Acta Biomed. - Vol. 90 - Suppl. 9 - September 2019 | ISSN 0392 - 4203

ACTA BIOMEDICA SUPPLEMENT

ATENEI PARMENSIS | FOUNDED 1887

Official Journal of the Society of Medicine and Natural Sciences of Parma and Centre on health systems' organization, quality and sustainability, Parma, Italy

The Acta Biomedica is indexed by Index Medicus / Medline Excerpta Medica (EMBASE), the Elsevier BioBASE, Scopus (Elsevier) and Bibliovigilance

Road to Rome 2020

Special issue to promote the 16th World Congress on Public Health (WCPH)

Guest Editor: Gaetano Maria Fara

Free on-line www.actabiomedica.it

Mattioli 1885

Pubblicazione trimestrale - Poste Italiane s.p.a. - Sped. in A.P. - D.L. 353/2003 (conv. in L. 27/02/2004 n. 46) art. 1, comma 1, DCB Parma - Finito di stampare September 2019

Acta Bio Medica

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OFFICIAL JOURNAL OF THE SOCIETY OF MEDICINE AND NATURAL SCIENCES OF PARMA AND CENTRE ON HEALTH SYSTEM'S ORGANIZATION, QUALITY AND SUSTAINABILITY, PARMA, ITALY

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Volume 90 / Suppl. 9 September 2019

Briefing on

Acta Biomed 2019; Vol. 90, Supplement 10: 5 DOI: 10.23750/abm.v90i9-S.8822

Foreword

The 16th World Congress on Public Health, to be held in Italy in 2020, will be a memorable event that deserves to be promoted and organized in the best possible way. For this reason the Publisher accepted our suggestion to promote two special issues of *ACTA BIOMEDICA*, also to implement the new section of the Journal dedicated to Public Health and Health Policies.

The aim of this initiative was to collect high-quality scientific contributions on various Public Health topics, with particular regard to Rome Congress' main theme: "PUBLIC HEALTH FOR THE FUTURE OF HUMANITY: ANALYSIS, ADVOCACY AND ACTION". In particular, we called upon our colleagues involved in the most significant scientific Public Health events of 2019, such as the ASPHER Deans' & Directors' Retreat, which took place last May 2019 in Erice: and the 12th European Public Health Conference 20-23 November 2019 in Marseille.

The present issue - the first of the two - includes 10 full papers and 4 short articles (Focus on) devoted to various areas of Public Health: the prevention of infectious diseses, the risk management, the health organization, the Public Health workforces. The multiplicity of the authors and of the academic institutions involved and the scientific validity of the contents, make this issue an important scientific testimony of the vivacity of our discipline and of our researchers, among them many brilliant, young health professionals.

At the end we take the opportunity to thank the members of the Board, the Editorial Office and the Publisher who have followed the different phases of this editorial work. A particular thank to Valeria Ceci from Mattioli; and to Deanna Rossi and Assunta Bizzarro - two young PH professionals - who contributed with their precise collaboration to the success of the editorial initiative.

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Acta Biomed 2019; Vol. 90, Supplement 9: 7-14 DOI: 10.23750/abm.v90i9-S.8695

Original article

Epidemiology of leprosy in Italy (1920-2019): a comprehensive review on existing data

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Summary. *Background and aims:* Incidence of leprosy in Italy has declined steadily over the last century, but available evidence remains fragmentary. Our review aims to summarize available data on the epidemiology of leprosy cases in Italy. *Methods:* The following keywords were used to explore PubMed and Embase: leprosy, Hansen's disease, (Mycobacterium) leprae, Italy, without any chronological restriction. *Results:* We identified a total of 39 reports, including 7 national reports, 11 international reports, 20 case reports. Notified leprosy cases were: 839 between 1925 and 1948; 434 between 1955 and 1979; 76 cases for the decade 1980-1989; 112 between 1990 and 1999; 62 between 2000 and 2009, and a total of 25 cases since 2009. Since 2003, 53% of all cases occurred in illegal residents. Focusing on individual cases, latency between early signs/symptoms and a proper diagnosis ranged between 2 and 20 years in 52.1% of individual cases. *Conclusion:* Imported cases of leprosy are responsible for most leprosy incidence in Italy, and social stigma, the unfamiliarity of healthcare professionals with such disorders, and difficulties of some high-risk groups to be appropriately assessed hint to a possible under-diagnosis. Professionals should be made more aware of the potential for leprosy incidence among patients from countries where the disease is endemic**.** (www.actabiomedica.it)

Key words: emigration and immigration, incidence, leprosy/epidemiology, retrospective studies, Italy/epidemiology

Introduction

Leprosy is an ancient illness caused by *Mycobacterium leprae* that mainly affects skin, peripheral nerves and upper respiratory tract (1). Following the introduction of multidrug treatment during the mid-1980s, global prevalence has decreased by over 90%, from 5.3 million cases in 1985 to around 192,713 cases at the end of 2017 (1-3). However, leprosy remains far from being eradicated (4,5). For instance, official statistics show that new cases increased worldwide from 210,758 in 2015 to 214,783 in 2016, and again in 2017 around 210,000 cases were reported from 150 countries (i.e. notification rate of 2.77/100,000 inhabitants) (2,6,7). As the surveillance systems from low-income countries are reportedly affected by significant inaccuracies, even in endemic areas, available figures are supposedly affected by significant underreporting (3,8).

Leprosy began being endemic in Italy during the early Roman Empire (4,9-11), but official epidemiological surveillance data have suggested a steady decrease during the last century, with autochthonous cases progressively disappearing during last decades (9,11,12); current epidemiology is affected by significant uncertainties and conflicting estimates (5,9). In Italy newly detected leprosy cases should be statutorily reported to the Ministry of Health, and a National Leprosy Register has been officially existing since 1923. Even though the last official report was published in 1983 (9), reports following the ongoing migratory crisis have underlined the possibility of reintroduction of leprosy from endemic areas, with a significant share of missed or late diagnoses (5,13).

In order to further understand the actual epidemiology of leprosy in Italy, we conducted this comprehensive literature review addressing all available evidence on Hansen's disease, specifically focusing on cases occurring after 1983.

Materials and Methods

This systematic review has been conducted following the PRISMA (Prepared Items for Systematic Reviews and Meta-Analysis) guidelines (14)**.** We searched into two different databases (PubMed and Embase) for relevant studies published from their inception to 31/05/2019, without any chronological restriction. The search strategy was a combination of the following keywords (free text and Medical Subject Heading [MeSH] terms): *leprosy, Hansen's disease, (Mycobacterium) leprae, Italy*. Records were handled using a references management software (Mendeley Desktop Version 1.19.5, Mendeley Ltd 2019), and duplicates were removed.

Articles eligible for review were original research publications available online or through inter-library loan. Articles had to be written in Italian, English, German, French or Spanish, the languages spoken by the investigators. Studies included were national and international reports, case studies, cohort studies, case-control studies and cross-sectional studies, case reports. Only articles reporting data from Italy, with relevant information on the prevalence of Hansen's disease were eligible for the full review. Articles were excluded if: (1) full text was not available; (2) articles were written in a language not understood by reviewers; (3) reports lacked significant timeframe (i.e. the year of diagnosis) and demographic data (i.e. sex, age, country of origin of the patient, etc.).

Two independent researchers reviewed titles, abstracts, and articles. Titles were screened for relevance to the subject of Hansen's disease. Any articles reporting original studies with information on leprosy in Italy, which did not meet one or more of the exclusion criteria, were retained for full-text review. The investigators independently read full-text versions of eligible articles. Disagreements were resolved by consensus between the two reviewers; where they did not reach consensus, input from a third investigator (MR) was obtained. Further studies were retrieved from reference lists of relevant articles and consultation with experts in the field.

Data abstracted included:

(1) Reports on incidence/prevalence: year of publication; level (i.e. all cases or selected risk groups); timeframe; the number of prevalent cases for index year; the number of incident cases; age at diagnosis; sex ratio; share of foreign-born people; share of lepromatous, tuberculoid or borderline cases.

(2) Case reports: year of publication; year of diagnosis; age at diagnosis; sex; country of origin; clinical characteristics following Ridley and Jopling classification (15); multibacillary vs. paucibacillary status; latency; individual risk factors (i.e. stay in high-risk areas; HIV+ status; refugee status; adopted status from high-risk areas). When Ridley and Jopling's classification was not openly reported, it was retrospectively defined by analysis of reported data.

Results

Briefly (Figure 1), a total of 1023 articles were initially identified. After removal of duplicates, titles of 680 remaining articles were screened, identifying a total of 33 publications, and 6 further reports were added following full-text analysis. Eventually, 39 publications

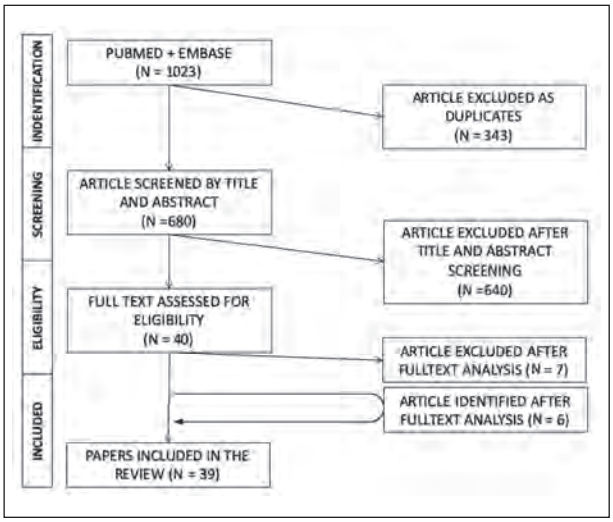

Figure 1. Flow of studies through the review

were retrieved, encompassing: 8 nationwide reports, 11 international reports (2,5-7,9,11-12,16-27) (Table 1) and 20 case reports (13,28-46) (Table 2).

Despite some inconsistencies for the years from 1920 to 1948, available data suggest that a total of 1658 leprosy cases have been notified between 1920 and 2018 (i.e. 16.7 cases/year). The number of reported cases decreased from 847 for the time period 1920 - 1949 (i.e. 28.2 cases/year), to 437 between 1950 and 1979 (14.6 cases/year), and eventually 307 between 1980 and 2018 (i.e. 6.3 cases/year) (9,11,12,24), with corresponding incidence rates ranging from 0.005 in 1979 to 0.25 in 1961 (9,11,24) (Figure 2).

Interestingly enough, after 1980 no official reports from National Health authorities are available. While a report of the National Institute for Statistics hints to

Table 1. Summary of the available reports on prevalence and incidence data for Leprosy in Italy (1925 - 2019). Notes: * = year of data analysis; FBP = foreign-born people; MB = multibacillary

		Incidence Data			Prevalence Data									
Reference	Level	Timeframe	All notified cases	(No.) cases by year	Year*	Prevalent cases (No.)	Age at diagnosis (mean)	Males (%)	FBP (%)	Lepromatous (%)	Tuberculoid (%)	Borderline (%)	Indefinite (%)	MB (%)
Greco D, Galanti MR (9)	Nationwide, all cases	1920-1980	734	12.3	1979	547	37.8	60.0%	17.2%	62.2%	15.4%	9.5%	2.9%	-
Greco D, Galanti MR, Moro ML (12)	Nationwide, all cases	1920 - 1980	678	11.1	1980	547	37.7	59.9%	19.3%	69.3%	10.4%	10.4%	3.2%	-
National Health Institute (24)	Nationwide, all cases	1955 - 1979	424	17.4	1981	543	-	61.1%	18.8%	73.6%	20.2%	6.4%	-	-
Terni M, Signorini FL (11)	Nationwide, all cases	1925 - 1948	839	35.0	1947	364	-	59.0%	23.1%	-	-	-	-	-
Massone C et al. (5)	Nationwide, Only FBP	2003 - 2009	59	9.8	2011	59	30.2	69.5%	100%	27.1%	3.4%	69.5%	-	51%
AIFO 2007 (25)	Nationwide, all cases	1970 - 2006	351	9.5	2007	351	-	-	47.0%	-	-	-	-	-
AIFO 2006 (26)	Nationwide, all cases	1970 - 2004	337	9.6	2006	337	36.5	64.0%	44.8%	-	-	-	-	-
ISTAT (27)	Nationwide, all cases	1992 - 2001	23	2.3	-	-	-	-	-	-	-	-	-	-
WHO (2,6,23,7, 16-22)	Nationawide, all cases	2005 - 2017	27	2.1	-	-	-	-	-	-	-	-	-	-

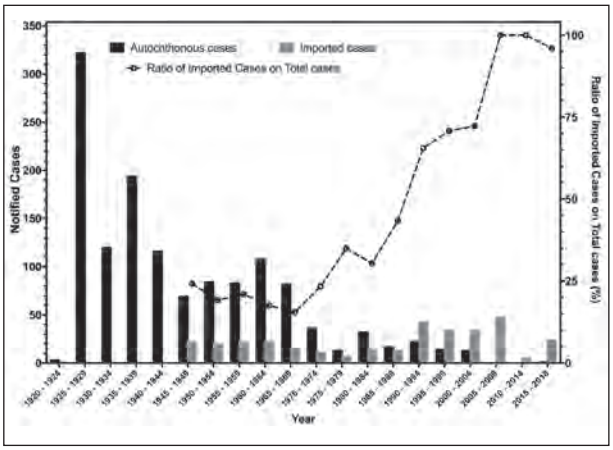

Figure 2. Epidemic curve of notification of leprosy cases in Italy by year and source of infection, 1920 - 2018 (2,5,19-27,6,7,9,11,12,16-18)

a total of 23 new cases (mean: 2.3, range 0 to 9) between 1992 and 2001 (27), analysis of data published by the Italian Society for Hansenology (SIHAN) suggests a mean of 9.5-9.8 cases/year between 1970 and 2006, and more precisely 76 cases for the decade 1980-1989 (mean: 7.6, range 2 - 10), 112 new diagnoses for 1990-1999 (mean: 11.2, range 6 - 17), and 62 new cases between 2000 and 2009 (mean: 4.9, range 0 - 14) (5,25,26). Since 2010, a total of 25 cases have been officially reported to the World Health Organization (mean: 2.1, range 0 - 12) (2,6,23,7,16-22), including 5 cases notified during 2018 (personal communication of the National Health Ministry). However, available data are heavily fragmentary. In fact, while no cases were officially reported between 2005 and 2006, 2008 and 2009, and then between 2011 and 2015, analysis of case reports that occurred during the index years suggests that such figure may be affected by significant underreporting (29,31,39-41,43,45).

Demographics of patients significantly changed over the years. While the majority of cases were consistently reported in males, ranging from 59.0% for 1925-1948 (11) and 69.5% in the report of Massone et al. (5), their mean age decreased from 37.7-37.8 years (1920 to 1980 timeframe) (9,12) and 36.5 years (1970-2004) (26) to 30.2 years (5). Such a trend possibly mirrored the increased prevalence of foreign-born patients, whose share increased from 17.8% of earlier reports to the 47.8% of the nationwide estimates 1970-2007 (5,25,26). After 2003, not only 67.0% to nearly all reported cases were identified among people having a migration background (91.8% of all case reports for the same timeframe), but a report from Massone et al. suggests that the majority of cases (i.e. 53%) occurred in illegal residents, with 28.6% of individual cases in refugees (26.1% in total) (5). Not coincidentally, analysis of individual cases reported between 1992 and 2017 identified an older mean age (39.7 years ± 20.6), and such figures included a significant share of Italian-born cases (34.8%), whose mean age was 65.0 years (range 30 - 78) (30,32-34,36-38,40,41) (Table 2).

In other words, after 2003 autochthonous cases occurred only in subjects who had spent abroad significant time in high-risk areas, either as adopted children, expatriate or missionaries, or who had been presumptively infected several decades ago, when leprosy was still endemic (32-34,36-38,40,41). As a consequence, while endemic areas were initially scattered across the Italian peninsula, having their roots in the medieval outbreaks of the Hansen's disease, in 1980 circulation remained significant only in Northern Tuscany, Eastern Sicily, Calabria, Puglia and Liguria, and new areas (e.g. metropolitan area of Milan) emerged as a consequence of imported cases from high risk countries (Figure 3).

On this regard, also the geographical origin of patients has radically changed: while in earlier reports the largest proportion of cases had a South American origin (36.1% for 1920 - 1980), last decades were characterized by a raising share of cases from Asian (Bangladesh, India, Pakistan, Philippines, Sri Lanka) and African countries (Cameron, Egypt, Nigeria, Senegal, Sierra Leone, Sudan, Tanzania) (5,9,12).

The changing demographics of leprosy was associated with a main shift in the clinical characteristics: while up to 1980 the majority of patients were lepromatous ones, borderline leprosy is nowadays the most frequently reported (5,9,11), with a share of highly infectious multibacillary leprosy ranging from 17.4% to 51.4% (5,28,32,43,46). Even in individual reports, not only borderline-borderline leprosy accounted for 26.1% cases, but considering also borderline-tuberculoid and borderline-lepromatous the total share climbed to 39.0%. However, as the Ridley and Jopling classification was introduced only in 1966, historical comparisons should be cautiously performed (15).

Table 2. Summary of single cases reported from Italy (1925 - 2019). Notes. * = year of actual diagnosis; BB = borderline borderline; TT = tuberculoid leprosy; TB = tuberculoid borderline; LL = lepromatous leprosy; LB = lepromatous borderline; N/A not specified; MB = multibacillary; IBP = Italian Born People; FBP = Foreign Born People

Reference	Year*	Age (years)	Gender	Country of origin	Familiarity	Diagnosis	MB	Latency (years)	Risk group
Fiallo P et al. (33)	1992	38	M	Italy	N	TB	-	2	Long stay, high-risk area
Passarini B et al (34)	2001	52	M	Italy	N	LL	-	2	-
Visco-Comandini U et al. (35)	2004	32	M	Brazil	N/A	TT	-	2	HIV positive
Mozzillo R et al. (36)	2006	68	M	Italy	N/A	LL	-	15	Long stay, high-risk area
Zammarchi L et al. (13)	2006 - 2010	29 49	M M	Philippines Sudan	Y N/A	TT LL	- -	14 N/A	- Refugee
Bongiorno MR et al. (32)	2008	43	M	Italy	N	LL	X	3	Long stay, high-risk area
Fiallo P et al. (31)	2008	51	W	Philippines	N/A	TT	-	3	Long stay, high-risk area
Filippetti R et al. (30)	2008	30	W	Italy	N	BB	-	< 1	Long stay, high-risk area
Aridon P et al. (29)	2009	15	M	Senegal	N/A	TT	-	< 1	Refugee
Rongioletti F et al. (46)	2009	43	W	Brazil	Y	BB	X	1.5	-
Giacomet V et al. (45)	2010	14	M	Brazil	N/A	LL	-	< 1	Adopted
Massone C et al. (44)	2010 2010 2010	28 22 14	M M M	Nigeria Columbia Brazil	N/A N/A N/A	LL BB BB	- - -	N/A N/A 1	Refugee - Adopted
Simeoni S et al. (43)	2011	20	M	India	Y	LL	X	4	-
Piras AM et al. (42)	2011	26	M	Nigeria	N/A	BB	-	N/A	Refugee
Massone C et al. (41)	2012	77	M	Italy	N	LB	-	20	-
Liguori R et al. (40)	2015	59	M	Italy	N	TT	-	2	-
Maritati M, Contini C (39)	2015	22	M	Ghana	N/A	BB	-	N/A	Refugee
Marotta M et al. (28)	2017	29	M	Nigeria	N	LL	X	3	Refugee
Cusini M et al. (37)	2017	75	M	Italy	N	LB	-	2	-
Beltrame A at al. (38)	2017	78	M	Italy	N/A	TT	-	4	Missionary, high risk area
Summary	Tot = 23	39.7 y ± 20.6	M: 20, 87.0% F: 3, 13.0%	IBP: 8, 34.8% FBP: 15, 65.2%	Y: 3, 13.0% N: 8, 34.8% N/A: 12, 52.2%	TT: 6, 26.1% TB: 1, 4.3% BB: 6, 26.1% LB: 2, 8.6% LL: 8, 34.8%	4, 17.4%	N/A: 5, 21.7% < 1y: 3, 13.0% 2y: 4, 17.4% 3y: 3, 13.0% 4y: 2, 8.7% ≥5y: 3, 13.0%	None: 8, 34.8% Refugee: 6, 26.1% Adopted: 2, 8.7% Long stay, high-risk area: 5, 21.7% Missionary, high-risk area: 1, 4.3% HIV positive: 1, 4.3%

Accurate data on latency were retrieved by individual cases, and 52.2% of them reported a delay between earlier symptoms and final diagnosis that ranged between 2 and 20 years, even for multibacillary ones (28,32,43,46).

Discussion

Our comprehensive review suggests that leprosy, once endemic in Italy, is nowadays a sporadically reported disease, that mainly affects subjects who were born or who spent several years in high-risk areas. De-

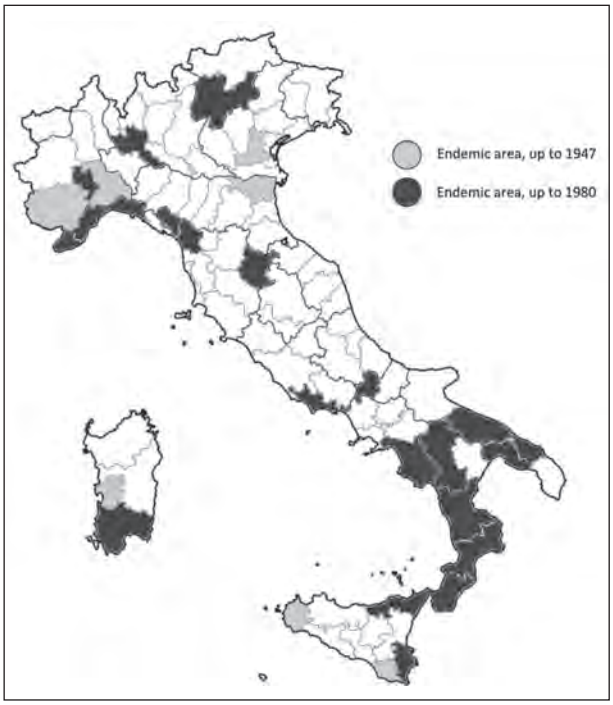

Figure 3. Distribution of leprosy cases in Italy, 1947 and in 1980 (9,11)

spite the potential public health relevance, our results should be carefully interpreted for several reasons.

Firstly, not only more recent reports are of heterogeneous quality and apparently inconsistent, but most of the available data have been only partially published in grey literature, without any external validation (25,26). In fact, a comparison of official data with available reports suggests that a significant share of cases has remained unknown to the National Authorities (28,37,38).

Secondly, actual figures for Hansen's disease are intrinsically inaccurate (3): not only a diagnosis of leprosy is generally difficult in initial stages, but the interplay between social and religious stigma, lack of access to appropriate healthcare services, unfamiliarity of Western medical professionals with a rare disease, diffusely hinder or at least delay appropriate diagnosis and treatment (4,5). Actually, the majority of individual cases we collected were appropriately diagnosed and treated only after several years (29,31,39-41,43,45). As accurate data collection on index cases was irregularly reported, and some of such patients are possibly unknown to the National Registry, we may guess whether the collection of personal history, analysis of familiarity, and identification of possible contacts had been appropriately performed (28,37,38). As a consequence, it is reasonable that a significant number of contact cases still remains unnoticed. More precisely as many refugees and illegal migrants actually come from highly endemicity areas, being frequently forced to living environments that facilitate the spreading of pathogens as *M. leprae*, it is possible that the ratio between notified cases and actual cases may range between 2 and 10 to 1, with around 40 to 50 new cases by year (2,5,22,23,47,6,7,16-21).

Third, it should be stressed that evidence drawn from individual reports is inherently biased, as cases characterized by a difficult diagnosis, or severe clinical involvement, are more likely to be published. In other words, the alarming share of patients who have received a very late diagnosis, even in multibacillary leprosy, may be largely overestimated (4,5).

Conclusions

In summary, our data reflect the need and importance of shedding light on this ancient but not vanished disease. As knowledge gaps of medical professionals may contribute to the unsatisfactory reporting rates we identified, teaching programs for medical specialties more likely to get in touch with possible cases (i.e. not only dermatologists and neurologists, but also general practitioners, pediatricians, and occupational physicians) are highly in need (29,44,45,48-50). Similarly, paramedical and social professionals that may interact with cases occurring in migrants and refugees should recall that a leprosy case remains possible even in the 21st century, addressing the suspected cases to an appropriate medical referral as soon as possible (2,4,5). As leprosy is a treatable infectious disease, and an untreated multibacillary patient can release more than 10,000,000 bacilli per day, which can survive for 4-5 weeks in the Italian climate, early identification and treatment of new cases is a public health priority that should not be forgotten.

Disclosures. This article is based on previously conducted studies and does not involve any new studies of human or animal subjects performed by any of the authors. Ethics approval was not required for this review. The facts, conclusions, and opinions stated in the article represent the authors' research, conclusions, and opinions and are believed to be substantiated, accurate, valid, and reliable. However, as this article includes the results of personal researches of the Authors, presenting correspondent, personal conclusions and opinions, parent employers are not forced in any way to endorse or share its content and its potential implications.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Received: 15 June 2019
Accepted: 18 July 2019
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Acta Biomed 2019; Vol. 90, Supplement 9: 15-20 DOI: 10.23750/abm.v90i9-S.8696

Original article

The accreditation system of Italian medical residency programs: fostering quality and sustainability of the National Health Service

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Summary. *Background and aim:* In June 2017, University and Health Ministries jointly enacted a decree implementing a new accreditation system for the Italian post-graduate medical schools (residency programs). We report the innovations introduced through the reform. *Methods:* Universities were called to submit post-graduate medical school projects to the National Observatory on medical residency programs, the inter-institutional committee responsible for the entire accreditation process, through an interactive web platform. The adherence to minimum standards, requirements and the performances were measured. After this first assessment, universities were asked to provide programs of improvement for critical schools. At the end of the evaluation, residency schools were proposed for a full or a partial accreditation. *Results:* Of the 1,431 post-graduate medical school projects submitted to the National Observatory by 37 public and 4 private Universities, 672 (47.0%) obtained a full accreditation, 629 (43.9%) a partial accreditation, with a gap to be filled within a two-year period according to a specific improvement programme, while 130 (9.1%) were not accredited. Further, 1,254 out of the 1,301 schools with a full or partial accreditation were activated according to the available public financial resources, excluding those performing the lowest. Annual surveys were in place to investigate the residents' level of satisfaction concerning the quality of the training programs. The National Observatory further developed an experimental methodology to conduct on-site visits to support quality improvement. *Conclusions:* This reform can be considered an important initiative to guarantee high standards in the quality of care and to face the challenge of sustainability for the National Health System. (www.actabiomedica.it)

Key words: Post-graduate medical education and training; residency programs; continuous quality improvement; standards and requirements; sustainability in healthcare; National Health System

Abbreviations:
MIUR: University and Research Ministry
NHS: National Health System
ANVUR: Agency for the Italian university system evaluation
AGENAS: Agency for regional health services

Background and aim

European Union has called member states to update educational standards and requirements needed to train physicians at the best level at the era of the cross-border healthcare in Europe (1). At the same time, national and international health authorities have underlined the importance of investing in public health policies to face the challenge of health systems' sustainability, which is undermined by populations' ageing and increased burden of preventable chronic diseases (2,3), impact of innovation in healthcare, related increasingly healthcare costs and ongoing financial crisis (4). These

all are drivers that should be taken into account by every medical education and training system (5).

