertinent privacy principles and measures. To ensure the completeness and quantity of the questionnaire, the researchers checked whether there were omissions and errors in the completed questionnaires.

Low-quality data such as too short questionnaire filling time and excessive overlap of item frequency were excluded from the audit process. Furthermore, two weeks later, 61 nurses (25%) were again chosen using the convenience sampling approach to complete the questionnaire, and the results of the retest were acquired.

Questionnaires

An email was sent to all twenty-one oncology departments involved in the study.

Attached to the email was a short letter which explained the project and a link to click to access the compilation of the questionnaire was sent. The email was presented by the five main authors. The questionnaire was sent online via Google Forms Platform. Google Forms is a tool that allows you to collect information from users via a personalized survey or a set of quiz. The information is then collected and automatically connected to a spreadsheet. The spreadsheet is populated with the survey and quiz answers. The collection of the questionnaires took place between 1 May 2024 and 30 May 2024. The editors were V.D. and L.M. Participants responded to the survey on a voluntary basis. The answer to the survey was considered a written consent participate. The questionnaire is made up of individual and multiple choice questions and is structured in two sections.

The first section concerned the collection of the nurses' general characteristics were surveyed using a self-administered questionnaire covering age, sex, academic degree, workplace location, position, duration of their nursing career, experience in the current department and pain management training.

The second section concerned the administration of the Nurses' Cancer Pain Management Competency Scale (NCPMCS) (12,13). The NCPMCS is designed to assess clinical nurses' competency in managing cancer pain. The scale is divided into 4 dimensions and 14 items. The 4 dimensions include Clinical conditions, Pain assessment and measurement, Management of pain, and Multidimensional nature of pain. There were 5 items describing nurses' competency to establish pain management strategy and carry out pain health education in time, 5 items describing nurses' competency to assess and measure cancer pain, 2 items describing their competency to manage cancer pain, and 2 items describing nurses' competency to understand the multidimensional nature of cancer pain. All items were assigned a score ranging from 0 to 4, with 1 representing very difficult (poor), 2 representing some what difficult (average), 3 representing almost complete (good), and 4 representing very good (excellent). A higher score indicated the nurse's competency to manage cancer pain. The Cronbach's α of the original scale was 0.890, and the Cronbach's α of each factor was 0.690-0.830 (12).

Statistical Analysis

A descriptive analysis was used to study the frequency distribution of all variables of interest. For normally distributed data, mean and standard deviation (SD) were applied.

Data were analyzed using SPSS 21.0 software package (IBM, Armonk, NY). The demographic data derived from the personal information form were analyzed using numbers and percentage.

Descriptive statistics were calculated to summarize quantitative data. The internal consistency reliability was identified using Cronbach's alpha (α). Exploratory factor analysis with principal component analysis and varimax rotation was used to investigate the construct validity of the NCPMCS.

Pearson correlation coefficient was calculated by the critical ratio method and correlation coefficient method for item analysis, and the scale reliability was described by Cronbach's α coefficient, Guttman split-half reliability, and retest reliability. Item level content validity index (I-CVI) and Scale level content validity index (S-CVI) in the expert evaluation were adopted. S-CVI evaluated the content validity of the scale and evaluated the structural validity of the scale through exploratory factor analysis and confirmatory factor analysis. The test level is $\alpha = 0.05$.

Maximum likelihood method was used to conduct confirmatory factor analysis to verify the stability of the substructures (the NCPMCS includes 4 sections) and the model fit using: fitting index, comparative fit index, chi-square degree of freedom ratio, goodness of fit index, root mean square error of approximation, and Tuck-Lewis index.

No missing data and no sensitivity analyses were addressed.

Ethical considerations

Recruitment of nurses began immediately after the lead author's approval of the creation of the NCPMCS scale (12).

The approval email was sent to us on May 3, 2024 by Doctor Young Sook Roh.

Nurses who showed interest for the study were recruited and asked to sign the informed consent prior to participating in the study and completing the questionnaires. The study questionnaire was introduced to each participant, and for each participant was asked to answer the questions. The study protocol was in line with the Declaration of Helsinki, as revised in 2013, and the Oviedo Convention for the protection of human rights and dignity of the human being with regard to the application of biology and medicine (1996).

The nurses belonging to the three different geographical area and twenty-one oncological departments completed the survey and were offered the possibility to remain anonymous. Data were collected in completely anonymous form. Therefore, the approval of an Ethics Committee was not necessary and the GDPR EU 2016/678 in force in Italy since 2018 does not apply for our study design.

Results

Sample

We sent the questionnaires to a sample of 409 oncology nurses and 21 Charge Nurses of a total of 21 oncological department. A total of 228 nurses (55.7%) and 15 Charge Nurses (71.4%) responded. The sample was predominantly female (65%), the average age was 42 years and 90% had a Bachelor's Degree in Nursing. Work experience was approximately 15 years of which at least 11 in the oncological department (Table 1).

Pain Management Educational Needs/Resources.

Of the 243 nurses, 109 (44.8%) nurses had received cancer pain management training in the last ten years, and 42 (17.3%) had no available protocols related to

Table 1 - General Characteristics of Oncology Nurses (n = 243).

Variable	Results
Age (year)	
Mean, SD	41.7 (± 11.9)
Range, n, %	
24-29	42 (17.4)
30-39	65 (26.7)
40-49	65 (26.7)
50-59	54 (22.2)
≥ 60	17 (7)
Sex n, %	
Male	86 (35.4)
Female	157 (64.6)
Level of Education n, %	
Diplome in Nursing	25 (10.3)
Bachelor's Degree in Nursing	218 (89.7)
Master's Degree in Nursing Science	59 (24.3)
1st level Master degree	40 (16.5)
Philosophiae Doctor (PhD)	1 (0.4)
Workplace Location n, %	
Northern Italy	142 (58.4)
Center-Italy	45 (18.5)
South-Italy	56 (23.1)
Position n, %	
Staff nurse	228 (93.8)
Charge Nurse	15 (6.2)
Work experience (year)	
Mean (SD)	15.4 (+ 10.2)
Range n, %	
< 5	48 (19.7)
5-10	48 (19.7)
11-19	37 (15.2)
20-30	92 (37.9)
> 30	18 (7.5)
Current department experience (year)	10.8 (+ 7.2)
Range n, %	
< 4	46 (18.9)
4-10	77 (31.7)
11-15	53 (21.8)
> 15	67 (27.6)

cancer pain management in their work department. The most preferred educational modality was simulation-based learning for 116 nurses (47.8), followed by web-based learning for 52 nurses (21.4%), lecture for 38 nurses (15.6%), and skills practice for 37 nurses (15.2%).

Linguistic validity and adaptation

To test the validity of the NCPMCS in its adaptation to Italian culture and in its adaptation to major nursing skills context, the following process was performed. The NCPMCS was first translated into Italian by VD and GD and then by one academic member. After conducting a review of the translated forms, a single version of the questionnaire was developed and adapted to the nurses'cancer pain management competency context. The translated forms were then back-translated into English by a linguistic fluent (master's degree in languages with 5 years of experience in linguistic translations) in both languages and closely familiar with both cultures (author: LF). The original questionnaire and the Italian translation were compared, and it was determined that the meaning of the items did not change. The translations made in both of the forms, were selected and submitted to 10 specialists for their opinions. The ten specialists who contributed to the evaluation of the linguistic translation were 10 Italian registered nurses. Since the Italian version retranslated into English did not present any differences, the author of the scale was not contacted for his new opinion.

Scale Item Analysis

The critical ratio method was used to rank the scale scores from low to high. The first 25% of samples were classified as high group, and the last 25% of samples were classified as low group. Independent sample T-test was conducted on their data to test the average difference between the scores of each item in the two groups. When the entry critical ratio (*t*-value) is greater than 3.000, it indicates that the entry has good discrimination and can be retained. The results showed that the *t*-values of each item ranged from 5.851 to 17.321 ($p < .05$ for all values), indicating high discrimination among the items. In addition, Pearson's correlation coefficient between the scores of each item and the total score of the scale was 0.489-0.719 ($p < .05$ for all values). The items of the Italian version of the Nurse Cancer Pain Management competency scale were reserved (Table 2).

Scale Validity Analysis

The item content validity index (I-CVI) of this scale was 0.853 - 1.000, and the S-CVI value was 0.969, based on the results of the expert consultation. Additionally, the study's exploratory factor analysis revealed that the KMO test value was 0.856 and the Bartlett's spheroid test χ^2 value was 2361.254 ($p < .001$), meeting the requirements for the analysis. The factors were extracted using principal component analysis, then the maximum variance method was

Table 2 - Expolative Factor Analysis of Nurses' Cancer Pain Management Competency Scale (n 243). The bold part represents the number of factor loads for different items in each factor.

Factor	Factor 1	Factor 2	Factor 3	Factor 4
I. Clinical conditions				
1. Implement an individualized pain management an that integrates the perspectives of patients, their social support systems, and health care providers in the context of available resources.	0.889	0.109	-0.028	0.116
2. Describe the role of the nurse as an advocate in assisting patients to meet treatment goals.	0.864	0.173	0.075	0.881
3. Explain how health promotion and self-management strategies are important to the management of pain.	0.875	0.115	0.115	0.131
4. Present theories and science for understanding pain.	0.847	0.126	0.141	0.191
5. Monitor effects of pain management approaches to adjust the plan of care as needed.	0.851	0.113	0.141	0.264
II. Pain assessment and measurement				
6. Assess patient preferences and values to determine pain-related goals and priorities.	0.134	0.878	0.113	0.611
7. Use valid and reliable tools for measuring pain and associated symptoms to assess and reassess related outcomes as appropriate for the clinical context and population.	0.081	0.884	0.109	0.109
8. Describe the unique pain assessment and management needs of special populations	0.134	0.876	0.176	0.102
9. Explain how cultural, institutional, societal, and regulatory influences affect assessment and management of pain.	0.116	0.888	0.135	0.156
10. Demonstrate the inclusion of patient and others, as appropriate, in the education and shared decision-making process for pain care.	0.147	0.836	-0.033	0.194
III. Management of pain				
11. Develop a treatment plan that considers the differences between acute pain, acute-on-chronic pain, chronic/persistent pain, and pain at the end of life.	0.251	0.201	0.151	0.871
12. Explain how to assess and manage pain across settings and transitions of care.	0.309	0.249	0.079	0.826
IV. Multidimensional nature of pain				
13. Describe the impact of pain on society.	0.139	0.148	0.885	0.108
14. Define terminology for describing pain and associated conditions.	0.168	0.149	0.876	0.085
Mean, SD	2.74 ±0.68	2.69 ±0.91	2.89 ±0.77	2.33 ±0.78
Cronbach's alpha	0.827	0.814	0.791	0.726
Eingenvalues	6.246	2.791	1.326	1.012
Percentage of variance (%)	22.416	19.038	17.426	12.558
Cumulative percentage of variance (%)	22.416	41.454	58.880	71.438

utilized to rotate the factors. They extracted common components with eigenvalue > 1 and factor load value > 0.400. Four common factors in all were extracted, according to the results, and no items were removed. The cumulative variance contribution rate was found to be 71.439%, and the factor load value of the 14 items in their dimensions ranged from 0.826 to 0.889, which was consistent with the original scale (Table 2).

In addition, the maximum likelihood method was used to conduct confirmatory factor analysis to verify the stability of the substructure and the model fit. The results showed that the chi-square degree of freedom ratio (χ^2 /df) was 2.773, the goodness-of-fit index (GFI) was 0.856, the root mean square of approximate error (RMSEA) was 0.087, the value-added fitting index (IFI) was 0.899, the comparative fitting index (CFI) was 0.932 (Table 3). The Tuck-Lewis index (TLI) was 0.935, indicating a good degree of model fitting and the Italian version of NCPMCS had a high agreement with the original scale (Table 3).

Table 3 - Maximum likelihood method was used to conduct confirmatory factor analysis to verify the stability of the substructure and the model fit.

Index	Acceptable Value	Normal Value	Values Found
X^2/SD	< 5	< 2	2.773
GFI	> 0.90	> 0.95	0.856
RMSEA	< 0.08	< 0.05	0.087
IFI	> 0.90	< 1.0	0.899
CFI	> 0.90	> 0.95	0.932
TLI	< 1	> 0.90	0.935

X^2/SD, chi-square degree of freedom ratio; GFI, goodness of fit index; RMSEA, root mean square error of approximation; IFI, value-added fitting index; CFI, comparative fit index; TLI, Tuck-Lewis index.

Reliability of the Scale

The Cronbach's alpha of the scale was 0.814 and ranged from 0.726 to 0.827. On a 4-point scale for total competency, the mean score was 2.65 ± 0.89. The multidimensional nature of pain (2.88 ± 0.76) was the factor that showed the highest mean score, whereas the management of pain factor was the lowest (2.52 ± 0.73).

The Guttman half-reliability of the scale was 0.819. Two weeks later, 61 nurses (25%) were selected to fill in the questionnaire twice, and the retest reliability of the scale was 0.922.

Discussion

In this study, the Italian version of the Nurses' Cancer Pain Management Competency Scale was introduced, as an effective assessment tool to provide reference for cross-sectional survey and intervention of cancer pain management and we also tested the scale's validity, reliability, and applicability. As of right now, the majority of cancer pain management research and investigation instruments in the world are patient-centered, and adequate instruments to assess nurses' cancer pain management proficiency are still lacking. The Italian version of the NCPMCS can be a useful tool for assessing nurses' competence in managing cancer pain. It can assess cognitive informations towards the creation of individualized intervention plans aimed at enhancing nurses' cancer pain management competency. Different departments can conduct individualized training to improve nurses' cancer pain management competency, enhance evidence-based pain management programs, and support nurses in regularly self-evaluations of their cancer pain management competency, all in accordance with current pain management guidelines and the unique characteristics of cancer pain. Low cancer pain management competency among nurses may have detrimental effects on patients' outcomes and reduce the effectiveness of their cancer pain management practice (14).

As participative advocate for pain management, the nurse's comprehension of cancer pain and the position itself are especially crucial. A thorough evaluation of pain should concentrate on the degree of pain, its location, kind and quality, length, history, and its radiating effects to other body areas (14).

Medical services ask nurses to become more proficient in managing cancer pain, since the percentage of cancer patients is rising. It is still vital for clinical nurses to find solutions for enhancing patients' quality of life and encouraging their physical and psychological recovery when providing pain management (2). In order to provide cancer care, nurses must understand the clinical importance of cancer pain management.

The critical ratio of every item in the Italian version of the nurses' cancer pain management competency scale was more than 3 and $p < .05$, according to item analysis, showing a high degree of item difference. Furthermore, there was a significant degree of homogeneity and connection among the scale's items, as seen by the correlation coefficients, which ranged from 0.489-0.719 (all $p < .05$), between the scores of each item and the scale's overall score. Furthermore, item analysis revealed that there was a high degree of differentiation among the items in the Italian version of the nurses' cancer pain management competency scale, with each item's critical ratio being greater than 3 and $p < .05$.

Validity refers to the fact that the measurement tool can measure what it is intended to measure. The validity of the scale is assessed in this study using both content validity and structural validity. Among these, the inclusion of experts is linked to content validity, and the choice and quantity of experts will affect content validity. In previous studies, it was considered better to select more than 6 experts (15) who scored the scale content relevance, the experts were given a four-point scale (1 = not relevant, 2 = weakly relevant, 3 = strongly relevant, 4 = highly relevant) with items scoring 3 or 4 being more representative. Dividing the number of experts scoring 3 or 4 by the total number was the I-CVI for the item. When the I-CVI is ≥0.780, it indicates that the overall content validity of the

scale is good (15). Ten experts in all were contacted for this study; the experts were chosen from a broad range of backgrounds, including scientific researchers, instructional personnel, and clinical workers. This study's I-CVI ranges from 0.853-1.000, and S-CVI was 0.969, suggesting that the scale's content validity was good and that nurses' competency in managing cancer pain can be accurately measured using the Italian version of NCPMCS. Exploratory factor analysis yielded four dimensions, and the cumulative variance rate was 71.44%, suggesting structural stability for the Italian version of the nurses' cancer pain management competency scale. The RMSEA study's value was 0.087 and its χ^2 value was 2.773. Analysis revealed that the fitting model created using the scale factors had good goodness of fit, suggesting that the Italian version of the scale had strong structural validity. The Italian version of the NCPMCS scale items was consistent with the measurement dimensions, which verified that the preset dimension structure matched well with the actual data. The consistency and stability of the measured findings can be represented by the scale's dependability; the better the reliability, the more stable and dependable the measuring device (16). The higher the internal consistency, the more accurately the measured topic reflects the research topic, and the stronger the correlation between the items in each dimension. It is generally believed that the Cronbach's α coefficient of the total scale is >0.800, the Cronbach's α coefficient of the subscale is >0.700, and the broken half reliability is >0.800, indicating good reliability. In this study, Cronbach's α coefficient was 0.814, and the reliability of each dimension was 0.726 to 0.827, indicating high internal consistency of the scale and strong reliability of the scale for evaluating nurses' cancer pain management competency. At the same time, the retest reliability is 0.922, indicating that the scale has good stability across time.

In contrast to the Korean validation study (12), which showed the lowest score for the pain assessment and measurement factor, the lowest score was obtained for the management of pain factor. While the best score was always obtained for the multidimensional nature of pain factor in line with the results of Hu and colleagues (12).

Regarding the current practice and training needs, although 45% of all nurses had received cancer pain management training, a high percentage of nurses did not have a cancer pain management- related protocol in their work department. Although the perceived importance and interest in cancer pain management are increasing, there are still insufficient resources to support nurses' cancer pain management practice in clinical settings. As nurses play an integral role in assessing, managing, and evaluating cancer pain, it is critical for nurses to perform cancer pain management proficiently. Nurses performed better on pain management after participating in training using action learning (17) and online learning (11,18), and the presence of a protocol in the work setting was shown to improve nurses' pain management competency (19). Therefore, it is necessary to adopt an in-hospital protocol for cancer pain management that is based on current clinical practice guidelines or reviews (14,20,21) that nurses can refer to at any time, along with competency-based training that can promote nurses' cancer pain management competency. Furthermore, nurses in the present study preferred multi-component educational modalities with the highest simulation-based learning experience.

Limitations

The first and most important limitation is the convenience and non-random sampling model, which makes the results influenced by the strict selection of cases. Random sampling would have allowed the instrument to be validated in a more heterogeneous nursing group.

Approximately 44% of the hypothetical nurses invited to our validation study did not respond to the questionnaire. This may have influenced the averages that emerged in the responses, as it is likely that the respondents were the greatest number of nurses motivated by the management of cancer pain and therefore offered the best responses.

In the translation and back-translation process, the author of the scale was not included and it probably could have been useful to obtain his new opinion on the back-translation of the questionnaire from Italian to English. However, the retranslated sentences matched the original version as stated by the 10 experts involved in the translation process and the linguist expert involved in the validation process.

It is currently not possible to perform the criterion control verification of the local version of the scale, nor are there any other pertinent instruments or translated versions available to assess the cancer pain treatment competency of nursing personnel in Italy. We should broaden the sample size and geographical reach of nurses in the future, add to the validation analysis, and investigate the use of this scale in Italy.

Conclusion

The NCPMCS, which includes 14 assessment items and 4 dimensions in the *'Italian version'*, is appropriate for assessing clinical nurses' cancer pain management competency in the Italian context. It also has strong reliability and validity. There is no reliable tool today in Italy to evaluate clinical nurses' skills in treating cancer pain. In addition to be a useful tool for clinical settings, this questionnaire makes it easy for researchers to learn more about the general degree of cancer pain management competency that clinical nurses in Italy already possess. The NCPMCS measures competency and may be useful in assisting faculty in developing a pain management curriculum to promote pain management competency. Training programs are needed that employ multi-component education and experimental learning to achieve optimal cancer pain management competency in nurses.

Data availability: The datasets used during the study are available upon reasonable request from the corresponding author.
The questionnaire translated into Italian is available upon request to the main author: VD.
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Riassunto

La versione italiana della Nurses' Cancer Pain Management Competency Scale: uno studio di validazione

Introduzione e obiettivo. La Nurses' Cancer Pain Management Competency Scale è uno strumento nato per esplorare le competenze e le esperienze soggettive degli infermieri nella gestione del dolore da cancro e per aiutare gli infermieri a comprendere le loro attuali carenze nella gestione del dolore. Inoltre, sulla base del punteggio specifico della scala, gli infermieri possono valutare la loro mancanza di comprensione nella gestione del dolore da cancro, far avanzare la ricerca in quest'area e migliorare la loro capacità di controllare il dolore da cancro durante l'assistenza. La scala è attualmente disponibile solo in inglese e in cinese. Lo scopo di questo studio era di tradurre questo strumento e misurarne l'affidabilità e la validità nel contesto italiano.

Disegno dello studio. Modello di ricerca metodologica.

Metodi. La popolazione di questo studio metodologico comprendeva infermieri italiani che lavoravano nei reparti di oncologia di 21 ospedali del Nord, Sud e Centro Italia; il campione ha coinvolto 243 infermieri che soddisfacevano i criteri di inclusione.

Risultati. L'alfa della scala di Cronbach era 0.814. La semi-affidabilità di Guttman della scala era 0.819. La competenza infermieristica nella gestione del dolore oncologico comprende quattro fattori, che rappresentano il 71.43% della varianza cumulativa: il contesto della gestione del dolore, la valutazione e misurazione del dolore, la gestione del dolore e la natura multidimensionale del dolore. Su una scala a 4 punti per la competenza totale, il punteggio medio era 2.65 ±0.89. La natura multidimensionale del dolore (2.88 ±0.76) è stato il fattore che ha mostrato il punteggio medio più alto, mentre la gestione del fattore dolore è stata quella più bassa (2.52 ±0.73).

Conclusioni. La competenza infermieristica nella gestione del dolore da cancro può essere valutata utilizzando la versione italiana della Nurses' Cancer Pain Management Competency Scale, che ha una forte validità e affidabilità.

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SHORT PAPER

Vaccinations at home: a new strategy to contain vaccine hesitancy? The experience of ASL Napoli 1 Centro, Italy

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Keywords: Home vaccination; mandatory vaccinations coverage; vaccine hesitancy; convenience; deprived socio-economic contexts

Parole chiave: Vaccinazione a domicilio, copertura delle vaccinazioni obbligatorie; esitazione vaccinale; convenienza; contesti socio-economici deprivati

Abstract

Vaccination coverage are generally geographically variable, even within large cities; furthermore, across target population are embedded difficult-to-reach clusters. To address this issue and improve coverage of mandatory vaccinations, a study group explored bringing vaccination at home as an interventional strategy.

In a pilot experience, parents of unvaccinated and under vaccinated children of the 2020 birth cohort living in Naples, Italy were contacted by telephone to offer home administration of vaccinations. A specifically trained team arranged vaccinations visits at home. Coverage rates were evaluated at baseline and one month after the intervention strategy. A significant positive increase in hexavalent vaccine (+1.43%) and measles-mumps-rubella (+1.85%) coverage was registered despite the short duration of the pilot program. Home vaccination turned out to be a medical resource consuming but feasible and successful strategy to increase mandatory vaccinations coverage among the most difficult-to-reach and fragile segments of the pediatric population.

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Abbreviations: *VC: vaccination coverage; LHU: Local Health Unit; AEFIs: adverse events following immunization.*

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Introduction

Vaccinations is recognized as one of the most effective and harmless approaches for the prevention of many even lethal infectious diseases (1). Despite this finding, in recent years there has been a decline in vaccination coverage (VC), which has led to the development of outbreaks of vaccine-preventable diseases (2).

Many factors can contribute to low immunization coverage, such as the lack of access to immunization services, missed opportunities for vaccination during healthcare visits alone with other determinants of vaccination hesitancy (3, 4).

Vaccine hesitancy refers to a delay in acceptance or the refusal of vaccination despite availability of vaccination services (5).

The reasons for this reluctance towards vaccinations are complex, varying across time and depend on multiple variables such as geographic barriers (6), perceived risk of adverse events following immunization and unfounded fear of serious vaccine-induced diseases including autism (7), but also the low perception of the risk/severity of the alternative, the natural disease (1).

Furthermore, low socio-cultural conditions and social risk negatively impact empowerment and generate the belief that the vaccination is not a priority (8).

In response to the progressive decline in VC, in Italy further to the National Plan for Vaccine Prevention (9) ten vaccinations: poliomyelitis, diphtheria, tetanus, hepatitis B, Haemophilus influenzae type b, acellular pertussis (hexavalent vaccine) and measles, mumps, rubella and chicken pox (MMRV vaccine) were declared mandatory for children aged 0 to 16 years (10). According to the law, the aforementioned mandatory vaccinations are required for admission to childcare up to primary school. Only children with health problems for which vaccinations are not indicated and those who have got immunization as a result of natural illness, such as varicella, can be declared exempt from the mandatory vaccinations (9, 11, 12).

Traditionally, in Italy, a relevant variability across Regions of vaccination coverage is observed; in the 2020 birth cohort a range of 86.28% - 96.42% for the hexavalent vaccine coverage and 89.20% and 96.05% for MMR vaccine coverage was reported for toddlers, being the national target of 95% (http://www.salute.gov.it/imgs/C_17_tavole_20_10_0_file.pd[1]). At regional or local figures can be even lower. In the area of the Local Health Unit (LHU) ASL Napoli 1 Centro, vaccination coverage for hexavalent and MMR vaccines are traditionally below 90%, due to the complexity and heterogeneity of community profiles.

Furthermore, the COVID-19 pandemic increased vaccine hesitancy (13, 14) for routine pediatric vaccinations throughout Italy (15).

To address this issue, in the LHU ASL Napoli 1 Centro, a home vaccination pilot program was implemented as an alternative strategy to improve coverage of mandatory vaccinations foreseen in toddlers.

Context

The Campania Health Information System (SINFONIA) was searched to find unvaccinated and under vaccinated toddlers belonging to the 2020 birth cohort by using poliomyelitis (as a proxy of the hexavalent vaccine) and measles (as a proxy of MMR vaccine) search terms. Parents of the selected subjects were contacted by telephone and informed on the possibility of receiving mandatory vaccines at home.

A devoted Project Team, composed by a physician and a nurse with previous experience in vaccination and proficient in pre-vaccinal screening interview including vaccination history, allergies, the history of adverse events following immunization (AEFIs) and specifically trained on vaccine storage and preservation techniques and equipped for the management of serious and potential life-threatening events in a no healthcare context (16).

A medical car belonging to the LHU was used by the Team to reach each vaccine destination. Upon arrival at home, project team performed a vaccination anamnesis, specifically checking for eventual contraindications and precautions. The parent informed consent was then obtained for each child to be vaccinated. Project Team monitored each toddler for 30 minutes after the administration of the vaccine. Afterwards, parents were contacted by phone by the Project Team within 10 to 14 days after the vaccination to check the insurgence of any AEFIs and to orally express their degree of perceived satisfaction on the experience of home vaccination. Administered vaccinations were recorded into the regional database.

The primary end point of the pilot program was to increase the vaccination coverage for the mandatory

[1] http://www.salute.gov.it/imgs/C_17_tavole_20_10_0_file.pd

vaccinations by hexavalent and MMR vaccines within 24 months of age, in the cohort of children been born in 2020, evaluated at the start and end (December 31, 2022, vs January 31 2023), of the observation period (one month). Coverage values were expressed as the number of vaccinated children (numerator) divided by the whole eligible pediatric population (denominator) of the 2020 birth cohort registered in the LHU Napoli 1 Centro.