Since the nineteen-eighties, post-graduate medical education in Italy has been provided by universities through residency programs, under the supervision of the University and Research Ministry (MIUR) (6). Although specialised physicians were trained to work for the National Health System (NHS), the role of national and regional health authorities was limited to answer the NHS's demand for health professionals by drawing up the health workforce plans, and to provide public financial support for the training contracts of about 25,000 medical residents.

In June 2017, MIUR and Health Ministry jointly enacted a decree implementing a new accreditation system for the post-graduate medical schools (residency programs) (7). This initiative followed the core curriculum revision for the 50 different typologies of post-graduate medical schools (Table 1) providing the residency programs (8).

The accreditation decree established three fundamental principles: first, implementation of a continuous quality improvement system, including i) the monitoring of every single structure as to adhere to minimum standards exploring different dimensions (structural, organizational, technological, healthcare), and ii) the adoption of a quality management system to register the educational and training activities dedicated to the residents, including clinical and surgical procedures, and to certificate knowledge, skills, and attitudes achieved by every single resident at the end of the training; second, the development of networks of training structures, including primary care facilities, meeting the minimum general and specific requirements (structural, organizational, technological defined per each health specialty discipline) introduced by the decree; and, lastly, the involvement of all the actors and the stakeholders (i.e. academics, professionals, scientific societies, junior doctors' associations and citizens' associations) in the reform developmental process and its future evolution.

We describe the main innovations introduced in the Italian post-graduate medical education and training system through a reform, based on a continuous quality improvement approach, implementing the new accreditation system of medical residency programs.

Methods

The entire accreditation process was up to the National Observatory on medical residency programs (National Observatory), the inter-institutional committee charged with the designing of the reform route and responsible for the continuously monitoring of standards and requirements to be met by every post-graduate medical school.

Health training facilities and services composing the training networks have been classified in main structure (directed by an academic role), associate (of the same specialty as the main one) and complementary (of a different discipline integrating the contribution of knowledge and skills by the future specialist). Interestingly, the decree stated the possibility to implement the training with elective programmes to be held both in national and international ranked highly qualified healthcare institutions or research centres, also in order to satisfy a demand for international experiences documented among Italian medical residents (9).

The continuous quality improvement system included the monitoring of every single structure as to adhere to the minimum standards exploring different dimensions as well as the development of networks of training structures, including primary care facilities, meeting the minimum general and specific requirements introduced by the decree. The adherence to standards and requirement was then measured. Furthermore, a set of indicators designed to measure healthcare and teaching performances was defined and then adopted in collaboration with the Agency for the Italian university system evaluation (ANVUR) and the national Agency for regional health services (AGENAS), respectively.

Universities were called to submit post-graduate medical school projects to the National Observatory through an interactive web platform. The adherence to minimum standards, requirements and the performances were then measured. After this first assessment, universities were asked to provide programs of improvement for critical schools. At the end of the evaluation, residency schools were proposed for a full or a partial accreditation. Schools projects were not accredited as a third option. According to the implemented continuous quality improvement approach,

the post-graduate medical schools with partial accreditation and not meeting the minimum standards and requirements, at the end of a three years period, will be deactivated, thus realizing an effective rationalization of the residency programs.

Furthermore, the National Observatory has developed an experimental methodology to conduct on-site visits and a structured questionnaire to survey the residents' opinion on the quality of the training. The adoption of a quality management system to register the educational and training activities dedicated to the residents, including clinical and surgical procedures, and to certificate knowledge, skills, and attitudes achieved by every single resident at the end of the training, has been also required to be implemented in a three year period.

Results

We report the results of the first step of accreditation, corresponding to the first year of a three years accreditation cycle.

In the global evaluation of the 1,431 post-graduate medical school proposals, submitted by 37 public and 4 private Universities, the National Observatory included the measurements of adherence to standards and requirement as well as of the healthcare and teaching performances scores provided by the two mentioned national Agencies.

Six hundred seventy-two (47.0%) post-graduate medical school proposals obtained a full accreditation, 629 (43.9%) a partial accreditation, with a gap to be filled in the next two years by providing outcomes consistent with the specific improvement programmes approved by the National Observatory, while 130 (9.1%) were not accredited (Table 1).

The accreditation status of the n. 1,431 post-graduate Italian medical school proposals by residency program is reported in Table 1.

Further, 1,254 out of the 1,301 schools with a full or partial accreditation were activated according to the available public financial resources, excluding those performing the lowest.

On-site visits, conducted by the Regional Observatories on behalf of the Regional Health Authorities or by the National Observatory in demand, are ongoing to verify quality improvement documented by the residency programs.

Moreover, annual surveys have been planned to be annually administered to investigate the residents' level of satisfaction concerning the integrated training system.

Conclusions

A new academic leadership was supported by a strong political, social and professional endorsement, and was addressed to the accreditation reform implementation, bridging together universities and NHS in order to overcome the existing dichotomy in the training process. In that direction, the renewal of post-graduate medical training must be considered an important initiative both to face the challenge of mobility of medical doctors in the European Union cross-border healthcare and to recognise the increasing demand for integrated, patient-centred and inter-professional education, which is mandatory to guarantee the sustainability of every NHS (10,11).

In this perspective, the role of a new generation of high qualified professionals, trained to face the challenge of implementing innovative technologies in healthcare while promoting the culture of quality and safety in healthcare, as well as the *value-based* and the *population-based* approaches, is increasingly recognized (12,13,14). Moreover, to shape a culture of stewardship and the value of leadership in healthcare all the stakeholders in higher medical education must rely on solid accreditation approach and, among them, are not only medical residents and patients, but also the general public and institutions (15). Accreditation should assure that public interest is respected, and particularly in relation to investments: public has a right to know more about quality of care, starting from the evidence that the credentials conferred by institutions are of the highest quality and that the education process tends to meet the standards of excellence (16).

Unfortunately, policy-makers missed the opportunity to include the general practitioners post-graduate training within the reform, as the proposal to evolve regional professional programs into general practice

Table 1. Accreditation status of the n. 1,431 post-graduate Italian medical school proposals, by residency program, submitted to the National Observatory on Residency Programs

Residency Programs		Accreditation Proposal n.	Full Accreditation n. (%)	Partial Accreditation n. (%)	No Accreditation n. (%)
1	**Allergology and Clinic Immunology**	**24**	11 (46)	11 (46)	2 (8)
2	**Anatomic-pathology and Histopathology**	**31**	3 (10)	23 (74)	5 (16)
3	**Anaesthesia**	**40**	17 (42.5)	21 (52.5)	2 (5)
4	**Audiology and Phoniatrics**	**14**	4 (29)	4 (29)	6 (42)
5	**Cardiac Surgery**	**23**	9 (39)	13 (57)	1 (4)
6	**General Surgery**	**41**	22 (54)	18 (44)	1 (2)
7	**Maxillo-facial Surgery**	**13**	2 (15)	7 (54)	4 (31)
8	**Paediatric Surgery**	**16**	2 (12)	7 (44)	7 (44)
9	**Plastic Surgery**	**24**	10 (42)	13 (54)	1 (4)
10	**Thoracic Surgery**	**23**	6 (26)	10 (44)	7 (30)
11	**Vascular Surgery**	**24**	4 (17)	18 (75)	2 (8)
12	**Dermatology and Venereology**	**28**	13 (46)	14 (50)	1 (4)
13	**Haematology**	**32**	14 (44)	16 (50)	2 (6)
14	**Endocrinology and Metabolic Diseases**	**34**	15 (44)	17 (50)	2 (6)
15	**Clinical Pharmacology**	**22**	9 (41)	5 (23)	8 (36)
16	**Medical Genetics**	**24**	12 (50)	7 (29)	5 (21)
17	**Geriatrics**	**36**	24 (67)	11 (30)	1 (3)
18	**Obstetrics and Gynaecology**	**41**	22 (54)	17 (41)	2 (5)
19	**Public Health and Preventive Medicine**	**38**	26 (69)	10 (26)	2 (5)
20	**Cardiology**	**40**	14 (35)	25 (62.5)	1 (2.5)
21	**Gastro-enterology**	**31**	20 (65)	9 (29)	2 (6)
22	**Respiratory Medicine**	**28**	13 (46)	14 (50)	1 (4)
23	**Communicable and Tropical Diseases**	**31**	14 (45)	17 (55)	0 (0)
24	**Emergency Medicine**	**34**	22 (65)	11 (32)	1 (3)
25	**Occupational Medicine**	**30**	11 (36)	16 (53)	3 (1)
26	**Sports Medicine**	**24**	12 (50)	10 (42)	2 (8)
27	**Physiatry and Physical Medicine**	**29**	6 (21)	20 (69)	3 (10)
28	**Internal Medicine**	**41**	27 (66)	14 (34)	0 (0)
29	**Legal Medicine**	**28**	14 (50)	7 (25)	7 (25)
30	**Nuclear Medicine**	**18**	13 (72)	5 (28)	0 (0)
31	**Thermal Medicine**	**5**	2 (40)	0 (0)	3 (60)
32	**Microbiology**	**29**	21 (73)	7 (24)	1 (3)
33	**Nephrology**	**29**	14 (48)	12 (41)	3 (11)
34	**Neuro-surgery**	**27**	10 (37)	11 (41)	6 (22)
35	**Neurology**	**39**	21 (54)	15 (38)	3 (8)
36	**Infant and adolescent Neuro-psychiatry**	**25**	4 (16)	18 (72)	3 (12)
37	**Ophthalmology**	**38**	14 (37)	21 (55)	3 (8)
38	**Clinical Oncology**	**34**	16 (47)	16 (47)	2 (6)
39	**Orthopaedic Surgery**	**41**	13 (32)	24 (58)	4 (10)
40	**Otolaryngology**	**34**	17 (50)	15 (44)	2 (6)
41	**Biochemistry and Lab Pathology**	**35**	24 (68)	8 (23)	3 (9)
42	**Paediatrics**	**37**	25 (67)	11 (30)	1 (3)
43	**Psychiatry**	**36**	14 (39)	20 (55.5)	2 (5.5)
44	**Radiology**	**41**	25 (61)	16 (39)	0 (0)
45	**Radiotherapy**	**26**	18 (69)	6 (23)	2 (8)
46	**Rheumatology**	**24**	6 (25)	17 (71)	1 (4)
47	**Nutrition Science**	**19**	13 (68)	3 (16)	3 (16)
48	**Health Statistics and Biometrics**	**13**	4 (31)	3 (23)	6 (46)
49	**Urology**	**32**	16 (50)	13 (41)	3 (9)
50	**Community Medicine and Primary Care**	**5**	4 (80)	1 (20)	0 (0)
	Total (%)	**1431 (100.0)**	672 (47.0)	629 (43.9)	130 (9.1)

and primary care post-graduate medical schools still remains in the political agenda.

Next step for the future is to improve transparency and accountability throughout the process by publishing the accreditation results so as to foster the academic social accountability in order to meet the demanding and pressing health care needs of society (17).

Acknowledgements

Authors would like to thank the University and Research Ministry and the Health Ministry for the strong political support and the Italian Agency for the university system evaluation (ANVUR) and the Italian Agency for regional health services (Age.Na.S.) for the technical support given to the reform conception and development. Authors are also grateful to all the members of the National Observatory on medical residency programs for the constant effort provided to the reform implementation.

Authors' contributions: All individuals listed as authors have contributed to the study. Conception of the study: WM, RV. Manuscript writing and drafting: WM, AS, RV. Revision of the manuscript: WM, AS, MG, RV. Approval of the final version of the manuscript: WM, RB, AS, MG. The document has been reviewed and corrected by a native English speaker with extensive scientific editorial experience to ensure a high level of spelling, grammar and punctuation.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Received: 15 June 2019
Accepted: 18 July 2019
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Acta Biomed 2019; Vol. 90, Supplement 9: 21-27 DOI: 10.23750/abm.v90i9-S.8699

Original article

On field vaccine effectiveness in three periods of 2018/2019 influenza season in Emilia-Romagna Region

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Summary. *Background and aim of the work*: Epidemic influenza is associated with significant morbidity and mortality, particularly in people at risk. The vaccine reduces complications, hospitalization and mortality excess, as well as health care and social costs. Aim of the study was to estimate the influenza vaccine effectiveness (VE) in Emilia-Romagna Region during the 2018/2019 season. *Methods:* Within the context of virological surveillance conducted at the Regional Reference Laboratory of Parma, nasal/throat swabs were performed by sentinel practitioners and clinicians, on patients with ILI (Influenza-like illness). VE estimates, overall and against subtype A(H1N1)pdm09 and A(H3N2), were evaluated in three periods of the season, using a test-negative case-control design. *Results:* From November 2018 to April 2019, 2,230 specimens were analyzed: 1,674 (75.1%) performed by clinicians and 556 (24.9%) by sentinel practitioners of the regional network. The season was characterized by the predominant circulation of influenza type A viruses: 57.4% belonged to subtype A(H3N2), 41.2% to subtype A(H1N1)pdm09. 23.5% of patients was vaccinated against influenza with quadrivalent or adjuvate vaccine. The overall VE was -5% (95% CI -33% - 18%) with a decreasing trend during the season. The overall VE against subtype A(H1N1)pdm09 was 39% (95% CI 11% - 58%) and remained stable during the season. The overall VE against subtype A(H3N2) was -43% (95% CI -89% - -9%), and showed an important decreasing trend. *Conclusions:* The possibility to make accurate and continuous VE estimates during the season will help to better define the composition of the vaccine for the following season. (www.actabiomedica.it)

Key words: influenza, influenza-like illness, virological surveillance, vaccine effectiveness, test-negative case-control design

Introduction

Epidemic influenza is associated with significant morbidity and mortality, particularly for the elderly and people at risk (1). The European Center for Disease Control (ECDC) estimates that, about 40,000 people, each year, die prematurely due to influenza in the European Union. A large proportion of influenza-related deaths occur in individuals older than 65 years, especially among those with chronic underlying conditions (2, 3). The prevention of influenza represents an important Public Health intervention, involving Health Services every year in the implementation of the vaccination campaign (4). The vaccine significantly reduces complications, hospitalization and mortality excess in those most at risk, as well as health care costs through the reduction of drug consumption, and the social costs associated with the flu epidemic (5-13).

The viral strains in influenza vaccines have to be evaluated and updated regularly because circulating influenza viruses continuously evolve. Annually, an advisory group of experts analyses influenza virus surveillance data generated by the WHO Global Influenza Surveillance and Response System (GISRS),

and issues recommendations on the composition of the influenza vaccines for the following influenza season. These recommendations are used by the national vaccine regulatory agencies and the pharmaceutical companies to develop, produce and license influenza vaccines. Approximately 6-8 months are needed to produce vaccines (14). Recommendations for the following influenza season are usually made in February in the Northern Hemisphere and in September in the Southern Hemisphere. According to the virological surveillance activity, in 2019, the formulation of the influenza vaccine for the Northern Hemisphere was postponed by about a month to allow a better definition of the A(H3N2) strain, genetically and antigenically different from the previous vaccine strain (15).

In recent years the need for Public Health to carry out rigorous and repeated studies, to obtain solid estimates of vaccine effectiveness (VE) performed at mid-season "interim" and at the end season, has been highlighted (16-21). Vaccine effectiveness refers to the impact of a vaccine assessed using observational studies (22). Since the 2008/2009 influenza season, in many European countries (8 to 12), including Italy, several studies have been conducted with the Test Negative design (TN) to assess this effectiveness (23-30). Starting from the 2014-2015 season, the Emilia-Romagna Region, with 5 other Italian Regions (Piedmont, Valle D'Aosta, Lombardy, Friuli Venezia Giulia and Puglia), was officially involved in the multicenter case-control observational study " I-Move "(Influenza Monitoring Vaccine Effectiveness in Europe) on field effectiveness of influenza vaccines, coordinated by the Istituto Superiore di Sanità (ISS) (31).

During the 2018/2019 season, within the context of integrated virological and epidemiological surveillance coordinated by the ISS and conducted in Emilia-Romagna, at the Regional Reference Laboratory of Parma, a test-negative case-control design was established in order to produce seasonal influenza VE estimates, and interim VE estimates.

Methods

During the 2018/2019 influenza season, 31 General Practitioners (GPs) and 18 Pediatricians (P) from the InfluNet network of Emilia-Romagna Region (Bologna, Ferrara, Forlì-Cesena, Modena, Parma, Piacenza and Reggio Emilia) performed nasal or throat swabs on not hospitalized infants, children and adults with ILI (Influenza-like illness). The Care Units of Piacenza, Parma and Reggio Emilia Hospitals performed nasal or throat swabs on patients admitted with influenza-like symptoms and/or severe acute respiratory diseases. According to operative InfluNet protocol (32), for each sample, information on age, sex, vaccination status, presence/absence of chronic diseases, and Care Unit for hospitalized patients, were collected. For data analysis, the subjects were stratified into 4 age groups: 0-4 years, 5-14 years, 15-64 years and $\geq$65 years. Laboratory diagnosis was undertaken by using one-step Real Time retro-transcription PCR assay (rRT-PCR), able to detect circulating influenza A and B viruses and subtypes. For rRT-PCR positive samples, influenza viruses were also isolated in MDCK or MDCK-SIAT1 cells (Madin-Darby Canine Kidney), specific for the growth of influenza viruses. Protocols and materials (kits, primers and probes) indicated by the CDC (Centers for Disease Control and Prevention) and WHO (World Health Organization) were used (33). Further strain characterisation was performed by the Reference Laboratory Network of the Italian National Influenza Center (NIC) on a selected number of influenza virus isolates.

Under the TN design, subjects who seek medical care for ILI and tested positive for influenza virus infection were cases, subjects who seek medical care for ILI and tested negative for influenza virus infection were non case/control.

To estimate the VE, the season in study was divided in three periods, considering the peak epidemic period (peak: 5^{th} - 7^{th} week/2019), the previous weeks (pre-peak: 46^{th} week/2018 - 4^{th} week/2019) and the following weeks (post-peak: 8^{th} - 17^{th} week/2019) at the peak period. VE was estimated as (1- ORadj) x 100 with the relative confidence intervals of 95% (95% CI). In particular, were estimated: the seasonal influenza VE (overall) and the VE against subtype A (H1N1)pdm09 and subtype A(H3N2) (adjusted for epidemic period, age group and sex); the interim VE estimates in the three considered periods of the season (adjusted for age group and sex).

The results were summarized in frequency tables and analyzed with the X^2 test with Yates continuity correction when necessary. A logistic regression model was used for the calculation of the adjusted VE for sex, age group and epidemic period. All statistical analyses were performed with SPSS 25.0 (IBM SPSS Inc., Chicago – IL).

Results

From November 2018 to April 2019, 2,230 specimens were analyzed. 1,674 samples (75.1%) came from hospital Care Units, in particular from the Medicine Unit (29.6%), Geriatrics and Long-term Care Units (27.1%) Emergency-Urgency Unit (12.2%), Pediatrics Unit (7.8%) and Intensive Care Unit (7%) (Figure 1); 556 swabs (24.9%) came from GPs and P of the regional network. Overall, 704 samples were positive (31.6%); 48.6% of swabs performed by sentinel practitioners and 25.9% by hospital Care Units, were positive (Table 1).

This influenza season was characterized by an initial period of low incidence, until the end of December 2018 and by an intensification of the viral activity at the beginning of the new year, with an incidence rate of 14 cases per 1000 person/years in the 5th week. In 2018/2019 season, the trend of the epidemic showed a peak around the 6th surveillance week. From a virological point of view, the season was characterized by the predominant circulation of influenza type A viruses (99.9%); of these, 57.4% belonged to subtype A(H3N2), 41.2% to subtype A(H1N1)pdm09 and the remaining 1.3% was not subtyped. Within type A, viruses of the two subtypes A(H3N2) and A(H1N1) pdm09 always co-circulated, although the A(H1N1) pdm09 strains were found to be prevalent in the first half of the epidemic season, and the A(H3N2) strains from the second half of February onwards. One virus type B, belonging to the B/Yamagata lineage, was isolated (Figure 2). Subtype A(H3N2) circulated more than subtype A(H1N1)pdm09, both in outpatients (56.3% vs 42.6%) and in inpatients (58.1% vs 40.3%) (Table 1). Although the highest number of swabs was performed on subjects older than 65 years (48.3%), the highest number of positive samples was identified in pediatric ages, 5-14 years (55.3%) and 0-4 years (42.3%). While in the age group 0-4 years, the subtypes A(H3N2) and A(H1N1)pdm09 co-circulated (50% vs 50%), in the classes 5-14 and over 65 years, circulated mainly the A(H3N2) (67.6% vs 30.9% and 69.8% vs 29.4% respectively). Subtype A(H1N1) pdm09, on the other hand, circulated more frequently in the age group 15-64 years (58.5% vs 38.5%). 23.5% of the subjects was vaccinated; considering subjects belonging to the age group greater than 65 years and/or with chronic diseases, for whom vaccination is strongly recommended, 36.6% of these, was vaccinated. According to the indications of Italian Ministry of Health (34), all vaccinated subjects were immunized with a quadrivalent or adjuvated (trivalent) vaccine; 29.1% of these, contracted influenza, and in particular 74.5% were positive for subtype A(H3N2) and 24.8% for subtype A(H1N1)pdm09. The overall VE was -5% (95% CI -33% - 18%) with a decreasing trend during the season: 37% (95% CI -3% - 62%) in the weeks preceding the epidemic peak , -9% (95% CI -63% - 27%) during the peak weeks and -41% (95% CI -109% - 5%) in the post-peak weeks. The overall VE against subtype A(H1N1)pdm09 was 39% (95% CI 11% - 58%) and remained stable during the season. The overall VE against subtype A(H3N2) was -43% (95% CI -89% - -9%), and showed a decreasing trend from values of 26% (95% CI -45% - 62%) at the beginning of the season (pre-peak), to -75% (95% CI -

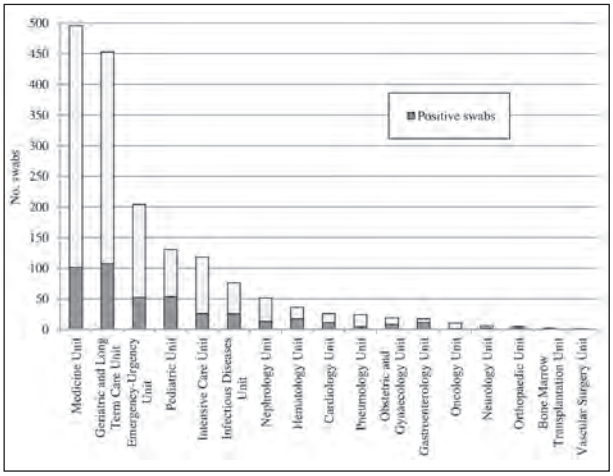

Figure 1. Number of swabs and specimens positive for influenza virus by hospital Care Unit

Table 1. Characteristics of patients in the 2018/19 influenza-season in Emilia Romagna-Region

Characteristic	Outpatients No. (%)	Inpatients No. (%)
Overall	556 (24.9)	1674 (75.1)
Province		
Bologna	41 (7.4)	-
Ferrara	72 (13.0)	-
Forli-Cesena	31 (5.6)	-
Modena	52 (9.3)	-
Parma	284 (51.1)	1370 (81.8)
Piacenza	29 (5.2)	200 (11.9)
Reggio Emilia	47 (8.4)	104 (6.3)
Sex		
Female	245 (44.1)	872 (52.1)
Male	311 (55.9)	802 (47.9)
Age group (years)		
0-4	194 (34.9)	85 (5.1)
5-14	204 (36.7)	42 (2.5)
15-64	144 (25.9)	484 (28.9)
≥65	14 (2.5)	1063 (63.5)
Vaccination Status		
Unvaccinated	476 (85.7)	1048 (62.6)
Vaccinated	77 (13.8)	448 (26.8)
Missing information	3 (0.5)	178 (10.6)
Target group for vaccination		
No	477 (85.8)	296 (17.7)
Yes	79 (14.2)	1316 (78.6)
Missing information	0 (0)	62 (3.7)
Influenza Laboratory Diagnosis		
Positive	270 (48.6)	434 (25.9)
Negative	286 (51.4)	1240 (74.1)
Influenza virus type or subtype		
A(H3N2)	152 (56.3)	252 (58.1)
A(H1N1)pdm09	115 (42.6)	175 (40.3)
A unsubtyped	3 (1.1)	6 (1.4)
Influenza B	0 (0)	1 (0.2)

168 - -15%) in the weeks following the peak period (Figure 3).

Molecular and phylogenetic analyses carried out on the HA (Haemagglutinin) gene of A(H3N2) strains (35) circulating in Emilia-Romagna, identified at the beginning of the season, have shown that A(H3N2) viruses were mainly grouped in subclade 3C.2a1b (vaccine reference strain: A/Singapore/INFIMH-16-0019/2016) and, in a small proportion, in subclade 3C.2a2; however, in the following weeks, A(H3N2) viruses belonging to clade 3C.3a started to circulate more widely. Viruses belonging to subclade 3C.3a are defined by the aminoacid substitutions S91N, N144K, F193S and K326R in HA1. Molecular and phylogenetic analyses carried out on the HA gene of A(H1N1)pdm09 strains (35), from January

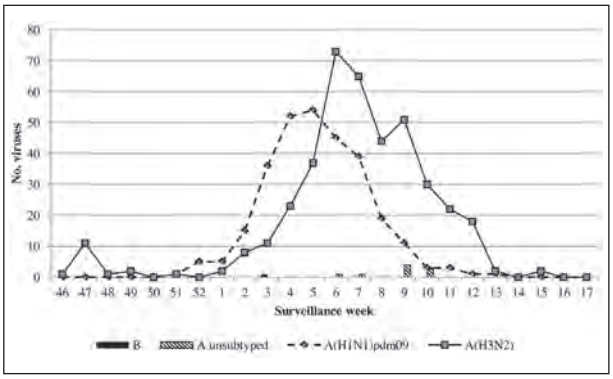

Figure 2. Number of specimens positive for influenza virus, by type or subtype and week of specimen collection

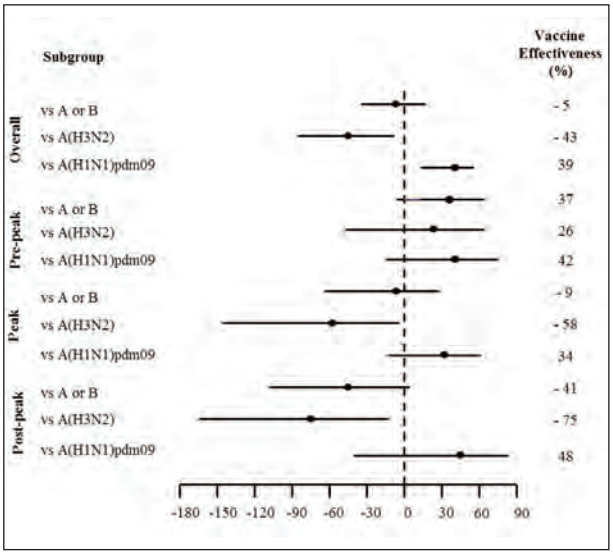

Figure 3. Adjusted estimates of Influenza Vaccine Effectiveness (VE) against virus type or subtype, overall and stratified according to epidemic period

onwards, have shown that they belong to subclade 6B.1A, defined, in HA1, by three additional aminoacid substitutions, S74R, S164T and I295V, compared to the vaccine strain A/Michigan/45/2015. Most of the A(H1N1)pdm09 strains analyzed, present further substitution, S183P, as the new vaccine strain selected for the 2019/2020 season, A/Brisbane/02/2019.

Conclusions

The 2018-2019 influenza season was particularly intense, with a high number of ILI cases and specimens collected, lower only than the 2009-2010 pandemic season. After 2 seasons in which the epidemic peak was anticipated by about 4 weeks, the trend of the epidemic returned to the usual timing, with a peak around the 6th week of surveillance; during this week there was the highest number of swabs performed and viral isolations. In Emilia-Romagna Region A(H1N1) pdm09 and A(H3N2) have co-circulated, with a greater prevalence of the A(H3N2) (57.4% vs 41.2%); the highest number of throat swabs was performed in people over 65 years, most of whom were hospitalized patients with influenza-like symptoms; however, the highest percentage of viral isolation concerned pediatric age groups. The first influenza viruses were identified in hospitalized patients and, only several weeks later, they also appeared in outpatients.

This study has some limitations: although the TN design controls for health care seeking behaviour bias, the VE estimates may not be generalizable to entire population (22). We adjusted the VE estimates for age, sex and epidemic season period. However, for a more correct estimate of the VE, it will be necessary to consider, in the future, also a severity score, based on the clinical symptomatology of the disease for each patient.

Our results, although referring to only one Region, suggest that the 2018/19 seasonal vaccine conferred a moderate protection against influenza viruses. The overall seasonal influenza VE was very moderate and showed a rapid decrease from the start of the season, throughout the peak period, until the end of the season.

A good VE against A(H1N1)pdm09 with stable trend in the 3 different periods of the season and a lack of protection against A(H3N2), due to antigenic and genetic mismatch between circulating A(H3N2) and the respective 2018/19 vaccine strain, were observed.

These results reflect what has been observed at national level and in most European Countries, and confirm a wide circulation of A(H3N2) variants antigenically distinct from the vaccine virus A/Singapore/INFIMH-16-0019/2016 (36). Phylogenetic analyses carried out in our Laboratory and at the NIC of the ISS, relating to the HA gene of a selection of viruses of subtype A(H3N2) isolated in Parma, have shown how, while in the first part of the season have circulat-

ed strains similar to the vaccine, with a moderate value of VE (26%), in the middle weeks of the season began to circulate in Parma, as well as Italy and in other parts of the world (35, 36), strains belonging to different genetic subgroups, and in particular to the subclade 3C.3a (reference strain: A/Kansas/14/2017) recently indicated by the WHO as an A(H3N2) component for the 2019/2020 influenza vaccine in the Northern Hemisphere.

In Italy, since the start of this influenza season, 8,104.000 cases of influenza syndrome have been reported; 809 severe cases of confirmed influenza have been reported in subjects with SARI (Severe Acute Respiratory Infection) and/or ARDS (Acute Respiratory Distress Syndrome) admitted to Intensive Care Units; among these, 198 died. In Emilia-Romagna Region, 72 severe cases of confirmed influenza and 53 deaths were reported (37).

The contribution given by Virological and Epidemiological Surveillance Programmes allows the correct identification of any variations (minor and major) in the circulating strains and, therefore, the preparation of more targeted vaccines, the effectiveness of which derives from the correct alignment between circulating viruses and antigens contained in the vaccine. The viruses characterization complemented with other available epidemiological and disease information, form the evidence base for Public Health decisions on epidemic response and pandemic preparedness, including seasonal vaccine virus selection and zoonotic influenza candidate vaccine virus development (38). Moreover, the timely identification of sick people and their contacts could contain the epidemic, at local level, and direct GPs and P towards more targeted therapies, reducing the risk of evolution in complicated cases, hospitalizations and deaths; in closed communities, and in inpatients it could reduce the risk of infections related to care (Healthcare Associated Infection), especially in subjects at risk for age or chronic disease.

The possibility to make accurate and continuous effectiveness estimates during the season, thanks to the availability of an acquired methodology based on the integration of virological and epidemiological data, combined with sensitive and standardized molecular biology methods, will help to better define the composition of the vaccine for the following season.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Received: 15 June 2019
Accepted: 18 July 2019
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Acta Biomed 2019; Vol. 90, Supplement 9: 28-34 DOI: 10.23750/abm.v90i9-S.8700

Original article

Immunity status against poliomyelitis in young migrants: a seroprevalence study

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Summary. *Background and aim of the work:* Recent seroprevalence studies in different population groups have shown low antibody titers against poliomyelitis, especially in young adults. This, together with the reduction of vaccination rates, could favor the reintroduction of poliovirus in long-time polio-free countries. Within the Surveillance system of acute flaccid paralysis, a prevalence study was conducted to estimate the immunological status associated with poliomyelitis in young migrants. *Methods:* Local Health Authority collected serum samples in young migrants, without vaccination documentation. Antibodies levels were assessed with a long incubation neutralization assay. Subjects were stratified by age and by WHO region. Seroprotection was defined by a titer equal or above 1:8 and titers > 1:2 were log-transformed and evaluated as geometric mean titers (GMTs). *Results:* From January 2004 to August 2017, 1138 blood samples were collected. Mean age was 13.3 years with no differences between WHO regions. The percentage of antibody titers below 1:8 was 6.0% versus poliovirus 1 (PV1), 7.7% versus poliovirus 2 (PV2) and 15% versus poliovirus 3 (PV3). The GMTs were 45.5, 29.5 and 20 towards PV1, PV2 and PV3 respectively. In each WHO region, the GMTs towards PV3 were consistently the lowest, and the Europeans showed the lowest GMTs both towards PV2 and PV3 (27.5 and 15.3 respectively). GMTs decreased with age. *Conclusion:* The low GMTs and the clear tendency to decrease with increasing age of the subjects, especially against to PV1, confirm the framework of attention that polio is receiving at national and international level. (www.actabiomedica.it)

Key words: serological survey, seroprevalence, immunity, migrants, poliomyelitis, WHO region

Introduction

Poliomyelitis epidemiology has radically changed since the introduction of intensive vaccination programs against the three polioviruses (PVs) (1,2). The last native case of polio due to wild-type poliovirus (WPV) infection detected in Italy occurred in 1982. At the time, the mandatory vaccination was performed entirely with trivalent oral poliovirus vaccine with Sabin strains (tOPV). In 1999, tOPV was substituted with a sequential schedule: two doses of enhanced inactivated polio vaccine (eIPV) followed by two doses of tOPV. When, in 2002, the European Region was declared "polio-free country" (the last case of indigenous wild poliomyelitis had occurred in Eastern Turkey in 1988) (3), Italy finally decided to adopt the four doses eIPV schedule as well as other high income Countries (4). Several seroprevalence studies, in which the level of neutralizing antibodies against poliovirus 1 (PV1), poliovirus 2 (PV2) and poliovirus 3 (PV3) are considered correlates of protection, conducted in Italy since the Eighties, both in general population and in selected subgroups, showed decreased protective values in terms of geometric mean titers (GMT) and titers considered protective by WHO (equal or higher than 1:8). These studies have also shown, despite good levels of seroprotection in the general population, a reduction in protection among adolescents and subse-

quently among young adults, probably due to the lack of natural boosters 10-15 years after the primary vaccination cycle (5-16). In addition, over the last years, the Italian Ministry of Health observed a lower vaccination coverage nationwide, explained by a loss of trust of the Italian population in these preventive measures. Due to vaccination hesitancy (17,18), anti-polio vaccination coverage dropped from 96.1% in 2013 to 93.4% in 2015, therefore below 95%, which is the requested threshold for polio elimination and to ensure herd immunity (19). For these reason, the 2017-19 National Immunization Prevention Plan confirmed the mandatory vaccination for children, alongside with a fifth booster dose of eIPV for adolescence (20).

Lower immunization rates, in fact, expose the Italian population, at least hypothetically, to a reintroduction of WPV or vaccine-derived polioviruses (cVDPV). Since 2005, when Environmental surveillance (ES, testing sewage for polioviruses) was introduced in Italy, becoming an important tool for early detection of silent reintroduction and circulation of polioviruses, no WPVs were spotted, although there have been several detections of Sabin-like PVs (21-26).

Migration flows towards Europe and Italy have constantly increased since the early Nineties. In many of the cases, migrants come from countries were OPV schedule is still recommended. Unfortunately in some of these areas there is a strong decline of vaccine coverage due to social disruption caused by civil war, Health Services collapse due to major epidemics, or even religious opposition by fundamentalists culminating with acts of violence against polio vaccination workers.

European countries registered an outbreak of 71 cases (59 paralytic and 2 death) in an unvaccinated religious community in the Netherlands in 1992 (27), whereas other 3 cases were identified among Roma children in Bulgaria in 2001 (28). A large outbreak caused by WPV1 imported from India in late 2009, with 463 laboratory-confirmed and 47 polio-compatible cases, took place in 2010 in Tajikistan and spread to neighbouring countries, Kazakhstan, Russia, Turkmenistan and Uzbekistan (29). Episodes like these ought to remind us that reintroduction of polioviruses cannot be completely ruled out (19).

Migrants who arrive in Italy legally, for work or study reasons, for international adoption or for family reunification and who decide to live permanently in the Italian territory, represent an important population group. Although immunization policies for migrants and refugees vary widely within the WHO European Region (30,31), the Italian Ministry of Health recommends to vaccinate, according to age, all refugee children who have never been vaccinated or who have insufficient documentation regarding prior vaccinations. Additionally, adults with the same characteristics should receive polio vaccination.

The aim of the present study was to estimate the prevalence of antibodies against the three poliomyelitis viruses in subjects of recent immigration who approached the vaccination services for the regularization of their vaccination calendars, to make them coherent with the polio eradication goal.

Methods

Study population

From January 2004 to August 2017, as part of the active surveillance of acute flaccid paralysis (AFP) and of the polio eradication process, all foreign migrants recently arrived in Italy, without or with insufficient vaccination documentation, who have turned to vaccination services of the Local Health Authority of Parma (a city with 190,000 inhabitants, in northern Italy) for the regularization of the vaccination schedule, were subjected to the determination of the antibody titers towards poliomyelitis. The survey was conducted according to the Good Clinical Practice Guidelines: the data collected - age, sex, period elapsed from arrival in Italy and country of origin - were treated anonymously for research purposes. This convenience sample was grouped into the six WHO regions: African Region (AFR), Region of the Americas (AMR), South-East Asia Region (SEAR), European Region (EUR), Eastern Mediterranean Region (EMR), and Western Pacific Region (WPR); by age groups (less than 2 years, 2 to 6 years, 7 to 18 years and equal or more than 19 years). To express graphically the trend of the GMTs in relation to age, instead, the distribution in quintiles of the age, treated as continuous variable, was used.

Serological analysis

Sterile serum samples were collected and kept at -20°C until they were examined. The determination of the three polioviruses antibodies levels was carried out with a long-incubation neutralization assay using 100 $TCID_{50}$, respectively, of poliovirus type 1 (Mahoney), poliovirus type 2 (Mef-1) and poliovirus type 3 (Saukett).

The search for neutralising antibodies (a) and the titration of the viruses (b) were carried out using a laryngeal carcinoma continuous cell line (HEP-2).

(a) The sera, heated to 56°C for 30 minutes, were tested simultaneously in triplicate at dilutions from 1:2 to 1:1024 with polioviruses type 1, type 2 and type 3, respectively. The serum/virus mixtures (0.025 mL each) were then incubated at 37°C for 6 hours in an appropriately humidified CO2 incubator and then at 4°C for 18 hours.

(b) Aliquots of 0.050 mL of a cellular suspension (5–6 x 104 HEP-2) were added to each well. While being incubated at 37 °C, the microplates were microscopically observed for cytopathic effects (CPEs) on the third and fourth days. The titers of the sera were calculated as the highest dilution capable of neutralising the CPEs. Each reaction included controls of the viral titer, the cells and the sera (32).

Statistical analysis

Seroprotection was defined as a titer equal to or above 1:8. Subjects with antibody titers <1:8 for all the three serotypes were classified as "triple negatives". Titers ≥ 1:2 were log-transformed and evaluated as GMTs. Continuous variables were summarised as the mean, standard deviation (*SD*) and minimum–maximum values. The Analysis of Variance (Two-Way ANOVA) and Student's t-test were performed when appropriate; to verify the association between GMT and quintile distribution of age, a linear regression test was carried out. A p-value of 0.05 was considered significant. All statistical analyses were performed with SPSS 24.0 (IBM SPSS Inc., Chicago, IL).

Results

From January 2004 to August 2017, 2,138 samples were analyzed to determine immunization levels in migrants recently moved to Italy. Such group was mostly composed of male subjects (59.07%), average age was 13.3 years old (sd 6.1), range, 1– 55 yrs, median 13.6 yrs, with no statistically significant differences regarding the WHO region of origin. The most represented age group was the one in school age (Table 1). Median time interval between arrival in Italy and sampling date was 3 months (range = 15 days-5 yrs), resulting higher in population arriving from the European Region (median, 7 months).

The African Region was the most represented with an elevated number of subjects coming from Senegal, Ivory Coast, Ghana and Nigeria (which is still an endemic country), followed by the EMR which includes two still endemic countries (Pakistan and Afghanistan). SEAR was extensively represented by the Indian sub-continent. Over time, the relative

Table 1. Characteristics of the study sample

WHO Region*		Age				Age group (%)			
	Subjects (No.)	Mean (sd)	Median	Min	Max	< 2 years	2 - 6 years	7 - 18 years	=>19 years
AMR	195	13.00 (5.38)	13.00	1	51	0.5%	9.9%	83.9%	5.7%
AFR	1,038	13.52 (6.01)	14.00	1	55	1.3%	10.8%	80.7%	7.2%
SEAR	223	12.61 (5.63)	12.2	2	44	0.0%	12.7%	80.1%	7.2%
EUR	240	13.56 (7.70)	14.00	1	49	1.3%	16.4%	72.3%	10.1%
EMR	271	13.18 (6.48)	13.40	1	40	0.7%	17.2%	73.9%	8.2%
WPR	171	12.38 (4.76)	13.00	0	31	2.4%	11.2%	82.2%	4.1%
Overall	2,138	13.25 (6.11)	13.63	0	55	1.1%	12.4%	79.2%	7.3%

* See abbreviations in the text

percentage of subjects from the African continent has increased, while the number of subjects coming from AMR has decreased (Figure 1).

The percentage of antibody titers below 1:8 was 6.0% versus poliovirus 1, 7.7% versus poliovirus 2 and 15% versus poliovirus 3. Twenty-seven subjects resulted triple negatives (antibody titers <1:8 for all the three serotypes).

Stratifying population by WHO region of origin, the WPR had the highest percent of non-seroprotected subjects against poliovirus 1 (8.8%), while the European Region had the highest percent of non-seroprotected against polio 2 and 3 (respectively 11.7% and 24.6%). Overall, the European subjects showed the highest percentages of seronegativity towards one or more serotypes, in fact only 70% of them, at the same time, showed protective antibodies to the three polio viruses. (Table 2).

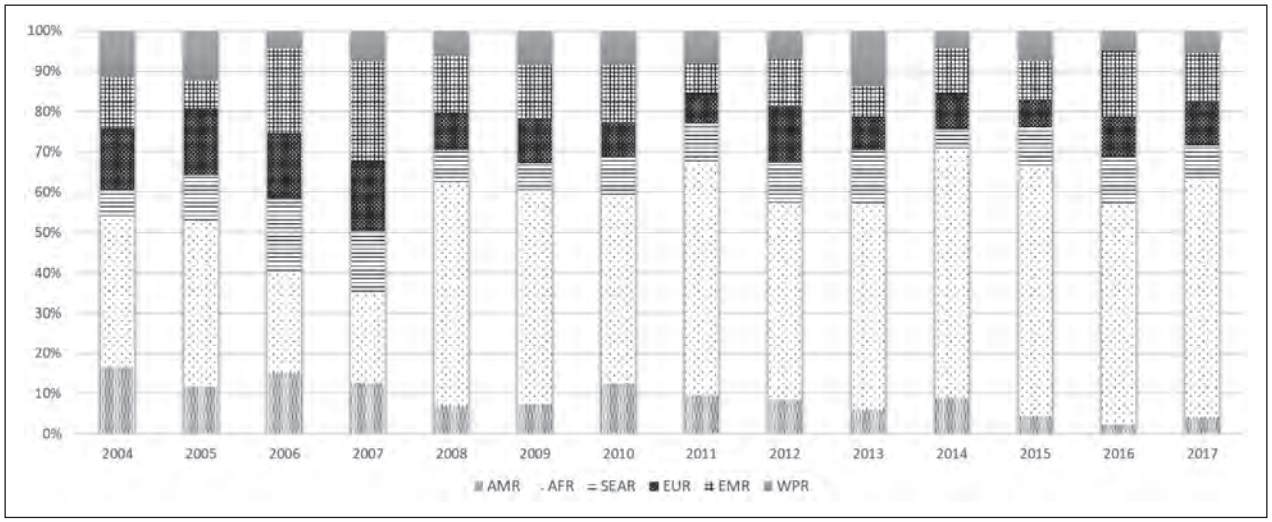

Figure 1. WHO regions of origin: distribution of subjects per year of study

Table 2. Numbers and percentages of subjects with protective (≥ 1: 8) and non-protective (<1: 8) antibodies and numbers and percentages of subjects without antibodies to one or more of the polioviruses, by WHO regions

WHO regions			Poliovirus 1		Poliovirus 2		Poliovirus 3		Triple	1/3	2/3	Triple
			≥ 1:8	< 1:8	≥ 1:8	< 1:8	≥ 1:8	< 1:8	positives	negatives	negatives	negatives
AMR	No.	195	185	10	180	15	159	36	147	37	9	2
	%		*94.9%*	*5.1%*	*92.3%*	*7.7%*	*81.5%*	*18.5%*	*75.4%*	*19.0%*	*4.6%*	*1.0%*
AFR	No.	1038	974	64	953	85	896	142	826	141	63	8
	%		*93.8%*	*6.2%*	*91.8%*	*8.2%*	*86.3%*	*13.7%*	*79.6%*	*13.6%*	*6.1%*	*0.8%*
SEAR	No.	223	212	11	213	10	206	17	195	19	8	1
	%		*95.1%*	*4.9%*	*95.5%*	*4.5%*	*92.4%*	*7.6%*	*87.4%*	*8.5%*	*3.6%*	*0.4%*
EUR	No.	240	226	14	212	28	181	59	168	48	19	5
	%		*94.2%*	*5.8%*	*88.3%*	*11.7%*	*75.4%*	*24.6%*	*70.0%*	*20.0%*	*7.9%*	*2.1%*
EMR	No.	271	257	14	254	17	230	41	221	33	12	5
	%		*94.8%*	*5.2%*	*93.7%*	*6.3%*	*84.9%*	*15.1%*	*81.5%*	*12.2%*	*4.4%*	*1.8%*
WPR	No.	171	156	15	161	10	145	26	137	23	5	6
	%		*91.2%*	*8.8%*	*94.2%*	*5.8%*	*84.8%*	*15.2%*	*80.1%*	*13.5%*	*2.9%*	*3.5%*
Overall	No.	2138	2010	128	1973	165	1817	321	1694	301	116	27
	%		*94.0%*	*6.0%*	*92.3%*	*7.7%*	*85.0%*	*15.0%*	*79.2%*	*14.1%*	*5.4%*	*1.3%*

Table 3. GMTs toward PV1, PV2, PV3, by WHO region

WHO Region	Subjects (No.)	GMT (Poliovirus 1)	GMT (Poliovirus 2)	GMT (Poliovirus 3)
AMR	195	44.8	31.1	17.2
AFR	1038	43.0	28.6	21.2
SEAR	223	50.9	35.0	22.8
EUR	240	56.0	27.5	15.3
EMR	271	50.7	29.3	20.6
WPR	171	35.1	30.2	19.2
Overall	2138	45.5	29.5	20.0

The GMTs towards the 3 polioviruses were 45.5 for PV1, 29.5 for PV2 and 20 for PV3 respectively (Table 3). In each WHO region, the GMTs for PV3 were consistently the lowest, and even in this case the EUR prevailing subjects showed the lowest GMTs for both PV2 and PV3 (respectively 27.5 and 15.3). The GMTs referring to each of the 14 years of study have experienced strong fluctuations (from 21.3 to 89.3 for the PV1, from 16.8 to 55.6 for the PV2, from 12.4 to 36.6 for the PV3). The analysis conducted on the distribution in quintiles of the ages, confirmed the reduction of GMTs that show a decrease in relation to age classes especially those towards polio 1 and polio 2. (Figure 2). The age group below 2 years of age showed the greatest prevalence of non-seroprotected subjects towards the 3 polioviruses; 34.8% of subjects had no protection against at least one of the 3 serotypes. Even the very large group of children and adolescents showed a high percentage of subjects lacking protective antibodies, in particular towards poliovirus 3 (15.4%) (Table 4).

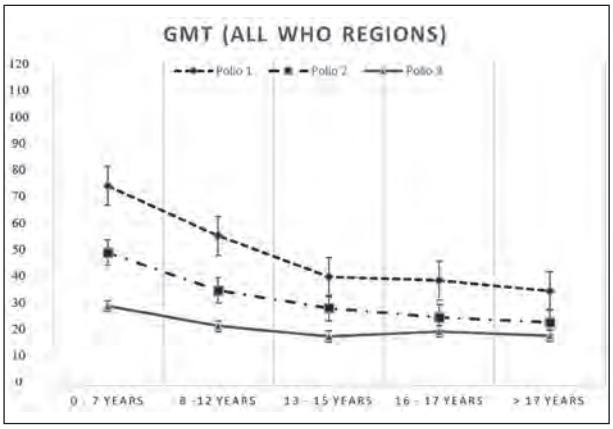

Figure 2. GMTs calculated by quintile of age group

Conclusions

Sub-optimal vaccination coverage, often the result of the disintegration of social and health systems due to ongoing conflicts, may be responsible for the circulation or reintroduction of wild polioviruses in polio-free populations as evidenced by recent episodes in Tajikistan (2010) or in the Arab Republic of Syria (2013-2014) (29,33).

In this survey, 79.2% of subjects showed protective antibodies to the three polioviruses. As in investi-

Table 4. Numbers and percentages of subjects with protective (> 1: 8) and non-protective (<1: 8) antibodies, percentages of subjects without antibodies to one or more of the polioviruses and GMTs by age class

Age	Subjects	Poliovirus 1			Poliovirus 2			Poliovirus 3			All strains	
	(No.)	titres ≥1:8	titres <1:8	GMT	titres ≥1:8	titres <1:8	GMT	titres ≥1:8	titres <1:8	GMT	triple positives	triple negatives
< 2 years	23	82.6%	17.4%	70.1	87.0%	13.0%	40.7	65.2%	34.8%	14.6	65.2%	13.0%
2 - 6 years	263	96.6%	3.4%	79.6	95.1%	4.9%	47.8	87.8%	12.2%	28.0	86.3%	1.9%
7 - 18 years	1,679	94.0%	6.0%	42.5	92.3%	7.7%	27.8	84.6%	15.4%	18.9	78.5%	0.9%
=>19 years	155	90.3%	9.7%	34.5	73.1%	6.1%	25.1	87.1%	12.9%	22.2	76.1%	2.6%
Overall	2,120	94.0%	6.0%	45.5	88.4%	11.6%	29.6	85.0%	15.0%	20.0	79.2%	1.3%

gations of the past and in recent seroprevalence studies on the Italian population, PV1 antigen was the most immunogenic with GMTs constantly higher than PV2 and PV3 during the 14 years of the survey and considering the WHO regions of origin. Fifteen percent of the subjects, on the other hand, were found not to have protective antibodies against PV3. In particular, subjects from the European region showed high percentages of low protection both towards PV2 (11.7%) and PV3 (24.6%). Children under the age of 2 were poorly represented (23 overall): they showed elevated GMTs, but a high percentage of unprotected subjects towards at least one of the 3 poliovirus.

GMTs tend to decrease significantly with age, especially PV1 and PV2 and, as in the case of the Italian population, low titers could depend on the absence of natural boosters.

The sample considered, coming from the 6 WHO regions and from 78 different countries, showed a low prevalence of subjects without antibodies; in 14 years of investigation only 27 subjects (1.3%) were triple-negatives.

However, a substantial percentage of sample showed not optimal antibodies levels as considered by the WHO, in a scenario of possible circulation of wild polioviruses. The low GMTs and the clear tendency to decrease with the increasing age of the subjects, especially against PV1, confirm the framework of attention that polio is receiving at national and international level.

The main limitation of this study is the convenience sample represented by the most stable foreign population that, for study and work reasons, turns to the Local Health Services to regularize its vaccination situation. Furthermore, due to the absence of vaccination documentation it was not possible to trace the type of vaccine used, however most of the subjects (> 95%) came from Countries where OPV Sabin is still used and, in this case, all subjects were hypothetically vaccinated with the trivalent vaccine (tOPV) before the switch to bivalent OPV (bOPV), which occurred between April and May 2016, due to the disappearance of PV 2 worldwide and the consequent removal of the type 2 component (OPV2) from immunization programmes. (34).

The population residing in Italy, vaccinated with eIPV, no longer exposed to vaccine polioviruses since 2002, if not those eventually imported by subjects with recent vaccination, could have GMTs and seroprotection levels lower than those found in our study (15,16).