The chi-square test was executed on proportions using the SPSS statistical program, version 12.0 for Windows (IBM, Armonk, NY, USA). Analysis findings were considered statistically significant at two-tailed p-value ≤ 0.05.

Results

A total of 142 toddlers eligible from the database query were vaccinated within the Pilot Project time frame.

We evaluated two-time points coverage rates for mandatory vaccinations: at baseline (31 December 2022) and after one month of the intervention strategy (31 January 2023) (Table 1).

We reported the number of vaccinated children (numerator) and the eligible pediatric population (denominator) registered in the Naples 1 Center Local Health Authority, ASL Napoli 1 Centro, of the 2020 birth cohort.

On 31 January 2023, 24-month coverage rates were 91.77% for poliomyelitis and 92.38% for measles corresponding to an increase of +2.62% and +3.75% respectively, as compared to the immunization rate of the previous month.

After the home vaccination implementation, the increase in poliomyelitis and measles vaccines coverage were +1.43% and +1.85% respectively (p-value < 0.05) (Table 1).

Many families (85 out of 142) preferred the coadministration of vaccines for their children. At the follow-up, 15 AEFIs were reported in 10 toddlers after MMR vaccines: of these, 10 reported fever and discomfort while 5 reported losses of appetite. All AEFIs were classified as mild in severity and managed by the toddler family pediatricians.

During the follow-up phone call, all participants (142/142, 100%) expressed a strong preference for home vaccine administration as compared to the traditional one. The reasons for this preference were mainly: the abolition of logistical access difficulties as distance, absence of their own means of locomotion, difficulty in accompaniment by partners absent for work reasons or detention measures, mothers themselves under house arrest, single-parent families, homes located on the upper floors of old buildings without a lift and presence of other young children that cannot be left disattended. In addition, most of the families (130 families, 91.5 %) belonged to deprived socio-economic and cultural contexts, and vaccination was not considered a priority (Table 2).

During the vaccination activities carried out at home, it was also possible to extend the offer for mandatory or recommended vaccinations to 13 brothers/sisters of the vaccinees, as their immunization profiles were incomplete.

The Pilot Project encompassed 20 working days where the Project Team personnel was dedicated full time to the project. A mean of 7.2 eligible subjects were vaccinated per day. In principle, for each eligible vaccinees, a mean of 10 minutes for visit preparation (including cold chain arrangements) and by phone post vaccination AEFIs monitoring, 20 minutes to obtain consent, vaccine administration and registration, 30 minutes for potential AEFIs waiting time, summing up to 1 hours per vaccinees could be postulated. Residual daily working time was devoted to car transfer from and back to LHU.

Table 1 - Vaccine coverage (VC) rate (%) registered for mandatory vaccinations at 24 months, stratified by vaccine type and month of administration, along with the percentage differences between the 31 January 2023 and 31 December 2022 rates in the Naples 1 center local health authority.

Vaccine	31 December 2022 VC rate (%)	31 January 2023 VC rate (%) with home immunizations alone	% difference	*p*-value	31 January 2023 Total VC rate (%)	% difference
Polio	89.15	90.58	+1.43	≤ 0.05	91.77	+2.62
Measles	88.63	90.48	+1.85	≤ 0.05	92.38	+3.75

Table 2 - Demographic characteristics, logistical access difficulties, socio-economic/cultural contexts for vaccinees families

Characteristics	Number
Vaccinated children	142
Third hexavalent + first trivalent vaccinations	85
Third hexavalent	14
First trivalent vaccination	43
Family size	
1 child	1
2 children	21
3 children	65
4 or more children	55
Difficulty in vaccination services access	
distance	51
absence of their own means of locomotion	35
absence of partners for work reasons	88
absence of partners for detention measures	23
mother under house arrest	12
single-parent families	26
homes located on the upper floors of old buildings without a lift	79
Socio-economic and cultural conditions of families	
Severely deprived/conditions of social and health risk	130

Discussion and Conclusions

The home vaccination Pilot Project reported here was implemented as an alternative strategy to improve mandatory vaccinations coverage in toddlers in a LHU in Italy.

A smooth but significant positive increase in poliomyelitis and measles vaccines coverage was measured with home immunizations despite the short duration of the Pilot Project implementation (one month). Interestingly, coverage rates for mandatory vaccinations were higher not only than in previous years but also in the Covid-19 pre-pandemic era.

During the COVID-19 pandemic we have witnessed, in Campania as in Italy, a drop in immunization coverage, mainly due to the fear of contagion but also, in some areas of the country, to the reduction in supply.

Alternative settings, such as home vaccination, were reported to be useful mainly for reaching children belonging to the most deprived and most fragile sections of the population and, therefore, at greater risk of contracting vaccine-preventable diseases (17). In the present Pilot Project, 100% of respondents firmly preferred home vaccination for convenience. Vaccination convenience refers to the influence of certain factors on the decision to get vaccinated such as physical availability, geographical accessibility, and quality immunization services and it is identified by the WHO Strategic Advisory Group of Experts (SAGE) as one of the key drivers of vaccine hesitancy (5).

The vaccination practice at home reduced the child's discomfort; the absence of waiting time and healthcare setting, the family environment and the presence of both parents or relatives proved to be reassuring. This intervention has also allowed the demedicalization of the vaccination act: the home setting, bringing the vaccination act back to a normal routine practice and therefore has reduced the parents' concern.

Home vaccination also proved to be an opportunity to educate, during the post-vaccination observation period, parents about the child's life habits, diet, the importance of reading aloud and interventions aimed at promoting responsive parenting.

In principle, home vaccination turned out to be expensive in the LHU public health perspective. It required full time engagement of healthcare workers highly trained in vaccine administration and routine procedures storage and transport of vaccines, the availability of emergency equipment on site. Roughly, time needed to vaccinate one toddler at home was 5 time higher (60 minutes vs 12 minutes) with respect to a routine single visit at LHU office. As a consequence, to be economically affordable home vaccination should be better framed in specific contexts and be limited to particular situations.

The experience reported here is affected by many methodological limitations. Due to restricted personnel availability out of the routine activity, it was possible to keep the project ongoing only for one month; consequently, Pilot Program sample size is too limited to conduct more detailed or statistical analysis. Furthermore, due to the preventive nature of the healthcare intervention, it is not possible to fully estimate the achieved benefit in terms of public health (further to the single subject protection), the direct and indirect medical costs and consequent cost/effectiveness of the Pilot Program. A longer period and a larger cohort of children are needed to establish the actual effectiveness and sustainability of the intervention.

Certainly, home vaccination represented a concrete example of a Public Health intervention inspired by the principles of equity and universality of assistance,

sensitive to the protection of the weakest groups and deprived segments of the population. This strategy may favor adherence to vaccination practice in disadvantaged and poor areas and in conditions in which access to healthcare offices is compounded by socio-cultural deprivation protecting children from transmissible and sometime life-threatening infectious diseases.

Contributorship: MT contributed to the conception/design of the study; CU drafted and revised the manuscript; LG, AV and IL collected the data, MC and MP analyzed and interpreted the data; CV approved the final version to be submitted. All authors contributed to multiple reviews and feedback on the manuscript and gave final approval before submission.
MT and CU contributed equally to this work and share first authorship.
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Riassunto

Vaccinazioni a domicilio: una nuova strategia per contenere l'esitazione vaccinale? L'esperienza dell'ASL Napoli 1 Centro, Italia

Le coperture vaccinali sono generalmente variabili geograficamente, anche all'interno delle grandi città; inoltre, all'interno della popolazione target ci sono cluster difficili da raggiungere. Per contenere questo problema e migliorare la copertura delle vaccinazioni obbligatorie, un gruppo di studio ha utilizzato la vaccinazione a domicilio come strategia di intervento.

In un'esperienza pilota, i genitori di bambini completamente o parzialmente non vaccinati della coorte di nascita del 2020 che vivono a Napoli, in Italia, sono stati contattati telefonicamente per offrire loro la somministrazione a domicilio delle vaccinazioni. Un'équipe appositamente formata ha organizzato le sedute vaccinali a domicilio. I tassi di copertura sono stati valutati all'inizio e dopo un mese di strategia d'intervento.

Nonostante la breve durata del programma pilota, è stato registrato un significativo aumento della copertura del vaccino esavalente (+1,43%) e di morbillo-parotite-rosolia (+1,85%). La vaccinazione a domicilio si è rivelata una strategia che richiede risorse mediche, ma fattibile e di successo, per aumentare la copertura vaccinale obbligatoria tra i segmenti più fragili e difficili da raggiungere della popolazione pediatrica.

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Respiratory Syncytial Virus associated hospitalisations in children up to 6 years of age in Italy: a systematic review

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Keywords: Respiratory infections; RSV; infants; paediatric population; inpatients; Hospital Discharge Records (HDRs); severe respiratory disease; bronchiolitis; pneumonia; LRTI

Parole chiave: RSV; virus repiratorio sinciziale; VRS; neonati; popolazione pediatrica; pazienti ricoverati; Schede di Dimissione Ospedaliera (SDO); malattia respiratoria grave; bronchiolite; polmonite; infezione delle vie respiratorie inferiori

Abstract

Introduction. *Respiratory syncytial virus is a leading cause of respiratory hospitalisations in infants. This systematic review (registration number: CRD42021248309) aims to synthesise the available evidence on Respiratory Syncytial Virus-related hospitalisations among children aged 0 to 6 years in Italy.*

Methods. *The literature search was conducted on PubMed, Embase, Scopus, and International HTA, covering the period from January 2000 to July 2022, with a focus on studies that reported information on Respiratory Syncytial Virus-associated hospitalisation in children aged 0-6 years in Italy.*

Results. *Eight articles were included after screening 20,845 records. These retrospective studies reported that most hospitalisations were among those <1 year (71.5%-88.8%), infants aged <1 year were also at higher risk of hospitalisation in intensive care unit. Respiratory Syncytial Virus infections typically peaked December-February, with an atypical early start in August 2021. Subtype analysis showed alternating prevalence of Respiratory Syncytial Virus-A and Respiratory Syncytial Virus-B across different seasons. Coinfections were not uncommon (1.1%-37.4%), with rhinovirus and bocavirus being the most frequent.*

Conclusions. *All infants at their first Respiratory Syncytial Virus season showed an increased risk of severe infection and hospitalisation, regardless of the gestational age at birth, compared to older participants. This systematic review will enrich the understanding about Respiratory Syncytial Virus disease and help support decisions regarding prevention efforts in Italy.*

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Introduction

Respiratory syncytial virus (RSV) is one of the major pathogens responsible for hospitalisations due to lower respiratory tract infections (LRTIs) in young children <5 years of age (1). RSV can indeed spread to the lower respiratory tract, causing severe LRTIs including bronchiolitis, and/or pneumonia (2). Also, RSV infections may have short-term direct and indirect consequences such as an increased incidence of acute otitis media, pneumonia, and excessive antibiotic usage (3), or long-consequences such as early transient or recurrent wheezing, asthma, and impaired lung function (4). Respiratory Syncytial Virus (RSV) is estimated to be the causative agent in 80% and 40% of hospitalisations due to bronchiolitis and pneumonia, respectively, among children (5). Globally, it's projected that RSV accounts for a total of 55,000 to 200,000 annual fatalities and 3.2 million hospitalisations among children below 5 years old (6). The most severe cases are predominantly observed in infants under 1 year of age, with a notably higher incidence in nations with limited economic resources (1,6). Several vaccines targeting infants, pregnant women, and older adults are currently under development: while two adult vaccines have recently been approved, including one specifically for pregnant women that will therefore protect newborns, there is no available vaccine to prevent RSV infections in infants as of now (7). An effective monoclonal antibody, palivizumab, is available for prophylaxis and is recommended for high-risk infants in Italy (8). It is reimbursed for preventing severe lower respiratory tract illnesses caused by RSV in children at high risk of RSV disease, such as those with a gestational age ≤35 weeks and an age <6 months at the start of the RSV season, those aged <2 years who have received treatment for bronchopulmonary dysplasia in the last 6 months, and those aged <2 years with hemodynamically significant congenital heart disease (9). In addition, the extended half-life mAb nirsevimab is approved for all newborns and infants to protect against RSV-LRTI with a single dose for their first RSV season (at least 5 months) and also for at-risk infants during their second RSV season in Canada and the USA (10). Universal implementation of long-acting monoclonal antibodies nirsevimab in newborns during RSV season has proven to be effective and safe as tested in Galicia, France, and in Valle D'Aosta region (11-14). In the future, nirsevimab may be included in the national immunization calendar as it has already been recommended by Italian scientific societies (15). Given the substantial estimated impact of the RSV disease burden on children, coupled with the advent of new preventive measures, this systematic review seeks to analyse the epidemiological data regarding RSV disease in hospitalised paediatric patients aged 0-6 years in Italy, spanning the years 2000 to 2022, and set the scene for a comprehensive understanding of the current burden of RSV disease in terms of hospitalisations in the country. Specifically, we have collected data related to the age of hospitalized children, the presence of co-infections with RSV, the distribution of RSV-A and RSV-B, and gestational age at birth.

Materials and Methods

1. Protocol registration and search strategy

The protocol of this systematic review was registered on the International Prospective Register of Systematic Reviews on August 8, 2021 (Registration number CRD42021248309). The review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (16) guidelines and a PRISMA Checklist was filled in (Supplementary File 1). Records were searched from 01 January 2000 until 14th July 2022 in the following databases: PubMed, Embase, Scopus, International HTA Database. The search query was built to search for all articles reporting data on patients hospitalised due to RSV infections in Italy. It was tailored to suit the specific requirements of each database, and it was developed to be as much sensitive as possible, to avoid the exclusion of any article that could be suitable for inclusion. As an example, the query used for searching on PubMed was as follows: (RSV OR hRSV OR Respiratory Syncytial Virus OR bronchiolitis OR ILI OR ARI OR SARI OR respiratory infection OR "respiratory tract infection" OR RTI OR URI OR URTI OR LRI OR LRTI OR "Viral pneumonia" OR otitis) AND (burden OR impact OR epidemiol* OR economic OR cost* OR hospital* OR incidence OR prevalence OR diagnos* OR diagnosis OR "laboratory confirm*" OR surveillance) AND (Italy OR Italian OR Italians OR Ital*) AND (paediatric OR child* OR toddler* OR newborn* OR infant* OR preterm OR pediatric*). The references of the included or relevant papers were then meticulously examined through a process of backward citation chaining.

1.1. Eligibility Criteria

This systematic review included studies conducted

in Italy between 2000 and 2022, focusing on RSV-related hospitalisations in patients aged 0 to 6 years. The review considered both observational studies and clinical trials for inclusion. To be eligible, a study had to exclusively include children hospitalized for RSV infection, ensuring that the inclusion criteria were 100% children hospitalized due to RSV. Studies that included and analyzed patients hospitalized due to other viruses were excluded. Additionally, the inclusion criteria required studies to provide at least one of the following data points: the proportion of RSV-associated hospitalizations by age, the distribution of RSV-A and RSV-B, RSV seasonality, and RSV co-infections with other infectious agents. Studies that did not meet the specified criteria were excluded from the final database: reviews, letters, posters, and conference abstracts reporting no data were excluded, as well as studies published in a language other than English or Italian.

1.2. Screening and study selection

All identified records were compiled in a Microsoft Excel sheet (Microsoft Excel® per Microsoft 365 MSO © Microsoft 2022 Microsoft Corporation). Duplicates have then been removed. Four reviewers worked in pairs in a double-blind manner to assess the eligibility of records based on title, abstract, and full text. Any discrepancies were resolved by a fifth, more experienced, investigator. Additionally, the reference lists of eligible papers and previously published literature reviews were further analysed to identify potentially relevant articles on the same topic.

1.3. Data retrieval, data analysis, and quality assessment

Following the selection process, the chosen articles underwent thorough analysis. Reviewers extracted key information from each record, encompassing general study details such as authors, title, and publication year. Study design, including cohort, case-control, and cross-sectional studies, was carefully noted. Additionally, geographical context and time of observation, along with participant characteristics such as age groups and sample sizes, were systematically recorded.

The data extraction process involved a comprehensive assessment of clinical and epidemiological outcomes. To ensure accuracy and reliability, data entries were cross validated by multiple reviewers. The data extraction encompassed identifying the clinical diagnosis of hospitalisation, the distribution of RSV cases among different age groups, and available characterization of RSV subtypes (RSV-A and RSV-B). When possible, information regarding coinfections with other pathogens and the seasonal patterns of RSV was also collected. The extracted data were then organized into designated tables for further analysis. The narrative analysis of this systematic review revolved around those topics identified as key during the data extraction (age distribution, seasonality, subtypes distribution, and coinfections identified in the hospitalised cases). The quality of the included studies was assessed using the Newcastle-Ottawa Scale (NOS). Each study received a score based on NOS criteria, with a maximum score of 9, representing the lowest risk of bias.

Results

1. Selection process

A total of 20,845 records were initially retrieved (Supplementary File 2): after removing duplicates (n = 1,991) and records not in Italian or English language (2,066), 16,788 records underwent initial screening based on title and abstract. Out of these, 16,541 records were excluded at this stage, leaving 247 records for further consideration. Subsequently, 239 articles were excluded based on specific criteria: studies entirely focused on children over 6 years old, geographical context outside Italy, period outside the scope (before the year 2000), incorrect study type (e.g. reviews, letters without original data), and outcomes unrelated to RSV-associated hospitalisation. Eight articles, all judged of low risk of bias (score range 7-9), were selected for inclusion in this study (Supplementary File 3).

1.1. Analysis of RSV-associated hospitalisations in children under 6 years in Italy

The 8 articles analysed in this review are summed up in Table 1 (17-24). All studies are retrospective analyses published between 2007 and 2022.Table 2 summarizes the proportion of RSV-associated hospitalisations by age for the included studies, reporting related data, including those age groups that encompass children older than 6 years when present. Kuhdari et al. 2018 (20), analysed the Hospital Discharge Records (HDRs) supplied by the National Archive of HDRs data (Italian Ministry of Health) in the period 2001–2014. The sample population was represented by all age groups (from 0 to >75 years); however, for the purpose of this review, we considered only data referred to the 0-4 years old

Table 1. Characteristics of the articles included in the systematic review, inverse chronological order, as reported in the included manuscripts.

Author	Hospital (Geographical region)**	Time of observation	Sample description
Loconsole D. et al., 2022	Giovanni XXIII Hospital (Bari, Southern Italy)	January 2017-December 2021	179 children aged 0-12 months, 13-24 months and >24 months
Barbati F. et al., 2020	Various centers in Tuscany, region of Central Italy	September 2014 - August 2019	624 children aged 0-6 years
Ciarlitto C. et al., 2019	Bambino Gesù Children's Hospital (Rome, Central Italy)	Winter seasons from 2015-2016 to 2017-2018	422 children aged < 1 year
Kuhdari P. et al., 2018	National Hospital Discharge Records	January 2001- December 2014	55,926* hospitalisations in children were children aged 0-4 years
Capizzi A. et al., 2017	Gaslini Hospital (Genova, Northern Italy)	Epidemic seasons from 2014-2015 to 2016-2017	366 children aged ≤ 1 year
Pierangeli A. et al., 2014	Umberto I Hospital (Rome, Central Italy), and United Hospitals (Ancona, Central Italy)	Epidemic seasons from 2010-2011 to 2012-2013	515 children: 165 in Rome (mean age: 4.8 months; median age: 2.75) and 350 in Ancona (mean age: 12.8 months; median age: 3 months; range: 0.1–163 months)
Scagnolari C. et al., 2012	Umberto I Hospital (Rome, Central Italy)	Winter seasons from 2006-2007 to 2009-2010	132 children (median age: 2.2 months, range: 0.23-32 months)
Rossi G.A. et al., 2007	Various centers in Northern, Central, and Southern Italy	Epidemic seasons from 2000-2001 to 2003-2004	145 children aged ≤ 4 years

*Calculated using data reported in the manuscript by Kuhdari et al.; **data retrieved from national or local medical records

Table 2. Distribution of RSV infections in hospitalised subjects by age group (%), when given.

Author	< 1 month	1-2 months	3-5 months	6-11 months	1-2 years	3-4 years	5-6 years	> 6 years
Loconsole et al., 2022	71.5				8.4	20.1*		
Barbati F. et al., 2020	41	21.5	19.1		18.4			
Kuhdari P. et al., 2018	88.8				8.2		3.0	
Capizzi A. et al., 2017 (full-term infants)	55.2**		21.4**	23.4**				
Capizzi A. et al., 2017 (pre-term infants)	62.5**		3.7**	33.8**				
Scagnolari C., 2012	78.6			21.4***				
Rossi GA. et al., 2007	41.4		33.1	21.4	4.1			

Note: * >24 months; ** calculated average value of three winter seasons; *** 6-32 months.

group hospitalised for RSV-related pathologies (97% of the entire population) with the following ICD9-CM codes: 466.11 (RSV bronchiolitis), 480.1 (RSV pneumonia) and 796 (RSV). Most hospitalisations involved patients < 1 year of age (88.8%), 8.2% referred to the 1–4 years age group and 3% the rest of the population. Moreover, the 1.7% of all RSV-related hospitalisations registered in the period 2001–2014 involved infants aged < 28 days of life (20). In Barbati et al., among 624 RSV-positive hospitalised children 0-6 years old from September 2014 to August 2019, 509 children were < 1 year, 390 were <3 months and 256 aged less than 30 days (81.6%, 62.5%, and 41% respectively). Prematurity (defined as <37 weeks of gestational age) was detected in 24.5% of children, of which 72.5% were born at 34-37 weeks. Furthermore, there were other predisposing factors for contracting RSV infection in 31 cases (5.0%), involving congenital heart conditions. Within the group of 624 children admitted to the hospital as part of the research, a total of 103 (16.5%) necessitated placement in the Intensive Care Unit (ICU), with the majority being infants aged less than 1 year (86.4% out of 103) (18).

In 2022, the research by Loconsole et al. retrospectively examined data related to the demographic and clinical characteristics, along with any existing health conditions and concurrent infections, of paediatric patients who had been hospitalised due to RSV infection. The study, conducted between August and December 2021, encompassed a total of 179 children (128 aged 0-12 months, 15 aged 13-24 months, 36 aged > 24 months). Among all children, 32 of them (equivalent to 17.9%) were born prematurely and 38 children (21.2%) have comorbidity (17).

The retrospective case-control study by Rossi et al. (23) shows the distribution of 145 children ≤4 years of age admitted to hospital for RSV-induced LRTI over four consecutive winter seasons (2000-2001 to 2003-2004), compared to LRTI cases due to other agents ("controls"). During the analysed period, the most represented age group were children aged <3 months old (41.4%), followed by those aged 3-5 months (33.1%), 6-11 months (21.4%) and those > 12 months (4.1%) (23). Scagnolari et al. enrolled 132 subjects (0-32 months) with a clinical diagnosis RSV-associated bronchiolitis between 2006 and 2010. The age distribution of RSV hospitalised patients was 78.6% in infants aged 0-5 months and 21.4% in the rest of the population analysed (24). In a retrospective analysis by Capizzi et al., three RSV epidemic seasons were analysed. A total of 366 infants (aged ≤12 months) were admitted to Gaslini Hospital due to RSV-induced ALRI: 137 in 2014-2015, 109 in 2015-2016, and 120 in 2016-2017. Notably, 7.7% of these cases involved preterm infants (29- < 36 weeks gestational age). The proportion of preterm admissions increased over the seasons. Among infants aged <6 months, 71.6%-80.8% of cases were full-term, with 48.2%-63.3% being younger than 3 months (21). In the study by Ciarlitto et al., all included children were 1 year old or less, and the median age at admission was 2 months and 10 days (no further detail was given), while in Pierangeli et al. (515 children), the median age at admission was 2.75 months. These two papers did not report an analysis by subgroup of age (19, 22).

1.2. RSV Seasonality

Three studies reported information on RSV seasonality for different seasons and are here reported in chronological order. In the winter seasons 2010-2011 and 2011-2012, Pierangeli and his team observed that the first hospitalisations due to RSV took place around mid-December and reached their peak during January and February. In 2012-2013 they observed an earlier start of both the RSV-season and RSV-associated hospitalisations (second half of November) (22).

The study by Barbati and cees described the trend of RSV infections in the paediatric population of Tuscany from September 2014 to August 2019. Their group observed a usual start of RSV epidemic in the late fall (November), with a peak during winter (January), and a variable end in early spring (April). Among 624 cases, 502 (80.4%) occurred in the period December-February, 584 (93.6%) if also considering the month of March (18).

The paper by Loconsole et al. studied the seasonal trends of RSV from 2017 to 2021 and reported that season 2021/2022 differed significantly from the previous years, being anticipated (first cases in August and peak in November) and with a higher peak, compared to the previous four seasons that saw the first cases in late October and the peak in late January/early February (17).

1.3. RSV-A and RSV-B distribution

Regarding the RSV subtype, three papers reported data on the percentage of RSV A and B (Supplementary File 4). RSV-A and RSV-B infections varied across the epidemic seasons considered, although RSV-A seemed to be more frequent (particularly, but not only, in preterm children) (17,19,22).

In the study conducted by Ciarlitto et al., it was

observed that among all the children examined, 64.4% were identified with RSV-A, 33.9% with RSV-B, and 1.7% exhibited a coinfection of both RSV-A and RSV-B. Throughout the investigated timeframe, RSV-A was the dominant strain in both term infants (64%) and preterm infants (68%). Specifically, during the first season (November 2015 - March 2016), RSV-A displayed predominance (90.1%), the second one RSV-B exhibited higher prevalence (62.3%), and the third one saw RSV-A as more frequent again (58.2%). The data reported by Ciarlitto et al., were consistent in both the term and pre-term groups of children. Although in terms of quantity the majority of children were infected with RSV-A, the data highlighted an alternating predominance between RSV-A and RSV-B strains in different seasons (19). Pierangeli et al. (who analysed seasons 2010-2011, 2011-2012 and 2012-2013) also reported an alternating trend with 83 cases of RSV-A and 97 RSV-B in 2010-2011, 119 RSV-A and 46 RSV-B in 2011-2012, 158 RSV-A and 12 RSV-B in 2012-2013 (22). Lastly, Loconsole et al. reported data for 179 children hospitalised between August and December 2021, being 136 of them infected with RSV-B (76%), 41 infected with RSV-A (23%), and 2 with both the RSV subtypes (1%) (17).

1.4. Coinfections with RSV

Finally, the coinfected association of RSV with other pathogens was assessed by molecular techniques by all studies, when reported (Supplementary File 5). The RSV coinfection rates ranged from 1.1% (21) to 37.4% (17). Among the other coinfection agents, rhinovirus was one of the most common pathogens found, ranging from 19% (19) to 47.8% (17) and bocavirus infections ranged from 26.9% (17) to 53.8% (24). Loconsole et al., 2022 reported that the 9% of the coinfected children was infected also with SARS-CoV-2 (17). Among 366 cases, Capizzi et al. 2017 reported 4 coinfections with a bacterial agent (Hib) (21).

Discussion

This systematic review aimed to collect and analyse the RSV-hospital burden in children aged 0-6 years old in Italy between 2000 and 2022.

Among the 8 retrieved studies in the period 2000-2021, we found that the RSV most affected age group were hospitalised children < 1 year old (71.5%-88.8%) (17,20) and especially those < 3 months (up to 62.5%, often requiring intensive care). Consistent information was reported by a recent modelling study aimed at estimating the number of RSV-associated hospitalisations in EU children under 5 years, that estimated that 78.3% (19,858/25,354) of annual RSV-associated hospitalisations occur among the age group 0-11 months in Italy (25). Other countries worldwide have reported interesting and similar data to what we hereby present. A Spanish study conducted from 2014 through 2018, in several hospitals of the Valencia Region, reported that the highest rates of hospitalisation related to RSV occurred in infants under 3 months old and in those born either before or at the onset of the RSV season (26). Moreover, a Swedish study showed that hospitalisations due to RSV have increased greatly between 2004 and 2011 and children < 1 year old were the most affected age group showing an annual incidence of 17/1,000 (27). Similarly, the average annual hospitalisation rates for RSV in the USA were 17/1,000 for children <6 months of age and 3/1,000 for children < 5 years of age (28). A recent European birth cohort study set in Spain, Finland, England, Scotland, and the Netherlands in children born between 2017 and 2020 showed again that the highest RSV-associated hospitalisations were reported in children <3 months (29). Loconsole et al. did not find a statistically significant association between prematurity and severity of the disease but highlighted that the symptoms severity was associated with younger age and chronic disease (17). Regarding the seasonality, RSV cases usually peak between December and February, in line with the data from the Temperate Northern Hemisphere (30). The reasons to explain this epidemiological pattern are described by the lower temperatures and low humidity conditions of the wintertime that may promote the stability of RSV in fomites; additionally, the consequent increased indoor crowding may also enhance viral transmission (30). Looking at the number of RSV cases in the period of our systematic review (2000-2021) it is remarkable to notice how the distribution of RSV hospitalised case changes in the different seasons: Rossi et al., 2007 reported that hospitalised patients were 17.2% in the season 2000-2001, 28.3% in the season 2001-2002, 34.5% in 2002-2003 and a slightly lower one in the 2003-2004 season (20%) (23). Alongside, Barbati et al., 2020 reported a similar distribution of RSV hospitalised patients in more recent seasons with values ranging from 13.3% in the 2014-2015 season to 25.2% in the 2018-2019 one (18). This trend can be related to the fact that clinicians become in the time more aware about the

RSV disease burden, requesting additional tests to have a more accurate diagnosis. Moreover, diagnostic tests have been developed greatly in the recent years, making the molecular characterization by RT-PCR the leading routine lab test for RSV, able also to discriminate between the RSV-A and RSV-B subtypes. It should be also highlighted that the COVID-19 pandemic greatly affected the global epidemiology of all infectious diseases, including RSV. The ban restrictions to reduce SARS-CoV-2 infections have significantly reduced hospitalisations due to RSV in Italy and worldwide in 2020 (31, 32), and disrupted seasonality, with one of the most recent seasons (2021-2022) being characterized by an unusual start of the season in August, as also reported by Loconsole et al (17). When analysing the subtypes, it is possible to notice how RSV-A and RSV-B prominence varied across the epidemic seasons considered, with no regular pattern, although RSV-A seemed to be generally more frequent. In this regard, two important factors should be mentioned, being that the subtype does not seem to be linked to a different severity of the symptoms (33) or to an increased risk of being infected (33-34), and that the current RSV preventive strategies target both RSV-A and RSV-B, including under investigation vaccines that are targeting protein F as the target molecule, which is conserved in both RSV-A and RSV-B (35). Regarding RSV infections in combination with other pathogens, the review reports a significant variability among the included studies, both in terms of coinfection rates and the involved pathogens. This considerable variability is likely due to the different circulation of pathogens linked to the extensive time frame considered in this review work. Nevertheless, it was possible to observe that rhinovirus ranks among the most prevalent infectious agents both in the pre-pandemic and pandemic eras.

Our study faces several challenges. The few studies we used could limit the scope of our findings, particularly as most predate the COVID-19 era and others follow it, with possible shifts in circumstances. In addition, the limited number of epidemic seasons represented in the studies is a limitation because it may not capture the full variability and trends in RSV hospitalizations over time. In terms of the precision of the selection process, we haven't calculated inter-rater reliability (IRR) to estimate inter-coder agreement, nor the κ statistic to measure accuracy and precision among researchers involved in the screening process. This could have helped identify inconsistencies or biases in study selection and ensure a more robust and reliable review process. We haven't assessed unpublished or unreviewed results (grey literature), which might have prevented us from retrieving more evidence on RSV in Italy. Finally, it must be noted that identification of RSV cases in most studies relies on ICD-9-CM coding, which introduces the potential for misclassification, miscoding, and missed opportunities for RSV testing, considering that physicians' coding practices may vary.

Conclusions

To our knowledge, this is the first study to collect data on Italian paediatric patients hospitalised for RSV infection. This comprehensive systematic review sheds light on the significant burden of respiratory syncytial virus hospitalisations among children aged 0-6 years in Italy from 2000 to 2021, underscoring the vulnerability of infants under 1 year old, who are more prone to severe RSV-related illnesses requiring ICU care. Notably, the dynamics of RSV hospitalisations have shown fluctuations over the years, possibly due to increased awareness among clinicians and advancements in diagnostic technologies. The influence of the COVID-19 pandemic on RSV epidemiology is undeniable, with significant declines in hospitalisations during the restrictions implemented to curb the spread of SARS-CoV-2. The disruption of seasonality in the 2021-2022 season further highlights the intricate interplay between infectious diseases. This study not only provides a deep understanding of RSV's impact on paediatric healthcare in Italy but also contributes to the broader global perspective on RSV-associated hospitalisations in young children. By offering detailed, region-specific data, it helps fill gaps in the global epidemiological understanding of RSV. Here, we emphasize the urgent need for good national data on RSV hospitalizations at the national level because of the imminent introduction of new prophylactic measures in Italy.

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Data availability statement: Template data collection forms, data extracted from included studies, data used for all analyses, and any other materials used in the review will be made available by the authors upon request.

PRISMA Checklist: A complete PRISMA Checklist is provided as supplementary material (Supplementary File 1). Items Nos. 13, 14, 15, 20, 21, and 22 were considered 'not applicable,' as they relate to a quantitative synthesis of results (e.g., meta-analysis), which was not conducted in this study.

Riassunto

Ospedalizzazioni dovute al Virus Respiratorio Sinciziale nei bambini minori di 6 anni in Italia: una revisione sistematica della letteratura

Introduzione. Il virus respiratorio sinciziale è una delle principali cause di ricoveri ospedalieri per problemi respiratori nei neonati. Questa revisione sistematica (numero di registrazione: CRD42021248309) ha lo scopo di sintetizzare le evidenze disponibili sulle ospedalizzazioni correlate al virus respiratorio sinciziale tra i bambini di età compresa tra 0 e 6 anni in Italia.

Metodi. La ricerca bibliografica è stata condotta su PubMed, Embase, Scopus e International HTA, coprendo il periodo da gennaio 2000 a luglio 2022, con un focus sugli studi che riportavano informazioni sulle ospedalizzazioni associate al virus respiratorio sinciziale nei bambini di età compresa tra 0 e 6 anni in Italia.

Risultati. Otto articoli sono stati inclusi dopo aver esaminato 20.845 voci bibliografiche. Gli studi retrospettivi inclusi hanno riportato che la maggior parte delle ospedalizzazioni riguardava bambini di età inferiore a 1 anno (71,5%-88,8%), e i neonati di età inferiore a 1 anno avevano anche un rischio più elevato di ricovero in unità di terapia intensiva. Il virus respiratorio sinciziale ha tipicamente raggiunto il picco tra dicembre e febbraio, con un inizio atipico precoce ad agosto 2021. L'analisi dei sottotipi ha mostrato una prevalenza alternata di virus respiratorio sinciziale-A e virus respiratorio sinciziale-B in diverse stagioni. Le coinfezioni non erano rare (1,1%-37,4%), con rhinovirus e bocavirus come i più frequenti.

Conclusioni. Tutti i neonati durante la loro prima stagione di virus respiratorio sinciziale hanno mostrato un rischio aumentato di infezione grave e ospedalizzazione, indipendentemente dall'età gestazionale alla nascita, rispetto ai bambini di età superiore a un anno. Questa revisione sistematica contribuisce a migliorare la comprensione della malattia da virus respiratorio sinciziale in Italia e fornisce un supporto importante nelle decisioni riguardanti le strategie di prevenzione in Italia.

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Supplementary File 1. Prisma 2020 Checklist

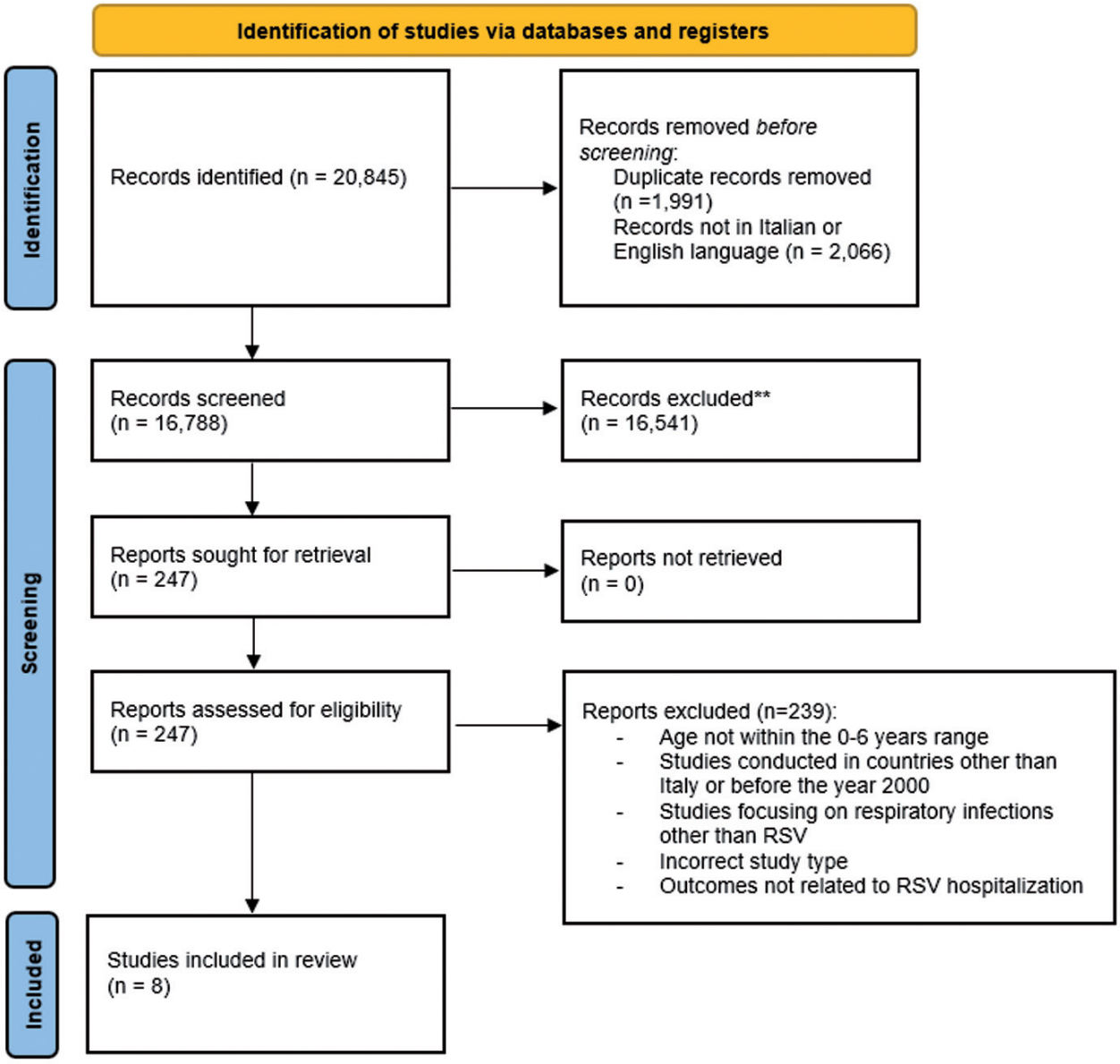
Section and Topic	Item #	Checklist item	Location where item is reported (page number; line number)
TITLE			
Title	1	Identify the report as a systematic review.	1; 2
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	2; 23-38
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	3; 51-74
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	4; 75-81
METHODS			Pages 4-6
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	5; 103-114
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	4; 85-90
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	4; 90-101
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	5; 117-122
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	5-6; 117-140
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	6; 130-140
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	6; 130-140
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	6; 138-140
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	6-7; 144-151
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Not applicable
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Not applicable
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Not applicable
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Not applicable
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Not applicable
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Not applicable
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Not applicable
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Not applicable
RESULTS			Pages 6-10
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	6-7; 142-151, Supplementary file 2
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	6; Supplementary file 2

Section and Topic	Item #	Checklist item	Location where item is reported (page number; line number)
Study characteristics	17	Cite each included study and present its characteristics.	7; 154, Table 1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	6; 150-151, Supplementary file 3
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	6-7; 144-151,Table 1
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Not applicable
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Not applicable
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Not applicable
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Not applicable
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Not applicable
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Not applicable
DISCUSSION			Pages 10-13
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	10-12; 244-294
	23b	Discuss any limitations of the evidence included in the review.	12-13; 295-306
	23c	Discuss any limitations of the review processes used.	12-13; 295-306
	23d	Discuss implications of the results for practice, policy, and future research.	13; 318-323
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	4; 85-86
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	4; 85-86
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	4; 85-101
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	13-14; 325-338
Competing interests	26	Declare any competing interests of review authors.	14; 340-343
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	14; 345-347

From: 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;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

Supplementary File 2. Flow diagram for the systematic review (PRISMA statement). Databases: Pubmed, Embase, PubMed, Embase, Scopus, International HTA Database

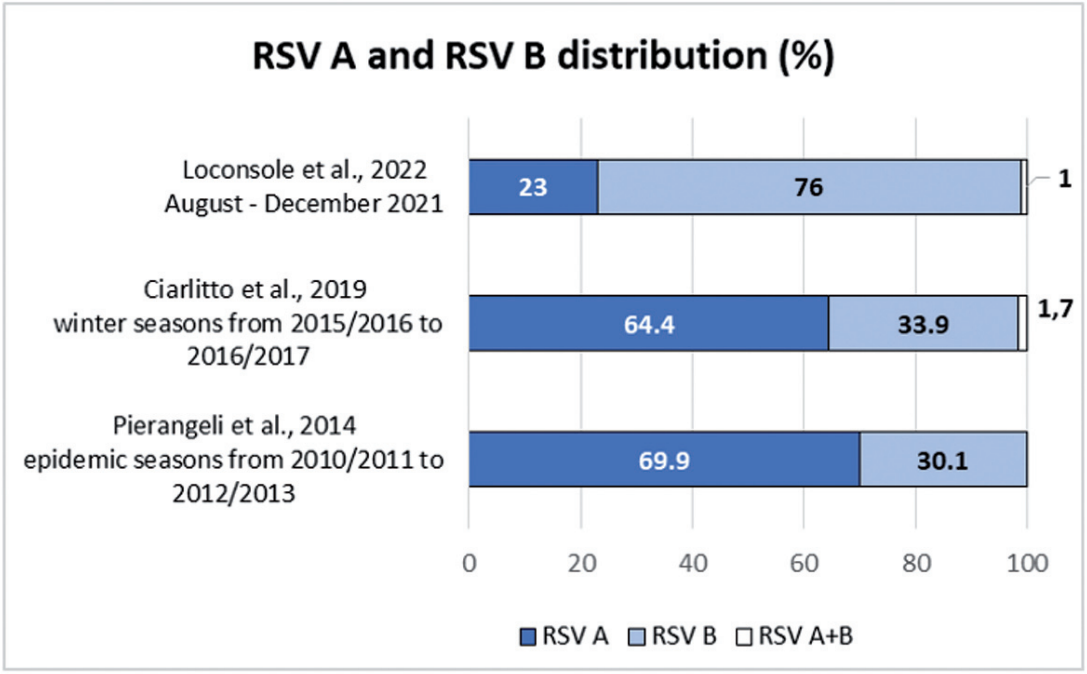


From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

Supplementary File 3. The Newcastle-Ottawa Scale (NOS) for assessing the quality of the selected studies

Author and year	Selection/ comparability	Exposure/outcome	Total quality score
Loconsole D., 2022	5	3	8
Barbati F., 2020	5	3	8
Ciarlitto C., 2019	5	3	8
Kuhdari P., 2018	4	3	7
Capizzi A., 2017	4	3	7
Pierangeli A., 2014	5	3	8
Scagnolari C., 2012	5	3	8
Rossi G.A., 2007	5	3	8

Supplementary File 4. Distribution of RSV A and RSV B (%).



Supplementary File 5. RSV coinfection rates with other pathogens

Author	Coinfection rates % (n/N)	Patients with agents of coinfection
Loconsole D. et al., 2022	37.4% (67/179)	32/67 (47.8%) with rhinovirus,18/67 (26.9%) with bocavirus, 12/67 (17.9%) with adenovirus, 12/67 (17.9%) with other viruses and (6/67; 9%) with SARS-CoV-2
Barbati F. et al., 2020	2.2% (7/320)	4/7 (57.1%) with Influenza A/H3N2, 2/7 (28.6%) with rhinovirus, 1/7 (14.3%) with Influenza B
Ciarlitto C. et al., 2019	35.6% (150/422)	19% with rhinovirus
Capizzi A. et al., 2017	1.1% (4/366)	100% with *Haemophilus influenzae*
Scagnolari C. et al., 2012	9.9% (13/132)	7/13 (53.8%) with bocavirus, 3/13 (23.1%) with rhinovirus, 3/13 (23.1%) with metapneumovirus

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Introduction to the Operation Room Management technology: Interrupted Time Series analysis in an urban acute care hospital facility in Rome, Italy

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Keywords: Hospital Management; Operating Room; Surgery; Time Series Analysis; Health Technology Assessment
Parole chiave: Management Sanitario; Blocco operatorio; Chirurgia; Serie temporale; Health Technology Assessment

Abstract

Background. *The surgical pathway represents a fundamental process in hospital productivity, and its digitalization is a major focus for hospital management. ASL Roma 1 health authority has taken up this digitalization challenge by introducing an Operation Room Management (ORM) system within the operating block of one of its hospital facilities in 2022.*
Study Design. *Interrupted Time Series analysis.*
Methods. *To evaluate the impact of Operation Room Management system adoption, data on surgery were collected from all interventions performed during two periods: January-June 2019 and January-June 2023. Analysis of the Operation Room Management system utilization rate since its introduction was performed, to estimate staff adaptation to the new software.*
Results. *As of June 2023, paper-registered interventions were 9%, nearing 100% for elective procedures only. The difference between the average intervention times was significantly in favor of the Operation Room Management cohort when restricting the analysis to Orthopedics (-9.02 minutes, p=0.006) and Surgery (8.47 min, p = 0.03). There was a modest but significant impact of Operation Room Management on the 'entering Operation Room to Incision' time (5 min, p < 0.01).*
Conclusion. *Overall, the adoption of the Operation Room Management did not worsen process outcomes. Operation Room Management offers advantages in real-time data quality, integrated with territorial and hospital platforms, contributing to a favorable cost-benefit assessment of digitalization.*

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Introduction

In 2005, the United Nations' World Health Assembly, in its resolution WHA58.28 concerning eHealth, called upon Member States "to consider drawing up a long-term strategic plan for developing and implementing eHealth services". Over 120 member states, including low- and middle-income countries, have joined (1). The recent COVID-19 pandemic has accelerated, in the healthcare world, several processes that were already in place, such as the need for greater proximity of care, environmental sustainability, and the digitalization of healthcare (2-5). The latter point in particular, initially driven by the lockdown and restrictions on mobility, then by the increased digital literacy of the population and the diffusion of "smart" devices, has rapidly become a goal embraced by governments, institutions, and companies (6). Improvement of the Operating Rooms (ORs) efficiency is also an important objective, since they absorb up to 40% of total hospital costs, but represent a major source of revenue (7). Their adequate management is paramount in guaranteeing the most optimal usage of available resources, in terms of personnel, time, and money. For public services, this is the main way to consistently deliver sustainable and high-quality health services to the population, while for private facilities this represents a major focus for marginal profit income (8-11). In recent years, hospital facilities have faced a significant increase in the cost-per-treated patient, particularly for public healthcare systems. Nevertheless, this rise in costs is not proportionate to the overall healthcare expenditure (12). Demographic trends, with an aging population as a well-established tendency (13), and macroeconomic conditions, with a global inflation rate well above the average of the last two decades, are also noteworthy factors (14).

Availability of ORs is also a must in any structure with associated Emergency Department (ED), as its availability represents a necessity for ED functioning, regardless of actual usage. This, on the other hand, means that at least a surgical équipe has to be available 24/7, and as such it is hardly sustainable without an associated surgical ward performing elective procedures. This means that, especially for low-volume centres, even clinical results may be suboptimal. Experiences such as itinerant équipes and partnerships between high- and low- volume centres are still few, but seem overall promising, at least under a clinical perspective, while management should do its best to guaranteeing them to be most effective. (15)

Overall, ORs can be seen as a core function of any hospital facility, even if medically-oriented, to the point that other hospital functions may be impacted (spatially or functionally) by its localization. Moreover, patient inflow and outflow from ORs can also impact on ED and wards performance, representing a factor in beds availability organization. Also, surgical wards may be organized towards day surgery\ week surgery regimens, impacting on personnel allocation and turnation. (16)

Local background

The Local Health Authority (ASL) Roma 1 is the Public Health Authority in charge of the Historical Centre and the Northwestern area of the Metropolitan city of Rome, Italy. It has a resident population of over 1 million, extending on an area of 524.0 km^2, which is almost 40% of the metropolitan city of Rome (17,18). It hosts 13 hospital structures with operating EDs out of a total of 22 in the Rome metropolitan area (19). It directly manages 3 large hospital structures (Santo Spirito Hospital, San Filippo Neri Hospital, Ophthalmologic Hospital) and two lesser centers for day hospital/day surgery activity (Nuovo Regina Margherita facility, and S. Anna gynecologic center). Three University Hospitals (Policlinico Umberto I, Policlinico Gemelli and Policlinico S Andrea, under a special cooperative management Region Lazio – Universities, all of them with ED, must be added.

Efficient resource management is a key focus, reflected in the integrated organization of various structures. All the Departments and Coordination Areas for related functions (except for EDs) are transversal within the whole Health Authority, and so are many operating units across the several hospital facilities. This transversal approach also includes hospitals staff.

In 2022, ASL Roma 1 decided to fully digitalize operating room functioning, using an Operation Room Management (ORM) software to enable the acquisition and accessibility of data that were difficult, if not impossible, to obtain with traditional paper records. This allows the implementation of a data-driven system capable of collecting field data to provide valuable information, which can implement continuous improvement in the management processes. In this specific case, the ORM software delivers data to clinical staff and administrators related to each surgical procedure, supporting the entire surgical process: planning, preparation, execution, and analysis. Moreover, all elective interventions are performed within assigned "slots" with a scheduled start and

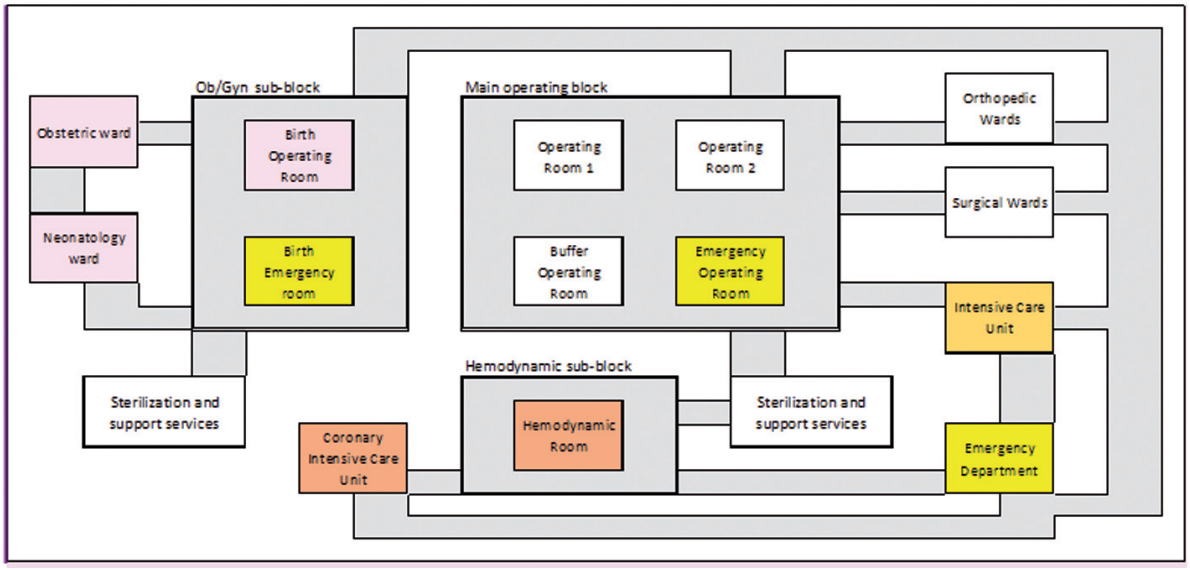

Figure 1 - Hospital Operating rooms functional organization.

end time, distributed among the surgical specialties depending on the volume of patients, and estimated intervention duration. Nursing and Anesthesiology coordinators were crucial in OR slot governance.

In the hospital facility chosen for ORM software implementation, the main operating block has two birth ORs, one hemodynamic OR, and four main ORs, of which one is dedicated to emergency-urgency activities, two to elective surgical activities, and a last one working as "buffer" room (Figure 1).

As for the intra-operative layout, each OR has two panel PCs: one installed on the wall, and one associated with the anesthesia machine. Nursing staff use the wall-mounted panel PC for completing application modules, gauze counts, and nursing checklists. The panel PC connected to the anesthesia machine is used by the anesthetist to record vital parameters and intervention phases. The surgical report is completed by the surgeon on the PC workstation in the operating block immediately after the intervention. Input for ORM may come from both Patient Data Management Systems (PDMS) and Electronic Medical Records (EMR) and integrated systems, such as wearable devices or connected electro-medical machinery (such as Anesthesiology monitors or defibrillators).

The ORM system is not only used for managing patients in the OR but also for preoperative intervention planning. The planning process involves two stages: the creation of operating sessions and their filling. The first phase, which is under the responsibility of the anesthesiologist and the nursing coordinator, defines the times of the operating slots and the assigned surgical specialty. The second phase, for which the Head of the Operational Unit is responsible, involves inserting patients into the slot of their specialty, defining each day's operating list.

Study objectives

The aim of this study was to describe and evaluate the impact of the introduction of the new ORM system in the ORs of a single acute care hospital in an urban area.

Primary end-points were:

- Technical effectiveness, as per intervention duration;
- Operators' compliance, as per number of interventions correctly registered using the ORM software instead of paper support;

Secondary end-points were:

- Saturation of operating slots;
- Delay in first patient admission to the OR.

Details on end-points and their measurement strategies are shown in Table 1.