The addition of a 5th dose of eIPV to the adolescent vaccination calendar, could be evaluated on serum epidemiological data collected in controlled investigations on representative population samples identified on the basis of age, origin and vaccination status.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Received: 15 June 2019
Accepted: 18 July 2019
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Acta Biomed 2019; Vol. 90, Supplement 9: 35-44 DOI: 10.23750/abm.v90i9-S.8722

Original article

Virological Surveillance of Influenza in the eight epidemic seasons after the 2009 pandemic in Emilia-Romagna (Northern Italy)

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Summary. *Background and aim of the work*: Influenza virological surveillance is essential for monitoring the evolution of influenza viruses (IVs) as well as for annual updating of the vaccine composition. The aim of this study is to analyse IVs circulation in Emilia-Romagna during the eight epidemic seasons after the 2009 pandemic and to evaluate their match with seasonal vaccine strains. *Methods:* A total of 7882 respiratory specimens from patients with influenza-like illness (ILI), were collected by regional sentinel practitioners and hospital physicians. Viral investigations were conducted by rRT-PCR assay. Genetic characterization was performed for a spatial-temporal representative number of influenza laboratory-confirmed specimens. *Results:* Influenza-positive samples per season ranged between 28.9% (2013-2014) and 66.8% (2012-2013). Co-circulation of IVs type A and type B was observed in all seasons, although with a different intensity. In all seasons, the highest number of positive samples was recorded in younger patients aged 5-14 years with relative frequencies ranging from 40% in the 2013-2014 season and 78% in the 2012-2013 season. Since the 2009 pandemic, A/H1N1pdm09 IVs circulating were closely related to the vaccine strain A/California/7/2009. Antigenic mismatch between vaccine strain and A/H3N2 IVs was observed in the 2011-2012 and 2014-2015 seasons. During 2015-2016, 2016-2017 and 2017-2018 seasons a complete or nearly complete mismatch between the predominant influenza B lineage of IVs type B circulating and vaccine B lineage occurred. *Conclusions:* This analysis confirms the importance of the virological surveillance and highlights the need of a continuous monitoring of IVs circulation, to improve the most appropriate vaccination strategies. (www.actabiomedica.it)

Key words: influenza virus, virological surveillance, antigenic characterisation, B lineage, vaccine virus strain, mismatch

Introduction

Seasonal influenza is an acute, highly contagious viral respiratory infection of great importance from clinical and epidemiological point of view. Worldwide, the annual attack rate is estimated at 5-10% in adults and 20-30% in children with about 3 to 5 million case of severe illness and 290.000-650.000 deaths (1).

Influenza epidemiology mainly depends on the particular characteristics of influenza viruses (IVs), able to spread all over the world and rapidly evolve. Furthermore, a gradual and relatively continuous change in the surface glycoproteins, hemagglutinin (HA) and neuraminidase (NA), allows them to escape the immunity that comes from prior infections or vaccination (2). Because of this, seasonal epidemics recur every year with different intensity and trend.

The impact of influenza also varies according to different age groups, in terms of morbidity, severe case illness and mortality among high-risk groups; the most

affected patients are the elderly, young children, pregnant women and individuals with comorbidity (1,3-9).

Periodically, in the range of 10-40 years, IVs type A caused pandemic events, due to the emergence of a new variant against which there is no pre-existing immunity in the population. The pandemic in 2009 was caused by a unique quadruple reassortant A/H1N1 IV, including a complex combination of swine, avian and human IV genes (10). This new variant, A/H1N1pdm09, has completely substituted the previous seasonal IVs of the same type and continues to circulate worldwide as seasonal IV, together with A/H3N2 subtype IVs and B type IVs. Moreover, a progressive diversification of B type IVs into two lineages, genetically and antigenically distinct, occurred starting from 1983 (11).

Within this context, influenza epidemiological and virological surveillance plays an essential role and it is carried out, at global level, by World Health Organization Global Influenza Surveillance and Response System (GISRS) (12) and at European level, by the European Centre for Disease Prevention and Control (ECDC) (13). The national influenza surveillance systems, together with the analysis of epidemiological features, have the specific goal to monitor the circulation of IVs, analyse antigenic, genetic and biological characteristics, also including the susceptibility to available antiviral drugs. Moreover, they work to recognize any new viral variants in order to implement the appropriate containment and prevention strategies in a timely manner (14). In Italy, these activities are carried out by influenza surveillance system, named InfluNet, coordinated by the National Influenza Centre at the Istituto Superiore di Sanità (NIC/ISS). Influnet is based on the collaboration of sentinel practitioners who, starting from the 46th week of each year until the 17th of the following year, perform respiratory samples from patients with a clinical presentation of influenza-like illness (ILI) (15-17). The regional influenza Laboratories perform isolations and antigenic characterizations of IVs during the epidemic season, to constantly monitor the different types/subtypes circulation and to evaluate the match between epidemic and vaccine strains. This is fundamental to formulate the vaccine composition of the following season, because the degree of match between circulating and vaccine strains is one of the factor, togheter with the characteristics of the person being vaccinated (such as their age and health), that contribute to the vaccine effectiveness (18-24).

Furthermore one of the main Public Health implication of the low vaccine effectiveness, togheter with the decrease and the poor vaccination uptake, even in the target population, is the real reduction of effectiveness of influenza vaccine on field. (19,25-28).

The aim of this paper is to describe the circulation of IVs in Emilia-Romagna and their matching with seasonal vaccine strains, during eight consecutive seasons (from 2010-2011 to 2017-2018) by analysis of virological surveillance data, performed by the regional influenza reference Laboratory of Parma (29-31).

Methods

Respiratory specimens from children and adults with a clinical presentation of ILI, were collected by regional sentinel physicians (general practitioners and pediatricians) and by hospital physicians of the care Units of Parma, Piacenza and Reggio Emilia hospital. Each clinical specimen was accompanied by a case report form filled in with epidemiological data. The "Virocult" diagnostic kit (MWE, England) and the commercial "UTM Viral Transport Media" kit (Copan, Brescia, Italy) were used to collect the clinical samples (32).

Viral isolation was performed in Madin Darby Canine Kidney cells (MDCK), and the presence of the virus was detected by a conventional haemagglutination assay using a 0,8% suspension in PBS of guinea pig red blood cells.

Viral nucleic acid was extracted from respiratory specimens and from viral cell culture supernatant, using the QIAamp Viral RNA Mini Kit (Qiagen, Hilden, Germany), according to the manufacturer's instructions. A one-step Real Time retro-transcription PCR assay (rRT-PCR) was performed with Quantifast Pathogen+IC Kit, (Qiagen, Hilden, Germany**)** with specific primer/probe sets targeting the matrix region of A type IV and the nucleoprotein region of B type IV. For A type IV, samples were further subtyped using specific primer/probe sets for the HA gene to dis-

criminate between A/H1N1pdm09 IVs and A/H3N2 IVs. The genetic lineage of confirmed B type IVs was determined by rRT-PCR. All assays were performed in compliance with institutional guidelines (33-34).

A representative number of influenza laboratory-confirmed specimens and viral isolates, were sent to the NIC/ISS for antigenic characterisations and phylogenetic analysis.

Results

During the study period, the reference Laboratory for influenza virological surveillance of Emilia-Romagna, analysed 7882 nasal or throat swabs, performed by regional sentinel practitioners and doctors working in hospital care Units of Parma, Piacenza and Reggio Emilia. The distribution of samples by season, provenience, age group, vaccination status, virological data, is reported in Table 1. Overall, the percentage of the samples range between 6.2% in 2013-2014 season and 18.6% in 2017-2018 season; 50.3% were outpatients and 49.7% were inpatients. In the first six seasons, the highest numbers of samples were collected in children ≤4 years of age and in school-aged children (5-14 years); in the two latest years, in young-adults (15-64 years) and in elderly ≥65 years of age. The percentage of influenza-positive samples per season ranged between 28.9% (2013-2014) and 66.8% (2012-2013). In the first three seasons after the 2009 pandemic, epidemics were particularly intense due to the highest number of specimens and influenza-positive samples, while in the following five seasons, the proportion of positive samples was lower (less than 50%) compared to the high number of samples (Table 1). In the surveyed area, epidemiological trends observed in the first six influenza

Table 1. Characteristics of patients during virological surveillance in Emilia-Romagna from 2010-2011 to 2017-2018 season

	FLU SEASON 2010-2011	FLU SEASON 2011-2012	FLU SEASON 2012-2013	FLU SEASON 2013-2014	FLU SEASON 2014-2015	FLU SEASON 2015-2016	FLU SEASON 2016-2017	FLU SEASON 2017-2018
Overall n.	747	695	922	491	1327	1134	1095	1471
Outpatients n (%)	478 (64%)	617 (88.8%)	511 (55.4%)	251 (51.1%)	645 (48.6%)	618 (54.5%)	415 (37.9%)	428 (29%)
Inpatients n (%)	269 (36%)	78 (11.2%)	411 (44.6%)	240 (48.9%)	682 (51.4%)	516 (45.5%)	680 (62.1%)	1043 (71%)
Age group (years) n (%)								
0-4	212 (28.4%)	298 (43%)	313 (33.9%)	158 (32.2%)	393 (29.6%)	340 (30%)	249 (22.7%)	311 (21.2%)
5-14	208 (27.9%)	192 (27.6%)	215 (23.4%)	111 (22.6%)	301 (22.7%)	324 (28.6%)	191 (17.5%)	168 (11.4%)
15-64	249 (33.3%)	155 (22.3%)	254 (27.5%)	122 (24.9%)	258 (19.4%)	258 (22.7%)	227 (20.7%)	401 (27.3%)
≥65	63 (8.4%)	45 (6.4%)	129 (14%)	99 (20.1%)	366 (27.6%)	209 (18.4%)	425 (38.8%)	591 (40.1%)
Unknown	15 (2%)	15 (0.7%)	11 (1.2%)	1 (0.2%)	9 (0.7%)	3 (0.3%)	3 (0.3%)	-
Vaccination Status n (%)								
Unvaccinated	514 (68.8%)	464 (66.8%)	695 (75.4%)	351 (71.5%)	977 (73.6%)	944 (83.2%)	867 (79.2%)	1104 (75.1%)
Vaccinated	151 (20.2%)	169 (24.3%)	136 (14.7%)	84 (17.1%)	233 (17.6%)	190 (16.8%)	228 (20.8%)	278 (18.9%)
Missing Information	82 (11%)	62 (8.9%)	91 (9.9%)	56 (11.4%)	117 (8.8%)	-	-	89 (6%)
Outcome n (%)								
Positive	379 (50.7%)	449 (64.6%)	616 (66.8%)	142 (28.9%)	581 (43.8%)	394 (34.7%)	392 (35.8%)	597 (40.6%)
Negative	368 (49.3%)	246 (35.4%)	306 (33.2%)	349 (71.1%)	746 (56.2%)	740 (65.3%)	703 (64.2%)	874 (59.4%)
Influenza Virus type/subtype n (%)								
A/H3N2	14 (3.7%)	447 (99.5%)	16 (2.6%)	103 (72.5%)	268 (46.2%)	34 (8.6%)	380 (97.2%)	15 (2.5%)
A/H1N1pdm09	177 (46.7%)	-	152 (24.8%)	37 (26.1%)	239 (41.1%)	49 (12.4%)	1 (0.2%)	233 (39.2%)
Influenza B	188 (49.6%)	2 (0.5%)	446 (72.6%)	2 (1.4%)	74 (12.7%)	311 (79%)	10 (2.6%)	347 (58.3%)

seasons were quite similar and analogous to that of the period prior to the 2009 pandemic. Concerning the official virological surveillance period, all six seasons after the 2009 pandemic started at the beginning of December (weeks 50-51) and peaked in February (weeks 5-6). The first IVs were detected between the end of the year and the beginning of the new one. All six seasons were characterized by temporally long epidemics, that declined on March and April. During 2016-2017 and 2017-2018 seasons, a clear shift was observed in epidemiological trend: influenza activity started about four weeks in advance, with a rapid increase of ILI and influenza-positive samples, and peaked between late December and early January (weeks 51-52).

The distribution of detected IVs is presented in Figure 1. During the study period, co-circulation of A type IVs and B type IVs was observed, although with a different intensity; in five seasons A type IVs predominated over B type IVs. An overview of the eight seasons shows a mixed IVs circulation: co-circulation of A/H1N1pdm09 IVs and B type IVs in 2010-2011 season (46.7% vs 49.61%); co-circulation of A/H1N1pdm09 IVs and A/H3N2 IVs in 2014-2015 season (41.1% vs 46.2%). During 2011-2012, 2013-2014, 2014-2015 and 2016-2017 seasons, A/H3N2 IVs were predominant (99.5%, 72.5%, 46.2% and 97.2% respectively); during 2012-2013, 2015-2016, 2017-2108 seasons, B type IVs were predominantly detected (72.6%, 79.0%, 58.3% respectively). In all seasons, the highest number of positive samples were recorded in younger patients 5-14 aged with relative frequencies ranging from 40% in the 2013-2014 season and 78% in the 2012-2013 season (Table 2, Figure 2). During every season, a spatial-temporal representative number of influenza-positive samples was genetically characterized and the phylogenetic analysis was performed by the NIC/ISS (16).

The antigenic and molecular characteristics of IVs circulating were analysed, with particular attention to the match with seasonal vaccine strains (Table 3).

In Emilia-Romagna most of IVs detected in the 2010-2011, and 2017-2018 seasons were A/H1N1pdm09 IVs. Since 2010-2011 season, A/H1N1pdm09 IVs were closely related to the vaccine strain A/California/7/2009. In particular, A/H1N1pdm09 IVs isolated in Emilia-Romagna during 2015-2016 season fell into genetic groups 6 and 8 (A/St.PetersburG/27/2011-like, A/Norway/2552/2010-like and A/South Africa/3626/2013-like). During 2016-2017 and 2017-2018, A/H1N1pdm09 IVs fell into genetic subgroup 6B.1, characterized by the amino acid substitutions S84N, S162N, I216T in HA1, antigenetically correlate to vaccine strains A/California/7/2009 and A/Michigan/45/2015 that was recommended vaccine strain for the 2018-2019 season (Table 3) (35).

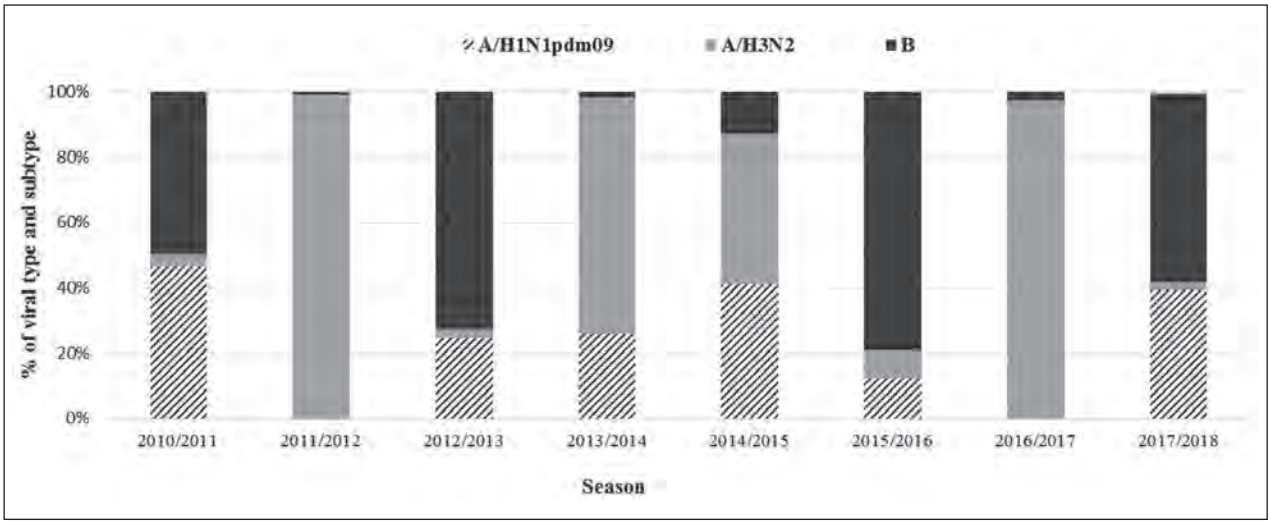

Figure 1. Influenza virus types/subtypes distribution in Emilia-Romagna from 2010-2011 to 2017-2018 seasons

Table 2. Number (%) of influenza virus positive by age groups and influenza season

Flu season	Age group (years)	Results		
		Flu negative n. (%)	Flu positive n. (%)	All n.
2010-2011	0-4	100 (47.2%)	112 (52.8%)	212
	5-14	66 (31.7%)	142 (68.3%)	208
	15-64	147 (59.0%)	102 (41.0%)	249
	≥65	47 (74.6%)	16 (25.4%)	63
2011-2012	0-4	98 (32.9%)	200 (67.1%)	298
	5-14	54 (28.1)	138 (71.9%)	192
	15-64	68 (43.9%)	87 (56.1%)	155
	≥65	23 (51.1%)	22 (48.9%)	45
2012-2013	0-4	106 (33.9%)	207 (66.1%)	313
	5-14	48 (22.3%)	167 (77.7%)	215
	15-64	95 (37.4%)	159 (62.6%)	254
	≥65	55 (42.6%)	74 (57.4%)	129
2013-2014	0-4	117 (74.1)	41 (25.9%)	158
	5-14	67 (60.4%)	44 (39.6%)	111
	15-64	86 (70.5%)	36 (29.5%)	122
	≥65	78 (78.8%)	21 (21.2%)	99
2014-2015	0-4	223 (56.7%)	170 (43.3%)	393
	5-14	136 (45.1%)	165 (54.8%)	301
	15-64	152 (58.9%)	106 (41.1%)	258
	≥65	232 (63.4%)	134 (36.6%)	366
2015-2016	0-4	237 (69.7%)	103 (30.3%)	340
	5-14	123 (38.0%)	201 (62.0%)	324
	15-64	197 (76.4%)	61 (23.6%)	258
	≥65	182 (87.1%)	27 (12.9%)	209
2016-2017	0-4	163 (65.5%)	86 (34.5%)	249
	5-14	87 (45.5%)	104 (54.5%)	191
	15-64	154 (67.8%)	73 (32.2%)	227
	≥65	296 (69.6%)	129 (30.4%)	425
2017-2018	0-4	164 (52.7%)	147 (47.3%)	311
	5-14	58 (34.5%)	110 (65.5%)	168
	15-64	254 (63.3%)	147 (36.7%)	401
	≥65	398 (67.3%)	193 (32.7%)	591

In Emilia-Romagna A/H3N2 IVs were identified only sporadically during 2010-2011 season, whereas they predominated in the 2011-2012, 2013-2014, 2014-2015 and 2016-2017 seasons.

A/H3N2 IVs circulating in 2010-2011 season were closely related to the vaccine strain A/Perth/16/2009, reconfirmed in the following season. In the first period of 2012-2013 season, A/H3N2

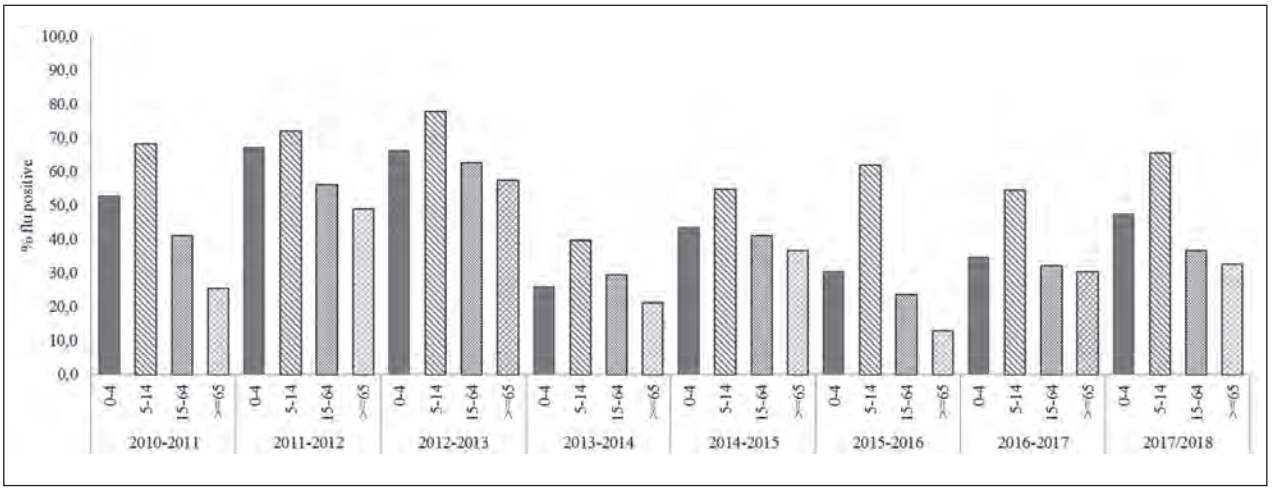

Figure 2. Distribution (%) of influenza positive samples by age group and by season (from 2010-2011 to 2017-2018)

Table 3. Circulating influenza viruses in Emilia-Romagna vs vaccine strains from 2010-2011 to 2017-2018 seasons (Predominant strain is indicated in bold; mismatch is highlighted)

Season	Trivalent vaccine composition (vaccine strains)			Circulating influenza viruses		
	A/H1N1pdm09	A/H3N2	B(lineage)	A/H1N1pdm09	A/H3N2	B(lineage)
2010-2011	A/California/7/2009	A/Perth/16/2009	B/Brisbane/60/2008 (VIC)	A/H1N1pdm09		VIC
2011-2012	A/California/7/2009	A/Perth/16/2009	B/Brisbane/60/2008 (VIC)		A/H3N2	
2012-2013	A/California/7/2009	A/Victoria/361/2011	B/Wisconsin/1/2010 (YAM)	A/H1N1pdm09		YAM
2013-2014	A/California/7/2009	A/Texas/50/2012	B/Massachusetts/2/2012(YAM)	A/H1N1pdm09	A/H3N2	
2014-2015	A/California/7/2009	A/Texas/50/2012	B/Massachusetts/2/2012(YAM)	A/H1N1pdm09	A/H3N2	
2015-2016	A/California/7/2009	A/Switzerland/9715293/2013	B/Phuket/3073/20132(YAM)			VIC
2016-2017	A/California/7/2009	A/Hong Kong/4801/2014	B/Brisbane/60/2008(VIC)		A/H3N2	YAM
2017-2018	A/Michigan/45/2015	A/Hong Kong/4801/2014	B/Brisbane/60/2008(VIC)	A/H1N1pdm09		YAM

IVs were correlated to the vaccine strain, while from January they were antigenically similar to variants of recent isolation (A/Alabama/5/2010-like, A/Hong Kong/3969/2011-like and A/Stockholm/18/2011-like). Genetic characterization showed different amino acid substitutions (K62E, K144N, T212A9) and molecular homology with a new variant, A/Victoria/361/2011, that replaced the vaccine strain of previous seasons. During 2012-2013 season, A/H3N2 IVs were antigenically correlated to the A/Texas/50/2012 strain, antigenically indistinguishable from the vaccine strain A/Victoria/361/2011, but more genetically stable for propagation and, for these reasons, recommended vaccine strain in the following season.

In 2013-2014 season, most of the A/H3N2 IVs were correlated to the different variants antigenically related to the vaccine strain A/Texas /50/2012. Phylogenetic analyses showed that most of them fell into genetic group 3C.3, with amino acid substitutions T128A, R142G and N145S in HA1 (reference virus: A/Samara/73/2013).

During 2014-2015 season A/H3N2 IVs presented with a mixed circulation of viral variants antigenically distinct from the vaccine strain. The HA

sequences of these viruses fell into two genetic subgroups: 3C.2, with amino acid substitutions N145S in HA1 and D160N in HA2 (reference virus A/Hong Kong/146/2013) and clade 3C.3a, with amino acid substitutions A138S, F159S, N225D in HA1, similar to A/Switzerland/9715293/2013, reference strain for 2015-2016 vaccine. The heterogeneous circulation of different A/H3N2 IVs strains was highlighted during the following seasons, with the emergence of variants grouped into genetic subgroup 3C.2, clade 3C.2a, with further amino acid substitutions (N144S, F159Y, K160T, N225D, Q311H). The reference strain A/Hong Kong /4801/2014, was the new vaccine strain. Also in the last two seasons, A/H3N2 IVs fell into genetic subgroup 3C.2a. However, in the last phase of 2017-2018 epidemic, viruses fell into sub-clade 3C.2a1, and shared similary with A/Singapore/INFIMH160019/2016, the reference strain for the vaccine of 2018/2019 season.

In Emilia-Romagna, type B IVs co-circulated with type A IVs in all seasons and predominated over type A during 2012-2013, 2015-2016, 2017-2018 seasons. With the exception of two seasons (2011-2012, 2013-2014), the co-circulation of both B lineages (B/Victoria/2/87 and B/Yamagata/16/88) was always observed, although with different intensity every year. The analysis of the HA gene sequence on a selection of type B IVs circulating in 2010-2011 season, showed that most of them belonged to B/Victoria lineage (B/Vic), antigenically similar to the vaccine strain B/Brisbane/60/2008 (B/Vic) and few to B/Yamagata lineage (B/Yam).

In 2012-2013 season, B/Yam viruses were predominant, related to B/Massachusetts/02/2012, strain recommended for 2013/2014 vaccine. During 2015-2016, 2016-2017 and 2017-2018 seasons a complete or nearly complete mismatch between the predominant influenza B lineage and vaccine B lineage occurred. In 2015-2016 season, type B IVs belonged to B/Vic lineage (clade 1A), related to B/Brisbane/60/2008, recommended in the 2016-2017 trivalent vaccine formulation.

During 2016-2017 season type B IVs circulating in Emilia-Romagna belonged to B/Yam lineage (clade 3), while in Italy, both B lineages co-circulated. The reference strain B/Brisbane/60/2008 (B/Vic) was reconfirmed for the following two season, where almost the whole B IVs belonged to B/Yam lineage circulated. Only one virus detected in Emilia-Romagna in 2016-2017 season belonged to B/Vic lineage.

Conclusions

This study provides the results of the virological surveillance in the eight epidemic seasons after the 2009 pandemic in Emilia-Romagna. The aim of this paper is to describe genetic and antigenic changes of IVs, and to evaluate their match with vaccine strains.

The circulation of IVs in Emilia-Romagna was similar to that of the other regions (36-39). Type B IVs co-circulated with type A IVs in all seasons. With the exception of 2011-2012 season during which only A/H3N2 subtype IVs circulated, in the others, both subtypes co-circulated, although with different intensity.

From a general point of view, yearly variations by distribution and frequency of viral types/subtypes were observed, as well as an alternation of the predominant type/subtype. The seasons with a modest circulation of a specific type/subtype, have been followed by seasons with its greater circulation and vice versa.

During all seasons, A/H1N1pdm09 IVs detected were closely related to the vaccine strain A/California/7/2009 and circulated intensely in 2010-2011 season, with the higher morbidity rates in school-aged children (aged 5-14 years) (Figure 2). Different considerations must be made for type A/H3N2 IVs and type B IVs. The continuous and rapid evolution of A/H3N2 IVs and the co-circulation of different A/H3N2 IVs strains during the same season caused an incomplete match between the vaccine strains and seasonal A/H3N2 IVs, so a new vaccine strain was recommended in the vaccine formulation in four seasons (35).

During seasons in which A/H3N2 IVs were predominant, the higher number of ILI occurred in the age group ≥65 years, more vulnerable to severe consequences of A/H3N2 IVs infection (40-47).

Furthermore, because of the presence of two genetically and antigenically distinct type B IVs lineages, co-circulating in the same season with different intensity, it was very difficult to predict the type of virus that will circulate in the following season. During the study

period, a complete mismatch between the type B IVs circulating and the vaccine strain, was observed in three consecutive seasons with a high number of cases and positive samples in children, young adults and elderly.

Overall, from this study we highlight that in none of the epidemic influenza season full match was achieved. Probably the Health Technology Assessment instruments, implemented with new studies on Artificial Intelligence, could help fill the information gap in the setting of the new influenza vaccine (48-55).