Materials and Methods

Study design

This study was conducted as an Interrupted Time Series Analysis using routinely collected data. The analysis was conducted on all surgical activity of the hospital ORs, from January to June 2019, and from

Table 1 - Study end-points and their measurement strategies.

End point		Definition	Measurement
Primary endpoints	Technical efficacy	Intervention duration is equal or less than paper-based recrding	Average intervention duration (Intervention end time - Intervention start time)
	Operators compliance	Attitude to use ORM instead of paper-based recording	Percentage of ORM recorded intervention / Total interventions
Secondary endpoints	Slots saturation	Saturation of operating slots	Sum of actual OR usage / Sum of assigned slots duration
	Start-time tardiness	Delay in first patient admission to the OR.	Average delay (Actual patient's access – Programmed OR starting activity)

January to June 2023. The 2020-2021 period was excluded due to the COVID pandemic having impacted on hospital activity (20-26). Since operators' ORM training began in January 2022, the said year was excluded as any comparison would have been inherently biased.

The data from January to June 2019, pre-dating the introduction of the ORM system, were extracted from the internal database managed by the Nurse Coordinator of the operating block. This database, faithful to the paper registry, requires manual data entry at the end of each working day and contains information for each intervention, including patient demographics, intervention setting (urgent or elective), intervention type, intervention date and progressive number, OR number, and timing details of various phases. This registry was also used as a rescue source, collecting data on interventions that, for some reason, were not recorded via ORM software (usually emergency ones). Intervention types were coded as per the International Classification of Diseases v. 9 – Clinical Modification (ICD9-CM).

From the ORM interventions database, the following information were retrieved:

- Intervention start time;
- Intervention end time;
- OR location;
- Intervention specialty type;
- Intervention assigned slot;
- Slot total duration.

From these variables, the percentage of ORs saturation per operational unit (OU), intervention duration (time from the first incision to the last suture), and time from entering the OR to the actual beginning of the procedure were calculated. Slot saturation, defined, for each specialty/type, as the ratio between total actual OR usage and total duration of assigned slots, represents a good indication of efficiency for that particular specialty or type of intervention. This value is usually considered acceptable when around 80% (27).

Statistical Analysis

Statistical analysis was performed using Stata v. 17.0 (StataCorp. College Station, TX, USA; https://www.stata.com; 2021). Descriptive analysis was conducted for quantitative variables by calculating mean and standard deviation (SD) and providing relevant graphical representations. Welsh t-test was used to test the association between certain variables when comparing two samples with potentially unequal variances and sample sizes. A time series analysis on intervention durations in the two different periods considered was conducted using a linear regression model to highlight potential differences in the temporal trend. The same procedure was used to verify potential differences in the time interval between entering the operating room and starting the intervention.

For the 2019 surgery group, interventions that were not performed (n=2), interventions with missing room exit time (n=4), those with missing incision start time (n=7), and interventions with missing entry room time (n=4) were excluded. The intervention time analysis was conducted on three groups: the first group included all interventions from the first semester of 2019 and the first semester of 2023 (TOT), while the second and third groups included interventions only for orthopedics (ORT) and surgery (CHIR) specialties, respectively, within the same time frame.

To assess the impact of using the ORM software on intervention duration concerning individual operational units, a multivariate linear regression model was employed, using individual operational units as covariates and intervention duration as the independent variable. The null hypothesis was that there was no difference between the paper-based group and the ORM group.

The STROBE guideline was used for study

reporting (28). Statistical significance level was set at $\alpha = 0.05$ for all inferential analysis.

Results

Primary endpoints

During the first six months of 2019, 1,373 interventions were performed, of which 316 (23%) were urgent. In the same period in 2022, 1,294 interventions were performed, of which 281 were urgent (22%). Details on the interventions, divided by subspecialty, are available in Table 2. Pearson's χ^2 test shows no significant difference between the intervention volumes ($p = 0.227$). Figure 2 represents interventions timing pre- and post- ORM introduction, by specialty.

The results of the analysis are described in **Table 3**. Overall, there are no statistically significant differences in intervention times between the first semester of 2019 (paper) and the first semester of 2023 (ORM); the average for each intervention is approximately 83 minutes. Intervention times for all specialties are represented in Figure 1. Focusing the analysis on the units producing higher volumes (Orthopedics and General Surgery, responsible for 57% of all interventions), an average reduction of 9.02 minutes (95% CI 1.96 – 16.08) for Orthopedics and 8.47 minutes (95% CI -0.31 – 17.25) for General Surgery was found.

Table 2 - Intervention numbers during the study period, by specialty type (wards indicated with * closed after 2019).

Specialty	2019	%	2023	%	Total	%
Anesthesiology	60	4,37	89	6,88	149	5,59
Cardiology	101	7,36	142	10,97	243	9,11
Gen. Surgery	320	23,31	303	23,42	623	23,36
Gastroenterology*	8	0,58	-		8	0,30
Gynecology	142	10,34	102	7,88	244	9,15
Orthopedics	438	31,90	452	34,93	890	33,37
Obstetrics*	79	5,75	-		79	2,96
Plastic Surgery	28	2,04	27	2,09	55	2,06
Breast Surgery	197	14,35	179	13,83	376	14,10
Total	1373		1294		2667	

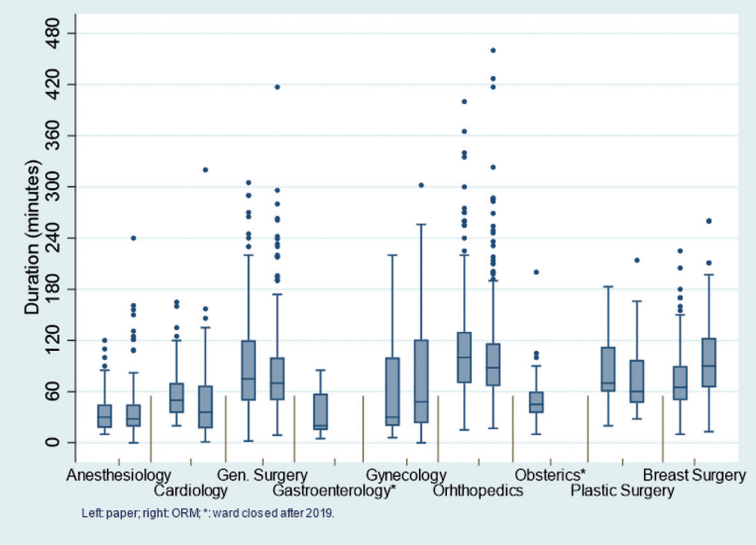

Figure 2 - Box plot of intervention times by specialty. Left: paper-based. Right: ORM based.

Table 3 - Mean of interventions duration, overall and for Orthopedics and General Surgery.

Overall:	N	Mean (min)	SD (min)	95%CI (Min)
Paper	1373	82.72	53.25	79.90 – 85.54
ORM	1294	83.09	55.04	80.09 – 86.09
DELTA	79	-0,37		-4.49 – 3.74 (p=0.570)
Orthopedics:	N	Mean (min)	SD (min)	95%CI (Min)
Paper	438	107.82	53.36	102.81 – 112.83
ORM	452	98.80	53.91	93.81 – 103,78
DELTA	14	9,02		1.96 – 16.08 (p=0.006)
General Surgery	N	Mean (min)	SD (min)	95%CI (Min)
Paper	320	91.40	58.79	84.93 – 97.86
ORM	303	82.93	52.80	76.96 – 88.90
DELTA	17	8.47		-0.31 – 17.25 (p=0.029)

A multiple regression analysis was then conducted between all paper-based interventions (2019) and all OMR-based interventions (2023), considering the intervention times of individual units (Table 3). Multivariable analysis did not reveal differences in intervention times between paper-based and ORM-based interventions.

Regarding operators' compliance, **Figure 3** represents ORM adoption trend within the operating block. It is evident that the majority of interventions still registered on paper in the first semester of 2023 regards urgent activities (n=96), while the use of ORM software for elective activities was close to 100%.

The timeframe between the entry time into the OR and the start of the surgery for the 2019 intervention group was analyzed compared to that of 2023 to assess the impact of ORM on pre-incision activities. In this analysis, operative units were not considered as the different types of intervention do not influence preoperative activities, performed by block personnel and not by operative unit personnel. A modest but statistically significant impact of the ORM system in the pre-incision phase was found, with an increase of approximately 5 min of phase duration ($p < 0.001$).

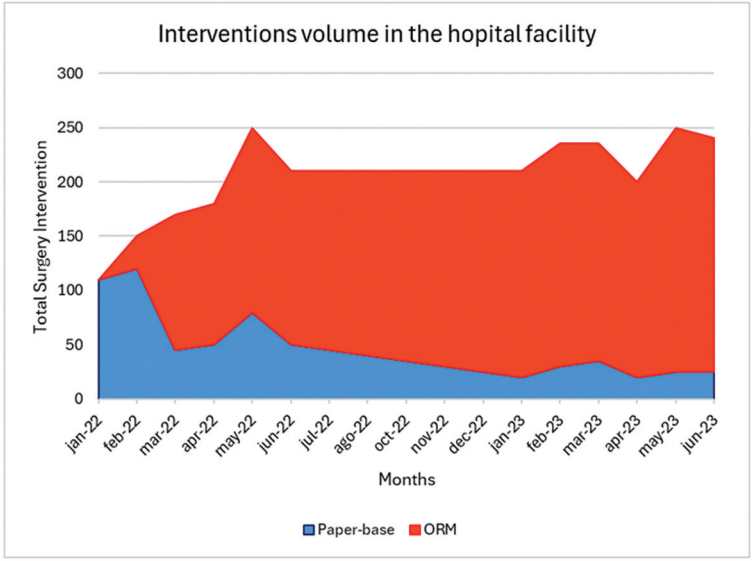

Figure 3 - Interventions volume in the hospital facility since January 1st, 2022. Blue: paper-recorded procedures. Red: ORM-recorded procedures.

Secondary endpoints

Data on the total intervention duration and the total assigned slot time were retrieved from the ORM system, by operating unit. The saturation percentage (sum of intervention times/total assigned slot duration) was then calculated. Unfortunately, this data was available only for 2023 since it was not recorded before ORM adoption. The results are synthesized in Table 4.

The Start-time delay represents the average timeframe between the time of entry into the OR of the first patient and the scheduled start time of the session. Its recorded values data are illustrated in Table 5, divided by surgical specialty. Again, this data was available only for 2023 since it was not recorded before ORM adoption.

Discussion and conclusions

Main Findings

After one-year since the adoption of the ORM system, the percentage of paper-based interventions has dropped below 10%, approaching 0% for elective procedures. However, some challenges persist in emergency/urgency activities, characterized by tighter timelines and inherently more hectic activity. Indeed, in emergency OR activities one-third of interventions still miss digital record. Nonetheless, the remarkable increasing of the ORM software usage, one year after its implementation, even for emergency/urgency interventions, highlights the critical role of personnel training in introducing new technologies and tools. This trend also suggests the potential for a complete digitalization of operating room processes, in line with eHealth transition.

In addition, the ORM system adoption had a marginal and non-detrimental impact on OR timings. This result is confirmed by multivariate analysis in an organization that, as indicated by the distribution of the number of interventions per operating unit, has remained unchanged. The analysis of intervention duration in the two units with higher surgical activity and complexity in the operating block (Orthopedics and General Surgery) has shown a slight improvement in intervention times (Table 3). The analysis of the intervening period between entry time to the OR and the start of surgery, less dependent on the type of surgery performed, shows a small difference in the pre-incision phase between the ORM group and the paper-based group. This result reinforces the concept that healthcare professionals require continuous and regular training to maximize the efficiency of the digital process (29).

Table 4. -Saturation rate of the operating block between January and June 2023, divided by specialty type.

Specialty	Scheduled slot Duration (min)	Total intervention Duration (min)	Saturation
Anesthesiology	7,200	4,295	59.65%
Cardiology	13,675	6,912	50.54%
General surgery	34,499	29,916	86.72%
Plastic surgery	4,075	2,904	71.26%
Breast surgery	23,676	15,807	66.76%
Gynecology	14,880	10,311	69.29%
Orthopedics	75,946	65,574	86.34%

Table 5 - Average start-time delay between January and June 2023, by specialty type.

Specialty	Average start-time delay	St.Dev.	N
Anesthesiology	48.26	13.44	19
Cardiology	44.87	33.34	38
General surgery	59.86	30.52	56
Plastic surgery	129.10	73.00	10
Breast surgery	75.11	61.92	46
Gynaecology	51.74	12.19	23
Orthopedics	53.07	28.50	122

The introduction of the ORM software does not seem to have brought a concrete alteration to intraoperative times. However, cost-benefit considerations cannot be limited to the intraoperative phase. The patient's surgical pathway is far from the "first come, first served" concept, as it is influenced by numerous clinical and organizational variables that impact times and outcomes (30,31). Additionally, the impact of the ORM software cannot be overlooked from a management perspective. The availability and standardization of data enable a quantitative evaluation of the impacts of organizational measures on the OR ecosystem, better management of operating slots, and more effective identification of process criticalities (missed interventions, unsaturated sessions).

Conclusions

This is among the few studies that investigate the effects of organizational changes in an operating room using real-world data. One of the study limitations is the impossibility, due to the nature of non-standardized 2019 data, to adjust the analysis for the type of surgical intervention according to the ICD9-CM code. Attempts were made to mitigate the bias by adjusting the data for individual operating units, assuming that similar types of interventions were performed within the same operating unit during both periods. Secondly, the 2019 data, generated through periodic manual data entry, is inherently of lower quality compared to ORM data, and are therefore more prone to random errors.

Another correction that cannot be applied is related to the intervention's regime (urgent, emergency, and elective) for saturation calculation, as the mixed nature of the organization of the ORs in the hospital does not allow for a correct estimation of the denominator in case of excluding urgent interventions. For the same reason, it was not possible to compare the 2019 saturation with the 2023 saturation, as the 2019 denominator data is exclusively based on elective activities. The specific distribution of surgical activities in the operating block, with a mix of urgent and elective interventions in the same room and shared rooms across multiple specialties, would have made room saturation monitoring and identifying criticalities impractical. Saturation is thus an indicator that cannot be abstracted from the surgical pathway context.

Access to high-quality, real-time data integrated across all territorial and hospital platforms is a linchpin in governing healthcare processes to meet the population's health needs (32). Increasing efficiency is essential for the future sustainability of any healthcare system, particularly the Italian National Health Service. An ORM system is a versatile and crucial tool in healthcare management, serving both the medical-nursing component to improve the quality of care, and the management component for processing analysis, identifying critical issues, and assessing the impact of adopted solutions. Ideally, once the software is integrated with an electronic clinical record, OR risk related to clinical conditions or ongoing therapy can be further monitored and, hopefully, reduced (33-35).

On the other hand, it should not be overlooked that digitalization inevitably creates a new critical node within the process, consisting of the combination of software and hardware. This requires a dedicated and cross-cutting approach in both training and organizing the entire structure. Services that were initially auxiliary in the organization, such as ICT, start to play a central and fundamental role in even the most basic care functions. Nevertheless, any new hardware and/or software introduction brings also multi-faced challenges, such as network malfunctions and program crashes/malfunctions which cause delays in the procedures and require extraordinary maintenance and support interventions. Adjustments to the presence of the new tool in established procedures also demanded modifications to the program and considerable organizational efforts. One of the main challenges that may arise with the introduction of a new digital tool, especially if the digitalization is entirely new and starts from an analog (paper-based) process, is the potential resistance from staff toward adopting new technologies, especially for non "digital natives," who might experience additional stress from using electronic devices. However, studies have shown that the ability to use digital and computer tools does not necessarily depend on the degree of digital literacy (29). Looking towards the future, we expect technology to play a more significant role in operating room scheduling and optimization, just as it is currently impacting on physicians' activity in both intra- and extra- hospital settings (36,37) Advanced software solutions, predictive analytics, and artificial intelligence will likely streamline the process further, enabling more precise and efficient scheduling. Additionally, healthcare facilities will continue to explore innovative ways to maximize resource utilization and deliver high-quality surgical care to an increasingly diverse patients' population.

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Data Availability Statement: Data are property of ASL Roma 1 Public Health Authority. The study used administrative data routinely collected by public service. Data usage granted by General Authorization of Italian National Privacy Board no. 9068972. Data are available from the Roma 1 Institutional Data Access (e-mail at: protocollo@pec.aslroma1.it), or from the corresponding author for researchers who meet the criteria for access to confidential data. [I dati sono di proprietà dell'ASL Roma 1. Lo studio ha utilizzato dati amministrativi raccolti routinariamente dal servizio pubblico. L'utilizzo dei dati è stato concesso dall'Autorizzazione Generale del Garante per la Privacy Italiano n. 9068972 (Provvedimento che individua le prescrizioni contenute nelle Autorizzazioni generali nn. 1/2016, 3/2016, 6/2016, 8/2016 e 9/2016 che risultano compatibili con il Regolamento e con il d.lgs. n. 101/2018 di adeguamento del Codice - 13 dicembre 2018 [9068972]). I dati sono disponibili presso la ASL Roma 1 (PEC: protocollo@pec.aslroma1.it, o dal corresponding author per i ricercatori che soddisfano i criteri di accesso ai dati riservati].
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Riassunto

Introduzione alla tecnologia di gestione digitale della sala operatoria: Serie temporale interrotta in un ospedale per acuti di Roma

Premessa. Il percorso chirurgico rappresenta un processo fondamentale nella produttività ospedaliera e la sua digitalizzazione è un obiettivo importante per la gestione ospedaliera. L'ASL Roma 1 ha affrontato questa sfida introducendo un sistema di Operation Room Management nel blocco operatorio di una delle sue strutture ospedaliere nel 2022.

Disegno dello studio. Analisi delle Serie Temporali Interrotte.

Metodi. Per valutare l'impatto dell'adozione del sistema Operation Room Management, sono stati raccolti dati sugli interventi chirurgici eseguiti durante due periodi: gennaio-giugno 2019 e gennaio-giugno 2023. È stata eseguita un'analisi del tasso di utilizzo del sistema Operation Room Management dalla sua introduzione per stimare l'adattamento del personale al nuovo software.

Risultati. A giugno 2023, gli interventi registrati su carta erano il 9%, raggiungendo quasi il 100% per le sole procedure elettive. La differenza tra i tempi medi degli interventi è risultata significativamente a favore del gruppo Operation Room Management quando l'analisi è stata ristretta a Ortopedia (-9,02 minuti, p=0,006) e Chirurgia (8,47 minuti, p=0,03). L' Operation Room Management ha avuto un impatto modesto ma significativo sul tempo "ingresso in sala -incisione" (5 minuti, $p < 0,01$).

Conclusione. Complessivamente, l'adozione dell'Operation Room Management non ha peggiorato i risultati del processo. L'Operation Room Management offre vantaggi in termini di qualità dei dati in tempo reale, integrati con le piattaforme territoriali e ospedaliere, contribuendo a una valutazione costo-beneficio favorevole della digitalizzazione.

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Sleep Patterns Among Athletes and Non-Athletes During Ramadan intermittent fasting: Systematic Review, Meta-Analysis and Meta-Regression

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Keywords: Sleep; Ramadan; Athlete; Meta-analysis; Public health
Parole chiave: Sonno; Ramadan; Atleta; Meta-analisi; Sanità publica

Abstract

Background. *Ramadan fasting is a religious observance practiced regularly by Muslims and may have an effect on sleep quality, especially for athletes. Our systematic review with meta-analysis aims to identify the effect of Ramadan observance on the sleep patterns of athletes and non-athletes during Ramadan fasting over the teen years (2014-2024).*
Study design. *A systematic search of Scopus, Web of Science, and Pubmed, was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-analyses.*
Methods. *After a deep search in the three databases, we downloaded all the references that respected our request. all the references were imported into the COVIDENCE platform. Two independent researchers were designated to look for the criteria inclusion and to appraise each study. A third reviewer resolved conflicts if there is a divergence of judgment. Then, we obtained an Excel file that compiles all the data collected. The meta-analysis and meta-regression were compilated.*
Results. *345 documents were found. Of these, 14 respected all the criteria. Our findings revealed that while sleep latency and disturbance remained unaffected by Ramadan, sleep duration and efficiency were negatively impacted, particularly among amateur athletes. Interestingly, the overall sleep quality, daytime dysfunction, and subjective sleep quality showed a positive impact from Ramadan, which was more evident among amateur athletes.*
Conclusions. *In the context of Ramadan fasting, these results suggest that Ramadan has a negative impact on the sleep patterns of athletes and non-athletes.*

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Introduction

An athlete's health depends on getting enough sleep, especially when training or recovering from an illness or injury. Sleep ideal for health and quality of life depends on age (adults should get between 7 and 9 hours per night) (1). For the best recuperation and most meaningful activity, athletes may need more sleep (between 9 and 10 hours) than non-athletes (2). The adverse effects of sleep deprivation on sports performance, including strength and speed, anaerobic and aerobic capacity, and psychomotor function, have been widely documented. Overall, athletes continue to experience a high prevalence of significant sleep disruptions, including insufficient sleep and poor sleep quality (3). Additionally, it was discovered that sleep deprivation impacted endurance performance but had no effect on anaerobic performance (4). Additional research demonstrated that getting enough sleep can enhance an athlete's mood, free throw and 3-point shooting ability in basketball (5), and improves service accuracy in tennis (6). According to several prior studies, diurnal fasting during Ramadan has been linked to disruptions in both quantity and quality of sleep (7). Another study found that during Ramadan, there was a noticeable significant delay in bedtime and wake time (8). Others did not note any significant fluctuations in the time spent sleeping at night throughout Ramadan (8). Nevertheless, some studies claimed no impact on physical performance (9), while others supported the opposite (10). The differences between the previous studies may be attributable to various subjective assessment methods or regional differences in culture and way of life (11). Overall, the research findings are varied, and each study revealed a different set of constraints and difficulties, making it challenging to draw broad conclusions.

In a systematic review and meta-analysis published in 2019 (12), the authors demonstrated that Ramadan and its associated practices significantly impact sleep duration and daytime sleepiness, as assessed by the Epworth Sleepiness Scale (ESS). However, this study did not present an effect size for Ramadan's impact on sleep quality or other sleep characteristics. Another meta-analysis published in 2020 (13) reported a moderate overall effect size for sleep duration, but did not conduct a meta-analysis for sleep quality or other sleep patterns. Additional recent systematic review and meta-analysis published in 2022 (14), reported that sleep duration and sleep quality altered during Ramadan, with no effect on daytime sleepiness levels. However, this study did not analyze the effect of Ramadan on all sleep patterns as measured by the Pittsburgh Sleep Quality Index (PSQI) (15) , only reporting on the global PSQI score and sleep duration.

In light of this limitations and the incongruent findings, this study aimed to conduct a systematic review with meta-analysis and meta regression to determine the effect of Ramadan fasting on sleep patterns among athletes and non-athletes who regularly practice physical activity during observance. This study is the first to examine six dimensions of sleep, as noted by PSQI (15). This meta-analysis and meta-regression will highlight new paths for future investigations.

Materials and methods

This present systematic literature review and meta-analysis adheres to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) (16) and registered in PROSPERO with ID: CRD42022327245. The COVIDENCE carried out data selection and extraction.

Data sources and search strategies

The literature search was conducted across 3 databases. We searched from January 2014 to January 2024 in Scopus, PubMed, and Web Science. The citations from the identified articles were traced. The last search was carried out on 03 January 2024. The following keywords [Sleep-wake cycle] x [Sleep quality] x [Sleep] x [Physical performance] x [Athlete] x [Non-athlete] x [Exercise] x [Performance] x [Physical exercise] were used in combination with [Ramadan] x [Fasting] x [Islamic fasting] x [intermittent Fasting]. Then we used a manual screening for more relevant studies. Indeed, the reference lists of relevant publications and reviews were searched to help ensure that all relevant publications were found.

Study selection and eligibility criteria

Two independent reviewers (ZM and RM) conducted the literature search. They screened the titles and abstracts. Then they reviewed the full texts of the manuscripts to look for the criteria inclusion. In the case of non-consensus, the Supervisor (L.S.) had the final decision. All members of the research team confirmed the inclusion and exclusion criteria. We used the PICOS criteria to define the main characteristics of our research. Population Subjects: athletes or non-athletes. Intervention: intermittent fasting of Ramadan. Comparators Baseline: before, during Ramadan. Outcomes: sleep patterns assessed by PSQI

(15). Study design: observational and experimental studies.

The search and selection procedure were based on the following criteria: English studies; Peer-reviewed journal papers published from 2014 to 2024; observational studies or controlled trials with measures of sleep quality with PSQI; healthy body; fasting during Ramadan with athlete or non-athlete profile. Studies were excluded if they used the animal model or unhealthy individuals; Shift workers; jetlag cases, diet or targeting the medication field.

Data extraction

COVIDENCE conducts data extraction. It is an extraction tool developed by Cochrane and dedicated to its authors. After a deep search in the three databases, we downloaded all the references that respected our request. The next step was to enter all the references into the COVIDENCE platform. Two independent researchers were designated as reviewers. Their mission is to screen the titles and abstracts of the records independently. All papers that were not relevant research rejected it. The reviewers performed an eligibility assessment by carefully scouring the full text independently. During this phase, any conflicts were resolved by discussions among the researchers until a consensus was achieved. The strategy starts by analyzing the title and the abstract. The reviewers accept the study and go to the next step or exclude it by stating the reason. Otherwise, they send it to a full-text analysis. The second step is to make the final extraction. For this, we have previously determined the information to be collected and analyzed the articles one by one to collect all the data we were looking for. Ultimately, we obtain an Excel file that summarize the data collected (Table 1).

Quality assessment of studies

Two independent reviewers appraised each study. A third reviewer resolved conflicts. The "QualSyst" scale was used to assess the risk of bias in studies included in the present review (17). There are 14 items, and each item was rated "Yes", "No", "Partial", or "Not applicable". We give 0 to "No" or "Not applicable", 1 to "Partial", and 2 to "Yes". A study with a score of more or equal to 75% has good quality, a score between 55% - 75% has moderate quality, and those less or equal to 55% have weak quality (Table 2).

Meta-analysis

The data were analyzed using the commercial software Comprehensive Meta-Analysis (CMA V.3.3.070, Biostat, Englewood, New Jersey, USA). An estimation of pooled measures, such as "subjective sleep quality", "sleep latency", "sleep duration", "sleep efficiency", "sleep disturbances", "daytime

Table 1 - Profiles of included studies in the meta-analysis

Study	Year	Country	Fasting time length	C°	Sample size	Level of practice	Age (SD)
Aziz et al. (10)	2017	Singapore	ND	30,5	14	Professional athlete	21.8 (2.4)
Aziz et al. (25)	2018	Singapore	ND	32,1	13	Non-athlete	20.1 (0.9)
Boukhris, H et al. (26)	2019	Tunisia	16,5	31	13	Non-athlete	21.2 (2.9)
Boukhris, T et al. (27)	2019	Tunisia	16	28	14	Non-athlete	21.6 (3.3)
Hsouna et al. (28)	2019	Tunisia	16	31,5	12	Non-athlete	21.9 (2.4)
Aziz et al. (29)	2021	Singapore	14	24,5	10	Professional athlete	22.8 (3.4)
Hsouna et al. (30)	2020	Tunisia	15,6	32	14	Non-athlete	22.0 (ND)
Hsouna et al. (31)	2020	Tunisia	16	30	12	Non-athlete	21.1 (3.2)
Lipert et al. (32)	2021	Liban	15	33	32	Professional athlete	28.3 (ND)
Saddoud et al. (33)	2022	Tunisia	16	ND	14	Professional athlete	19.0 (ND)
Boukhris et al. (34)	2022	Tunisia	16,33	32	15	Non-athlete	21.0 (ND)
EL-Jaziz et al. (35)	2023	Morocco	15,5	21	50	Non-athlete	17.2 (1.15)
EL-Jaziz et al. (36)	2023	Morocco	13,5	21	96	Non-athlete	16.9 (1.09)
EL-Jaziz et al. (37)	2023	Morocco	15,5	21	117	Non-athlete	16.9 (1.07)

ND: Not determined. C°: average temperature during the month of Ramadan.

Table 2 - Quality assessment of the 14 included studies (The "QualSyst" scale)

Author	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total score (%)	Quality assessment
Aziz et al. (10)	2	2	2	2	N/A	N/A	N/A	2	2	2	1	1	2	2	90,91%	Strong
Aziz et al. (25)	2	2	2	2	N/A	N/A	N/A	2	2	2	1	1	2	2	90,91%	Strong
Boukhris, H et al. (26)	2	2	2	1	N/A	N/A	N/A	2	2	2	1	1	2	2	86,36%	Strong
Boukhris, T et al. (27)	2	2	2	2	N/A	N/A	N/A	2	2	2	1	1	2	2	90,91%	Strong
Hsouna et al. (28)	2	2	1	2	N/A	N/A	N/A	2	1	2	1	1	2	2	81,82%	Strong
Aziz et al. (29)	2	2	2	2	N/A	N/A	N/A	2	1	1	1	1	2	2	81,82%	Strong
Hsouna et al. (30)	2	2	2	2	N/A	N/A	N/A	2	2	2	1	1	2	2	90,91%	Strong
Hsouna et al. (31)	2	2	2	2	N/A	N/A	N/A	2	2	2	1	1	2	2	90,91%	Strong
Lipert et al. (32)	2	2	1	2	N/A	N/A	N/A	2	1	2	1	1	2	2	81,82%	Strong
Saddoud et al. (33)	2	2	1	2	N/A	N/A	N/A	2	1	1	2	1	2	2	81,82%	Strong
Boukhris et al. (34)	2	2	2	2	N/A	N/A	N/A	2	2	2	2	1	2	2	95,45%	Strong
EL-Jaziz et al. (35)	2	2	1	2	N/A	N/A	N/A	2	2	2	1	1	2	2	86,36%	Strong
EL-Jaziz et al. (36)	2	2	1	2	N/A	N/A	N/A	2	2	2	1	1	2	2	86,36%	Strong
EL-Jaziz et al. (37)	2	2	1	2	N/A	N/A	N/A	2	2	2	1	1	2	2	86,36%	Strong

1: Objective, 2: Design, 3: Subject selection, 4: Subject characteristics, 5: Random allocation, 6: Blinding investigators, 7: Blinding subjects, 8: Outcomes, 9: Sample size, 10: Analysis, 11: Estimate of variance, 12: Confounding, 13: Results, 14: Conclusion, NA: Not applicable

dysfunction", and the "total PSQI score", was calculated using a random-effect model, following the DerSimonian–Laird method (18), both before and during Ramadan. The interpretation of PSQI results was conducted by utilizing the reference ranges provided in the PSQI questionnaire, where a score less than 5 signifies good sleep quality and a score greater than 5 signifies poor sleep quality (15).

The meta-analysis was undertaken by doing one-group meta-analyses (pre-post) utilizing means and standard deviations (SDs) before and during Ramadan. The sample size and pre-post correlation values were adjusted for this study. The means were chosen from empirical investigations, and in instances where the correlation was not given, a cautious estimate of $r = 0.5$, as suggested by Higgins et al., (19) was utilized.

The meta-analysis employed Cohen's guidelines to determine effect sizes (ES) with 95% confidence intervals (CIs). These effect sizes represent standardized variations in averages between total sleep patterns before and during Ramadan. The scores of ES were classified into different categories, namely trivial (ES <0.2), minor (ES 0.2–0.6), moderate (ES 0.6–1.2), big (ES 1.2–2.0), very large (ES >2.0), or extremely large (ES >4.0).

In order to assess statistical heterogeneity, the Q statistic (20) and I^2 (21) were employed. The presence of significant heterogeneity was determined when the I^2 value surpassed 50%. The values were classified into levels of statistical heterogeneity, namely low (25%), moderate (50%), or high (75%) (21). Moderator analysis, including subgroup analysis for categorical variables (e.g., sports category, level of practice), and meta-regression for both integer or decimal variables (e.g., fasting time length, age, temperature, and body mass index) and categorical variables, was performed to identify potential sources of variance and heterogeneity.

Sensitivity analyses were conducted to figure out the stability of pooled ES by assessing the impact of taking out specific investigations (leave-one-out). Additionally, a cumulative meta-analysis was carried out to further establish the stability and reliability of the outcomes.

Potential publication bias was investigated by examining funnel plot asymmetry and executing Begg and Mazumdar's rank correlation test (Kendall's S statistic P–Q)(22), Egger's linear regression test (23), and Duval and Tweedie's trim-and-fill test (24). A significance level of $p < 0.05$ was utilized for all analyzes.

Results

Study Selection

A total of 345 records were found via the initial search. Of these articles, 239 were screened by titles and abstracts for eligibility, of which 73 published studies met the inclusion criteria. After a careful review, 14 articles were included in this systematic

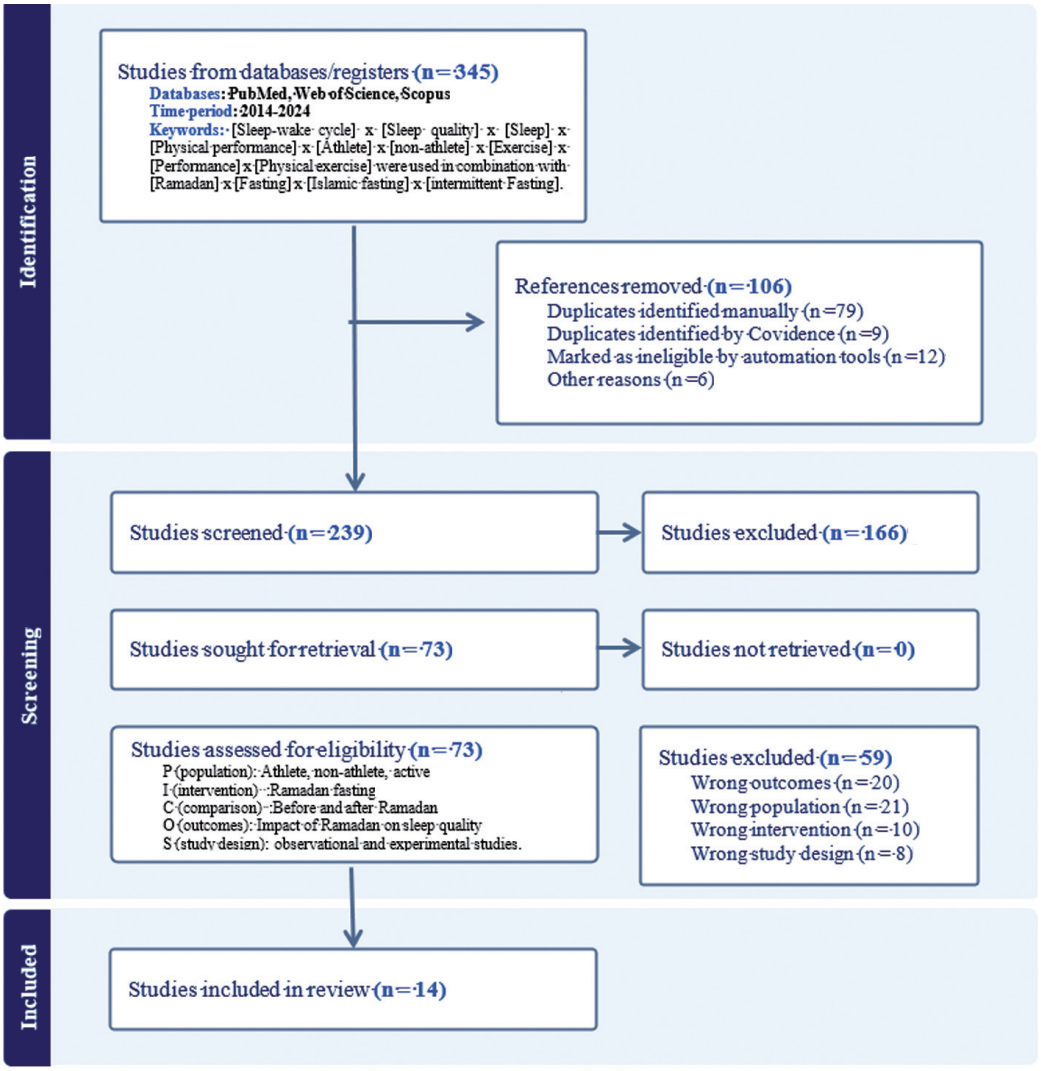

Figure 1 - PRISMA flow diagram for literature review search with a brief summary of the adopted search strategy.

review (10, 25-37). Figure 1 provides the flow diagram of this search process.

Study characteristics

A total of 14 studies, comprising 83 athletes and 343 non-athletes (non-sedentary), recruited 290 athletes from team sports and 136 from individual sports from four countries were included in this meta-analysis. All studies included fasting participants who practice regularly the training or participate in competition events during Ramadan. Three studies were conducted in Asia (Singapore), and the rest in Africa (Tunisia, Morocco, Lebanon). The average duration of fasting per day during Ramadan was 15.49 hours, with temperatures ranging between 21-33°C. The average age of participants ranged from 18 to 24 years. The highest number of participants was 117 in the study. All research papers were published between the years 2014 and 2024.

Quality Assessment

After checking the scores of 14 studies, the included research showed high methodological quality (Table 2). The most significant number of points were lost due to the lack of control of confounding factors (50%), lack of Estimating of variance (42.86%) and sample size (14.29%).

Meta-Analysis outcomes

Subjective sleep quality

The meta-analysis of subjective sleep quality before Ramadan revealed that participants obtained (1.103, 95% CI [0.799, 1.407]) with a significative heterogeneity ($Q = 231.147$, $df = 8$, $p = 0.000$; $I^2 = 96.539\%$). Analysis by subgroups found that non-athlete population had an overall pooled estimate of subjective sleep quality greater than athlete population (1.121;95% CI [0.769,1.473]) and (1, 95% CI [0.774,1.225])

respectively. However, during Ramadan, the subjective sleep quality increased to (1.777, 95% CI [1.600, 1.955]), with significant heterogeneity (Q = 58.784, df = 8, p = 0.000; I^2 = 86.391%), and it has observed among non-athlete more than athlete population (1.790, 95% CI [1.589, 1.991]) and (1.693, 95% CI [1.407, 1.980]).

Meta-analysis of pre-post subjective sleep quality indicated a significant large effect size of Ramadan (ES = 0.924, SE = 0.089, 95% CI [0.750, 1.099], Z-value = 10.389, p = 0.000), with an insignificant heterogeneity (Q = 12.806, df = 8, p = 0.119; I^2 = 37.530%); thus, a subgroup analysis and meta-regression analysis were completed. In the subgroup analysis, we computed nine research reports (27, 30-37) among two categorical variables: "level of practice", "Sports category". On one hand, the results confirmed that Ramadan fasting had a more significant effect size among individual sports participants than team sports participants (ES=1.129, SE= 0.158, 95% CI [0.820, 1.438], Z-value= 7,161, p= 0.000) and (ES= 0.789, SE= 0.069, 95% CI [0.653, 0.925], Z-value= 11.383, p= 0.000) respectively. On the other hand, the finding revealed that Ramadan observance had a more significant impact on subjective sleep quality in non-athlete population than professional athletes (ES=0.991, SE = 0.114, 95% CI [0.768, 1.215], Z-value= 8.691, p= 0.000) and (ES=0.782, SE= 0.165, 95% CI [0.458, 1,106], Z-value= 4.733, p= 0.000).

To verify if the characteristics of studies are associated with the effect size observed in this study, a meta-regression analysis performed and indicated no impact of the level of practice (coefficient= -0.184, SE= 0.25, t= -0.74, p = 0.485), fasting time length (coefficient= 0.153, SE= 0.094, 95% CI [–0.069, 0.376], t= 1.63, p= 0.073), sports category (coefficient= -0.284, SE= 0.170, 95% CI [-0.687, 0.119], t= -1.67, p= 0.069), age (coefficient= 0.011, SE = 0.027, 95% CI [-0.052, 0.075], t =0.43, p = 0.341) and temperature (coefficient= 0.026, SE= 0.019, 95% CI [-0.022, 0.074], t= 1.33, p= 0.115). However, we discovered a significant impact of the body mass index BMI (coefficient= 0.220, SE= 0.095, 95% CI [-0.013, 0.454], z= 2.31, p= 0,030).

Publication bias

The funnel plot and the results of Begg and Mazumdar's test (Kendall's S statistic P–Q = 30; tau without continuity correction = 0.833, z = 3.128, p = 0.000; tau with continuity correction = 0,805, z = 3.023, p = 0.001) and of the Egger's linear regression test (intercept = 2.173, SE = 0.450, 95% CI [1.108 to 3.239], t = 4.823, df = 7, p = 0.000) provided evidence of publication bias. Indeed, with the Duval and Tweedie trim-and-fill analysis, four studies were trimmed in the plot, and the overall effect size became 0,802 with 95% CI [0.603, 1].

Stability and Reliability

The sensitivity analyses were conducted to determine the stability of pooled ES. The effect of Ramadan on subjective sleep quality is robust and not significantly driven by any single study. In addition, the cumulative meta-analysis of the pooled effects confirmed the strong stability of the results over time.

Sleep Latency

A meta-analysis was carried out using evidence from eleven studies, and the pooled results showed no significant effect of Ramadan intermittent fasting on sleep latency (ES= -0.258, SE= 0.157, 95% CI [-0.565, 0.565], Z-value= -1.644, p = 0.100). However, the heterogeneity was highly significant (Q= 68.606, df= 10, p= 0.000; I^2= 85.424%).

Publication bias

The funnel plot and the results of Begg and Mazumdar's test (Kendall's S statistic P–Q = -2; tau without continuity correction = -0,030, z = 0,137, p = 0.445; tau with continuity correction = -0,015, z = 0,068, p = 0.0,472) and of the Egger's linear regression test (intercept = 0,288, SE = 2,097, 95% CI -4,386 to 4,962, t = 0,137, df = 10, p = 0.447) provided robust evidence of the absence of publication bias. In fact, with the Duval and Tweedie trim-and-fill analysis, one study was trimmed in the plot, and the overall effect size became -0,166 with 95% CI [-0.510, 0,177].

Stability and Reliability

The sensitivity analyses were conducted to figure out the stability of the pooled effect size. The effect of Ramadan on sleep latency is robust and not driven by any single study. In addition, a strong stability of the findings was confirmed according to the cumulative meta-analysis of the pooled effects.

Sleep duration

Meta-analysis of pre-post sleep duration indicated a significant moderate effect size of Ramadan (ES = -0.613, SE = 0.168, 95% CI [-0.943, -0.283], Z-value = -3.642, p = 0.000), with a significant heterogeneity (Q = 99.157, df = 13, p = 0.000; I^2 = 86.890%); thus, a subgroup analysis and meta-regression analysis were completed. In the subgroup analysis, we computed

fourteen research reports (10, 25-37), among two categorical variables: "Level of practice", "Sports category". On one hand, the results confirmed that Ramadan fasting had a more significant effect size among individual sports than team sports (ES= -0.726, SE= 0.281, 95% CI [-1.277, -0.176], Z-value= -2.584, p= 0.000) and (ES= -0.574, SE= 0.191, 95% CI [-0.948, -0.200], Z-value= -3.010, p= 0.003) respectively. On the other hand, the finding revealed that Ramadan observance had a significant impact on sleep duration in non-athlete but not on athlete population (ES=-0.840, SE = 0.203, 95% CI [-0.442, -0.442], Z-value= -4.141, p= 0.000) and (ES=-0.197, SE= 0.201, 95% CI [-0.590, 0.196], Z-value= -0.983, p= 0.326).

To verify if the characteristics of studies are associated with the effect size observed in this study, a meta-regression analysis performed and indicated no impact of the level of practice (coefficient= 0.622, SE= 0.452, t= 1.37, p = 0.098), fasting time length (coefficient= 0.110, SE= 0.488, 95% CI [-0.952, 1.172], t= 0.23, p= 0.443), sports category (coefficient= -0.284, SE= 0.170, 95% CI [-0.687, 0.119], t= -1.67, p= 0.069), age (coefficient= 0.079, SE = 0.072, 95% CI [-077, 0.235], t =1.11, p = 0.145), temperature (coefficient= 0.037, SE= 0.051, 95% CI [0.077, 0.150], t= 0.71, p= 0.245) and BMI (coefficient= -0.015, SE= 0.244, 95% CI [-0.551, 0.522], t= 0.06, p= 0,477).

Publication bias

The funnel plot and the results of Begg and Mazumdar's test (Kendall's S statistic P–Q = -17; tau without continuity correction = -0,187, z = 0,930, p = 0,176; tau with continuity correction = -0.176, z = 0.876, p = 0.190) and of the Egger's linear regression test (intercept = 0.575, SE = 1.686, 95% CI [-3.099, 4.248], t= 0,341, df = 12, p = 0.369) provided robust evidence of the absence of publication bias. This further strengthens the credibility of our findings. In addition, the Duval and Tweedie trim-and-fill analysis did not trim any study in the plot.

Stability and Reliability

The sensitivity analyses were conducted to figure out the stability of the pooled effect size. The effect of Ramadan on sleep duration is robust and has not been driven by any single study. In addition, the strong stability of the findings was confirmed according to the cumulative meta-analysis of the pooled effects.

Sleep Efficiency

Meta-analysis of pre-post sleep efficiency indicated a significant low effect size of Ramadan (ES = -0.375, SE = 0.085 95% CI [-0.541, -0.208], Z-value = -4.411, p = 0.000), with an insignificant moderate heterogeneity (Q = 16.223, df = 9, p = 0.062; I^2 = 44.524%); thus, a subgroup analysis and meta-regression analysis were completed. In the subgroup analysis, we computed teen research reports (26-28, 30, 31, 33-37), among two categorical variables: "Level of practice", "Sports category". On one hand, the results confirmed that Ramadan fasting had a more significant effect size among individual sports than team sports (ES= -0.578, SE= 0.129, 95% CI [-0.829, -0.322], Z-value= -4.453, p= 0.000) and (ES= -0.229, SE= 0.061, 95% CI [-0.349, -0.109], Z-value= -3.742, p= 0.000) respectively. On the other hand, the finding revealed that Ramadan observance had a significant impact on sleep duration in non-athlete population (ES= -0,332 SE = 0.080, 95% CI [-0.490, -0.174], Z-value= -4.128, p= 0.000).

To verify if the characteristics of studies are associated with the effect size observed in this study, a meta-regression analysis performed and indicated no impact of the level of practice (coefficient= -0.531, SE= 0.380, t= -1.40, p = 0.099), fasting time length (coefficient= -0.092, SE= 0.100, 95% CI [-0.323, 0.138], t= -0.93, p= 0.191), temperature (coefficient= -0.028, SE= 0.016, 95% CI [-0.065, 0.010], t= -1.75, p= 0.061) and BMI (coefficient= -0.140, SE= 0.074, 95% CI [-0.315, 0.036], t= -1.87, p= 0.051). However, there is a significant impact of sports category (coefficient= 0.343, SE= 0.140, 95% CI [0.019, 0.667], t= 2.44, p= 0.020) and age (coefficient= -0.072, SE = 0.036, 95% CI [-0.155, 0.011], t =-2, p = 0.04).

Publication bias

The funnel plot and the results of Begg and Mazumdar's test (Kendall's S statistic P–Q = -27; tau without continuity correction = -0.60, z = 2.41, p = 0.007; tau with continuity correction = -0.578, z = 2.325, p = 0.01) and Egger's linear regression test (intercept = -1.780, SE = 0.689, 95% CI [-3.368, -0.192], t = 2.584, df = 8, p = 0.0162 provided robust evidence of publication bias. In addition, the Duval and Tweedie trim-and-fill analysis did not trim any study in the plot.

Stability and Reliability

The sensitivity analyses were conducted to figure out the stability of the pooled effect size. The effect of Ramadan on sleep efficiency is robust and not driven by any single study. In addition, a strong stability of the findings was confirmed according to the cumulative meta-analysis of the pooled effects.

Sleep disturbance

A meta-analysis was carried out using evidence from teen previous studies, and the pooled results showed an insignificant low effect size of Ramadan intermittent fasting on sleep disturbance (SE= 0.186; 95% CI [-0.113, 0.484]; z= 1.220; p= 0.223). However, the heterogeneity was moderate and significant (Q= 54.891; p= 0.000; df= 9; I²= 83,604%).

Publication bias

The funnel plot and the results of Begg and Mazumdar's test (Kendall's S statistic P–Q = 21; tau without continuity correction= 0.467, z= 1.878, p= 0.030; tau with continuity correction= 0.444, z= 1.789, p= 0.036) and Egger's linear regression test (intercept= 1.031, SE= 1.568, 95% CI [-2.585, 4.646], t= 0.657, df= 8, p= 0.265 provided robust evidence of publication bias Indeed, with the Duval and Tweedie trim-and-fill analysis, one study was trimmed in the plot, and the overall effect size became 0.072 with 95% CI [-0.239, 0.383].

Stability and Reliability

The sensitivity analyses were conducted to figure out the stability of the pooled effect size. The effect of Ramadan on sleep disturbance is robust and not driven by any single study. In addition, a strong stability of the findings was confirmed according to the cumulative meta-analysis of the pooled effects.

Daytime dysfunction

The meta-analysis of daytime dysfunction before Ramadan revealed that participants obtained (0.741, 95% CI [0.462, 1.020]) with a significative heterogeneity (Q= 397.219, df= 9, p = 0.000; I² = 97.734%). Analysis by subgroups found that non-athletes had an overall pooled estimate of daytime dysfunction less than the professional athletes (0.672, 95% CI [0.365, 1.158]) and (1.010, 95% CI [0.861, 1.158]), respectively. However, during Ramadan, daytime dysfunction increased to (1.145, 95% CI [0.793, 1.498]), with significant heterogeneity (Q = 381.301, df = 9, p = 0.000; I² = 97.640%), and it has observed among professional athletes more than non-athlete population (1.262, 95% CI [0.618, 1.905]) and (1,121, 95% CI [0.722, 1.519]).

Meta-analysis of pre-post daytime dysfunction indicated a significantly small effect size of Ramadan (ES = 0.731, SE = 0.0.173, 95% CI [0.392, 1.070], Z-value = 4.225, p = 0.000), with a significant high heterogeneity (Q = 58.366, df= 9, p= 0.000; I²= 84.580%); thus, subgroup analysis and meta-regression analysis were completed. In the subgroup analysis, we computed teen reports (27, 28, 30-37), among two categorical variables: "Level of practice", "Sports category". On one hand, the results confirmed that Ramadan fasting had a significant effect size among team sports more than individual sports participants (ES= 0.912, SE = 0.072, 95% CI [0.771, 1.052], Z-value= 12.680, p= 0.000) and (ES=0.713, SE= 0.336, 95% CI [0.055, 1.371], Z-value= 2.124, p = 0.034) respectively. On the other hand, the finding revealed that analysis by subgroup of level of practice showed a significant impact on daytime dysfunction in non-athletes more than professional athletes respectively (ES= 0.831, SE= 0.185, 95% CI [0.468, 1.194], Z-value= 4.486, p= 0.000) and (ES= 0.327, SE= 0.573, 95% CI [-0.797, 1.450], Z-value= 0.570, p= 0.000).

To verify if the characteristics of studies are associated with the effect size observed in this study, a meta-regression analysis performed and indicated no impact of the level of practice (coefficient = -0.496, SE= 0.664, t= -0.75, p= 0.238), fasting time length (coefficient= -0.20, SE= 0.344, 95% CI [-0.992, 0.592], t= -0.58, p= 0.288), sports category (coefficient= 0.274, SE= 0.571, 95% CI [-1.043, 1.592], t= 0.48, p= 0.322), age (coefficient= 0.006, SE= 0.082, 95% CI [-0.185, 0.197], t= 0.07, p= 0.471), temperature (coefficient= -0.007, SE= 0.075, 95% CI [-0.109, 0.237], t= 0.85, p= 0.209) and BMI (coefficient= 0.074, SE = 0.306, 95% CI [-0.650, 0.799], t= 024, p= 0.407).

Publication bias

The funnel plot and the results of Begg and Mazumdar's test (Kendall's S statistic P–Q = -5; tau without continuity correction= -0.111, z = 0.447, p = 0.327; tau with continuity correction = -0.088, z= 0.357, p= 0.360) and of the Egger's linear regression test (intercept= -0.760, SE= 1.854, 95% CI [-5.037, 3.516], t= 0.410, df = 8, p= 0.346) provided no evidence of publication bias. Indeed, with the Duval and Tweedie trim-and-fill analysis, two study was trimmed in the plot, and the overall effect size became 0.538 with 95% CI [0.172, 0.904].

Stability and Reliability

The sensitivity analyses were conducted to determine the stability of pooled ES. The effect of Ramadan on daytime dysfunction is robust and not significantly driven by any single study. In addition, the cumulative meta-analysis of the pooled effects confirmed the robust stability of the results over time.

Total PSQI score

The meta-analysis of total PSQI scores before Ramadan revealed that participants obtained (4.497, 95% CI [3.796, 5.199]) with a significative heterogeneity (Q= 211.903, df= 10, p= 0.000; I^2= 95.281%). Analysis by subgroups found that non-athletes had an overall pooled estimate of total PSQI Scores less than the professional athletes (4.366, 95% CI [3.572, 5.160]) and (5.084, 95% CI [4.561, 5.607]) respectively. However, during Ramadan, total PSQI scores increased to (6.253, 95% CI [5.395, 7.110]), with significant heterogeneity (Q= 312.144, df= 10, p= 0.000; I^2 = 96.796%), and it has observed among athletes more than non-athlete population respectively (6.537, 95% CI [5.957, 7.116]) and (6.203, 95% CI [5.228, 7.178]).

Meta-analysis of pre-post total PSQI scores indicated a significantly high effect size of Ramadan (ES= 0.809, SE= 0.226, 95% CI [0.366, 1,152], Z-value= 3.579, p= 0.000), with a significant high heterogeneity (Q= 100.728, df= 10, p= 0.000; I^2= 90.072%) (Figure 2); thus, subgroup analysis and meta-regression analysis were completed. In the subgroup analysis, we computed eleven reports (26-28, 30-37), among two categorical variables: "Level of practice", "Sports category". On one hand, the results confirmed that Ramadan fasting had a significant effect size among individual sports participants more than team sports participants (ES= 1.092, SE= 0.477, 95% CI [0.157, 2.027], Z-value= 2.289, p= 0.022) and (ES= 0.862, SE = 0.071, 95% CI [0.723, 1.001], Z-value= 12.173, p= 0.000) respectively. On the other hand, the finding revealed that Ramadan observance had a significant impact on total PSQI scores in non-athlete more than professional athletes respectively (ES=0.888, SE= 0.280, 95% CI [0.340, 1.437], Z-value= 3.174, p= 0.002) and (ES= 0.696, SE= 0.204, 95% CI [0.297, 1.095], Z-value= 3.417, p= 0.001).