This study also confirms the importance of the virological surveillance and the integration of epidemiological and virological data, and highlights the need of a continuous monitoring of types/subtypes of IVs circulation during epidemic season, to acquire useful informations for improve the most appropriate vaccination strategies.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Received: 15 June 2019
Accepted: 18 June 2019
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Acta Biomed 2019; Vol. 90, Supplement 9: 45-53 DOI: 10.23750/abm.v90i9-S.8703

Original article

Healthcare workers' vaccination at European and Italian level: a narrative review

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Summary. Today some vaccine-preventable diseases remain an important cause of morbidity and mortality worldwide despite the availability of new vaccines. Healthcare workers are particularly at risk to acquire an infection disease, playing a fundamental role in nosocomial transmission, which makes them an important target group for vaccination. The vaccination recommendations of HCWs, as well as the general population, differ from country to country. Furthermore, coverage rates vary widely a lot over the world, making HCWs vulnerable to disease and so healthcare settings to outbreaks. The motivations of vaccine hesitancy are many and maybe other studies would help policymakers and stake-holders to shape programs to improve vaccination coverage and the control of infectious diseases through the correct application of guidelines on prevention. (www.actabiomedica.it)

Key words: healthcare workers, vaccination, coverage

Introduction

Healthcare workers (HCWs) were frequently implicated as the source of nosocomial infection by vaccine preventable disease (VPD) in health care settings. World Health Organization (WHO) estimates that all over the world about 59 million HCWs are potentially exposed every day to multiple occupational biological hazards, working with infectious patients and contaminated fluids and materials (1).

In hospital setting HCWs had frequent contact with high risk patients and they could lead to potential lethal infectious diseases and also, they could infect their colleagues (2,3).

So, the benefits of vaccinations of HCWs were many: they reduced the risk of outbreaks in health care facilities, decreased staff illness and absenteeism and also reduced costs resulting from loss of productivity (4-7).

Vaccines recommended for HCWs were summarized in Table 1

In the 2017- 18 influenza season, 29 of European Member States recommended vaccination for HCWs: particularly, 23 of them reported that influenza immunisation was recommended for all HCWs; in Belgium, Norway, Portugal, Slovakia and Sweden flu was recommended for some HCWs (e.g. those working in out-patient, in-patient and long-term care departments). Also, within the United Kingdom vaccine recommendations varied: in Scotland vaccination was recommended for all HCWs, in England, Northern Ireland and Wales only for frontline or HCWs that have direct contact with patients. Although there is no national recommendation to vaccinate HCWs in Denmark, most regions and municipalities offer vaccinations to HCWs free of charge. In Sweden, vaccination was only recommended for staff caring for severely immunocompromised persons. In Slovakia, vaccination was recommended for HCWs in close contact with patients or the foci of infection. In all Member States that responded, the vaccination of HCWs is voluntary (8).

Table 1. Vaccines recommended for HCWs

Disease	Vaccination recommendations
Influenza	Recommended for all HCWs in the Europe, the USA and Japan. In Italy is mandatory for HCWs in Apulia, Emilia Romagna and Marche for all operative units.
Hepatitis B	Recommended for all HCWs in high-income countries. Mandatory for medical students in France. In Italy is mandatory for HCWs in Apulia, Emilia Romagna and Marche for all operative units.
Tetanus, diptheria and pertussis	Recommended for all HCWs in high-income countries. Pertussis, in Italy is mandatory for HCWs in Apulia, Emilia Romagna and Marche for all operative units.
Measles, mumps and rubella	Recommended for all HCWs in high-income countries. Measles is mandatory in Finland and for female workers in Slovenia. In Italy is mandatory for HCWs in Apulia, Emilia Romagna and Marche for some operative units.
Varicella	Recommended for some or all HCWs in European countries

Also, almost all (29 of 30) European countries have established recommendations or requirements for hepatitis B vaccination, but with difference across Europe (9).

For tuberculosis (not here discussed) national recommendations regarding the immunization of healthcare workers differ throughout Europe; a recent review evaluated the different recommendations in European countries: in four countries, BCG is required or recommended for all previously unvaccinated Mantoux-negative HCWs that may have contact with patients. In five other countries, immunization is only recommended for HCWs who are employed in high-risk sectors. In one country, the recommendations vary according to the HCWs' age. Finally, 4 countries do not currently recommend immunization against TB for HCWs (10). In France since April 2019, the BCG vaccination requirement not exists for healthcare workers and the social sector (11). Vaccination guidelines against tetanus, diphtheria, and pertussis varied across the countries but generally it is administered every 10 years with some exceptions (12,13).

MMR immunization is mandatory for HCWs in Finland for female workers in Slovenia and voluntary for all or specific groups of HCWs in 18 European countries; no immunization policies for HCWs against measles are in place in the remaining 11 European countries (14).

For CDC the following vaccinations was recommended for HCWS: hepatitis b, flu, MMR for born in 1957 or later not naturally or artificial immunized, Tdap, chickenpox and those who are routinely exposed to isolates of N. meningitidis should get one dose of meningococcal vaccine (15).

Despite the above mentioned issues, several Authors have reported suboptimal immunization rates for some relevant VPDs among HCWs in most of countries, including Italy; even with professionals at high-risk of exposure to hazardous biological agents, such as those employed in obstetric or neonatology departments, this issue is important taking into account the evidence of nosocomial transmission, as reported in recent reports (16-22).

Below, we report the findings of a narrative review of the literature for some VPDs (i.e., HBV, measles, rubella, chickenpox and influenza) carried out in order to update the socio-demographic and professional characteristics, the susceptibility and the vaccination rates among HCWs in the world.

Hepatitis B

This is a vaccine preventable disease but despite this, today approximately 360 million carriers were present worldwide (23). HCWs are at particularly high risk, primarily due to their increased risk of exposure to blood (24).

The prevalence of chronic HBV varies widely around the world and WHO estimates that in

2015, 3.5% of the population were living with chronic HBV infection in the world. The African and Western Pacific regions accounted for 68% of those infected. In 2015, global coverage with the third dose of hepatitis B vaccine reached 84%, but the European, Eastern Mediterranean and African regions faced coverage gaps (25).

Benefits and risk in healthcare settings

Approximately 3 million healthcare workers per year receive an injury with an occupational instrument, with around 2.000.000 HCWs exposures to hepatitis B virus; today the rates of HBsAg positivity in healthcare workers reported in several studies published in the last three decades range from 0.1% to 8.1% (26-28). Low rates of HBsAg positivity were found in two seroprevalence studies conducted on healthcare workers in the United States (0.1%) and Brazil (0.8%)(29).

So, a cycle of vaccination is required for HCWs; if there isn't any serological response (HbsAB< 10 UI/ml) HCWs should repeat the 3-dose series and test for anti-HBs 1-2 months after the last dose of vaccine. If the HCW is still negative after the second vaccine series, the HCW is considered a non-responder to hepatitis B vaccination. It is also possible that the non-responder is chronically infected with HBV. HBsAg testing can be offered or suggested to determine if this is the case (30). Also Hepatitis B immunoglobulins were necessary if the HCWS are exposed to a unknown source or serological positive within 48 hours (31).

Vaccination coverage

Notwithstanding these recommendations, vaccination coverage against HBV remains suboptimal, albeit higher than with other recommended vaccines. For example, in a recent multicentre study in Italy, vaccination coverage was 77.3% for HBV (26).Vaccination coverage of HCWs against HBV in the USA was 63.4% and higher in French healthcare students (91.8%), probably for mandatory vaccination (20,32-34). In a study in China 86% of respondents reported having received at least one dose of the hepatitis B vaccination and 60% reported having completed ≥3 doses of the hepatitis B vaccination (35). In Africa the coverage was very low the estimated full hepatitis B vaccination coverage was 24.7% (95% CI: 17.3-32.0)(36). In a study on Greek the HBV vaccination coverage of students was high (83%), being higher among medical students (88.1%, vs. 81.4% among nursing and 80.1% among paramedical students; $p < 0.001$). The vast majority of Greek medical students (95%) have been vaccinated during childhood and 30% of the unvaccinated students declared fear over HBV safety (37). In a study in Georgia the rate of HBV vaccination coverage was 12% and 54% of respondents indicated that they would recommend vaccination to other HCWs (38).

Tetanus, Diphtheria and Pertussis

Tetanus and diphtheria are very serious diseases, luckily were rare in the high-income countries today, but people who do become infected often have severe complications (39). Whooping cough can cause serious illness in babies, children, teens and adults. Symptoms of pertussis usually develop within 5 to 10 days after you are exposed (40). TDPa or TD vaccine (only for booster in adult age) is used to protect adolescents and adults from these diseases.

Benefits and risk in healthcare settings

Recommendations regarding diphtheria vaccine vary across countries for HCWs and the general population (39). In general, there are no specific recommendations for HCWs compared to the general population (see Table 1).

The protection against pertussis (which usually occurs in an oligo-asymptomatic form in adults) is particularly important for the staff of neonatology, paediatrics and obstetrics clinics where contact with infants is frequent and so there is a high risk of transmission of infections (41).

Pertussis outbreaks have been reported from a variety of healthcare settings, including neonatal wards, surgical units and residential homes (42,43). Despite CDC recommended a booster every 10 years transmission has been described from HCWs after vaccina-

tion in the previous 3 years, showing a partially effectiveness of vaccination and transmission from HCWs to their patients has been documented (44).

Vaccination coverage

In a recent review the higher initial coverage rate observed was 63.9%, but most studies showed coverage rates under 40.0% (8, 45). USA and France are the only two countries with studies evaluating Tdap coverage within HCWs using national data (46-48). In France Pulcini et al. reported a national coverage rate of 63.9% among physicians (49). In a study data from 21 American states using the 2013 Behavioral Risk Factor Surveillance System industry/occupation module were analysed in 2016 with a national coverage of 47.2% (range:38.8- 56.7%) while another study in 2014 showed a coverage of 42.4% (95% CI=38.7%, 46.0%) (50). Paranthaman et al described a higher coverage (90%) and reasons for non-acceptance: included having had pertussis infection or vaccination in childhood, fear of adverse effects, being pregnant or a lack of national policy/colleague recommendation (51). In Italy a multicentre cross sectional study showed a vaccination coverage of 29.5%(16).

Globally the same data described for DT were detected for pertussis with a variable range (40-63.9%) (8,45-52). In a recent survey vaccination data showed a value between 78.6% and 96.5% in healthcare workers in maternity and paediatric care (53). A recent cross-sectional study aimed to assess pertussis seroprevalence among healthy healthcare workers in Tunisia detected a seropositivity rate of 11.4% (95% CI 7.4- 15.5)(54). In USA national coverage varied from 38.7 to % 56.7% while, in Italy, the national coverage was 29.5%, according to a national survey (45-52, 16).

Measles, Mumps, Rubella

Mumps, measles and rubella (MMR) are serious diseases that can lead to potentially fatal illness, disability and death. Due to their transmission way the immunization of healthcare workers could be important to avoid several cases of outbreaks, such as described in literature (55,56).

In fact, compared to the general population, HCWs are estimated to be at 13- to 19-fold greater risk of acquiring measles (57-59).

Even though a safe and cost-effective vaccine is available, in 2017, there were 110 000 measles deaths globally, mostly among children under the age of five. In 2017, about 85% of the world's children received one dose of measles vaccine by their first birthday through routine health services (60).

Vaccination coverage

In a retrospective epidemiological study of 1060 HCWs, 90.1% were protected against varicella, 65.6% against mumps, 95.6% against rubella and 92.9% against measles (61). Two studies performed in Turkey found a rate of 94% for measles, 98% for rubella and for mumps of 90-91%% (62,63). In a study on 1128 HCWs measles and rubella antibodies were detected in 95.4% and 86.2% of the HCW, with 11.9% of females being unprotected against rubella (64). In a cross-sectional study 71% had ever received an MMR and 42% had received the most recent flu vaccination (65).

Vaccination coverage among HCWs in ten countries of Samu-social international sites was 81.3% (66). In a study of Australian HCWs the vaccination coverage was higher for hepatitis B, tetanus and polio than measles (59.8%), mumps (60.7%), rubella (70.5%), influenza (42.1%) or pertussis (58.2%) (67). Another study in Argentina showed a triple or double viral vaccine coverage of 50.32% with higher levels among those workers with a higher level of education and less seniority (68). In a review by the European Center for Disease Control, coverage rates were 43.6% in France and 62.3% in Denmark (69). In a Japanese seroprevalence survey a total of 1811 HCWs were tested, 91.8% were seropositive to measles, 92.1% to mumps, 89.5% to rubella and 96.3% to varicella (70).

In Italy the coverage reported in several studies was very low, under the target required for herd immunity (16, 71-77).

Chickenpox

Chickenpox is a high contagious disease and so healthcare setting are at particular risk of transmission with possible case of outbreak (defined as the occurrence of five or more cases in a specific setting that are epidemiologically linked). Varicella transmission in healthcare settings from HCWs to susceptible patients has been reported, mostly in tropical countries or in HCWs who received only 1 vaccine dose (78,79).

Varicella vaccine coverage depends on vaccine recommendations for people entering the healthcare workforce.

In Turkey the rate was 98% (63,64) while in Japan the rate coverage was 95% (71). In a study on Saudi Arabia previous history of VZV infection was reported by 1303 HCWs of which 262 (13%) had a history of positive test for varicella antibody, and only 44 (2%) had a history of varicella vaccination (80). In Italy we found a vaccine rate under 20%, in line with other studies (16).

Flu

Influenza is a contagious acute viral infection, with a short incubation period, spreading mainly by droplets, and characterized by respiratory and systemic symptoms. Despite the availability of antiviral drugs vaccines remain the most effective tool for preventing flu. Every year the flu vaccine is offered to HCWS in order to prevent the spread of flu to vulnerable patients and to their colleagues and so to protect themselves, their families and their patients (81).

Vaccination coverage among HCWs is low in Europe (generally less than 30%) despite several recommendations. A significant difference comparing data reported in the USA vs. Europe and other countries exists. According to the CDC data report the 2017- 18 flu vaccination coverage among health care personnel was 78.4%, similar to coverage during the 2016- 17 season (78.6%)(82).

In Europe the rate coverage was also variable: in Spain the 2014 European Health Interview Survey for Spain (N = 22,842) found a value of 18.9% immunized HCWs(83).

In Italy a survey in province of Taranto of the 2015/2016 influenza season detected vaccination coverage among the general practitioners of 76.4% (84). Also, in a multicentre study conducted in ten Italian cities the coverage rate detected was 14% (16).

In a survey of 5141 Belgian HCWs from 13 hospitals and 14 nursing homes, the mean vaccination coverage detected by the authors was 40.4% in the hospitals and 45.3% in the nursing homes (85).

In other countries the vaccination coverage was also variable: for example, 88.3% of the participants of a study in Saudi Arabia declared to get vaccine (80).

Conclusion

These findings underline the low vaccine coverage of HCWs in the World and so the importance of mandatory vaccine (86-89). In some Italian regions and also in some countries mandatory vaccine has been introduced but in literature we found some contrasting opinion about this (90-92). The motivations of vaccine hesitancy are many and maybe other studies would help policymakers and stake-holders to shape programs to improve vaccination coverage and the control of infectious diseases through the correct application of guidelines on prevention (93-98).

Furthermore, the prevention of infectious diseases through vaccinations falls within the competence of the Occupational Physicians, a figure of absolute centrality for its traditional role in the complex system of protection of health and safety in the workplace and also for the role of "health promoter" entrusted by Legislative Decree 81/08. So, it is important in this optic the engagement of OP as well as hygienists to ensure adequate vaccination rates as part of an effective nosocomial infection prevention through vaccinations in an age of antimicrobial resistance (99-104).

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Received: 15 June 2019
Accepted: 18 July 2019
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Acta Biomed 2019; Vol. 90, Supplement 9: 54-63 DOI: 10.23750/abm.v90i9-S.8713

Original article

Measuring hospital qualities. A preliminary investigation on Health Impact Assessment possibilities for evaluating complex buildings

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Summary. *Background and aim of the work:* World Health Organization states that is possible evaluating projects' qualities via Health Impact Assessment (HIA) but there are not specific HIA tools on hospital buildings assessment. Researchers show significant relationships between built environment and health. The research purpose is investigating how existing tools for healthcare building assessment are encouraging the development of possible hospital HIA evaluation. *Methods:* Based on previous works, 13 assessment tools have been included and a comparison of the criteria has been conducted to understand which the most prevalent topics are. The tools have been analyzed through literature, technical manuals and official websites. The authors identified 12 thematic categories where criteria from different tools have been clustered and discussed. *Results:* The most prevalent criteria are related to *Indoor Environmental Quality (IEQ)* (20%). In the oldest tools the evaluation was mainly on technical features while in recent instruments several indicators are related to *Architectural features and innovation (48%), Education (23%)* and *Food* (11%). *Conclusions:* There is growing interest in tools capable of addressing healthy hospitals encouraging IEQ, physical activity and healthy food provision related to occupants' health outcomes. This preliminary study set the basis for further development on hospital facility HIA tools. (www.actabiomedica.it)

Key words: evidence based design, assessment tool, hospital, built environment, quality, public health, healthcare facility, health impact assessment

Background and aim of the work

Public health and architecture

Recent trends such as globalization, digitalization and urbanization, combined with an ageing population and population growth, result in new challenges for public health and healthcare settings (1, 2). To address those complex issues a social multidisciplinary approach has to be considered and various professional figures have to collaborate in analysis, advocacy and action. In this paper the authors argue that decision makers, healthcare managers and public health workforce can benefit from the support of architects, designers and urban planners when dealing with complex decisions about healthcare facilities and built environment in terms of health promotion possibilities both at the urban and at the building scale (3, 4). In particular, contemporary healthcare systems are facing the challenge of delivering high level services in complex economic and social environments. Hospital facilities reflect this complexity and, as building type, they host diverse and multiple daily users, try to integrate advanced technologies and systems and have a public role as health venue and promoters, constantly transforming during time (5-7).

The Italian context and built environment criticalities

In the Italian context one hospital over three has been built before 1970 demonstrating the obsolescence of this important asset (8). This figure is reinforced by data from Piedmont region where 42% of the healthcare estate is not adequate to the contemporary organizational models and technological innovation due to their construction period or the need for consistent extraordinary maintenance (9). Moreover, recent declaration from the Italian Minister of Health confirms the needs of a consistent investment plan of about Euro 32 billion for the improvement of the overall quality and safety of hospital architectural assets (10). Although this consistent amount of money is requested for the economic sustainability of the system, strategic tools are needed to target the most important aspects to design or refurbish high quality hospital, eventually avoiding the repetition of obsolete and inefficient models.

Hospital built environment and Health Impact Assessment

Researchers demonstrated that physical healthcare environment is an important factor in the overall health care performance outcomes. Architecture and physical space are considered an important component that contributes to the creation of a high-quality health service to promote health and well-being (11-13). Indeed, the Donabedian's quality assurance model states that the quality of healthcare is related to three domains: process, outcome and, lastly, structure, which is defined as the "*physical and organizational characteristics where health care occurs*" (14). In western countries well established systems (i.e. Joint Commission International) are important in the process of quality measurement and improvement with criteria and indicators related to clinical, organizational and managerial fields. Nevertheless, they rarely mention the built environment and no indicators are provided to evaluate the physical settings where healthcare is delivered (Figure 1).

Research gap and problem statement

Although the concept of design quality is very difficult to define (15), several studies at the edge of architecture, environmental psychology, health management and service design fields, demonstrated the impact of built environment on the final building users (16-20). Moreover, the World Health Organization (WHO) states that is possible to evaluate the quality of a project via Health Impact Assessment (HIA)

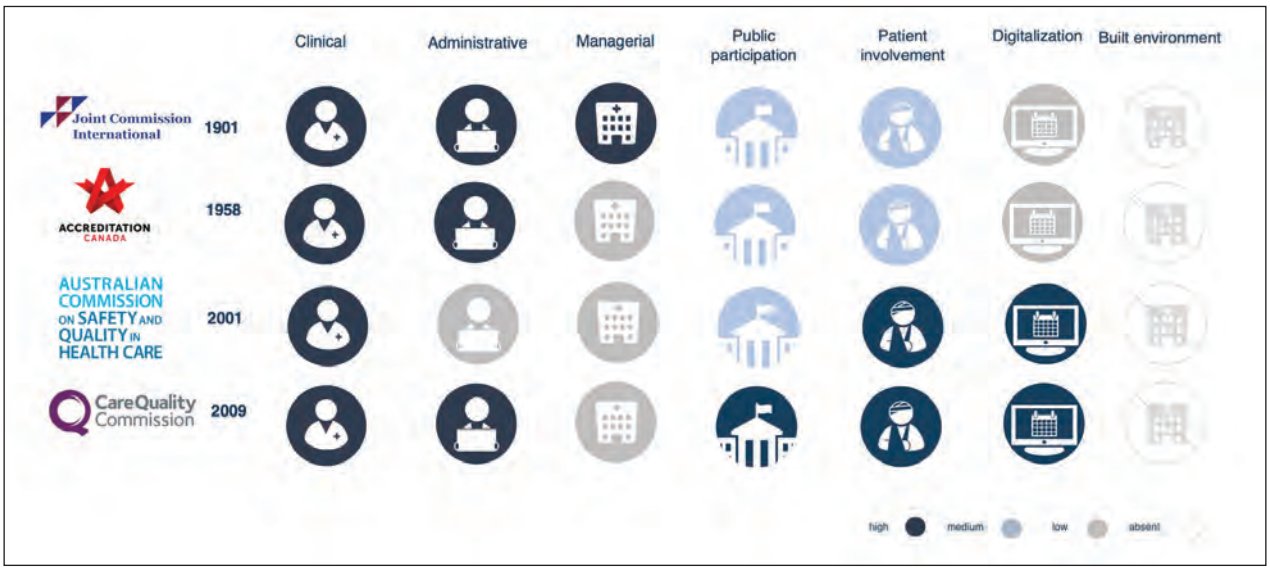

Figure 1. Comparison between the most common organizational quality assessment tools

which is a means of assessing the health impacts of policies, plans and projects in diverse economic sectors using qualitative, quantitative and participatory techniques (21). To the best of our knowledge, no HIA tools are available for the assessment of hospital design qualities. However, Ulrich's Evidence Based Design (EBD) studies demonstrated the importance of green views and several other design elements on different health-related outcomes and organizational domains such as patient stay reduction, fall reduction and staff satisfaction (22-25). Furthermore, in the last 20 years, within the real estate sector of corporate office buildings a similar approach started to be diffused mainly in the field of environmental sustainability with the development of some evaluation instruments, also applicable to hospital settings (26-28). Since in Italy hospital design regulations are generic, prescriptive and obsolete there is an urgent need to study and develop specific assessment tools.

Purpose and research questions

Therefore, the general research purpose is to investigate how the existing tools for hospital built environment assessment can encourage the development of possible HIA tools. Specifically, two research questions have been framed in order to clarify the boundaries of the study:

i) If hospital's physical qualities are measurable through assessment tools, on which criteria those evaluations are based, which topics are the most prevalent and, therefore, important in the evaluation?
ii) Within the available tools, are there emerging topics that were not present in the past and, therefore, can define a possible trend for the future?

Methods

In order to collect most of the information about the topic a literature review has been conducted and different tolls have been extracted and differently analyzed. With the objective of highlighting blank or weakly covered areas for grounding incremental studies in the field, the search has been conducted with sets of keywords derived from preliminary search and relevant references (29-32) (Table 1). Based on previous works by the authors (24, 33) 13 tools have been included.

Table 1. Synthesis of the literature search and review conducted, upon which the analysis presented in the paper is based; extensive description and PRISMA flow diagram is provided in previous works by the authors (23, 32)

Date of search	May and April 2018
Keywords	Quality • AND hospital AND design • OR architecture OR built AND environment
Repositories	• Scopus; PubMed • Center of Health Design (CHD); Health and Care Infrastructure Research and Innovation Centre (HaCiCR); International Academy for Design & Health (IADH)
Papers collected	2228
Inclusion criteria	Physical qualities; Assessment or evaluation methodology; Published after 2010; English language
Papers included	172
Tools founded	44
Inclusion criteria	Post Occupancy Evaluation; Applicable to hospital building
Tools included	13
Full methodology available in:	Brambilla et al, 2019 (24); Brambilla & Capolongo, 2019 (33)

A comparison of the criteria has been conducted in order to understand which the most prevalent topics are. Each tool has been analyzed based on the criteria level of detail and in line with previous studies on the topic (28, 33-37). All the included tools have a hierarchic structure of macro areas, criteria and indicators. The analysis has been conducted exclusively at the criteria level and the importance of each criterion has been considered based on the total number of indicators related to that specific criterion. The tools have been analyzed through the literature, technical manuals and official websites by the authors. During the tools screening the authors identified a series of thematic areas in which criteria from different tools can be related and clustered them in 12 categories. The prevalence of a category (p) within each tool has been calculated according to the following formula:

$$p = n/T \times 100$$

where n is the number of indicators related to a specific criterion and T is the total number of indicators of the tool. The prevalence has been calculated for each single tool ($p1$; $p2$; …; $p13$) and for the overall set of criteria collected (P).

The included tools, with the corresponding number of indicators (n) are:

- BREEAM - Building Research Establishment Environmental Assessment Method (n=193)
- LEED - Leadership in Energy and Environmental Design (n=49)
- CASBEE - Comprehensive Assessment System for Building Environment Efficiency (n=20)
- GS - Green Star (n=30)
- ASPECT - A Staff and Patient Environment Calibration Toolkit (n=46)
- AEDET - Achieving Excellence Design Evaluation Toolkit (n=57)
- GGH - Green Guide for Healthcare (n=57)
- SUSTHEALTH - Sustainable High Quality Healthcare (n=37)
- BUDSET - Birthing Unit Design Spatial Evaluation Tool 2.0 (n=92)
- HBS - Healthcare Building Sustainability Assessment tool (n=52)
- DQI - Design Quality Indicator (n=66)
- WELL - Well Building Standard (n=117)
- CHD-CHC - Community Health Center Facility Evaluation Tool (n=94)

Results

All the tools are based on a hierarchic structure, the framework is composed by fundamental and interconnected macro-areas (39) and each one is evaluated through a hierarchic set of criteria and indicators (Figure 2). The tools collected have up to 5 macro areas, between 6 and 24 criteria and between 21 and 193 indicators. Each indicator might have one or more item with different techniques of measurement, either qualitative or quantitative. Globally the total number of indicators is 910.

Data analysis

Among the total number of tools and criteria, 12 categories have been highlighted by the authors in order to be able to cluster a significant number of similar topics of measurement. The categories are hereafter listed and described from the most prevalent to the least (Table 3).

Indoor Environmental Quality (IEQ) is the most prevalent category among all the criteria and it collects 20,9% (n=190) of the total amount of indicators. IEQ performance of buildings affects lifecycle costs and energy consumption but also the wellbeing, health and

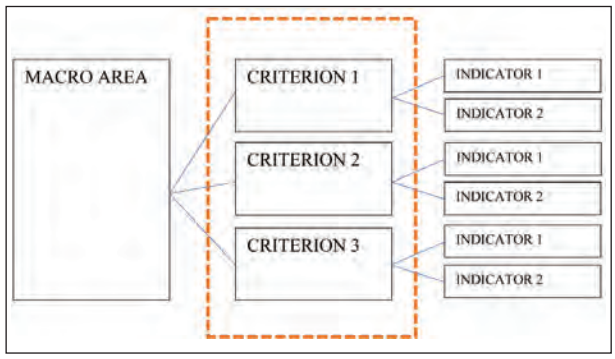

Figure 2. Hierarchic framework of a generic assessment tool with highlighted the criteria level where the analysis has been conducted

productivity of building occupants (39). It includes the subtopics of health and wellbeing (BREEAM *p*=15%), humanization, comfort and in general the qualities of the indoor environment (LEED *p*=24%), including privacy, views, colours, air and sound (WELL *p*=29%). Researches in this direction shown the importance of qualitative issues for the hospital's occupants, patients and staff (40, 41).