To verify if the characteristics of studies are associated with the effect size observed in this study, a meta-regression analysis performed and indicated no impact of the level of practice (coefficient= -0.211, SE= 1.217, t= -0.17, 95% CI [-2.664, 2.541], p = 0.433), fasting time length (coefficient = -0.203, SE = 0.598, 95% CI [-1.556, 1.150], t= -0.34, p= 0.371), sports category (coefficient= 0.026, SE= 0.1.042, 95% CI [-2.331, 2.383], t= 0.02, p= 0.490), age (coefficient= 0.007, SE= 0.148, 95% CI [-0.327, 0.340], t= 0.05, p= 0.482), temperature (coefficient= -0.003, SE= 0.095, 95% CI [-0.2033, 0.227], t= 0.13, p= 0.90) and BMI (coefficient= 0.148, SE = 0.583, 95% CI [-1.197, 1.492], t = 0.25, p = 0.403).

Publication bias

The funnel plot and the results of Begg and Mazumdar's test (Kendall's S statistic P–Q= 7; tau without continuity correction= 0.127, z= 0.544, p= 0.34; tau with continuity correction= 0.109, z= 0.467, p= 0.320) and the Egger's linear regression test (intercept= 0.416, SE= 1.864, 95% CI [-3.800, 4.633], t= 0.223, df= 9, p= 0.414) provided no evidence of publication bias. Indeed, with the Duval and Tweedie trim-and-fill analysis, three studies were trimmed in the plot, and the overall effect size became 0,385 with 95% CI [-0.105, 0.877] (Figure 3).

Study name	Std diff in means	Standard error	Lower limit	Upper limit	Z-Value	p-Value
Boukhris et al. (26)	-0,776	0,310	-1,384	-0,169	-2,504	0,012
Boukhris et al. (27)	1,380	0,366	0,663	2,097	3,771	0,000
Hsouna et al. (28)	-1,718	0,445	-2,590	-0,845	-3,860	0,000
Hsouna et al. (30)	4,508	0,875	2,793	6,222	5,153	0,000
Hsouna et al. (31)	5,879	1,209	3,509	8,249	4,861	0,000
Lipert et al. (32)	0,862	0,203	0,464	1,260	4,250	0,000
Saddoud et al. (33)	0,447	0,275	-0,092	0,985	1,626	0,104
Boukhris et al. (34)	1,176	0,329	0,531	1,821	3,574	0,000
EL-Jaziz et al. (35)	0,732	0,156	0,426	1,037	4,689	0,000
EL-Jaziz et al. (36)	0,869	0,117	0,639	1,099	7,405	0,000
EL-Jaziz et al. (37)	0,919	0,108	0,707	1,130	8,505	0,000
	0,809	0,226	0,366	1,252	3,579	0,000

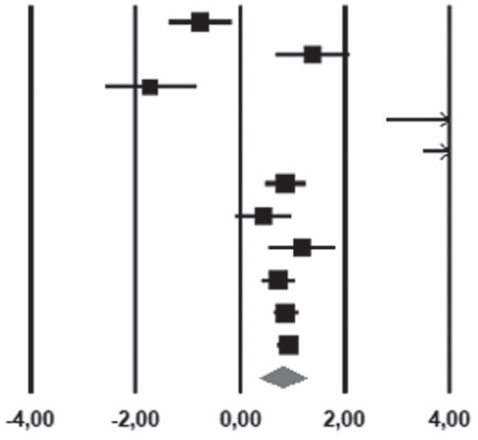

Figure 2 - Forest plot of the total PSQI Score

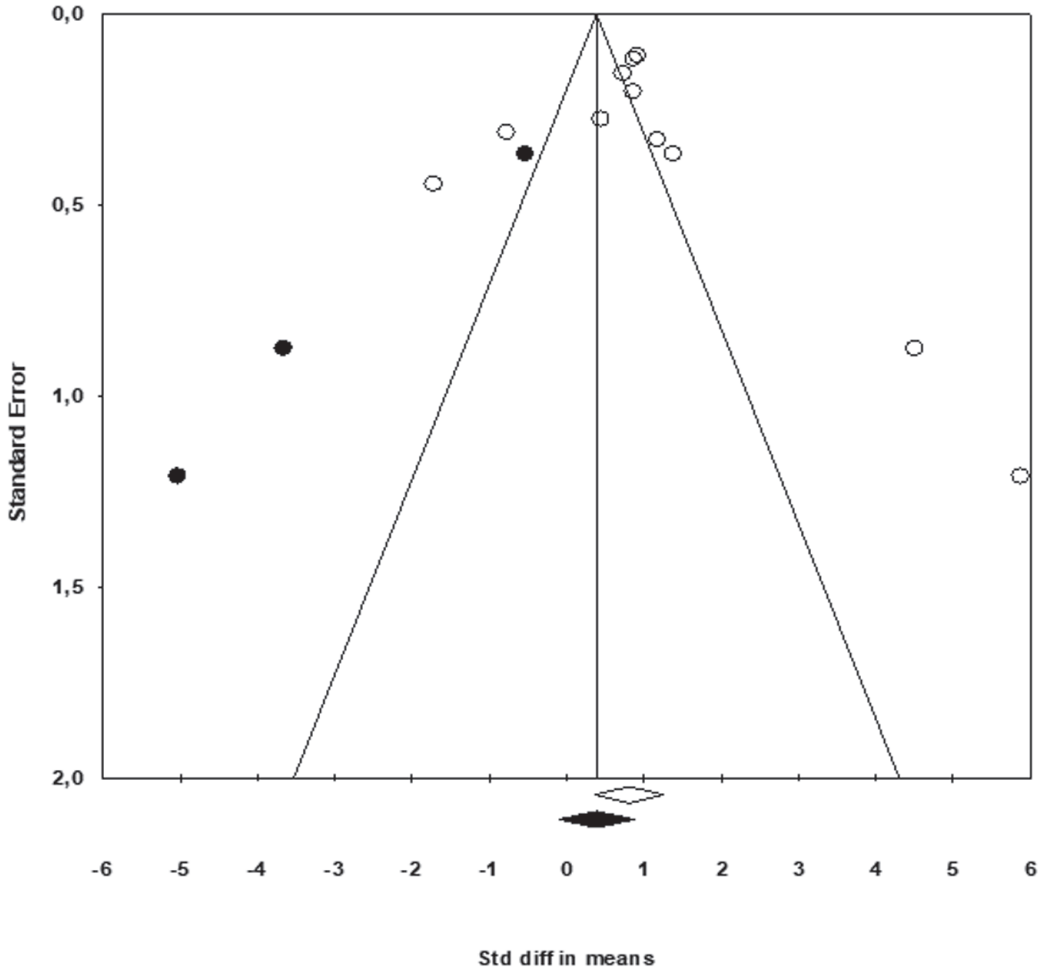

Figure 3 - Funnel plots of the total PSQI score

Stability and Reliability

The sensitivity analyses were conducted to determine the stability of pooled ES. The effect of Ramadan on total PSQI Scores is robust and not significantly driven by any single study. In addition, the cumulative meta-analysis of the pooled effects confirmed the robust stability of the results over time.

Discussion and conclusions

This systematic review and meta-analysis, crucial for researchers, coaches, and athletes, delved into the sleep quality of athletes (professional/amateur) before and during intermittent fasting of Ramadan. Our findings revealed that while sleep latency and disturbance remained unaffected by Ramadan, sleep duration and efficiency were negatively impacted, particularly among amateur athletes. Interestingly, the overall sleep quality, daytime dysfunction, and subjective sleep quality showed a positive impact from Ramadan, which was more pronounced among amateur athletes.

In this meta-analysis, the significant finding was that Ramadan does not impact sleep disturbance for non-athlete and athlete population. Lipert et al. (38) confirmed this outcome and showed that the sleep disturbance was the same before and during Ramadan. However, this result does not align with previous studies suggesting that Ramadan is associated with dietary changes that could induce gastrointestinal disorders and impair sleep interruption (39-41). In addition, other studies suggested that the risk of this interruption is due to the late Suhoor meal (the

last meal before starting the day fast) (42) or to the excess drinking water during night-time which may lead the athlete to wake-up at night many times to urinate (43).

The analysis yielded no discernible impact of Ramadan on sleep latency among non-athlete and athlete population. Our findings align with previous research (44). This consistency persisted even after controlling for various circadian moderators, including the sleep/wake schedule, prior sleep duration, caloric intake, energy expenditure, and light exposure (45). One potential explanation for these results is that athletes may compensate for daytime fasting by incorporating naps into their routine, thus regulating their sleep patterns and mitigating any potential impact on latency. However, contrasting findings from other recent studies (46, 47) suggest the opposite. It is conceivable that alterations in the timing of nocturnal meal consumption and delays in nocturnal training or competitions contribute to changes in sleep patterns, promoting nocturnal wakefulness.

The research findings indicate that Ramadan has a negative impact on sleep efficiency among non-athlete, while professional athletes do not experience significant changes. Our findings diverge from previous research outcomes. According to clinical guidelines, a sleep efficiency >85% reflects good sleep efficiency during Ramadan (48), and many studies found that the average sleep efficiency values were higher than this cut-off. Therefore, there was no significant change in sleep efficiency during the fasting period compared to baseline (42, 44, 49-51).

The meta-analysis findings suggest that Ramadan negatively affects the sleep duration in non-athlete population, whereas professional athletes do not undergo significant alterations. Our results are in accordance with another meta-analysis that found the Total sleep time decreased during Ramadan (27) in athletes and non-athlete people (12). Nevertheless, not with others (26, 28, 52) that they reported a need for more change in sleep duration during Ramadan. In the present meta-analysis, the total studied population was 7.65 h, which decreased by 62 minutes during Ramadan; this result is in line with the last meta-analysis (12), which found the average was 7.2 h, which decreased by ~60 min during Ramadan observance. One possible explanation for this reduced sleep duration may be the increased exposure to nocturnal light (53) resulting from heightened nighttime social activities during Ramadan (12, 54). BaHammam (55) also proposed another explanation, suggesting that sleeping with a full stomach after the late Suhoor meal could lead to gastroesophageal reflux and reduced diet-induced thermogenesis, affecting sleep duration. Moreover, future analyses should consider factors such as mental and psychological stability throughout the month when training and competing activities are undertaken, as these parameters are likely to influence total sleep duration significantly.

The current study found that subjective sleep quality and the total PSQI score are positively impacted by Ramadan, particularly among non-athletes compared to professionals. Our findings are consistent with previous studies that demonstrated a significant increase in subjective sleep perception during Ramadan compared to before (47, 56, 57), especially towards the end (57). However, these results differ from some published meta-analyses (14) that did not find any change in global PSQI scores, especially among individuals who continued to train during Ramadan. This discrepancy may be attributed to the fact that Ramadan observance is generally associated with changes in training programs, sleep routines (39, 58), alterations in food composition and quantity, as well as meal timing and frequency (59). These dietary changes could induce gastrointestinal disorders (39), which have been previously suggested to impair athletes' sleep quality through sleep interruption (40). It is pertinent to highlight that while physical activity during Ramadan influences sleep quality, it remains elusive to discern whether specific forms of physical exercise exert a differential impact on sleep quality during this period. Hence, there is a necessity for future studies centred on Ramadan to adopt experimental designs, transcending reliance on subjective assessments.

The results of this study indicate that daytime dysfunction was positively influenced by Ramadan, particularly among non-athletes compared to professionals. These findings appear to align with previous meta-analyses that documented a substantial increase in daytime sleepiness during Ramadan (12, 54). Other research corroborated these findings, suggesting that Ramadan leads to a significant, substantial, and robust increase in daytime dysfunction among athletes (46). This observed increase in daytime dysfunction may arise from the cumulative effects of sleep deprivation during Ramadan, compounded by daytime fatigue associated with training schedules or competition schedules, which may be further exacerbated by inadequate hydration throughout the day. However, other meta-analyses did not support our results and reported no significant effect of Ramadan on daytime sleepiness (14). A possible explanation might be that athletes take daily naps or employ other adaptive

responses to counteract daytime sleepiness (13). In future investigations, it might be possible to explore different forms of sleep recuperation during Ramadan observance.

Practical implications

The findings of this review have several practical and research implications. It would be advisable for Sports psychologists, Sports nutritionists, Coaches, adolescent university students and athletes to conduct regular assessments of the effect of Ramadan intermittent fasting on their sleep quality to increase physical performance and anticipate the effects of possible coping strategies and overcome sleep disturbance. Thus, we suggested the need for self-help management strategies and program training for athletes to identify and enhance sleep quality, especially before competitions.

Limitations and strengths

The current review possesses several strengths. It represents the first systematic review with meta-analysis and meta-regression, reporting pooled effect sizes for six dimensions of sleep among both athletes and non-athletes. While the majority of previous meta-analyses have presented information solely on sleep duration and the total score of the PSQI, no study - to our knowledge- has addressed all dimensions previously comprehensively. However, it is crucial to acknowledge the limitations of the present study when assessing the effect of Ramadan intermittent fasting on sleep patterns. Firstly, during the realization of this meta-analysis, other authors have published similar projects, necessitating several modifications to ensure the originality of our study. This process led to a considerable time investment, with occasional revisions required to our inclusion and exclusion criteria. Secondly, due to the relatively small number of studies included in this meta-analysis and an insufficient representation of athlete participants compared to non-athletes, caution should be exercised in generalizing the conclusions of the current review. Thirdly, certain research studies may not be included in this meta-analysis, even if published between 2014 and 2024, despite using MeSH keywords and various databases. Fourthly, we were constrained to rely on the published data available to extract information regarding participants' sleep and level of practice during Ramadan. However, the data was sometimes insufficient or unavailable, so we did not verify physical performance as a moderator variable susceptible to association with sleep quality during Ramadan.

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Riassunto

Modelli di sonno tra Atleti professionisti e Atleti dilettanti durante il digiuno intermittente del Ramadan Systematic Review, Meta-Analysis and Meta-Regression

Contesto. Il digiuno del Ramadan è un'osservanza religiosa osservata periodicamente dai musulmani praticanti e può avere un effetto sulla qualità del sonno, in particolare per gli atleti. La nostra revisione sistematica con meta-analisi (2024-2024) mira a identificare l'effetto dell'osservanza del Ramadan sui modelli di sonno di atleti e non atleti durante il digiuno del Ramadan negli anni dell'adolescenza.

Disegno dello studio. È stata condotta una ricerca sistematica su Scopus, Web of Science e Pubmed, utilizzando gli elementi di reporting preferiti per revisioni sistematiche e meta-analisi.

Metodi. Dopo una ricerca approfondita nei tre database, abbiamo scaricato tutti i riferimenti che rispettavano la nostra richiesta. Tutti i riferimenti sono stati importati nella piattaforma COVIDENCE. Due ricercatori indipendenti sono stati designati per definire i criteri di inclu/esclusione e valutare ogni studio. Un terzo revisore ha risolto i conflitti in caso di divergenza di giudizio. Quindi, abbiamo ottenuto un file Excel con in evidenza tutti i dati raccolti. Sono state compilate la meta-analisi e la meta-regressione.

Risultati. Sono stati recuperati 345 documenti. Di questi, 14 rispettavano tutti i criteri. I nostri risultati hanno rivelato che - mentre la latenza e i disturbi del sonno non sono stati influenzati dal Ramadan - la durata e l'efficienza del sonno sono state influenzate negativamente, in particolare tra gli atleti amatoriali. È interessante notare che la qualità complessiva del sonno, la disfunzione diurna e la qualità soggettiva del sonno hanno mostrato un impatto positivo da parte del Ramadan, che è stato più evidente tra gli atleti amatoriali.

Discussione e Conclusioni. Nel contesto del digiuno del Ramadan, questi risultati suggeriscono che il Ramadan ha un impatto negativo sui modelli di sonno degli atleti e dei non atleti.

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Pulmonary embolism: incidence and outcomes in a twelve-year historical series, in Tuscany - Italy (2010-2021)

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Parole chiave: Embolia polmonare; Trend di incidenza; Analisi epidemiologica; Determinanti di mortalità; Farmaci anticoagulanti; Differenze di genere

Abstract

Background. *Pulmonary embolism poses a global health concern. Administrative databases serve as valuable sources for broad epidemiological studies on the prevalence and incidence of major diagnoses or diseases**.** The primary scope is to provide up-to-date insights into Pulmonary Embolism incidence trends, examining shifts in management and outcomes.*

Design. *This retrospective observational study examines a 12-year dataset from hospitals in the Tuscany Region, covering the first two years of the Covid-19 pandemic.*

Methods*. Administrative data from residents aged 18 and older discharged from hospital between 2010 and 2021 were used for the analysis.*

Results. *Hospitalized pulmonary embolism incidence slightly declined from 2010 to 2019 (64.7 to 60.9 x 100,000; p=0.152). Males under 75 showed a higher incidence rate, while females had higher incidence rates in older age groups. In-hospital and 30-day mortality decreased from 2010 to 2019 (p=0.001 and 0.020 respectively). In 2020, 30-day mortality increased (12.4% vs 10.1%, p=0.029), while in-hospital mortality remained stable. One-year mortality was stable from 2010-2019 but increased in 2020 (32.6% vs 29.4%, p=0.037). Considering the multivariable model, one-year mortality is significantly associated with sex, age, and comorbidities.*

Conclusions. *Our study shows that Pulmonary Embolism persists as a relevant burden in Tuscany region, but with improvements in management over the past decade and a decisive change in pharmacological treatment. Gender-related differences emerge, highlighting the need for a gender-specific healthcare approach.*

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Introduction

Pulmonary embolism (PE) is a worldwide health issue representing a common disorder with high mortality and morbidity rates (1). Patients with PE have a case fatality rate of 8% and approximately 10% of symptomatic PE cases are fatal within the first hour after symptoms onset (2). Moreover, PE is the third cause of cardiovascular death after myocardial infarction and stroke, and it is the leading preventable cause of death in hospitalized patients (3,4). Longitudinal data have revealed an increasing trend in annual PE incidence rates over time. Since the incidence of the disease rises with age and due to the aging of Western societies, it can be expected that a larger number of patients will be diagnosed with PE in the future (5). Despite the overmentioned tendency, there is evidence of a decrease in the mortality rate of PE. Such decrease may be attributed to improvements in risk management, but also to a higher number of patients with smaller emboli and low risk of PE-related complications and mortality (6). Nevertheless, in the modern era, since the introduction of computed tomographic pulmonary angiography (CTPA) to establish the diagnosis, an increase of the total number of PE cases and a corresponding decrease in case fatality have been observed (7).

Most of the published information on the prevention, current therapy, and natural history of patients with venous thromboembolism (VTE) came from randomized clinical trials (RCTs), mostly focused to obtain data on efficacy and safety of drugs. Randomized control studies usually involve well-defined study populations excluding complex patients and adopt standardized protocols that are sometimes difficult to implement in routine clinical practice (8). Moreover, RCTs-based recommendations might not be applied to different, broader populations so that the resulting outcomes could not be inferred to different persons with respect to those observed in RCTs. Real world data are crucial for describing the management of PE, because a significant percentage of the affected patients have at least one exclusion criterion preventing their inclusion into randomized clinical trials (8). Administrative structured database data collection can provide complementary data to those from the trials, help understanding the treatment pathway of patients, inform the generation of new hypotheses, and verify the already emerged ones (8). Taking into account databases fueled by real world data, we must consider possible epidemiological differences among populations, due to different prevalence of risk factors, and other distal determinants, such as those regarding the socio-economic status, or the geographical nationality of the recruited persons. So far, for instance, only few studies evaluated the incidence and prognosis of PE in the southern European countries (9).

In the last few years several findings have shown that administrative databases might represent one of the best available sources for wide epidemiological studies regarding prevalence and incidence of major diagnoses or diseases, especially when they are focused on a clearly identified event (10).

This study employs a methodological approach using data from Tuscany Region hospitals' discharge records over a 12-year period, including the initial two years of the Covid-19 pandemic. Our objective is to conduct a trend analysis of pulmonary embolism incidence, offering robust and updated data to enhance understanding of the disease burden. We focus on an unselected population to evaluate changes in management and outcomes over the years, with attention to the pandemic's impact in the last two years of the examined period.

Materials and Methods

We conducted a retrospective observational study, including all individuals resident in Tuscany, aged 18 years or older, discharged from one of the regional hospitals with diagnosis of PE from 2010 to 2021.

The primary outcome measures were trends in incidence rates (crude and adjusted for sex and age), patient's characteristics (sex, age, Charlson Comorbidity Index (11)), length of hospital stay (LOHS), pharmacological treatment at discharge and hard outcomes in terms of in-hospital mortality (IHM), 30-day mortality and one year mortality.

Data were provided by Tuscan Regional Healthcare Agency that is a public entity (Regional Law n. 40/2005) entitled to perform research and analysis. Individual, anonymous data on people residing in Tuscany come from the Regional Healthcare Administrative Data System (RHCADS). The RHCADS comprises several healthcare data sources, including Hospital Discharge Abstracts (HDAs), Registry Offices and data on drug dispensing registry (DDR). Each individual has a unique and anonymous identifier within the RHCADS.

The HDA collects information on demographic characteristics, admission and primary and secondary diagnoses and procedures coded according to the

International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). Date of death was reported in Registry Office, while information on medications dispensed in private, public and hospital pharmacies were identified on DDR through the Anatomical Therapeutic Chemical index (ATC).

According to the relevant regulatory provisions and guidelines, the opinion of the Ethics Committee, thus the Institutional Review Board (IRB) approval, was not required for the present activity. This exclusion is determined by the circumstance that in carrying out the activity no relevant ethical issues arise, as the subject matter is regulated by current legislation on planning, management, control, and evaluation of healthcare, as set forth in sheet No. 12 (Attachment A) to the Regional Regulation on data protection (Regulation dated October 26, 2021, No. 37/R, Implementation Regulation of Article 1, paragraph 1, of Regional Law dated April 3rd, 2006, No. 13, concerning the treatment of special categories of personal data and that relating to criminal convictions and crimes by the Tuscany Region, healthcare agencies, entities, companies, and regional agencies, and public entities in respect of which the Region exercises direction and control powers).

The study population includes all Tuscany region residents with a first hospital admission for PE in a calendar year (PE hospital events). More specifically, patients with a primary diagnosis of PE (ICD-9-CM codes 415.11 or 415.19) or with a secondary discharge diagnosis of PE associated with a primary code compatible with PE (ICD-9-CM codes 51881, 51882, 51884, 7991, 4534, 4538, 4536 78551, 4275, 4589) in the hospital discharge form were included. In order to estimate the incidence of PE events requiring hospital care, the first hospitalization in a year was considered for each subject, excluding any hospitalizations in the subsequent 365 days. Other exclusion criteria were admission in a rehabilitation ward and incorrect unique encrypted identifier. According to the clinical characteristics of the index episode, high-risk PE (HRPE) was defined by the presence of at least one of the following criteria: cardiogenic shock (ICD-9-CM code 785.51), cardiac arrest (427.5), transient severe hypotension (458.9), need for mechanical ventilation (96.70, 96.71, 96.72), orotracheal intubation (96.04), cardiopulmonary resuscitation (96.60). Comorbidities were measured using the Charlson Comorbidity Index (CCI).

Pharmacological treatments prescribed within 30 days of hospital discharge considered in the study include: low-molecular-weight heparin (LMWH) therapy (ATC codes B01AB01, B01AB04, B01AB05, B01AB06, B01AB07, B01AB08, B01AB12, B01AX05), indirect anticoagulation therapy (B01AA03, B01AA07), direct oral anticoagulants (DOACs) (B01AF01, B01AE07, B01AF03, B01AF02).

Baseline patient characteristics were expressed using descriptive statistics. Continuous variables were reported as mean with standard deviation (SD) or median with interquartile range (IQR). Categorical variables were reported as counts and percentages. In order to identify changes in trends between 2010 and 2019 (pre-pandemic period), the Mann-Kendall test for trend has been performed. Data between 2020 and 2021 were compared to 2019 to evaluate changes in the burden of disease of PE due to COVID-19 pandemic. A descriptive analysis (chi-square test for categorical data and nonparametric Kruskal-Wallis/ median test for quantitative measurements) were performed. For each analysis, an αlevel of 0.05 is considered as significant. To study determinants of in-hospital, 30-days and one-year mortality, multivariate logistic regression models were conducted over the 12-year period. The statistical software Stata 15 SE [tm] was used for the analysis.

Results

During the twelve-year study period (2010-2021), a total of 22,361 PE hospital events in 21,774 subjects were recorded. The proportion of patients with High Risk Pulmonary Embolism (HRPE) decreased from 2010 to 2019 (5.9% vs. 4.2%, $p < 0.001$). Incidence rate of hospitalized pulmonary embolism slightly decreases from 2010 to 2019 from 64.7 x 100,000 to 60.9 x 100,000 (Mann-Kendall test p-value 0.152). The trend is maintained even after standardization by age and sex (Appendix). Notably, this trend remained stable between 2019 and 2021 (Mann-Kendall test p-value 1.000). The reduction in incidence is higher in individuals aged over 85 years (see Figure 1).

The cumulative crude incidence of PE was significantly higher in females (63.1 x 100,000) than in males (55.8 x 100,000, $p<0.001$). Since the median age of the population is 78 years, we subsequently stratified the study population into three age classes (< 75 yo, 75-84 yo, >=85 yo). The incidence rate was more than ten-fold higher in 85 years old or older people than in people younger than 75 years (303.7 per 100,000 inhabitants vs. 27.8 per 100,000 inhabitants).

Sex distribution revealed a higher incidence rate of PE among males under 75, while females exhibited a higher incidence rate in the older age classes (Figure 1). In Table 1 we show in detail the clinical features of patients comparing the first study year (2010), the last pre-pandemic year (2019) and the 2020-2021 pandemic years compared to 2019. Complete data are listed in Appendix. Between 2010 and 2019 we observed significant differences in the proportion of HRPE, Charlson comorbidity index, length of hospital stay (LOHS). Following a substantial reduction between 2010 and 2019, LOHS significantly increased during the pandemic years.

The overall in-hospital mortality (IHM) and the 30-day mortality decreased significantly between 2010 and 2019 (Mann-Kendall test p-value 0.001 and 0.020, respectively, see Figure 2). During 2020, 30-days mortality showed a significant increase compared to 2019 (12.4% vs 10.1% p=0.029) while in-hospital mortality remained stable during the pandemic years (Mann-Kendall test p-value 0.296). No significant differences exist between females and males (8.5% vs. 8.0% respectively, p=0.182 for in-hospital and 13.1% vs 13.4% respectively, p=0.393, for 30-day mortality). Considering the multivariable models, in-hospital and 30-day mortality rates are not associated with sex (OR 0.968, p=0.515) while both increase with age and comorbidities (Table 2). While reduction in IHM was constant during the study periods, 30-days mortality increased between 2010 and 2013, especially in males, and decreased for both sexes beginning 2014 (Figure 2).

Figure 1 - Incidence of PE by sex and age, 2010-2021, Tuscany. (a) Cumulative PE incidence rate; (b) PE incidence rate in individuals younger than 75 years old; (c) PE incidence rate in individuals aged 75 to 84 years; (d) PE incidence rate in individuals older than 85 years.

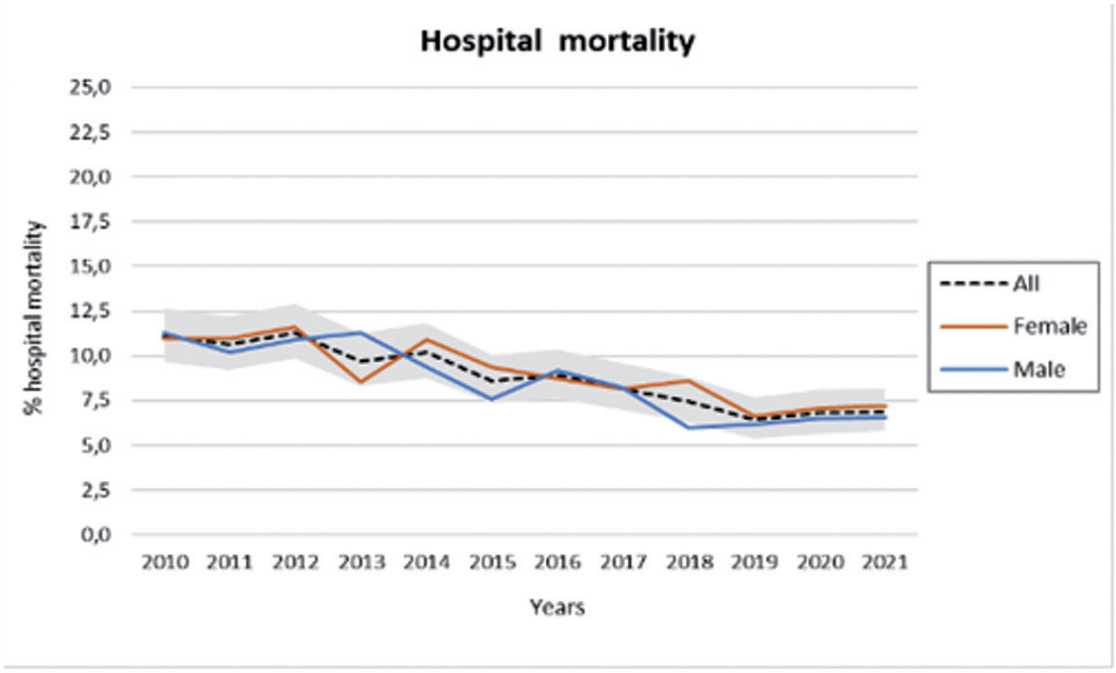
Table 1 - Baselines characteristic of patients across study years: 2010 - pre-pandemic 2019, and pandemic years 2020-2021 vs. 2019.

Characteristics	2010-2021 N (%)	2010 N (%)	2019 N (%)	19 vs 10 p-values	2020 N (%)	20 vs 19 p-values	2021 N (%)	21 vs 19 p-values
Hospital admissions	22,361	1,963	1,924		1,707		1,966 (8.8)	
Massive EP	1,010 (4.5)	115 (5.9)	81 (4.2)	0.019	66 (3.9)	0.600	76 (3.9)	0.585
Sex								
Female	12,646 (56.6)	1,149 (58.5)	1,071 (55.7)	0.071	907 (53.1)	0.126	1,110 (56.5)	0.618
Age								
Mean (SD)	75 (13)	75 (13)	74 (14)		74 (14)		75 (13)	
Median [IQR]	78 [69;85]	78 [69;85]	78 [68;84]	0.773	77 [67;84]	0.150	78 [68;84]	0.858
<75 year	8,745 (39.1)	740 (37.7)	777 (40.4)	0.219	734 (43.0)	0.247	762 (38.8)	0.558
75-84 year	7,997 (35.8)	727 (37.0)	675 (35.1)		583 (34.2)		716 (36.4)	
85+ year	5,616 (25.1)	496 (25.3)	472 (24.5)		390 (22.8)		488 (24.8)	
Charlson index								
CCS 0	7,787 (34.8)	674 (34.3)	740 (38.5)	0.044	647 (37.9)	0.963	734 (37.3)	0.345
CCS 1	4,524 (20.2)	400 (20.4)	389 (20.2)		342 (20.0)		431 (21.9)	
CCS 2-4	6,403 (28.6)	590 (30.1)	528 (27.4)		472 (27.7)		508 (25.8)	
CCS 5-6+	3,647 (16.3)	299 (15.2)	267 (13.9)		246 (14.4)		293 (14.9)	
LOHS								
Mean (SD)	10 (7.5)	11.4 (9)	8.7 (8)		9.3 (7)		9.5 (7)	
Median [IQR]	8 [5;12]	10 [6;14]	7 [5;11]	<0.001	7 [5;12]	0.076	8 [5;12]	0.004
Pharmacological treatments at hospital discharge	%	N (%)	N (%)		N (%)		N (%)	
At least one treatment	87.7	1,455 (83.4)	1,640 (91.1)	<0.001	1,431 (89.9)	0.270	1,640 (89.6)	0.143
low-molecular-weight heparin therapy	40.4	840 (48.1)	576 (32,0)	<0.001	486 (30.5)	0.381	503 (27.5)	0.003
indirect anticoagulation therapy	24.4	830 (47.6)	117 (6.5)	<0.001	68 (4.3)	0.004	65 (3.6)	0.001
DOACs	35.0	21 (1.3)	1,111 (61.7)	<0.001	1,000 (62.9)	0.498	1,212 (66.2)	0.005
Mortality	%	N (%)	N (%)		N (%)		N (%)	
- In-hospital	8.9	218 (11.1)	124 (6.4)	<0.001	116 (6.8)	0.671	136 (6.9)	0.555
- 30-days	13.3	264 (13.4)	195 (10.1)	0.001	212 (12.4)	0.029	223 (11.3)	0.224
- 1-year	33.6	661 (33.7)	566 (29.4)	0.004	557 (32.6)	0.037	616 (31.3)	0.194
Hospital readmissions								
- all causes		236 (13.5)	193 (10.7)	0.011	170 (10.7)	0.972	192 (10.5)	0.822
- for symptoms related to PE		65 (3.7)	63 (3.5)	0.720	42 (2.6)	0.149	58 (3.2)	0.579
- for any major complications of anticoagulation therapy		6 (0.3)	15 (0.8)	0.058	12 (0.8)	0.796	16 (0.9)	0.893

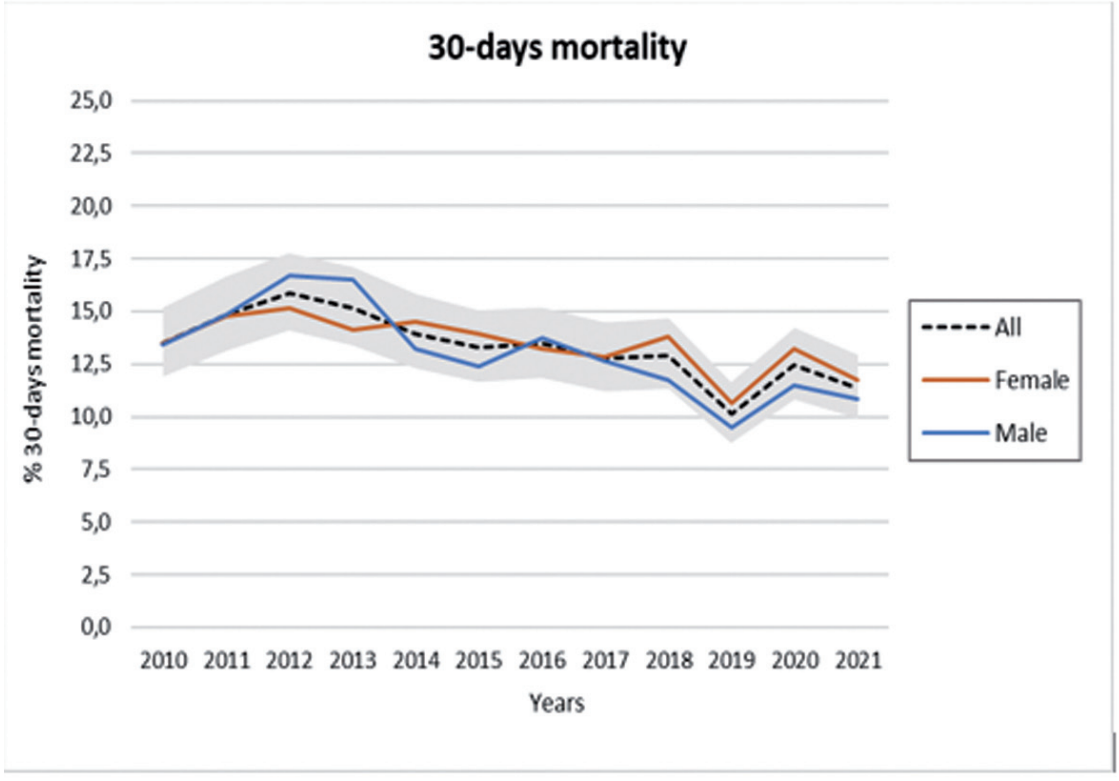
SD, standard deviation; CCI, Charlson comorbidity index; IQR, interquartile range; LOHS, length of Hospital Stay; DOACs, Direct Oral Anticoagulants

Regarding the pharmacological treatments, they were prescribed at the time of discharge from the hospital in 87.7% of patients. During the years, we observed a reduction in the prescription of low molecular weight heparin (LMWH) therapy, from 48% in 2010 to 32% in 2019, and in indirect anticoagulation therapy, from 47.6% in 2010 to 6.5% in 2019 (p<0.001). On the other hand, the prescription of direct oral anticoagulants (DOACs) increased over time, from 1.3% in 2013 to 61.7% in 2019 (p<0.001). Throughout the pandemic years, a similar pattern in pharmaceutical prescriptions as that seen in the years 2010-2019 was observed (see Appendix and Table 1).

The 30-day hospital readmission rate for all causes decreased from 2010 to 2019, but there was



(a)



(b)

Figure 2 - PE Mortality rate by sex, 2010-2021, Tuscany. (a) In hospital mortality rate; (b) 30 days mortality rate

Table 2 - Multiple regression model of variables associated with mortality after a first episode of PE. From the left: the first column shows the variables included in the model. The second, third and fourth columns show the in-hospital mortality, the 30-days mortality and the 1 year mortality. Statistically significant results are highlighted

	In-hospital mortality		30-days mortality		1 year mortality	
	OR	P-value	OR	P-value	OR	P-value
Female	0.968	0.515	0.975	0.554	0.929	0.027
Age (baseline: "Age<75")						
Age 75-84	1.667	<0.001	1.615	<0.001	1.612	<0.001
Age 85+	2.920	<0.001	3.234	<0.001	3.604	<0.001
CCS (baseline: "CCS 0-1")						
CCS 2-4	1.461	<0.001	1.602	<0.001	1.963	<0.001
CCS 5	2.005	<0.001	2.528	<0.001	3.743	<0.001
CCS 6+	2.920	<0.001	2.520	<0.001	17.038	<0.001
Year (baseline year 2010)						
2011	0.949	0.626	1.115	0.256	0.997	0.966
2012	1.000	0.997	1.180	0.079	1.035	0.648
2013	0.843	0.120	1.119	0.243	1.093	0.249
2014	0.906	0.363	1.031	0.749	1.083	0.301
2015	0.730	0.005	0.947	0.578	1.020	0.791
2016	0.769	0.017	0.973	0.779	0.973	0.719
2017	0.697	0.001	0.912	0.353	0.960	0.601
2018	0.634	<0.001	0.941	0.538	0.905	0.195
2019	0.570	<0.001	0.758	0.007	0.865	0.059
2020	0.609	<0.001	0.971	0.779	1.044	0.581
2021	0.602	<0.001	0.841	0.084	0.932	0.355

OR, Odds Ratio; CCI, Charlson comorbidity index

no significant reduction in readmission rates for symptoms related to PE or for any major complication of anticoagulation therapy over the years. The readmission rates remained stable during the pandemic years compared to 2019.

One-year mortality did not change between 2010 and 2019 (Mann-Kendal test: p=0.107). Between 2011 and 2014, males showed a significantly higher one-year mortality. Moreover, one-year mortality shows a significant increase during 2020 compared to 2019 (32.6% vs 29.4%, p=0.037). Considering the multivariable model, one-year mortality is significantly associated with sex, age and comorbidities (Table 2).

Discussion

Based on our findings, the incidence of hospitalized PE in the Tuscany Region, Italy, between 2010 and 2021 was relatively high and exhibited stability throughout the entire observation period, surpassing rates observed in other studies (1, 9). According to other recent analyses, the incidence rate of high-risk pulmonary embolism has decreased over the years. This may be partly attributed to improved diagnostic workup and more effective management right from the initial phases of onset at the emergency department (12). The in-hospital and 30-days mortality was in line with literature findings (13-16), but there was a discernible downward trend until 2019. Furthermore, a notable and statistically significant reduction of the mean duration of hospitalization throughout the study period was found.

Our findings, consistent with existing literature (17), underscore age-stratified differences in PE incidence by gender. Among younger age groups, males exhibited a higher incidence rate compared to females, likely influenced by physiopathological factors associated with venous thromboembolism (18). Conversely, in older age groups, females constituted a larger proportion of patients, possibly reflecting demographic trends in advanced age cohorts (19). Our data confirmed PE as predominantly affecting older individuals, with incidence rates in the over-85 exceeding over tenfold those in people under 75

(17,20,21]. These disparities in PE incidence highlight the complex interplay of age, gender, and underlying health conditions (21).

Unlike the results reported in previous studies showing an increasing trend, our time series analysis indicated a stable incidence rate of PE in patients during the study period. (1,13,22,23). One factor that may explain this trend is that our case definition did not include patients discharged directly from the emergency room (24-27). In recent years, an increasing number of low-risk pulmonary embolism (PE) cases have been managed through rapid discharge and outpatient care, supported by continued anticoagulant treatment at home (28). Another potential factor that could explain the stable trend of incidence rate reported are the preventive strategies to reduce PE in acute ill patients. Preventive strategies, encompassing pharmacological and mechanical approaches, play a critical role in mitigating the risk of PE, especially among elderly patients. Anticoagulant prophylaxis, supported by findings from a comprehensive meta-analysis by the Cochrane Collaboration showing a reduction in PE incidence by up to 60% in medical patients (29). Combining anticoagulants with intermittent pneumatic compression (IPC) further enhances efficacy, reducing PE risk by 70% in high-risk surgical patients (30). Tailored preventive strategies may play a pivotal role in controlling the incidence of new events, contributing to the stable trend of reported incidence rates.

Our study identified a consistent decrease in IHM, consistent with previous research (31-34). This trend may be primarily attributed to an increasing referral to high-volume centers, leading to enhanced interventional and pharmacological treatment. As expected, age and CCI showed a significant association with increase in mortality rate.

It is interesting to note that the COVID-19 pandemic did not significantly influence the incidence of hospital-admitted PE. During the years of the highest pandemic impact (2020-2021) for the hospital admissions burden, the number of hospitalized PE cases showed a slight reduction. Gender differences concerning the incidence rate disappeared. At the same time, in-hospital mortality slightly increased in both sexes, possibly reflecting a higher appropriateness of hospitalization for severe cases of PE, in addition to the direct effect on PE caused by COVID-19 itself, attributable to a higher likelihood of systemic coagulation activation and thrombotic complications in people suffering from COVID-19 (33).

Despite the increasing aging, which affects all the western populations, we observed a decrease in LOHS over time in our study. Age significantly influences hospital stay length in elderly patients due to complex medical conditions, reduced physiological reserves, and increased susceptibility to complications post-surgery or during acute illnesses (34). Despite these challenges, our findings, as reported in recent literature, indicates a global trend towards reducing LOHS (35). Factors contributing to this reduction include streamlined internal diagnostic processes, development of less invasive surgical techniques, simplified discharge procedures, organization of outpatient clinics for follow-up, and shifting preoperative activities to outpatient settings (36).

In our analysis, we observed a 1-year mortality of 33.6%. While several studies indicate a relatively low risk of mortality directly from pulmonary embolism (PE) during anticoagulant therapy (1.5-4%) and even lower post-treatment (less than 0.5% per person-year) (37-39), all-cause mortality rates within the first year after a PE event are notably higher, ranging from 17% to 32% (40,41). It's clear that although the risk of dying specifically from PE while on anticoagulant therapy is relatively low, patients with PE often have underlying medical conditions, contributing to a significantly higher overall mortality rate.

Strengths and limitations

Our study presents both strengths and limitations. Notably, strengths include the substantial number of patients assessed (over 3.5 million), which allowed for further stratification by age and sex, and the extended 12-year period, providing valuable insights into trends in PE hospitalizations and more.

However, a primary limitation of our study stems from the method used to identify patients hospitalized for PE, which relied on ICD-9-CM diagnosis codes. While these codes may have a low accuracy in identifying hospitalized patients with the disease (42), we took precautions by including only patients with a principal diagnosis of PE and those with a secondary diagnosis of PE along with a primary diagnosis of conditions compatible with PE. This approach aimed to prevent the inclusion of cases where pulmonary embolism was associated but not the determining factor for hospitalization. Moreover, we used a washout period of one years, considering only incident cases of PE, potentially leading to underestimation of admission rates.

Another significant limitation pertains to the inability of hospital discharge diagnostic codes to distinguish between PE developed during hospitalization and

cases that pre-existed before admission. Consequently, we lack information about the setting of the origin of PE. Furthermore, we acknowledge that detailed clinical data, including laboratory parameters, as well as specific pharmacological and interventional procedures like thrombolysis and catheter-based procedures, are not adequately captured in the current healthcare data flow. As a result, these treatments were not available for analysis.

Additionally, our assessment of mortality was limited to all-cause mortality, both in-hospital and one year after the event. However, prior studies have shown that in-hospital mortality is primarily related to acute PE episodes, while other causes of death, such as comorbidities, impact mortality over the long term (17).

Conclusions

Our investigation shows that PE remains a significant burden, yet it strongly supports the notion that the management of PE has seen remarkable improvement over the years. The results also emphasize the need to redefine care models and healthcare services in both hospital and outpatient settings, given the influence of chronic diseases and age. Considering the ongoing global trend of population aging, we anticipate a continued increase in the overall medical, societal, and economic burden associated with hospital admissions and deaths due to PE in the future. Additionally, in our dataset, we found that female gender was associated with a higher crude incidence of PE. These results agree with findings from previous studies conducted in a similar context (1, 9). The findings highlight significant gender-related differences for PE, emphasizing the importance of addressing gender health disparities (43).

Declarations

Disclosures: The authors have no relevant financial or non-financial interests to disclose.

Data Availability Statement: Data supporting reported results are available upon request to the corresponding author. Data were collected and managed in aggregated form according to European Union Regulation 2106/679 of the European Parliament and the Italian Legislative Decree 2018/101.

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Riassunto

Embolia polmonare: incidenza ed esiti in una serie storica di dodici anni, in Toscana - Italia (2010-2021)

Contesto. L'embolia polmonare è un problema per la salute a livello globale. I database amministrativi rappresentano fonti per ampi studi epidemiologici sulla prevalenza e incidenza delle principali diagnosi e malattie. L'obiettivo principale è fornire informazioni aggiornate sulle tendenze di incidenza dell'embolia polmonare, esaminando i cambiamenti nella gestione e negli esiti.

Disegno dello studio. Questo studio osservazionale retrospettivo esamina un dataset di 12 anni proveniente dagli ospedali della Regione Toscana, coprendo i primi due anni della pandemia di Covid-19.

Metodi. Per l'analisi sono stati utilizzati i dati amministrativi dei residenti di età pari o superiore a 18 anni dimessi dagli ospedali tra il 2010 e il 2021.

Risultati. L'incidenza di embolia polmonare nei pazienti ospedalizzati è leggermente diminuita dal 2010 al 2019 (da 64,7 a 60,9 x 100.000; p=0.152). Gli uomini al di sotto dei 75 anni hanno mostrato un tasso di incidenza più elevato, mentre le donne hanno registrato tassi di incidenza più alti nei gruppi di età più avanzata. La mortalità in ospedale e a 30 giorni è diminuita dal 2010 al 2019 (p=0.001 e 0.020 rispettivamente). Nel 2020, la mortalità a 30 giorni è aumentata (12.4% vs 10.1%, p=0.029), mentre la mortalità in ospedale è rimasta stabile. La mortalità a un anno è rimasta stabile dal 2010 al 2019, ma è aumentata nel 2020 (32.6% vs 29.4%, p=0.037). L'analisi multivariabile ha mostrato che la mortalità a un anno è significativamente associata a sesso, età e comorbilità.

Conclusioni. Il nostro studio mostra che l'embolia polmonare continua ad avere un peso rilevante in Regione Toscana, ma con miglioramenti nella gestione nell'ultimo decennio e un cambiamento decisivo nel trattamento farmacologico. Emergono differenze legate al genere, sottolineando la necessità di un approccio sanitario orientato alle differenze di genere.

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Best practices for disinfection in dental settings: insights from Italian and European regulations

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Keywords: Disinfection; antiseptics; sterilisation; dental settings; dentistry; medical devices
Parole chiave: Disinfezione; antisettici; sterilizzazione; ambienti odontoiatrici; odontoiatria; dispositivi medici

Abstract

Disinfection practices in dental settings are fundamental to clinical safety, playing a pivotal role in preventing cross-infections and protecting the health of patients and healthcare professionals. This article examines the key components of effective disinfection, based on evidence-based protocols developed by international organizations such as the WHO and the U.S. CDC, alongside European and Italian regulatory standards.

Dental instruments require stringent sterilization by autoclave or chemical methods, while high-level disinfection is essential for non-sterilizable items. Clinical surfaces require routine biocidal treatment tailored to microbial hazards and material compatibility. The European Biocidal Products Regulation and the Medical Devices Regulation provide critical oversight, ensuring product safety and effectiveness while preventing resistance. Antiseptics also play a vital role in oral care, with applications ranging from infection prevention to the treatment of periodontal disease, and are governed by strict regulatory frameworks.

Disinfection effectiveness is significantly affected by factors such as microbial load, presence of biofilm, pH, temperature and biocide exposure time. Preventing bacterial resistance requires appropriate germicide selection, adherence to manufacturer protocols, robust sterilization and cleaning procedures. In addition, the increased use of disinfection during public health emergencies highlights the need for adaptability to mitigate evolving risks.

Regular audits, biological tests, and training for healthcare personnel ensure the consistent application of these rigorous protocols. By integrating international and national standards, dental facilities achieve a uniform approach to hygiene and safety, advancing public trust and compliance. This article highlights the imperative for ongoing research and dissemination of best practices to enhance infection control in dental care environments.

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Introduction

Disinfection in dental facilities is a cornerstone of modern clinical practice, aimed at ensuring the safety and health of both patients and healthcare personnel. In a setting where daily operations involve close contact with blood (1), saliva, and other bodily fluids, the risk of infection transmission is particularly high (2). Consequently, the implementation of stringent disinfection and sterilization protocols is critical to prevent cross-infections and maintain a safe and hygienic environment.

Disinfection practices in dental facilities are guided by well-established protocols developed by international organizations such as the World Health Organization (WHO) (3), the U.S. Centre for Disease Control and Prevention (CDC) (4-7), and, at the national level, the Italian National Institute of Health (*Istituto Superiore di Sanità, ISS*) (8,9). These guidelines encompass standardized measures for hand hygiene, the use of Personal Protective Equipment, and the safe handling of contaminated instruments and surfaces.

Dental instruments are an important route for the transmission of infection if not handled correctly, as well as for the generation of potentially contaminated aerosols during certain dental procedures (10).

Reusable instruments must undergo rigorous sterilization processes using autoclaves, dry heat, or chemical methods to ensure the complete elimination of microorganisms, including bacteria, viruses, and spores. Instruments that cannot be sterilized require high-level disinfection to ensure maximum safety.

Clinical surfaces, such as dental chairs and workstations, must be disinfected after each patient using the most appropriate biocidal products, selected on the basis of their effectiveness against a broad spectrum of microorganisms and their compatibility with the surfaces being treated (11). In addition, routine cleaning of non-clinical and common areas is essential to maintain a hygienic environment. During public health emergencies, such as epidemics or pandemics, dental facilities must take additional measures (12), including the use of protective barriers, patient triage, and the implementation of enhanced disinfection protocols.

Disinfection procedures must be regularly monitored and reviewed to ensure their effectiveness. This includes routine internal audits of established protocols, biological testing to verify instrument sterilisation, periodic quality control of disinfected surfaces and dental unit waterline, and continuous feedback to staff (13).

By adhering to these rigorous and standardized practices, dental facilities can significantly reduce the risk of infections, safeguard the health and safety of all involved, and ensure the delivery of high-quality dental care.

This manuscript addresses the application of disinfection and sterilisation techniques for the control and prevention of transmissible infections in the dental setting, focusing on a general European context, including Italy. The authors acknowledge that this work is not exhaustive, as it does not include a detailed analysis of the regulations specific to each European country. Consequently, it does not assess the comparability of procedures and protocols currently adopted in each country. However, the authors emphasize the importance of this discussion, particularly in light of several recognized challenges: the limited awareness and dissemination of updates to Italian and European regulations, the occasional neglect of proper disinfection and sterilisation procedures, and the inadequate scheduling of refresher courses for dental professionals. These issues highlight critical gaps that may compromise infection control in the dental environment.

The aim of this manuscript is to stimulate dialogue at the European level to encourage participation and knowledge sharing both on this topic and on the standardization of environmental sampling methods (14). By promoting a more cohesive and informed approach, the authors hope to stimulate collaboration with other European countries' researchers to fill existing gaps and facilitate comparison of regulatory frameworks to jointly establish uniform and effective standards. The establishment of a common platform for research, discussion, training and standardization of protocols would be highly desirable, allowing the development of common guidelines to improve safety and best practice in the dental sector.

Sanitization of environments and non-medical devices

According to the Italian Ministerial Decree No. 274 of 7 July 1997, which defines the technical, economic, financial and professional capacity requirements for performing cleaning, disinfection, pest control, rodent control and sanitization activities, the term "sanitization" refers to a set of procedures and operations aimed at ensuring the healthiness of certain environments (15). These operations may

include cleaning and/or disinfection and/or pest control, as well as the control and improvement of microclimatic conditions such as temperature, humidity and ventilation, or factors such as lighting and noise. Thus, sanitization may include an initial cleaning phase followed by disinfection, or it may consist of cleaning or disinfection alone, using one or more products placed on the market in accordance with specific regulatory standards.

During the cleaning phase, it is essential to use products authorized under Regulation (EC) No. 648/2004 of the European Parliament and of the Council of March 31, 2004, on detergents for environmental sanitizers, (16) or Regulation (EC) No. 1223/2009 of the European Parliament and of the Council of November 30, 2009, on cosmetic products for skin sanitizers (17). These types of products act physically or mechanically to remove unwanted residues, exerting a purely mechanical action on harmful organisms, which are removed from the treated surface. Within this function, although they provide a sanitizing effect, they do not possess disinfectant or biocidal properties and are therefore marketed as general consumer products.