Architectural features and innovation category have a prevalence of 17,9% (n=163) and embeds several topics such as distribution, layout features, space flexibility and adaptability (HBS=8%), character and innovation (DQI=36%) and other design considerations able to improve overall safety and quality of care (CHD-CHC=49%). Indeed, within the evolution of hospital typology several strategies such as flexibility have been recognized as very effective in terms of medium and long term management by several authors as well as practitioners that are constantly experimenting new technological systems for improving the ability of a space to change function during time (42).

The third most prevalent category is ***Energy efficiency*** that contains 127 indicators (P=14%) with specific performance-based criteria such as envelope technologies, environmental life cycle, engineering systems, sustainability and energy measurements (SUSTHEALTH=27%). Hospital facilities are energy demanding systems and although several aspects are demanded to technical regulations and standards, the different tools provide clear and performance-based indicators to improve the overall energy management,

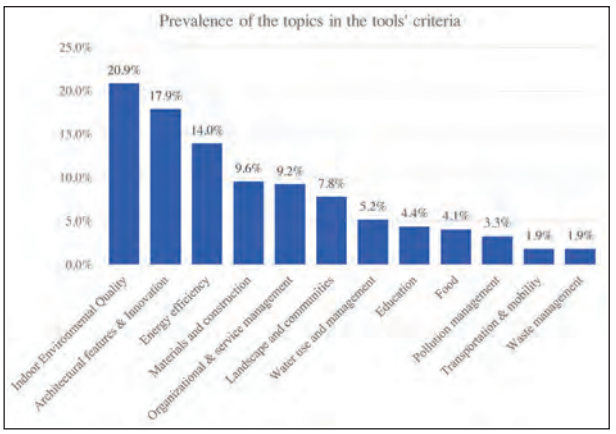

Figure 3. Prevalence of the different categories in the whole tools' criteria

reduce the cost and contribute to the contemporary environmental issues related to climate change.

Below a prevalence of 10% is possible to find the ***Materials and construction*** topics (P=9,6%; n=87), the ***Organizational and service management*** (P=9,2%; n=84), the ***Landscape and communities*** issues (P=7,8%; n=71) and the ***Water use and management*** (P=5,2%; n=47) categories.

The least prevalent criteria are ***Education*** (P=4,4%; n=40), ***Food*** (P=4,1%; n=37), ***Pollution management*** (P=3,3%; n=30), ***Transportation and mobility*** (P=1,9%; n=17) and, finally, ***Waste management*** (P=1,9%; n=17) (Figure 3).

Evolution during time and innovative criteria

Most of the criteria highlighted are related to environmental sustainability categories such as Energy efficiency, Materials, etc. Nevertheless, looking at the included tools from a chronological point of view it is interesting to notice that an increasing attention in the assessment criteria is devoted to the categories of: *Architectural features & innovation*, *Education* and *Food strategies*.

Indeed, in the tools developed in the early 90s (i.e. BREEAM or LEED) only few criteria related to architectural features and innovation were present. On the contrary, in the most recent hospital built environment quality evaluation instruments, up to 48% of the indicators are related to Architectural features and innovation (i.e. CHD CHC) and up to 23% and 11% are respectively related to Education and Food (i.e. WELL). This evolution confirms what highlighted in previous works (33) and an overview of this pattern is provided in Figure 4.

Discussion

Several categories have a direct or indirect impact on hospital performances, quality of the service and on occupant's health. For example, in the Indoor Environmental Quality category, criteria like DQI's "Internal patient environment" contains several indicators that allow a better patient or staff satisfaction i.e. layout legibility, wayfinding, provision of natural light, views

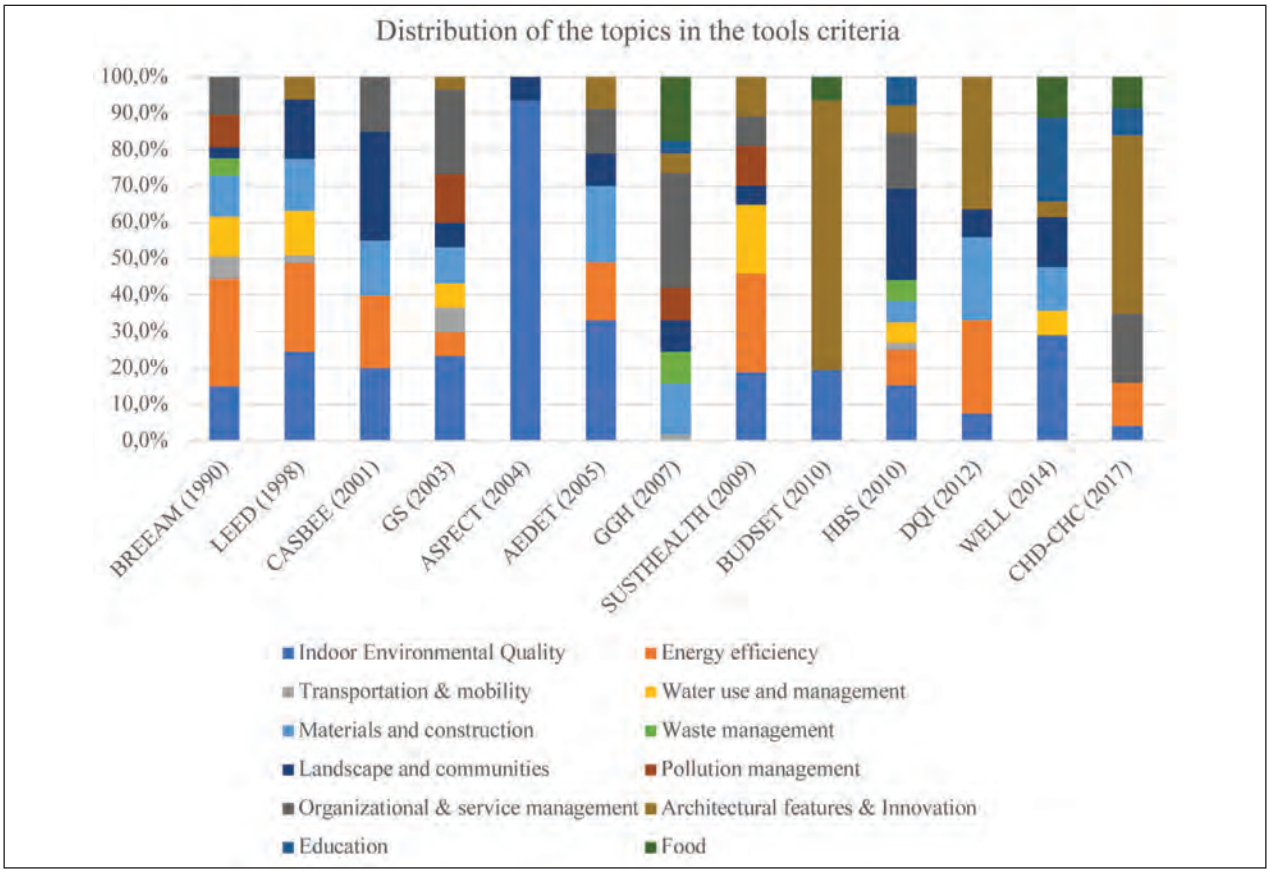

Figure 4. Distribution of the 12 categories in the 13 different tools during time

and accesses to green areas (43, 44). Additionally, in the WELL's "Movement" criteria, most of the indicators are related to the possibility of enhancing, through different layout and organizational strategies, the use of stairs for the buildings' occupants or the provision of gym services in order to foster a culture of physical activities and health prevention in the workplaces (45, 46). Furthermore, the whole "Food" category embeds, through the different tools, several strategies to provide healthy diets with attention to the different intolerances and culture-related issues, not just with organizational strategies but also with the implementation of graphical signages, layout interventions and ad-hoc surveys (45, 47). Finally, even if the criteria related to sustainability might seem very technical, as defined by WHO and the Health Care Without Harm initiative, those strategies are capable of addressing healthy hospitals, healthy planet and healthy people in the view of climate change (48, 49).

Conclusions

Although most of the hospital service evaluation instruments do not consider the built environment, criteria from hospital facility assessment tools can be related to well defined categories and embeds several indicators of measurement that have a direct or indirect impact on hospital occupant's health. Qualitative issues in the field of IEQ, sustainability, organizational qualities are evaluated and recently released tools includes specific issues from the architectural field, the education of the occupants and the services related to the provision of healthy food. Hospital built environment have an important role within the whole national health system and therefore the design of those facilities has to be based on the best available knowledge from solid research (43). Therefore, Public Health and Built Environment researchers have to collaborate in developing strategic tools and methods for the im-

provement of the physical qualities of the healthcare settings that can have important impacts on occupants' health and wellbeing (50). Further investigation of the tools and their relationship with the direct or indirect health outcomes will provide the basis to structure HIA tools for the evaluation of hospitals built environment design and operations.

Limitations

The tools have been studied assuming that all the indicators included in each criterion are coherent with the criterion main objective. Further investigation at the indicator level might result in slightly different outcomes in terms of category prevalence. Nevertheless, the authors are confident that the methodology is solid enough to provide consistent results.

Future developments

Starting from the results achieved and the limitations highlighted, further research are encouraged to deepen specific categories and unfold the possible relationship that the built environment variables have with the health outcomes. This development is encouraged to be fostered with collaborations between built environment and public health scholars in order to possibly define hospital facility HIA tools.

Acknowledgements

The authors certify that the submitted manuscript is an original article. Moreover, the authors would like to acknowledge that a wider version of the research based on the same literature and tools set is available as declared in chapter Methodology (24, 33) and has been presented at 2019 ASPHER (The Association of Schools of Public Health in the European Region) Deans' and Directors' Retreat.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Received: 15 June 2019
Accepted: 18 July 2019
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Annex 1. List of the 13 tools included in the analysis with the most relevant information

	Indoor Environmental Quality	Energy efficiency	Transportation & mobility	Water use and management	Materials and construction	Waste management	Landscape and communities	Pollution management	Organizational & service management	Architectural features & Innovation	Education	Food
BREEAM (n=193)	Health & Wellbeing	Energy	Transport	Water	Materials	Waste	Land use & ecology	Pollution	Management	-	-	-
	15%	30%	6%	11%	11%	5%	3%	9%	10%	-	-	-
LEED (n=49)	Indoor Environmental Quality	Energy and Atmosphere	Location and transportation	Water Efficiency	Materials and Resources	-	Sustainable sites	-	-	Innovation; Regional priority	-	-
	24%	24%	2%	12%	14%	-	16%	-	-	6%	-	-
CASBEE (n=20)	Indoor Environment	Energy	-	-	Resources & Materials	-	Outdoor Environment on Site + Off-site Environment	-	Quality of Service	-	-	-
	20%	20%	-	-	15%	-	30%	-	15%	-	-	-
GS (n=30)	Indoor Environmental Quality	Energy	Transport	Water	Materials	-	Land Use & Ecology	Emissions	Management	Innovation	-	+
	23%	7%	7%	7%	10%	-	7%	13%	23%	3%	-	-
ASPECT (n=46)	Privacy, company and dignity; Views; Comfort and control; Legibility of place; Interior appearance; Facilities; Staff	-	-	-	-	-	Nature and outdoors	-	-	-	-	-
	93%	-	-	-	-	-	7%	-	-	-	-	-
AEDET (n=57)	Staff and patient environment; Access; space	Performance; Engineering	-	-	Form and materials; construction	-	Urban and social integration	-	Use	Character & Innovation	-	-
	33%	16%	-	-	21%	-	9%	-	12%	9%	-	-
GGH (n=57)	-	-	Transportation Operations	-	Environmetally Preferable Purchasing	Waste Management	Sustainable Sites Management	Chemical Management	Facilities Management; Environmental Services	Innovation in Operation	Integrated Operations & Education	Food service
	-	-	2%	-	14%	9%	9%	9%	32%	5%	4%	18%
SUSTHEALTH (n=37)	Humanization; Comfort	Saving with efficiency; 'Envelope technologies; 'Combined heat and power; 'Unconventional Source supply	-	Watercare	-	-	Urban planning	Clinical waste; technological waste	Managerial waste	Distribution	-	-
	19%	27%	-	19%	-	-	5%	11%	8%	11%	-	-
BUDSET (n=92)	Light; colour; noise control	-	-	-	-	-	-	-	-	Space (arrival-reception,...); privacy; sense of domesticity; physical support; birthing bath; en-suite facilities; accomodation for companion	-	Food for woman
	20%	-	-	-	-	-	-	-	-	74%	-	7%
HBS (n=52)	User's health and comfort; Controllability by the user	Energy; 'Environmental life cycle impact assessment; passive design	Mobility plan	Water	Technical systems; Durability	'Materials and Solid Waste	Soil use and biodiversity; Landscaping; 'Local community; 'Cultural value; 'Facilities	-	Life cycle costs; Local economy; Environmental management systems; Security	Space flexibility and adaptability	Awareness and education for sustainability; Skills in sustainability	-
	15%	10%	2%	6%	6%	6%	25%	-	15%	8%	8%	-
DQI (n=66)	Internal (Patient) Environment	Performance; Engineering	-	-	Construction; Form and Materials	-	Urban and Social integration	-	-	Access; use; space; Character and Innovation	-	-
	8%	26%	-	-	23%	-	8%	-	-	36%	-	-
WELL (n=117)	Air; Light; Thermal comfort; Sound	-	-	Water	Material	-	Community	-	-	Innovation	Movement; Mind	Nourishment
	29%	-	-	7%	12%	-	14%	-	-	4%	23%	11%
CHD-CHC (n=94)	Physical Environment: Air & Water Quality, Noise, Environmental Impact, Transit	Sustainability (alternate considerations to LEED)	-	-	-	-	-	-	Clinical Care - Access to Care (location), Co-located Services, Team Care, Technology	OPTIONAL: Other Design Considerations to Improve Quality & Safety of Care	Social-Economic Factors: Education, Community/ Personal Safety, Socio-demographic Balance	Healthy Behaviors: Activity, Nutrition, Green Spaces
	4%	12%	-	-	-	-	-	-	19%	49%	7%	9%

Acta Biomed 2019; Vol. 90, Supplement 9: 64-70 DOI: 10.23750/abm.v90i9-S.8710

Original article

Out-of-hospital cardiac arrest (OHCA) Survey in Lombardy: data analysis through prospective short time period assessment

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Summary. *Background and aim of the work:* The results of out-of-hospital cardiac arrests (OHCA) are usually reported through data collected collected via "ad hoc" registries, but in large populations, samples of short time periods can be used to apply the results to the entire population. We would like to describe the situation of Lombardy to provide evidence on successful procedures, which may be carried out in a larger context. *Methods:* Observational, prospective, analytical, single cohort study in Lombardy population. Data of OHCA of cardiac aetiology, according to "Utstein Style", with resuscitation attempts started by the Emergency Medical Service (EMS), were collected for 40 days subdivided in 10-day-periods in all seasons 2014-15 via Operating System "Emergency Management" (EmMa). *Results:* Of 1219 cases, 536 events of witnessed OHCA of presumed cardiac etiology were analyzed. Outcomes were: sustained Return Of Spontaneous Circulation ROSC (25.6%), Survival Event in Emergency Department (22.8%), Survival after 24 hours (21.2%) and Survival after hospital discharge at home 30 days after (11.2%). Statistically significant results were found in age, rhythm of presentation, and resuscitation by bystanders. Sex, seasonality and rescue timing did not differ statistically. *Conclusions:* Overall the thirty-day survival rate was similar to studies with larger databases. Our data are consistent with the concept that all emergency service should provide CPR instructions for every citizen who activate the EMS in the suspect of a SCA; further investigation should clarify how long interval could be useful for ROSC and sustained ROSC in patients resuscitated by lay people using CPR instructions. (www.actabiomedica.it)

Key words: Resuscitation, OHCA, EMS, Utstein Style, Lay Persons, bystanders-CPR, ROSC, sustained ROSC

Glossary

Azienda Regionale Emergenza Urgenza, (Emergency Medical System Regional Trust): AREU
Advanced Life Support (ALS)
Out-of-hospital cardiac arrest: OHCA
Sudden Cardiac Arrest: SCA
Emergency Medical Service: EMS
Return Of Spontaneous Circulation: ROSC
Cardiopulmonary Resuscitation: CPR
Automated external defibrillator: AED
Medical Emergency Dispatch Centers: MEDC
Emergency Department: ED
Italian National Institute of Statistics: ISTAT
Joints Territorial Systems: JTS
Cerebral Performance Categories: CPC
Intensive Care Unit: ICU
Cardiac/Coronary Care Unit: CCU
Ventricular fibrillation: VF
Public Safety Answering Points: PSAPs

Introduction

Survival from out-of-hospital cardiac arrest (OHCA) is closely related to the application of the maneuvers detailed in the four links of the "Chain of Survival" (1,2), where bystander Cardiopulmonary Resuscitation (CPR) and early defibrillation are synergic with the interventions performed by the Emergency Medical System (EMS).

The restoration of spontaneous cardiac function is closely related to an early recognition of the sudden cardiac arrest (SCA) condition by those who can witness the event and immediately begin chest compression, and by an early defibrillation in presence of a shockable rhythm (3). Early defibrillation also depends on the prompt availability of an Automated External Defibrillator (AED), which requires their diffusion in public places to increase the likelihood of immediate availability (4-7).

Systematic data on SCA in our country are scarce and limited to earlier investigations (8,9) and a few more recent studies (10). All these studies identified a prevalence of approximately 1000 SCA per year per million of inhabitants. These results were obtained with data collected through registries, reporting the exact number of events; the following data acquisition was then feasible thanks to some co-investigation reviewing each case and following them during hospital-stay and after discharge. The relatively limited number of events and hospitals in those areas were important elements affecting the study design and subsequent results.

Lombardy is the most populated Italian region with a resident population of approximately 10 million people. According to previous estimates SCA incidence accounts for approximately ten thousand events/year.

A complete reorganization of EMS took place in recent years, with the introduction of the European Unique Emergency Number 112, the reduction of the Medical Emergency Dispatch Centers (MEDC) (from twelve to four Operative Centers covering more provincial territories), the re-organization of emergency calls and vehicles delivery. Only after accomplishment of these tasks, it was possible to acquire regional data in a more uniform way also thanks to a brand-new technology linking together the four MEDC and facilitated a more homogeneous data acquisition. Closer relationships between operators involved in the out-of-hospital (OH) setting or in the in-hospital services offered the opportunity to follow the patients till the hospital discharge, at least in the major hospital facilities.

We recognized that previous data in Lombardy were collected only in very small areas, and referred to only the OH setting until the arrival at the Emergency Department (ED). There was no information on outcome following hospital admission. We realized that the new uniform system would offer the opportunity of a more complete data recording in the entire region. We are convinced that the promotion of awareness of all operators should begin by improving the data acquisition.

Materials and methods

The study population included all residents in Lombardy, estimated 9924447 people in 2013 according to the Italian National Institute of Statistics (ISTAT). The territory covered by AREU, Azienda Regionale Emergenza Urgenza, Regional EMS Trust in Lombardy taking care of Emergency and Urgency, is estimated at 23861 square kilometers, 1544 municipalities distributed in 12 provinces. The management of the interventions includes 12 provincial Joints Territorial Systems (JTS) and 4 regional Medical Emergency Dispatch Centers (MEDC), with the purpose of coordinating every ambulance or advanced rescue vehicle (cars and helicopters).

Territorial rescue is ensured by 265 ambulances (with 2-3 rescuers that are qualified to perform Basic Life Support maneuvers only), 50 Intermediate Rescue Vehicles with a nurse on ambulance or car, 59 Advanced Rescue Vehicles with a physician certified to perform Advanced Life Support (ALS) and 5 helicopters with ALS crew members. All operators were sensitized through their chiefs of services to register every case of SCA. Some operators of the MEDC personnel were also identified to follow the patients admitted to the hospitals to follow up until the 30th day after hospital discharge.

Data were prospectively collected over four 10-day periods, each one representing a season, all starting on Monday, for a total of 40 days: from 14th to 23rd October 2013 (Autumn), 14th to 23rd January 2014 (Winter), 14th to 23rd March 2014 (Spring) and from 14th to 23rd July 2014 (Summer). The data were extrapolated from the regional database and built by the information of the records of the operators of territorial EMS. Whenever missing, data were requested to the physician of the MEDC.

The data, reported according to the Utstein Style, refer to SCA of presumed cardiac origin (11,12). The exclusion criteria were: undiagnosed OHCA, unwitnessed OHCA, events where cardiopulmonary resuscitation (CPR) by EMS was not attempted for injuries incompatible with life (as beheading, charring, etc.) or for the body conditions such as hypostatic stains, "rigor mortis", etc.

We considered sustained Return Of Spontaneous Circulation (ROSC) as defined by the maintenance of perfusing spontaneous cardiac activity lasting longer than 20 minutes.

Patients with sustained ROSC were transported to the most appropriate hospital. In case of non-return of spontaneous circulation, patients were declared deceased on site. In case of patients transported with ongoing CPR, the outcome was evaluated on arrival at the ED.

For the assessment of "outcome" the "Survival Event" was used for the following time intervals: sustained ROSC on-site, survival at arrival in the emergency room, survival after 24 hours, survival at hospital discharge and at home at 30 days after the cardiac event. In those survivors at 30 days, neurological conditions were determined by the "Cerebral Performance Categories" (CPC) scale (CPC 1-2 good neurological performance, CPC 3-4 compromised neurological performance).

Age, sex, time intervals (emergency call-to-target), bystander resuscitation (CPR or chest compression only), use of an Automated External Defibrillator - AED), presenting rhythms (by either an AED or an EMS monitor-defibrillator), seasons were also investigated.

Non-ROSC patients were used as comparative group. Frequencies were analyzed by the chi-square test with contingency tables. A p-value less than 0.05 was considered statistically significant. Statistical analysis was carried out with the "Statistical Package for Social Science" (SPSS).

Results

A total of 1219 OHCA were collected, corresponding to an incidence of about 1000 SCAs per 1000000 inhabitants every year (1: 1000/year).

Among these, resuscitation maneuvers were started by the EMS personnel in 854 patients (70.1%), while in the remaining 365 (29.9%) CPR was not initiated.

A presumed cardiac etiology was attributed to 762 cases of the 854 patients (89.2%) while in 92 cases (10.8%), SCA was attributed to non-cardiac causes. The presence of witness lay people occurred in 439 (57.6%) whereas in 97 patients SCA occurred in presence of EMS personnel (12.7%) accounting for a total of 536 cases (70.3% of the total) (Fig. 1).

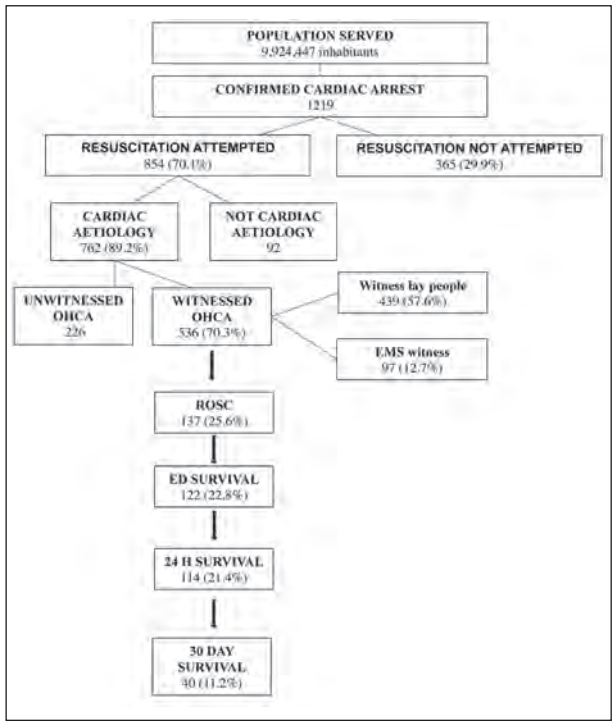

Figure 1. Utstein template of Lombardy's OHCA
Legend: OHCA: Out of Hospital Cardiac Arrest; ROSC: Return Of Spontaneous Circulation; ED: Emergency Department

Of the 536 presumed cardiac etiology arrests witnessed by bystanders there were 320 males (59.7%), mean age 71 years, and 196 females (36.6%), mean age 78 years; sustained ROSC was obtained in 137 cases (25.6%), survival at ED arrival occurred in 122 cases (22.8%) and survival at 24 hours regarded 114 patients (21.2%). Hospital discharge occurred in 40 patients (11.2%) and was coincident with survival at 30 days at home. In this group of patients, the neurological outcome highlighted a CPC 1-2 in 36 cases (6.7%) and a CPC 3-4 in 18 cases (3.3%).

A comparison between ROSC vs non-ROSC patients related to presenting rhythms, call-to-target time intervals, bystanders-CPR, use of public AED and numbers of events in relationship to the periods is reported in Table 1.

In patients in whom the first rhythm was shockable the mean interval was 9.5 minutes (range: 3'- 25'), while in the non-shockable rhythms it was 11 minutes (range: 4'- 32').

Before EMS arrival, CPR was started in 162 cases (30%) and the use of an AED in 10 cases (1.8%). In the 162 patients in which CPR maneuvers were begun by bystanders, ROSC was observed in 52 patients (32.1%), whereas in the 374 in which the CPR interventions were performed only after EMS arrival the survival occurred in 85 patients (22.7%) (Table 2).

One-hundred patients experienced a shockable rhythm (18.7%) as presenting rhythm, while in 312 cases the rhythm was non shockable (58.2%) (Table 1). In the 10 patients in whom an AED was used by lay people a shockable rhythm was detected in 3 patients while 2 had a non-shockable rhythm and in 5 it was unknown.

Table 2. Outcome's analysis in patients with and without bystander CPR (p value 0.022)

	ROSC	non-ROSC
Bystander CPR, No./162 (%)	52 (32.1%)	110 (67.9%)
No bystander CPR, No./374 (%)	85 (22.0%)	289 (78.0%)

Legend: ROSC: Return Of Spontaneous Circulation; CPR: Cardiopulmonary Resuscitation

Defibrillating and non-defibrillating rhythms in relationship to time intervals are described in Fig. 2.

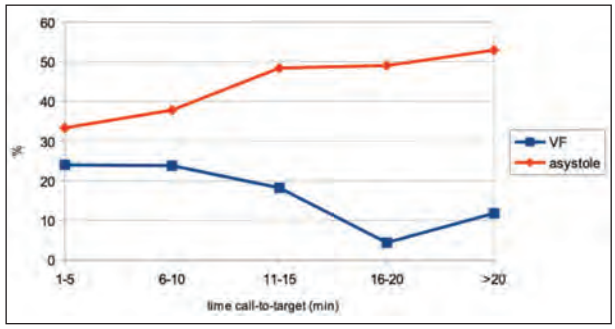

Figure 2. Correlation between defibrillating and non-defibrillating rhythms, and time intervals
Legend: VF: Ventricular Fibrillation

Table 1. Statistical validity of the variables when comparing patients characterized by Return Of Spontaneous Circulation (ROSC) vs non-ROSC patients

	ROSC No./137 (%)	Non-ROSC No./399 (%)	P-value
VF/pulseless VT	56 (40.9)	44 (11.0)	< 0.001
PEA/asystole	51 (37.2)	261 (65.4)	< 0.001
Age	65,3 ± 18	76 ± 14	< 0.001
Male sex	91 (66.4)	229 (57.4)	0.079
Time call-to-target (min)	10.6 ± 4.0	11.4 ± 4.0	0.045
Bystander CPR	52 (38.0)	110 (27.6)	0.030
Use of public-access AED	4 (2.9)	6 (1.5)	0.490
October	37 (27.0)	94 (23.6)	0.487
January	38 (27.7)	116 (29.1)	0.850
March	32 (23.3)	111 (27.8)	0.364
July	30 (21.9)	78 (19.5)	0.640

Legend: ROSC: Return Of Spontaneous Circulation; VF: Ventricular Fibrillation; pulseless VT: pulseless Ventricular Tachycardia; PEA: Pulseless Electrical Activity; CPR: Cardiopulmonary Resuscitation; AED: Automated External Defibrillator

Of the 162 patients rescued by bystanders 44 (27.1%) had a shockable rhythm and 87 (53.7%) had a non-shockable rhythm, while in the remaining 31 (19.2%) the pace was unknown.

Regarding the 374 patients not rescued by bystanders a shockable rhythm was documented in 56 (14.9%), whereas in 225 (60.2%) the rhythm was non shockable; in the remaining 93 (24.9%) the pace was not detected.

Discussion

Worldwide survival after SCA remains poor despite 50 years of continuing efforts to spread the CPR maneuvers to large proportions of population (10,13-16).

The concept of the Chain of Survival introduced in 1992 has maintained his validity. Prompt EMS service activation, early beginning of CPR and early defibrillation are of paramount importance to improve survival.

Our regional EMS service in Lombardy Region has striven to improve the response to SCA situations not only through a wide training campaign among the population, also through an improvement of the whole service in terms of implementation of rescue means on the territory, AED located in every emergency ambulance and a continuous rescuer re-training. We therefore aimed to measure the effects of both EMS effectiveness in the CPR setting and the effects of CPR intervention started by lay people.

According to the Utstein Style (11,12) we considered only presumed cardiac etiology.

The importance of the bystander-CPR is widely recognized (17). We could confirm their relevance as almost 33% of patients had a ROSC, in contrast to the 22% who had ROSC when the first intervention was performed only after EMS arrival. Results are coherent with the widely recognized importance of early CPR.

Among the 107 patients who had a sustained ROSC on the spot, almost 90% were successfully admitted to the ED and more than 80% were then admitted to the ward (either ICU or CCU) in almost all instances. Only half of the patients admitted to the ward were successfully discharged at home, 63% of whom had a CPC of 1-2. These data support the concept that an early onset of CPR is of paramount importance to promote not only a cardiac restoration but also an intact neurological function. To achieve this goal our regional dispatch centers are instructing every person who witnesses a SCA to start chest compressions, guided by the dispatch operators.

A shockable rhythm was found in 19% of the cases. This proportion is consistent with an increasing evidence that ventricular fibrillation is no longer the most frequent rhythm detected in SCA patients, in part explained by the progression of SCA in which a Ventricular fibrillation (VF) rhythm evolves toward an asystole within few minutes. This fact would be supported by the time elapsed in defibrillating and non-defibrillating rhythms (18), in which the higher proportion of non-defibrillating rhythms was observed in the group of patients who had a longer (although non-significant) time interval until the EMS arrival. On the other hand, the changes in the epidemiology of ventricular fibrillation may be accounted by the interventions on myocardial ischemia which are likely to have reduced the proportion of ischemic events, as reported in a previous publication (9).

This fact would be coherent with the observations of other several studies who consistently reported a diminished proportion of VF in their studies on SCA (8,19-22).

In the present survey we could realize that only 7 witnesses were able to use a public AED thus accounting for a very low proportion of public AED use. Our data are consistent with other studies in which the use of a public AED is very limited since it accounts for a proportion of 2.2% of people defibrillated with a public AED. The limited number of our observations does not allow us to draw conclusions although it is evident that where the public AED were used early survival was much higher raising up to 65% (4-7).

We also decided to investigate possible effects of the season on survival, not finding any evidence in the literature. Our data however did not allow us to identify specific relationships between the SCA event and the season.

Anyway, this study has some evident limitations.

First of all, it was limited to short distinct time

periods unlike the majority of the investigations which report longer periods of observation (10,13,14). However, the proportion of cases approximates the prevalence of SCA in other studies.

Secondly the quality of CPR by the witnesses could not be assessed. Nevertheless, it is likely that these maneuvers, although imprecise, may have determined some cardiac perfusion as the proportion of ROSC in this group of patients was significantly higher than those that not experienced bystander CPR.

It is widely recognized that telephone CPR instructions are associated with an increased rate of successful outcome (23,24). A study by Sutter and coworkers conducted in USA among more than 5600 Public Safety Answering Points (PSAPs), to identify those who provide telephone CPR (T-CPR) instructions, highlighted that nearly half of the nation's PSAP does not provide T-CPR and very few provide compression-only instructions. Despite the number of PSAP involved, there are no data to ascertain whether T-CPR was associated with an increased proportion of successful outcome (25).

Another limitation is related to the proportion of unknown rhythms even when a defibrillator was used. Despite the improvement in data collection, this result implies that data recording is as yet suboptimal and therefore a progressive sensitization of the personnel is necessary. This is indeed an area of improvement for our EMS personnel.

Conclusions

We suggest that short time periods of data acquisition for cardiac arrest patients may be useful to extrapolate data for the entire cardiac arrest population. The feasibility of a sample analysis is a strength that should be highlighted and applied to our advantage. These data can be useful for monitoring the events and further develop new strategies to improve their management. The ultimate goal in the study design, however, is to accomplish the requirements of the registries with full recording of all cardiac arrest data together with a close collaboration with those who work in the hospital setting to obtain the follow-up after hospital admission.

Our data support the importance of an early as possible treatment by lay people who witness a cardiac arrest and are consistent with the concept that all emergency services should provide CPR instructions for every citizen who activate the EMS in the suspect of a cardiac arrest.

Despite discussion's limitations, we emphasize the importance of an early treatment as possible by lay people who witness a SCA. Yet our data are consistent with the concept that all emergency service should provide CPR instructions for every citizen who activate the Emergency Medical Service in the suspect of a SCA.

Besides that, these data further investigation should verify the time interval from the arrest to the EMS arrival to clarify how long interval could be useful to have ROSC and a sustained ROSC in the patient resuscitated by lay people using CPR instructions.

Acknowledgements

The Authors gratefully acknowledge the precious support and the data provided by the Directors of Lombardy provincial EMS and Information Communication Technology Service (ICT) of AREU.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Received: 15 June 2019
Accepted: 18 July 2019
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Acta Biomed 2019; Vol. 90, Supplement 9: 71-75 DOI: 10.23750/abm.v90i9-S.8704

Knowledge, attitudes, and practices of General Practitioners from the Province of Parma (Northern Italy) towards vaccinations in adults ≥65 year-old

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Summary. *Backgrounds and aims:* This study aims to characterize attitudes and knowledge towards immunization practice of people aged >65 years for seasonal influenza (SIV), pneumococcus (PNV), and Herpes zoster (ZV) in a sample of Italian general practitioners (GPs). *Materials and Methods:* During 10/2018, a structured questionnaire was emailed to 274 GPs operating in the Province of Parma, Italy. Association between willingness to perform aforementioned vaccines and individual factors was assessed through a multivariate regression analysis by calculating multivariate Odds Ratio (mOR). *Results:* A total of 73 GPs (26.6% of original sample) completed the questionnaire. Knowledge gaps were identified on the targeted vaccination rates for PNV and ZV (31.6% and 21.9% of correct answers), on the formulation of VZ (41.1%), and on the simultaneous immunization SIV/ZV (12.3%). The majority of respondents had high/very high trust on safety and efficacy of assessed vaccines. In multivariate analysis, recommending PNV was associated with having previously received SIV (mOR 5.44, 95%CI 1.08-27.31). In turn, ZV was negatively associated with a self-assessed knowledge gap (mOR 0.07, 95%CI 0.01-0.63). *Discussion:* Despite a generally favorable attitude towards vaccines, GPs exhibited knowledge gaps deserving appropriate intervention. However, lack of association between knowledge status and willingness to vaccinate enlighten the complex interplay between attitudes and personal behaviors. (www.actabiomedica.it)

Key words: healthcare workers, immunization, elderly infections, general practitioner, vaccination recommendation, vaccine hesitancy

Introduction

The National Immunization Program 2017-2019 specifically recommends Seasonal Influenza Vaccine (SIV), Pneumococcus vaccines (PNV), and Zoster-Vaccine (ZV) in people older than 65 years (1,2). The aim of the present study was to evaluate knowledge, attitudes and practices (KAP) among a sample of Italian general practitioners (GPs) towards SIV, PNV and ZV.

Materials and Methods

An anonymous online survey was administered to all 274 GPs from the province of Parma (449,191 inhabitants) during October 2018. All recipients received by email two reminds at day +10 and day +20. The questionnaire was specifically designed, including a total of 26 structured items from similar studies (2-6), and retrieved following information: demographic data; knowledge of official recommendations for SIV,

PNV and ZV; specific attitudes towards aforementioned vaccinations; whether participant had or not received SIV; whether participant had or not performed SIV, PNV and ZV in assisted patients; previous interactions with severe cases of seasonal influenza, pneumococcal infections, zoster infections. Having recommended SIV, PNV and ZV was the outcome variable, whose association with individual factors was initially assessed through univariate analysis (i.e. chi squared test). All factors associated with a proactive status with a p value <0.250 were included in three logistic regression models, calculating correspondent multivariate Odds Ratios (mOR).

Results

A total of 73 GPs completed the questionnaire (response rate 26.6%). As shown in Table 1, the majority of them were males (67.1%), with a mean age of 58.1±9 years, and a mean seniority of 30.4±9.4 years. Participants assisted a mean of 1446 patients (actual range 400 to 1800), with a share of subjects aged ≥ 65 equals to 39.2%±13.2 (actual range, 18 to 80%). Significant uncertainties were reported on the targeted vaccination rates for SIV (i.e. 75% of all at risk groups; 32.9% of correct answers), PNV (i.e. 55%, 31.6% of correct answers), and ZV (i.e. 20%, 21.9% of correct answers) as well as on the actual composition of VZ (41.1%). Similarly, only 12.3% of participants correctly reported the possible simultaneous immunization with SIV and ZV. The majority of respondents had high or very trust on safety (possible range 1 to 10; actual scores: 9.1±1.1, 8.8±1.6, and 8.2±1.6 for SIV, PNV, and ZV respectively) and efficacy (i.e. 8.9±1.0, 8.8±1.1, 8.0±1.0) of assessed vaccines. Severe cases of seasonal influenza were reported by 75.3% of participants, while pneumococcal infections and zoster cases were reported by 32.9% and 26.0%, respectively.

SIV was reportedly recommended by 98.6% of participants, and 60.3% had received SIV in the previous winter season, whereas PNV recommendations were reported by 84.9%, and ZV by 65.6%. While 98.6% and 93.3% had performed SIV and PNV among their patients, none of them had previously vaccinated any patient for ZV (this vaccine was administered only by doctors of the local health unit), but 95.9% planned to vaccine against zoster in the future.

Among the reasons for avoiding vaccine recommendations, the most frequently reported was the lack of information (5/11, 45.5% for PNV and 19/25, 76.0% for VZ), followed by doubts on the vaccine efficacy (27.3% and 12.0% for PNV and VZ, respectively).

In the multivariate analysis, recommending PNV was associated with having previously received SIV (mOR 5.44, 95%CI 1.08-27.31), and a proactive attitude for VZ (mOR 13.67 95%CI 2.41-77.64), while ZV was positively associated with familiarity with zoster cases (mOR 6.61, 95%CI 1.11-44.43), and recommending PNV (mOR 19.36, 95%CI 2.60-139.61), while it was negatively associated with a self-reported knowledge gap of the respondent (mOR 0.07, 95%CI 0.01-0.63).

Discussion and conclusions

In conclusion, we identified a generally positive attitude towards SIV, PNV and ZV, that was associated with significant knowledge gaps, particularly on the targeted vaccination rates (1,2). Similar uncertainties were reported for the actual composition of ZV: as such vaccine is based on a live but weakened strain of Varicella Zoster Virus, ignoring its formulation may elicit misbeliefs on its actual recommendations (i.e. history of neoplasia, high-dose steroidal therapy, immunodeficiency etc.) (7,8). Similarly, the lack of information on simultaneous SIV and PNV immunization may improperly inflate patients' interactions with Vaccination Services, with eventual unnecessary costs and discomforts for the recipients (9,10).

Our survey is one of the first Italian studies about this topic and, despite the small sample size, can have a potential interest for several reasons. Firstly, there is a significant lack of evidence on the KAP towards vaccinations in the elderly (2,6,9,11–13). Second, our results confirm that in some Healthcare Workers, the attitude towards vaccinations results from a complex interplay of individual and educational factors, not fully included in the Health Belief Model (3,14,15). However, our results are limitedly generalizable because of the characteristics of the sample. Moreover,

Table 1. Characteristics of 73 General Practitioners (GPs) from the Province of Parma participating to our survey (2018) (Notes: SIV = seasonal influenza vaccine; PNV = pneumococcal vaccines; ZV = Zoster Vaccine)

Variable	No., %	Mean ± S.D.
Gender		
Male	49, 67.1%	
Female	24, 32.9%	
Age (years)		58.1 ± 9.0
Seniority (years)		30.4 ± 9.4
No. of assisted patients*		1445.6 ± 309.2
Share of patients ≥ 65 year-old		39.2 ± 13.2
Working settings		
Private practitioner	27, 37.0%	
Group of associated GPs	27, 37.0%	
Community Healthcare Center	19, 26.0%	
Knowledge test (No. of correct answers)		
Subjects ≥ 65 year-old should receive trivalent / quadrivalent formulations of SIV	69, 94.5%	
Minimal SIV rates should be 75% among subjects ≥ 65 year-old	24, 32.9%	
Subjects ≥ 65 year-old should firstly receive PCV13 and then PPSV23	57, 78.1%	
Targeted 2018 PNV rate in subjects ≥ 65 year-old is ≥ 55%	23, 31.6%	
Simultaneous administration of SIV and PNV is officially recommended	54, 72.6%	
ZV contains a live but weakened strain of Varicella Zoster Virus	30, 41.1%	
Targeted 2018 ZV rate in subjects ≥ 65 year-old is ≥ 20%	16, 21.9%	
Simultaneous administration of SIV and ZV is possible	9, 12.3%	
ZV is recommended also in subjects naïve for varicella infection	55, 75.3%	
ZV is recommended also in subjects reporting previous zoster	57, 78.0%	
Perceived safety of … (range 1 to 10)		
SIV		9.1 ± 1.1
PNV		8.8 ± 1.6
ZV		8.2 ± 1.6
Perceived efficacy of … (range 1 to 10)		
SIV		8.9 ± 1.0
PNV		8.8 ± 1.1
ZV		8.0 ± 1.5
Reported familiarity with cases of …		
Seasonal influenza	35, 75.3%	
Pneumococcal infections	24, 32.9%	
Herpes zoster	19, 26.0%	
Proactive attitude in patients towards …		
SIV	72, 98.6%	
PNV	62, 84.9%	
ZV	48, 65.6%	
Reasons for hesitating towards SIV recommendation (No. = 1)**		
Patient-specific	1, 100%	
Reasons for hesitating towards PNV recommendation (No. = 11)**		
Lack of information on the vaccine	5, 45.5%	
Doubts on the vaccine efficacy	3, 27.3%	
Patient-specific	1, 9.1%	
Increasing risk for disorders associated with strains not included in the vaccine	1, 9.1%	
GPs can perform PNV only since 2017 (i.e. lack of opportunity)	1, 9.1%	
Unspecified	*1, 9.1%*	

(continued)

Table 1 ***(continued)*****.** Characteristics of 73 General Practitioners (GPs) from the Province of Parma participating to our survey (2018) (Notes: SIV = seasonal influenza vaccine; PNV = pneumococcal vaccines; ZV = Zoster Vaccine)

Variable	No., %	Mean ± S.D.
Reasons for hesitating towards ZV recommendation (No. = 25)**		
Lack of information on the vaccine	19, 76.0%	
Doubts on the vaccine efficacy	3, 12.0%	
Herpes Zoster is a not severe disorder	3, 12.0%	
Doubts on the actual length of vaccine efficacy	2, 8.0%	
At the moment ZV is offered only to subjects born in 1953 (i.e. lack of opportunity)	1, 4.0%	
Unspecified	1, 4.0%	
Practices of SIV, PNV and ZV		
SIV received during previous influenza season	44, 60.3%	
SIV performed in assisted patients	72, 98.6%	
SIV not performed in assisted patients but willingness to perform it	1, 1.4%	
SIV not performed in assisted patients and unwillingness to perform it	0, -	
PNV performed in assisted patients	68, 93.2%	
PNV not performed in assisted patients but willingness to perform it	5, 6.8%	
PNV not performed in assisted patients and unwillingness to perform it	0, -	
ZV performed in assisted patients	0, -	
ZV not performed in assisted patients but willingness to perform it	70, 95.9%	
ZV not performed in assisted patients and unwillingness to perform it	3, 4.1%	

* self-reported
** more answers allowed

the share of assisted 65 year-old patients was nearly double that that reported by other studies, potentially inflating the number of respondents who had interaction with severe cases of assessed disorders (10,16). In conclusions, the commitment of public health authorities will require specifically targeted interventions that should stress the role of SIV, PNV and ZV in avoiding more severe clinical cases.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

Funding: This study is part of a research project supported by the Cariparma Foundation (N 2015.0094)

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Received: 15 June 2019
Accepted: 18 July 2019
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Acta Biomed 2019; Vol. 90, Supplement 9: 76-86 DOI: 10.23750/abm.v90i9-S.8164

Ricerca e formazione sul Risk Management in Italia

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Risk Management in healthcare: results from a national-level survey and scientometric analysis in Italy

Summary. Risk management in healthcare, intended as all processes employed to detect, monitor, assess, mitigate, and prevent risks in healthcare facilities and safeguard patient safety, is a crucial component of Italy' National Health Service. Aim of the current study is to assess the role and progress of research and training, in the field of Risk Management. We carried out a scientometric analysis to quantify and describe scientific outputs on Risk Management at the global and national level, over the last forty years; in addiction, we conducted a national-level cross-sectional survey to systematically retrieve and assess research and training activities within Italian postgraduate medical programmes in Hygiene and Preventive Medicine. We report increasing scientific production on Risk Management-related topics from 1980 to 2017 at the global level (12% annual increase rate). Clinical Trials and Systematic reviews/meta-analysis make up for respectively 5% and 6% of global scientific output. Italy ranks 4th for scientific production, after USA, UK and Germany. 88% of Italian postgraduate medical programmes in Hygiene and Preventive medicine research on Risk Management, 42% through international collaborations. The main research themes are Healthcare-Associated Infections (HAIs) (97%), analysis of organizational models for safety in healthcare (62%), while training is focused on internships (87%) and academic lectures (73%). While *research* provides the evidence required to plan, implement and monitor effective interventions in healthcare risk management, *training* allows its dissemination in a synergic action to promote the value of patient safety and quality of care. (www.actabiomedica.it)

Key words: Risk Management in healthcare, Research, Training, Italy

Riassunto. *Introduzione:* La gestione del Rischio Clinico (Risk Management) è un tema di cruciale importanza ed attualità in Italia, alla luce dei più recenti assetti nomativi e piani programmatici. Obiettivo del presente lavoro è analizzare il ruolo della ricerca e della formazione a supporto del Risk Management. *Materiali e Metodi:* Abbiamo condotto un'analisi scientometrica per quantificare e descrivere la produzione scientifica globale sui temi del Risk Management negli ultimi quarant'anni, completata da un'analisi cross-sectional estesa a tutte le Scuole di Specializzazione in Igiene e Medicina Preventiva italiane per mappare, in maniera sistematica, le attività di formazione e ricerca in corso in Italia. *Risultati:* La produzione scientifica globale sui temi del Risk Management è in progressivo aumento (12% di incremento annuo). I trials clinici e le revisioni sistematiche/metanalisi costituiscono il 5% e 6% del totale. L' Italia è al quarto posto per produzione scientifica dopo Stati Uniti, Regno Unito e Germania. L' 88% delle Scuole di Specializzazione conduce attività di ricerca sui temi del Risk Management, di cui il 42% attraverso collaborazioni internazionali. I principali ambiti di ricerca sono le infezioni correlate all'assistenza (ICA) (97%) e lo studio di modelli organizzativi per la sicurezza delle cure (62%), mentre le principali modalità formative sono le attività di tirocinio (87%) e le

lezioni frontali (73%). *Discussione:* La *ricerca* fornisce le evidenze necessarie per la pianificazione, implementazione e monitoraggio di efficaci interventi di gestione del rischio clinico; in maniera sinergica, la *formazione* consente di diffonderne i contenuti e le metodologie, al fine di creare la cultura della sicurezza delle cure tra le diverse figure professionali coinvolte.

Parole chiave: Risk Management, Ricerca, Formazione

Introduzione

La gestione del Rischio Clinico (Risk Management) – dove per rischio clinico si intende la probabilità che un paziente subisca un qualsiasi "danno o disagio imputabile, anche se in modo involontario, alle cure mediche prestate durante il periodo di degenza, che causa un prolungamento della durata del ricovero, un peggioramento delle condizioni di salute o la morte" (1,2) - è tema di cruciale importanza ed attualità (3). Questa definizione fu enunciata per la prima volta nel 1999 dall' Institute Of Medicine (IOM) americano, nella pubblicazione *"To err is human. Building a safer healthcare system*", pietra miliare nella cultura della sicurezza delle cure, che gettò luce sulla rilevanza del problema, quantificando nel 50% la percentuale di eventi avversi conseguenza di errori medici prevenibili (vedi Box I) in America e in 98.000 i decessi annui conseguenti a errore medico (2,4,5). Già vent'anni fa le raccomandazioni dell'Institute Of Medicine ponevano l'accento sulla necessità di individuare e monitorare indicatori di sicurezza e di promuovere progetti di miglioramento della qualità dell'assistenza nelle strutture sanitarie (1).

In una recente pubblicazione, l'OCSE ha rilevato come il 17% delle ospedalizzazioni sia caratterizzato da uno o più eventi avversi, di cui il 30-70% potenzialmente prevenibile con adeguati sistemi per la sicurezza del paziente, con conseguente riduzione delle giornate di degenza nell' ordine di centinaia di migliaia (6). Lo studio ha altresì quantificato gli eventi avversi prevenibili come costi prevenibili, stimati attorno al 2-10% della spesa degli ospedali pubblici (6).

Il presente lavoro raccoglie i contributi originali presentati durante la sessione plenaria *"Il Risk Management nelle strutture sanitarie: una nuova frontiera per la Sanità Pubblica"* del 51° Congresso Nazionale della Società Italiana di Igiene, Medicina Preventiva e Sanità Pubblica (SItI), con l' obiettivo di inquadrare il tema della sicurezza delle cure e gestione del rischio clinico in Italia, alla luce dei più recenti assetti nomativi e piani programmatici, nonché di analizzare il ruolo della ricerca e della formazione a supporto del Risk Management.

E' interessante osservare come nel 2005 il programma enunciato dal documento WHO *"World Alliance for patient safety*" dedichi un capitolo all'aspetto della formazione e dell'apprendimento in tema di miglioramento della sicurezza del paziente (7). Apprendere dagli errori significa osservare, registrare le osservazioni, analizzarle e imparare dagli eventi avversi avvenuti o mancati; rendere oggetto di riflessione e di apprendimento gli eventi che potrebbero compromet-

Box I – Tipologie di errori: definizioni

Nell'ambito del Risk Management, viene utilizzata una terminologia specifica, poiché ciascun tipo di evento viene opportunamente inquadrato e definito sulla base delle cause e delle conseguenze ad esso correlate:

L'evento evitato *(Near miss o close call) è un errore che ha la potenzialità di causare un evento avverso che non si verifica per caso fortuito o perché intercettato in quanto non ha conseguenze avverse per il paziente (12).*

L'evento sentinella *(Sentinel event) è un evento avverso di particolare gravità, potenzialmente indicativo di un serio malfunzionamento del sistema, che può comportare morte o grave danno al paziente e che determina una perdita di fiducia dei cittadini nei confronti del servizio sanitario. Per la loro gravità, è sufficiente che si verifichi una sola volta perché da parte dell'organizzazione si renda opportuna a) un'indagine immediata per accertare quali fattori eliminabili o riducibili lo abbiamo causato o vi abbiano contribuito e b) la conseguente implementazione delle adeguate misure correttive (12).*

L'evento avverso *è definito come un "evento inatteso correlato al processo assistenziale e che comporta un danno al paziente, non intenzionale e indesiderabile". Gli eventi avversi possono essere prevenibili o non prevenibili. Un evento avverso attribuibile ad errore è "un evento avverso prevenibile" (12).*

tere la sicurezza degli operatori e dei pazienti è considerato un modo efficace anche di ricerca delle soluzioni.

In Italia, dal punto di vista normativo, si può osservare un percorso che presenta degli snodi cruciali: il Decreto del Ministro della Salute 10 Gennaio 2007, attiva il Sistema nazionale di riferimento per la sicurezza dei pazienti; il 20 Marzo 2008 viene sottoscritta l'Intesa tra il Governo, le Regioni e le Province Autonome concernente la gestione del rischio clinico e la sicurezza dei pazienti e delle cure, nella quale si sancisce l'impegno a promuovere il monitoraggio e l'analisi degli Eventi Avversi (vedi Box I) e l'implementazione di buone pratiche per la sicurezza. Riguardo a quest'ultima attività, Agenas ha avviato nel 2008 le attività dell'Osservatorio delle Buone Pratiche per la Sicurezza dei Pazienti: attraverso un sistema web di rilevazione delle esperienze di miglioramento della sicurezza dei pazienti, vengono annualmente raccolte, e rese disponibili ai professionisti, ai cittadini e ai diversi stakeholder, una molteplicità di pratiche realizzate dalle organizzazioni sanitarie.