Conversely, in the disinfection of environments and surfaces of objects outside the scope of Medical Devices (MD), the products used fall under the national regulatory framework for Medical-Surgical Products (*Presidi Medico Chirurgici,* PMC) or the European framework for biocides, as will be detailed in the next section. Disinfectant products labelled with terms such as "sanitizing" or "sanitizing agents" should be considered equivalent to biocides and are therefore subject to the relevant authorization regime (18).

Regulation of biocidal products for the disinfection of environments and non-medical devices

In accordance with Regulation (EU) No. 528/2012 of the European Parliament and of the Council of May 22, 2012, concerning biocidal products (Biocidal Products Regulation, BPR), a disinfectant is defined as a biocidal product intended to destroy, eliminate, render harmless, prevent the action of, or otherwise exert control over any harmful organism by any means other than mere physical or mechanical action (19). Specifically, the regulation categorizes biocides into several groups, classifying disinfectants under the first group, "Disinfectants", which is further divided into five product types (PTs). These PTs encompass various applications, including the disinfection of surfaces, equipment, air conditioning systems, and human and veterinary hygiene.

The BPR aims to improve the functioning of the European market by harmonizing rules regarding availability and use of biocidal products while ensuring a high level of protection for human and animal health and the environment. To achieve this, biocidal active substances are subject to a review program under Article 15 of the BPR, where their effectiveness and safety are periodically reassessed. Following successful evaluation, active substances are approved and included in the Union list, which is publicly available for each specific product type on the website of the European Chemicals Agency (ECHA) (20). Subsequently, all biocidal products containing approved active substances must undergo an additional authorization process, either at the national or European level, before they can be marketed. It is essential that each final product is assessed in its entirety, even when it contains pre-approved active substances, to safeguard human health and the environment while ensuring the product's effectiveness against specific targets (e.g., bacteria, fungi, virus) as declared on the label by the manufacturer. This robust and detailed regulatory system is crucial to maintaining high safety standards and preventing potential risks associated with the use of biocidal products.

Due to the ongoing nature of the review programme, the EU regulatory framework is currently in a prolonged and complex transitional phase in which both authorized active substances and those still under evaluation (BPR review) coexist. At present, the latter can be placed on the Italian market as PMC, provided they are authorized by the Ministry of Health after evaluation by the Italian National Institute of Health. This authorization process is governed by Italian Presidential Decree No. 392 of 6 October 1998 ("Regulation on the simplification of procedures for the authorization of the production and marketing of medical-surgical devices pursuant to Article 20, paragraph 8, of Law No. 59 of 15 March 1997") (21) and Italian Ministerial Decree of 5 February 1999 ("Approval of the requirements for applications and related documentation to be submitted for the authorization of marketing and for the modification of previously granted authorizations for medical-surgical devices") (22).

Regulation of products used for the disinfection of medical devices

The disinfection of medical devices (MDs) through the use of disinfectants is governed by Regulation (EU) 2017/745 of the European Parliament and of the Council of April 5, 2017, on medical devices (Medical Device Regulation, MDR) (23). This regulation amends Directive 2001/83/EC, Regulation (EC) No. 178/2002, and Regulation (EC) No. 1223/2009, and repeals Council Directives 90/385/EEC and 93/42/EEC. Specifically, this regulation applies to:

- all devices intended for the disinfection or sterilization of non-invasive MDs;
- disinfectant solutions or washing and disinfecting devices intended for the disinfection of invasive MDs after treatment;
- all devices designed for the disinfection, cleaning, rinsing, or hydration of contact lenses.

In this context, "invasive" is defined as any device that penetrates partially or entirely into the body through a body orifice or the body surface.

Disinfectants mentioned in point 1 are classified under Class II.a of the MDR, which encompasses medium to low-risk devices, while those mentioned in points 2 and 3 are classified under Class II.b, which includes medium to high-risk devices. Consequently, the disinfectants used in the disinfection of MDs are themselves considered MDs, intended to ensure the absence of pathogenic microorganisms before the treated MDs are used. Specifically, these disinfectants must meet the essential safety and performance requirements outlined in the MDR, including biological safety, disinfection effectiveness, and compatibility with the materials of the treated MDs.

The conformity assessment of disinfectants used for MDs disinfection with regulatory requirements necessarily involves a Notified Body, which conducts an independent external evaluation. Once authorized, these disinfectants must bear the CE marking, certifying their compliance with EU regulations and their eligibility for unrestricted commercialization in the European market.

Antiseptics for dental use

Antisepsis encompasses a set of procedures aimed at inhibiting the growth of microorganisms on living tissues or destroying them through the use of chemical substances known as "antiseptics." Antiseptics are generally defined as germicidal agents applied to living tissues, which must possess both microbicidal activity and compatibility with, and non-toxicity for, the tissues to which they are applied.

Dental antiseptics are chemical agents specifically designed to reduce or eliminate pathogenic microorganisms in the oral cavity and on dental surfaces. These products play a fundamental role in the prevention of post-operative oral infections, the treatment of gingivitis and periodontitis, the disinfection of oral cavities and the maintenance of oral hygiene. Their effectiveness and safety are critical in the context of dental practice.

Antiseptics intended for disinfecting damaged skin (e.g., wound disinfection) or intact skin prior to a medical procedure are classified as medicinal products (24) and must be authorized accordingly under the Italian Legislative Decree No. 219 of April 24, 2006 "Implementation of Directive 2001/83/EC and subsequent amending directives on a Community code concerning medicinal products for human use, as well as Directive 2003/94/EC", known as the "Medicines Code" (25), which transposes Directive 2001/83/EC of the European Parliament and Council of November 6, 2001, into Italian law. This classification necessitates a rigorous evaluation process by the Italian Medicines Agency (*Agenzia Italiana del Farmaco, AIFA*) to ensure their safety, effectiveness, and quality. Products meeting all the regulatory requirements are granted Marketing Authorization (*Autorizzazione all'Immissione in Commercio*, *AIC*).

Conversely, antiseptics intended exclusively for application on intact skin for general preventive purposes fall under Product Type 1 of biocides and are regulated by the Biocidal Products Regulation (BPR) or national legislation governing PMC. These are primarily disinfectant products for hand hygiene, which may also include the disinfection of the wrist and forearm.

Bacterial resistance to disinfection procedures

Bacterial resistance, which can occur in both intrinsic and acquired forms, is one of the most critical factors affecting the effectiveness of disinfection. Microorganisms naturally possess various intrinsic mechanisms that limit the action of germicidal agents. Among these, bacterial spores have the highest innate resistance to chemical germicides after prions, due to the presence of a specialized coating and cortex that act as barriers. They are followed by coccidia, mycobacteria (which have a waxy cell

wall that inhibits the penetration and absorption of germicidal agents), small non-lipid-enveloped viruses, parasites, Gram-negative bacteria (characterized by an outer membrane that inhibits the penetration and absorption of antimicrobial agents), fungi, large non-lipid-enveloped viruses, Gram-positive bacteria and vegetative forms, and finally medium-sized lipid-enveloped viruses. The innate resistance of Gram-positive and Gram-negative bacteria is generally similar, with some exceptions (e.g. *Pseudomonas aeruginosa* is more resistant to certain disinfectants). In contrast, acquired bacterial resistance refers to the ability of a microbial population to adapt and survive in the presence of a disinfectant. Over time, these bacteria develop mechanisms that confer resistance to the disinfectant, allowing them to survive even at progressively higher concentrations. This issue frequently arises with disinfectants used at extremely low dilutions, as insufficient dosages can:

• promote the genetic selection of mutant microbial strains resistant to the biocide;

• facilitate the expulsion of the biocide from cells via molecular efflux pumps, which are typically used to prevent the accumulation of toxic substances within bacterial cells;

• trigger bacterial chemical stress adaptation responses, activating specific defence mechanisms such as the production of enzymes that degrade the biocide and/or reducing the permeability of cellular membranes to the biocide;

• prevent the biocide from penetrating physical and chemical barriers formed by microbial community structures, known as biofilm, due to local consumption by external cells and limited diffusion within these structures.

For instance, high bacterial loads have been detected within containers of diluted disinfectants. This type of resistance typically regresses spontaneously if the bacterial population is not exposed to the disinfectant for a sufficient period of time.

When selecting a disinfectant, careful consideration must be given not only to its actual germicidal activity, but also to the risk of developing bacterial resistance as a result of its use. This concern is particularly relevant when the same disinfectant is used repeatedly at low concentrations, such as in water systems.

Equipment and surfaces as potential infection sources in dental settings

The CDC guidelines (26) specify disinfection requirements for surfaces and medical devices (MDs), categorizing them based on the potential risk of infection associated with their specific use. For this purpose, the widely adopted classification by Earle Spaulding, recently updated by the Robert Koch Institute, is utilized. This classification divides instruments and surfaces into critical, semi-critical, and non-critical categories, each requiring different levels of disinfection (26-31). Specifically:

• critical instruments are those that penetrate tissues or the vascular system;

• semi-critical instruments come into contact with mucous membranes or non-intact skin;

• non-critical instruments come into contact with intact skin but not mucous membranes.

For critical items, absolute sterility is mandatory, necessitating sterilization procedures using physical methods, such as steam autoclaving.

For semi-critical items, absolute sterility is recommended whenever possible, and at minimum, high-level disinfection is required. Specifically, for instruments made of heat-sensitive materials, steam sterilization may cause irreversible damage. In such cases, low-temperature sterilization methods, including gas plasma or ethylene oxide autoclaves, or cold sterilization using high-level disinfectants with extended contact times (up to 10 hours), are advised.

For non-critical instruments, given the lower risk of cross-infection, medium- to low-level disinfection or, in some cases, simple cleaning procedures are sufficient.

Selection of the most appropriate disinfectant

An ideal disinfectant should possess the following characteristics: broad-spectrum antimicrobial activity, rapid action, persistent effect, absence of toxicity and harmful environmental effects, compatibility with various treated materials, chemical stability, ease of use, cost-effectiveness.

Unfortunately, no single product fulfils all these requirements. Therefore, it is necessary to evaluate the specific needs of each situation to identify the product that offers the best compromise between effectiveness and potential drawbacks, prioritizing hygiene objectives, the required disinfection level, and compatibility with treated materials.

Based on their mechanism of action, disinfectants can be classified as bacteriostatic, which inhibits microbial reproduction, or bactericidal, virucidal

or fungicidal, which are capable of destroying microorganisms. According to Block's classification, disinfectants are divided into three levels of activity (32-34):

- low-level disinfectants, which are effective against many vegetative forms of bacteria, some fungi and certain viruses, but not against resistant microorganisms such as spores and *Mycobacterium* spp. (minimum contact time: 10 minutes);
- intermediate disinfectants, which are effective against a wider range of micro-organisms (e.g. *Mycobacterium tuberculosis*, most viruses and fungi) but not spores (minimum contact time: 5-10 minutes);
- high-level disinfectants, which are effective against almost all types of micro-organisms except certain spores, especially at high concentrations (minimum contact time: 20-45 minutes).

Some high level disinfectants can also kill spores when used at appropriate concentrations and for longer contact times (6-10 hours). In such cases, they are considered disinfectants/sterilisers and are suitable for 'cold sterilization', a process used for heat-sensitive items that cannot be physically sterilized in an autoclave without damage.

Table 1 provides a brief overview of the main active ingredients found in disinfectants and antiseptics used in dentistry, highlighting their commonly used concentrations, levels of activity and potential risks associated with their use (32,34).

Table 1 - Active ingredients in disinfectants and antiseptics for dental applications.

Active Ingredient	Concentration (%)	Action time (min)	Level of activity	Precautions and limitations
Glutaraldehyde or Orthophthalaldehyde	0.55	5-10	High (less effective against spores)	Volatile, irritant
Hydrogen Peroxide	10, 3, 0.1	60, >20, >30	High (including spores), Intermediate, Low	Corrosive, irritant, unstable, organic materials may reduce effectiveness
Peracetic Acid	1	10	High (including spores)	Corrosive
Tetraacetylethylenediamine + Sodium Perborate	2	10	High (including spores)	Irritant, limited effectiveness in the presence of reducing agents
Chlorine derivatives as Cl_2	0.5, 0.1, 0.01	20, 10, 20	High (including spores), Intermediate, Low	Irritant, inactivated by organic substances, activity reduced by organic material
Iodophors as I_2	0.003-0.015	10	Intermediate	Corrosive, stains, inactivated by organic substances
Iodine + alcohol	0.5 + 70	10	Intermediate	Corrosive, irritant, stains, inactivated by organic substances
Alcohols	70	10	Intermediate	Flammable, irritant, inactivated by organic substances
Phenols	0.5-3	10	Intermediate	Corrosive, irritant, toxicity and environmental risks limit use
Quaternary Ammonium Compounds	0.1	10	Low	Irritant, easily contaminated, inactivated by soap and anionics
Amphoteric	2	20	Intermediate/Low	Low toxicity
Chlorhexidine	0.2	10	Low	Easily contaminated

Factors influencing disinfectant effectiveness and speed of action

The real effectiveness and speed of action of a disinfectant depend on several factors, including:

• *Microbial load and biofilm*

A high microbial load requires longer contact times to ensure effective germicidal action. Additionally, microbial cell aggregates, such as biofilms, have demonstrated increased resistance to disinfection. Thorough cleaning of instruments before disinfection is essential to mitigate these issues.

• *Product concentration*

For solutions requiring preparation, adhering to the concentrations specified by the manufacturer is crucial. Product concentration also impacts the speed of action.

• *Contact methods and application time*

Effective disinfection requires that all surfaces come into contact with the disinfectant for the required time. Instruments with complex shapes, crevices, or cavities must be disassembled to allow the disinfectant to penetrate all parts of the object.

• *pH*

The antimicrobial activity of a disinfectant may be influenced by pH, which can alter the disinfectant's composition or the molecular structure of microbial cell surfaces. For example, an increased pH enhances the antimicrobial effectiveness of some disinfectants, such as glutaraldehyde and quaternary ammonium compounds (QACs), but reduces the effectiveness of others, such as phenols, hypochlorite, and iodine.

• *Temperature*

The effectiveness of some disinfectants is temperature dependent. In general, most disinfectants are more effective at higher temperatures.

• *Presence of inactivating substrates*

Certain substances can neutralize the effect of disinfectants, including detergents, hard water, and organic material. For example, hard water containing magnesium and calcium reduces the germicidal activity of some disinfectants by forming insoluble precipitates. Organic material (e.g., serum, blood, pus, faeces) can interfere with disinfection by chemically reacting with the germicide, reducing the active product available, or by serving as a physical barrier that shields microorganisms from the disinfectant. These factors highlight the importance of thorough cleaning before disinfection or sterilization procedures.

• *Product stability during storage*

Not all disinfectants retain their properties over time, especially when diluted. Adhering strictly to the manufacturer's instructions for preparation, use, and storage is essential.

• *Material compatibility*

When selecting a disinfectant for surface or medical device sanitization, it is critical to consider the compatibility of the product's components with the materials to be treated. Disinfectants containing acids, alkalis, electrolytes, or hypochlorite may corrode metallic parts, while those containing organic solvents may degrade plastics and rubber.

Manufacturer information and safety protocols

Comprehensive understanding of the conditions for using each disinfectant product, including operator safety protocols and appropriate disposal procedures, is essential to ensure safe and effective application. This critical information is typically provided in the product label, technical data sheet, and Safety Data Sheet (SDS) issued by the manufacturer:

• *Product label*

The label must comply with Regulation (EC) No. 1272/2008 (CLP Regulation: Classification, Labelling, and Packaging), providing all necessary information for the lawful marketing of disinfectant products (35). This includes specific indications, such as "for professional use only" for products requiring specialized training, and instructions for the mandatory use of Personal Protective Equipment (PPE).

• *Technical Data Sheet*

The technical data sheet offers supplemental details beyond those on the label, such as the spectrum of target organisms, recommended contact times, and optimal product concentrations.

• *Safety Data Sheet*

For hazardous disinfectants or non-classified products containing hazardous substances in significant concentrations, the SDS outlines essential safety measures. These include information on chemical composition, associated hazards, first aid measures, accidental release management, handling and storage recommendations, and PPE requirements for exposure control.

Furthermore, strict adherence to the operational instructions provided by the manufacturers of instruments and equipment is imperative to maintain both safety and effectiveness in disinfection procedures.

Conclusions

Disinfection practices in dental settings are an essential element of clinical safety, serving as a cornerstone for preventing cross-infection and ensuring a hygienic environment for both patients and healthcare professionals. This manuscript has provided an in-depth analysis of the complex aspects of disinfection, drawing on international guidelines,

European regulatory frameworks and Italian legislation to highlight the key protocols and practices required in modern dental facilities. The effective integration of international and national standards is essential to achieve consistency in disinfection practices. Guidelines issued by WHO and the CDC, alongside the ISS guidelines, provide a solid foundation for infection control. These standards ensure the implementation of evidence-based practices that include hand hygiene, dental instrument sterilisation and surface disinfection.

The proper management of dental instruments and clinical surfaces is critical for minimizing microbial risks. The sterilization of reusable instruments using validated methods, including autoclaves and chemical disinfectants, ensures the elimination of pathogens, while surface disinfection protocols tailored to the specific requirements of dental facilities further mitigate infection risks. Regulatory compliance with frameworks such as the BPR and the MDR guarantees the safety, effectiveness, and environmental compatibility of the disinfectant products employed.

Antiseptics play a vital role in dental practice, particularly in the prevention of oral infections and the management of conditions such as gingivitis and periodontitis. The regulation of these products under Italian and European laws ensures their safe and effective use in clinical settings, contributing significantly to oral health. However, the potential for bacterial resistance, both intrinsic and acquired, underscores the need for careful selection and correct application of germicides. Avoiding suboptimal concentrations and ensuring proper cleaning prior to disinfection are critical strategies for mitigating resistance risks.

The selection of disinfectants must balance a range of considerations, including antimicrobial effectiveness, compatibility with treated materials, and safety for both operators and the environment. Factors such as microbial load, pH, temperature, and the presence of inactivating substrates significantly influence the effectiveness of disinfection procedures, requiring careful adherence to established protocols and manufacturer instructions. Furthermore, in public health emergencies such as pandemics, the adoption of enhanced disinfection measures, patient triage systems, and protective barriers becomes imperative to manage increased infection risks.

To ensure the safety and effectiveness of disinfection practices, holistic training of healthcare workers is needed, starting with students in specialist training (36,37) supported by detailed technical and safety information provided by manufacturers. The use of PPE and compliance with waste disposal protocols are essential components of a safe and effective disinfection strategy. Regular monitoring, internal audits, and biological verification tests further enhance the reliability and consistency of disinfection procedures. Continuous feedback and the periodic update of protocols based on emerging scientific evidence are equally important for maintaining high standards of hygiene and safety.

By adhering to these rigorous and evidence-based practices, dental facilities can effectively safeguard the health of both patients and healthcare providers, fostering trust and compliance within the community. Moreover, the findings presented in this work underscore the importance of ongoing research and dissemination of best practices, which remain critical for advancing public health in the context of dental care.

Riassunto

Le migliori pratiche di disinfezione in ambito odontoiatrico: approfondimenti dalle normative italiane ed europee

Le pratiche di disinfezione negli ambienti odontoiatrici sono fondamentali per la sicurezza clinica, svolgendo un ruolo cruciale nella prevenzione delle infezioni crociate e nella protezione della salute di pazienti e operatori sanitari. Questo articolo analizza i componenti chiave di una disinfezione efficace, basandosi su protocolli scientificamente validati sviluppati da organizzazioni internazionali come l'OMS e il CDC statunitense, insieme a standard normativi europei e italiani.

Gli strumenti odontoiatrici richiedono una rigorosa sterilizzazione tramite autoclavi o metodi chimici, mentre per gli strumenti non sterilizzabili è essenziale una disinfezione di alto livello. Le superfici cliniche necessitano di trattamenti biocidi regolari, adeguati alle minacce microbiche e compatibili con i materiali trattati. Il Regolamento europeo sui prodotti biocidi e il Regolamento sui dispositivi medici offrono un controllo critico, garantendo la sicurezza e l'efficacia dei prodotti e prevenendo la resistenza. Gli antisettici, inoltre, svolgono un ruolo vitale nella cura orale, con applicazioni che spaziano dalla prevenzione delle infezioni al trattamento delle malattie parodontali, regolamentate da rigidi quadri normativi.

Fattori come la carica microbica, la presenza di biofilm, il pH, la temperatura e il tempo di esposizione del biocida influenzano significativamente l'efficacia della disinfezione. La prevenzione della resistenza batterica richiede una selezione appropriata dei germicidi, l'aderenza ai protocolli e alle procedure di sterilizzazione, pulizia energiche. Inoltre, misure di disinfezione potenziate durante le emergenze sanitarie pubbliche sottolineano l'adattabilità necessaria per mitigare i rischi emergenti.

Audit regolari, test biologici e formazione del personale sanitario garantiscono l'applicazione coerente di questi protocolli rigorosi. Integrando standard internazionali e nazionali, le strutture odontoiatriche raggiungono un approccio uniforme all'igiene e alla sicurezza,

promuovendo la fiducia e la conformità del pubblico. Questo articolo evidenzia l'importanza di una ricerca continua e della diffusione delle migliori pratiche per il controllo delle infezioni negli ambienti odontoiatrici.

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LETTER TO THE EDITOR

Environmental and Climate Challenges: Implications for Food Safety, Food Security, and Public Health Protection

Rischi ambientali e climatici: sicurezza alimentare-nutrizionale e tutela della salute

Keywords: Climate change; food safety; food security; Public Health

Abstract

Climate change poses a significant threat to global Food safety and security, but it also offers a unique opportunity to transform food systems towards more sustainable and resilient practices.

Sir,

Climate has a complex, critical impact on food safety and security, influencing all stages of the agricultural system from planting to consumption, including transport and storage. Climate change, weather variability, and extreme events significantly contribute to the spread of foodborne pathogens and related diseases (1). Higher temperatures, heavy rainfall or flooding can contaminate agricultural fields with pathogens from polluted surface water seeping into the soil. Marine waters are also at risk. *Vibrio* infections have increased in Europe over the last 20 years. Warmer coastal waters have expanded the areas where *Vibrio* bacteria can multiply, increasing the risk of infection through consumption of raw seafood (2). In addition, changing conditions can favour the establishment of invasive alien species that damage plant and animal health, while warming surface waters and increased nutrient inputs lead to the proliferation of toxin-producing algae, causing epidemics through the consumption of contaminated seafood (3). Similarly, prolonged droughts can increase the concentration of chemical contaminants such as nitrates, pesticides or mercury in seafood, which can enter the human food chain (4). Climate change also affects the distribution and prevalence of parasites and other vectors such as mosquitoes and rodents, which can lead to increased use of pesticides and veterinary drugs.

These extreme events can destroy crops, cause significant damage to storage and transportation infrastructure, contaminate water supplies, and disrupt food supply chains. They also increase the risk of food spoilage and contamination, reducing the availability of safe food (5).

The impact of climate change on food safety and food security is becoming increasingly clear. Studies conducted between 1960 and 2010 have documented a significant increase in infections caused by pathogens such as *Campylobacter*, *Salmonella*, and *Escherichia coli*, particularly during the summer months. This phenomenon highlights how warm climates can favor the proliferation of these harmful microorganisms. In contrast, Noroviruses, known to cause acute gastroenteritis, are responsible for an increase in cases during the winter months, demonstrating how different pathogens can respond to climate conditions in opposite ways (6).

Effective management of the risk of food-borne diseases in an era of climate change requires a concerted effort by governments, the scientific community and the communities in general. International cooperation and continuous updating of practices based on the latest scientific evidence are essential to anticipate and mitigate the impact of

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climate change on food security. Governments, in particular, have a critical role to play in implementing policies that can incentivize sustainable food production and appropriate food choices (7). These include reforming agricultural subsidies, promoting research, supporting technological innovation, providing public education on nutrition, and creating social safety nets to protect vulnerable communities from economic and health impacts (8). Regular and timely implementation of control systems used by the food industry is also a good preventive measure. One example is the Hazard Analysis and Critical Control Points (HACCP) system, which helps food businesses identify, assess and control significant food safety hazards. The adoption of good agricultural and manufacturing practices, supported by HACCP, is therefore essential to ensure the safety of the final product (9). By implementing this system, food business operators can manage and minimize the risk of contamination during production, processing, distribution and storage of food. Only through a proactive and well-coordinated approach will it be possible to protect public health in an increasingly warming and meteorologically unstable world (10,11).

Another of the most alarming manifestations is "nutrient dilution": rising atmospheric carbon dioxide levels reduce the concentration of proteins, essential minerals, and other key nutrients in major food crops such as wheat and rice (12). The reduction in nutritional value occurs because high levels of CO_2 can stimulate rapid plant growth, but with less efficient nutrient production than biomass growth. As a result, although the total amount of food produced may increase, the nutritional quality of food is compromised (13). This phenomenon represents a significant threat, weighing on malnutrition problems, particularly for populations in low-income areas where wheat and rice are essential components of the daily diet and a primary source of protein, vitamins, and minerals.

Proactive measures are needed to address the growing risk of reduced food nutrition and to ensure safer and more reliable food distribution. One strategy could be to develop and promote crop varieties that are more resilient to the effects of climate change and can maintain their nutritional value despite high CO_2 concentrations. In addition, better water and soil management can help maximize the nutritional efficiency of crops and strengthen food supply chains by investing in more appropriate food storage infrastructure.

Promoting sustainable and low impact diets is one of the most promising approaches to address the challenges of climate change and global food security. Such diets not only help reduce the greenhouse gas emissions responsible for global warming, but also promote public health. Eating a wider variety of foods, with less meat and more plant-based products, can have a significant impact not only on individual well-being, but also on the health of the planet. The relationship between diet, health and the environment are complex and require detailed study to fully understand its potential (14). Indeed, the modern diet, characterized by a high consumption of meat and animal products, is a major risk factor for many chronic diseases, including diabetes, cardiovascular disease and some forms of cancer (15). These conditions reduce the quality of life and place a significant burden on global health systems. The intensive agriculture required to support these diets is a major contributor to greenhouse gas emissions, deforestation and biodiversity loss. In addition, conventional agricultural practices often consume large amounts of natural resources such as water and energy and use pesticides and fertilizers that can have adverse effects on the environment and human health. Some researchers have reported that diets rich in meat, especially red and processed meat, are among the most impactful in terms of CO_2 emissions, water pollution and land use. In contrast, low meat or vegetarian diets (e.g. the Mediterranean diet, rich in fruits, vegetables, whole grains, legumes and nuts) can reduce these emissions by almost 50% (14). These diets not only require fewer natural resources to be produced but are also associated with a lower risk of developing chronic diseases. Furthermore, shifting to more sustainable and biodiversity-based agricultural systems can help conserve ecosystems, improve soil and water quality, and increase resilience to climate shocks and adversities.

In summary, while climate change poses a significant threat to global food security, it also offers a unique opportunity to transform food systems towards more sustainable and resilient practices. The challenges are immense, but so are the opportunities for improvement. A future where everyone has access to safe, nutritious and sustainable food is possible, but it will require concerted global commitment, unprecedented intergovernmental cooperation and strong, enlightened political leadership. With timely and coordinated action, it is possible to create food systems that not only nourish the bodies, but also protect the planet.

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