Rispetto alla rilevazione degli eventi avversi, con il Decreto 11 Dicembre 2009 il Ministero del Lavoro, della Salute e delle Politiche Sociali istituisce il Sistema Informativo per il Monitoraggio degli Errori in Sanità (SIMES), con lo scopo di rilevare informazioni relative agli Eventi Sentinella (vedi Box I), cioè quegli eventi di particolare gravità indicativi di un serio malfunzionamento del sistema sanitario, e rilevare altresì informazioni relative alle denunce dei sinistri, in modo da determinare anche il rischio assicurativo. Nell'ambito delle metodologie e degli strumenti del governo clinico, il Ministero della Salute, fin dal 2005, si è impegnato nella stesura e diffusione di "Raccomandazioni" finalizzate proprio alla prevenzione degli eventi sentinella; ad oggi sono state pubblicate dal Ministero diciotto raccomandazioni.

Anche il livello regionale ha svolto un ruolo importante nelle politiche e nelle azioni sulla sicurezza delle cure, attraverso un proprio coordinamento, oggi rappresentato da una Sub Area dell'Assistenza Ospedaliera nel contesto della Commissione Salute della Conferenza delle Regioni e Province Autonome. L'obiettivo del coordinamento è quello di promuovere le politiche sanitarie per la sicurezza delle cure e favorire lo sviluppo della cultura della sicurezza nei diversi contesti regionali e nelle aziende sanitarie.

A dieci anni dal primo decreto del Gennaio 2007, è stata infine emanata una norma che affronta in maniera articolata e complessiva il tema: la Legge 8 marzo 2017, n. 24 *"Disposizioni in materia di sicurezza delle cure e della persona assistita, nonché in materia di responsabilità professionale degli esercenti le professioni sanitarie"*, che all'articolo 1 sancisce che la sicurezza delle cure è parte costitutiva del diritto alla salute e che tutto il personale deve concorrere al soddisfacimento di questo diritto attraverso le attività di prevenzione. La legge prevede inoltre che le strutture pubbliche e private che erogano prestazioni sanitarie predispongano una relazione annuale consuntiva sugli eventi avversi verificatisi all'interno della struttura, sulle cause che hanno prodotto l'evento avverso e sulle conseguenti iniziative messe in atto. Anche le regioni sono chiamate ad un ulteriore livello di responsabilità attraverso l'istituzione in ciascuna di esse di un Centro per la gestione del rischio sanitario e la sicurezza del paziente, che ha come compito basilare quello di raccogliere dalle strutture sanitarie e sociosanitarie pubbliche e private i dati regionali sui rischi, sugli eventi avversi e sul contenzioso e di trasmetterli annualmente all'Osservatorio nazionale delle buone pratiche sulla sicurezza nella sanità. Come evidenziato dal decreto attuativo del 29 Settembre 2017, che istituisce l'Osservatorio, quanto contemplato dalla norma amplia lo scenario, andando ben oltre il tema della rilevazione dei soli "eventi avversi", per richiamare quello della misurazione della sicurezza delle cure e delle relative fonti informative da cui attingere le informazioni.

Un altro importante tema affrontato dalla norma è quello delle competenze che devono possedere i soggetti che sono chiamati a svolgere il coordinamento delle attività di gestione del rischio sanitario: la legge 24/2017, all'articolo 16, precisa che tale attività di coordinamento deve essere svolta da personale medico dotato delle specializzazioni in Igiene, Epidemiologia e Sanità pubblica o equipollenti, in Medicina Legale, ovvero da personale dipendente con adeguata formazione e comprovata esperienza almeno triennale nel settore.

È altresì vero che il processo formativo in tema di sicurezza del paziente non può prescindere dalle conoscenze di base nei Corsi di Laurea di Medicina e Chirurgia e nelle Lauree delle professioni sanitarie; lo

studente, nelle attività di tirocinio, si avvicina all'attività assistenziale e necessita di una conoscenza della possibilità di errore, del suo riconoscimento, dell'utilità di una risposta preventiva efficace. A maggior ragione, la formazione specialistica medica e chirurgica richiede attenzione formativa, approfondita e specifica.

In realtà la lettura del D.L. n. 402/2017, recante la definizione degli standard, dei requisiti e degli indicatori di attività formativa e assistenziale delle Scuole di specializzazione di area sanitaria ai sensi dell'art. 3, comma 3, del D.I. n. 68/2015, all'Allegato 2 (Requisiti minimi generali e specifici di idoneità della rete formativa), ha evidenziato attenzione al problema della formazione in tema di governo clinico e di gestione del rischio solo per le specializzazioni in Pediatria, Anestesia, Rianimazione e Terapia Intensiva e del Dolore, Igiene e Medicina Preventiva e Medicina Legale.

Il documento *"WHO Patient Safety Curriculum Guide for Medical Schools"* (8), che ha avuto successive traduzioni in lingua francese (9) e in lingua italiana (10), e la sintesi elaborata a Firenze nel 2016 (11), sottolineano diversi aspetti della formazione in ambito sanitario: apprendere dagli errori, riconoscere e comunicare gli eventi avversi, comunicare in modo efficace con il coinvolgimento di pazienti e caregiver, fare formazione basata sulle evidenze di efficacia.

In questo contesto ben si evince come, rispettivamente, ricerca e formazione siano strumenti essenziali, imprescindibili, a supporto di ogni fase, operativa e programmatica di gestione del rischio clinico. Infatti, se da un lato la *ricerca* fornisce le evidenze necessarie per la pianificazione, implementazione e monitoraggio di interventi efficaci, dall'altro, e in maniera sinergica, la *formazione* consente di diffonderne i contenuti e le metodologie, al fine di creare la cultura della sicurezza delle cure tra le diverse figure professionali coinvolte.

Materiali e Metodi

La ricerca originale condotta per il presente studio si è articolata in due parti:

- Un'analisi scientometrica, con l'obiettivo di quantificare e descrivere la produzione scientifica sui temi del Risk Management negli ultimi quarant'anni, a livello globale e in Italia.
- Un'analisi cross-sectional estesa a tutte le Scuole di Specializzazione in Igiene e Medicina Preventiva italiane con l'obiettivo di mappare, in maniera sistematica le attività di Formazione e Ricerca sui temi del Risk Management condotte sul territorio nazionale.

Analisi scientometrica

La banca dati bibliografica Medline è stata interrogata al fine di individuare la produzione scientifica sul tema del Risk Management pubblicata tra il 1980 e il 2018 (aggiornamento al 11.10.2018). In particolare, la strategia di ricerca è stata condotta utilizzando i termini Mesh: *Risk Management, Patient Safety, Risk Assessment, Safety Management e Accident Prevention* (vedi Box II). Le risultanze della ricerca sono state analizzate: nel tempo (trend temporali), nello spazio (per Paese), nonché descrivendone la distribuzione: per rivista, per argomento, per disegno di studio (sperimentale vs. osservazionale), e per figura professionale coinvolta. Nel dettaglio, la ricerca è stata condotta partendo dall'impostazione della stringa di ricerca del termine Mesh (ad esempio, "risk assessment[MeSH Terms]") considerando la produzione scientifica suddivisa per ciascun anno analizzato mediante l'applicazione

Box II – Definizioni dei termini MeSH utilizzati nell'analisi scientometrica. Fonte: PubMed

Risk Management: *Processo di minimizzazione del rischio di un'organizzazione mediante lo sviluppo di sistemi per identificare ed analizzare i rischi potenziali, per prevenire incidenti, danni o altri eventi avversi, con l'obiettivo di gestire e ridurre eventi o incidenti che hanno un impatto sui costi.*

Patient Safety: *Sforzi per ridurre il rischio, affrontare e ridurre gli incidenti che possono impattare negativamente sulla salute.*

Risk Assessment: *La stima quantitativa o qualitativa della probabilità di eventi avversi che possono derivare dall'esposizione a specifici rischi per la salute o dall'assenza di benefici.*

Safety Management: *Lo sviluppo di sistemi per prevenire incidenti, infortuni o altri eventi avversi in un setting istituzionale. Il concetto include la prevenzione e la riduzione di eventi avversi o incidenti che coinvolgono dipendenti, pazienti o strutture. Alcuni esempi includono piani per ridurre le lesioni da cadute o piani per la sicurezza antincendio per promuovere un ambiente istituzionale sicuro.*

Accident Prevention: *Sforzi e progetti per ridurre l'incidenza di eventi indesiderati ed imprevisti in vari ambienti e situazioni.*

dell'apposito filtro in PubMed. Successivamente è stato applicato il filtro per categoria di rivista scientifica considerata (Core Clinical Journals, Dental Journals e Nursing Journals) ed in seguito per disegno di studio (con focus sui Trials clinici e sulle Revisioni Sistematiche); infine è stata anche valutata la distribuzione della produzione scientifica relativa a ciascun termine Mesh nei Paesi europei e negli Stati Uniti (USA), impostando una stringa di ricerca composta da entrambe i componenti (ad esempio "risk assessment[MeSH Terms] AND Austria[Affiliation]").

Analisi cross-sectional

Un questionario rivolto ai Direttori delle 35 Scuole di Specializzazione in Igiene e Medicina Preventiva è stato elaborato *ad hoc*, sulla base di ricerche di letteratura e consulto con esperti di settore attraverso numerose revisioni e discussioni sulle tematiche da approfondire (il questionario è disponibile integralmente come materiale supplementare). Lo strumento indagava con domande sia aperte che a scelta multipla i seguenti aspetti: le attività di ricerca sui temi del Risk Management in corso nelle diverse sedi accademiche, con focus sugli ambiti specifici e tematiche trasversali affrontati nei progetti di ricerca, le fonti e i flussi informativi a disposizione nei diversi centri, le collaborazioni con gli enti territoriali, con altre sedi accademiche, nonché le collaborazioni internazionali, ed infine la presenza di un modulo di insegnamento sul Risk Management e la modalità di svolgimento dell'attività formativa nel contesto della Scuola di Specializzazione.

Lo strumento è stato pilotato da personale medico ed infermieristico per verificarne la coerenza di contenuto e il grado di comprensibilità e successivamente somministrato su piattaforma elettronica tra il 12.09.2018 e l'11.10.2018.

Risultati

Analisi scientometrica

La produzione scientifica globale sui temi del Risk Management è cresciuta in maniera esponenziale nel periodo di studio considerato, passando da 821 pubblicazioni del 1980 a 33.536 del 2017, con un trend annuale di crescita del 12% tra il 1980 e il 2015 (Figura 1).

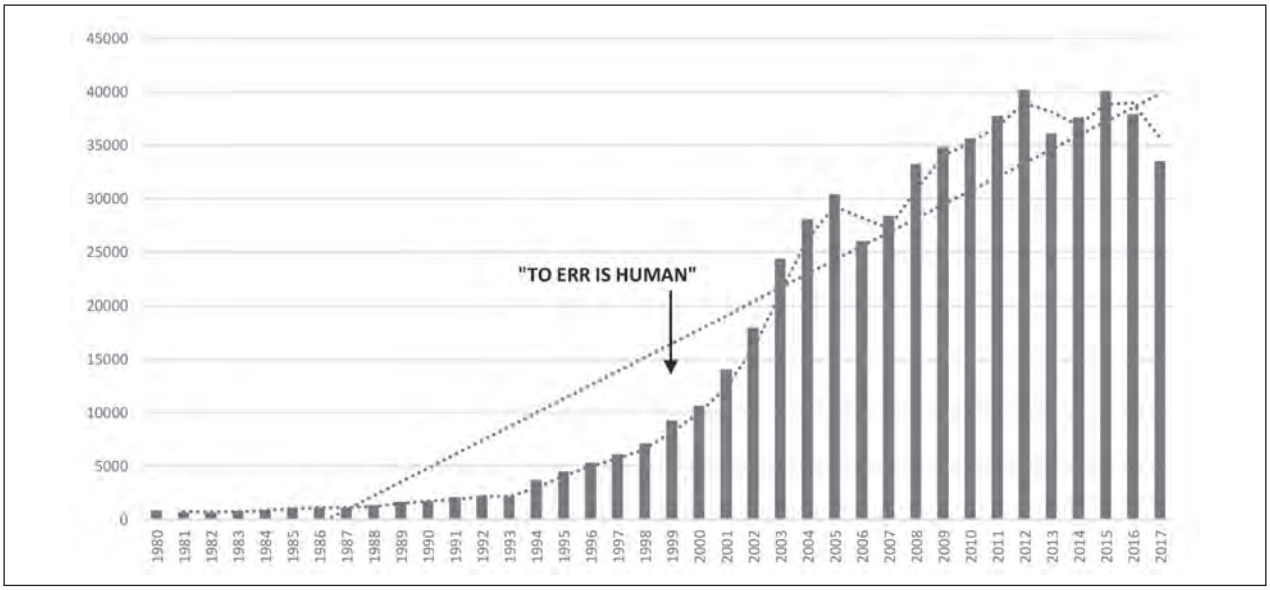

Figura 1. Totale Produzione scientifica (n. di articoli) sul tema della gestione del rischio clinico (1980-2017)
Fonte: Pubmed, combinazione termini Mesh: Risk Management, Patient Safety, Risk Assessment, Safety Management e Accident Prevention (aggiornamento 11.10.2018)

La maggior parte della produzione scientifica è negli Stati Uniti, Paese in cui si concentra il 90% (n=162.099 articoli) del totale delle pubblicazioni mondiali nel periodo di studio considerato. In Europa, la distribuzione geografica della produzione vede il Regno Unito al primo posto con il 24.4% del totale delle pubblicazioni europee inerenti i cinque termini Mesh, seguito dalla Germania (12%) e dall'Italia (11.6%) (Figura 2). In Italia, in particolare, si osserva un aumento esponenziale della produzione scientifica nel tempo, con un tasso di crescita annuale tra il 1980 e il 2015 del 24% (materiale supplementare, Figura 1s), doppio rispetto al dato globale; con oltre 1000 pubblicazioni all'anno dal 2008 in poi.

La distribuzione degli articoli per i diversi termini Mesh è sovrapponibile nei diversi Paesi Europei, con netta prevalenza degli articoli sui temi del Risk Management e Risk Assessment, rispettivamente 46% e 43% sul totale della produzione, rispetto ai temi dell'Accident Prevention (8%) e Patient Safety (2%) (materiale supplementare, Figura 2s). Negli USA le proporzioni sono allineate ai Paesi europei (46% Risk Management, 40% Risk Assessment, 12% Accident Prevention e 2% Patient Safety), tuttavia, complessivamente, la produzione statunitense risulta essere circa quattro volte maggiore rispetto alla produzione britannica e più di sette volte maggiore rispetto a quella italiana e tedesca.

Sul totale della produzione scientifica, i trials clinici e le revisioni sistematiche/metanalisi costituiscono, rispettivamente il 6% il 5%, con un trend temporale netto in aumento per le revisioni sistematiche/metanalisi (per tutti i termini Mesh considerati), che passano dallo 0.35% della produzione totale nel decennio 1991-2000, al 7.66% dal 2011 in poi (Figura 3) e un aumento dei trials clinici a partire dagli anni '90, anni di particolare rilevanza nella sensibilizzazione ai temi del rischio clinico e dell'errore in sanità (Figura 3). Il termine Mesh associato ad una maggiore produzione di trials clinici risulta Accident Prevention (14.32% della produzione scientifica nel periodo 1991-2000, seguito dal 7.38% del periodo 2001-2010), mentre tra le revisioni sistematiche prevalgono i termini Risk Assessment (8.04% della produzione scientifica nel periodo 2011-2018), Patient Safety (7.90% nel periodo 2011-2018 e 7.26% nel periodo 2001-2010) e Risk

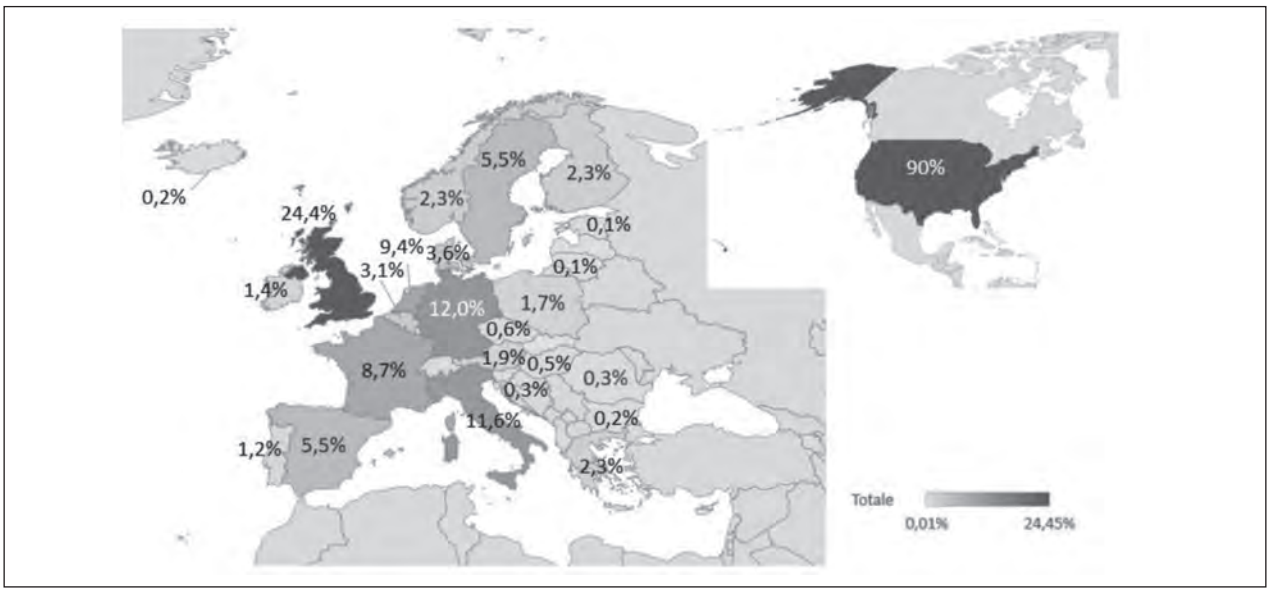

Figura 2. Distribuzione percentuale della produzione scientifica complessiva dei cinque termini Mesh nei Paesi europei sul totale della produzione europea. Gli Stati Uniti, da soli, rappresentano circa il 90% del totale della produzione globale.
Fonte: Pubmed, combinazione termini Mesh: Risk Management, Patient Safety, Risk Assessment, Safety Management e Accident Prevention (aggiornamento 11.10.2018).

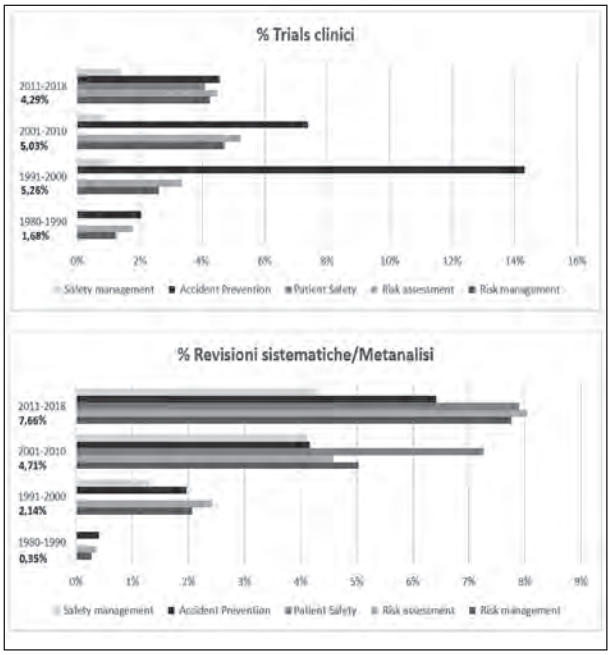

Figura 3. Distribuzione della Produzione scientifica, per tema, per decennio e per disegno di studio (% trials clinici e revisioni sistematiche/metanalisi sul totale della produzione scientifica)
Fonte: Pubmed, (aggiornamento 11.10.2018)

Management (7.76% nel periodo 2011-2018) (Figura 2).

Complessivamente, il 64% della produzione scientifica è pubblicata su riviste mediche, il 30% su riviste infermieristiche ed il 4% su riviste di interesse odontoiatrico. Nello specifico, i termini Mesh Risk Assessment e Risk Management includono articoli scientifici pubblicati prevalentemente su giornali di ambito medico (rispettivamente, 79% e 69%), al contrario dei Mesh Patient Safety, Accident Prevention e Safety Management, nettamente prevalenti in pubblicazioni su riviste infermieristiche (rispettivamente, 56%, 51% e 73%).

Analisi Cross-sectional

Trentaquattro Scuole su 35 hanno risposto al questionario (rispondenza 97%), di cui l'88% (29 Scuole su 33) ha dichiarato di svolgere attività di Ricerca su tematiche inerenti il Risk Management in ambito sanitario.

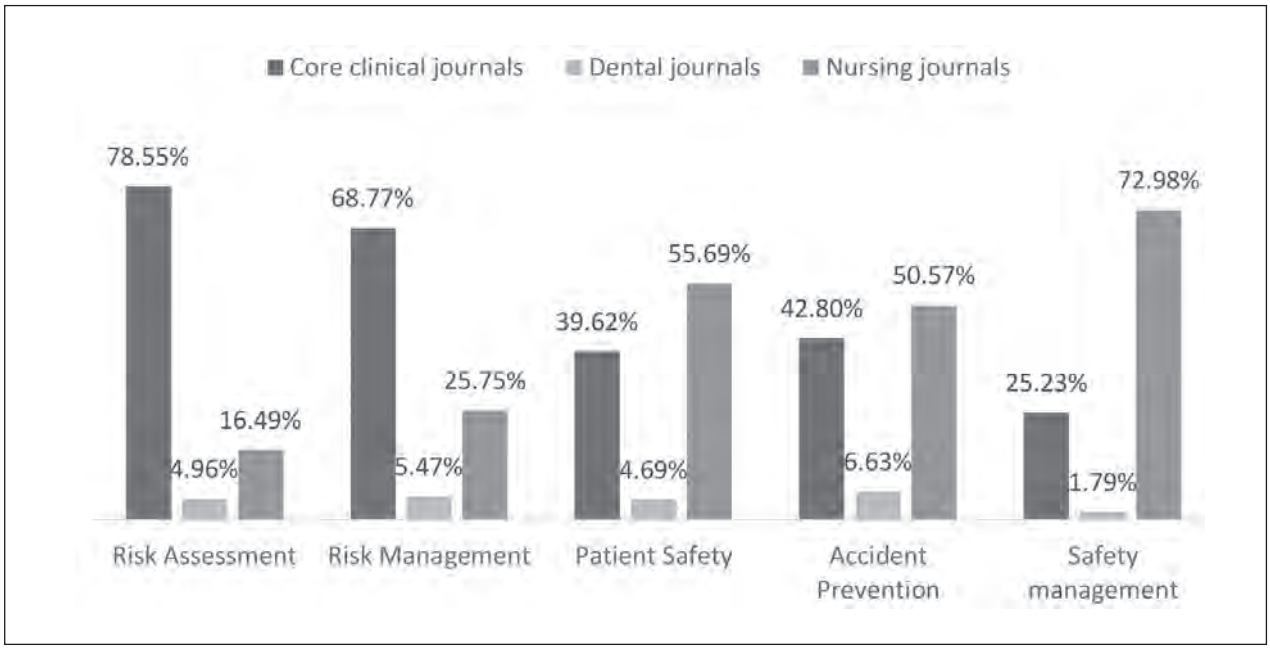

Figura 4. Distribuzione della Produzione scientifica dei termini Mesh Risk Management, Patient Safety, Risk Assessment, Safety Management e Accident Prevention, per categoria di giornale.
Fnte: Pubmed, (aggiornamento 11.10.2018)

Tabella 1. Ambiti specifici o temi trasversali su cui si concentra l'attività di ricerca sul Risk Management nelle sedi accademiche delle Scuole di Specializzazione in Igiene e Medicina Preventiva

Ambito di ricerca	%
Infezioni correlate all'assistenza (ICA)	97%
Occorrenza degli eventi avversi nelle strutture sanitarie	62%
Modelli organizzativi per la sicurezza delle cure	62%
Cadute	45%
Integrazione dei sistemi di sicurezza nelle organizzazioni sanitarie (pazienti, operatori, amministrativa)	41%
Errori di terapia/diagnosi/chirurgici	38%
Corretta identificazione del paziente	31%
Parto ed Area materno infantile	28%
Tecnologie informatiche ed informative per la sicurezza dei pazienti	28%
Sicurezza nella pratica trasfusionale	24%
Lesioni da pressione	21%
Coinvolgimento dei cittadini nel miglioramento della sicurezza	21%
Altro*	10%*

* Handover, Risk Assessment, Health Impact Assessment, Audit, M&M (rassegna di mortalità e morbilità), Indicatori di rischio clinico

La Tabella 1 riporta Ambiti specifici o temi trasversali su cui si concentra l'attività di ricerca sul Risk Management nelle sedi accademiche. Complessivamente, in tutte le sedi accademiche, il principale *ambito di ricerca* sono le infezioni correlate all'assistenza (ICA) (97%), seguite dallo studio degli eventi avversi nelle strutture sanitarie (62%), dei modelli organizzativi per la sicurezza delle cure (62%). Due specifiche aree di interesse sono il tema della sicurezza Materno-infantile (28%) e della pratica trasfusionale (24%). Altri temi di ricerca riguardano: le cadute (45%), i sistemi di sicurezza nelle organizzazioni sanitarie (41%), gli errori di terapia/diagnosi e chirurgici (38%), la corretta identificazione del paziente (31%), le tecnologie informatiche ed informative per la sicurezza del paziente e il coinvolgimento dei cittadini (21%).

La quasi totalità (97%) dei centri accademici dichiara di svolgere *attività di ricerca in collaborazione* con unità ospedaliere, il 45% con unità territoriali, il 55% con istituzioni regionali; solo il 3% ha dichiarato di non avere collaborazioni con enti esterni, ma di svolgere l'attività di Ricerca sul Risk Management solo in ambito accademico.

Le *Fonti/Flussi informativi* utilizzati comprendono: i monitoraggi aziendali trasversali (lesione da pressione, cadute, infezioni ecc…) per il 79% delle Scuole, i monitoraggi regionali/aziendali sugli indicatori derivati dalle SDO (64%), l'analisi dell'Incident Reporting (61%), il Report delle attività di audit interni ed esterni (57%), il monitoraggio dell'applicazione delle raccomandazioni ministeriali (54%), l'analisi delle richieste di risarcimento e dei reclami dell'Ufficio Relazioni con il Pubblico (URP) (36%).

Inoltre, il 46% delle Scuole dichiara di avere *collaborazioni di ricerca in Italia*, principalmente con istituzioni come l'Istituto Superiore di Sanità (ISS), l'Agenzia italiana del farmaco (AIFA), l'Agenzia nazionale per i servizi sanitari regionali (AGENAS), la Scuola Superiore Sant'Anna, altre sedi universitarie e con il Gruppo Italiano di Studio di Igiene Ospedaliera (GISIO). Il 42% delle sedi accademiche dichiara di avere *collaborazioni di ricerca all'estero*, incluse agenzie internazionali (Organizzazione Mondiale della Sanità-OMS, European Centre for Disease Prevention and Control-ECDC), Commissione Europea e altre sedi universitarie in Europa e negli Stati Uniti.

Sono state poste poche domande sulla *formazione* specifica svolta nelle Scuole di Specializzazione in Igiene e Medicina Preventiva; delle scuole rispondenti, il 90% dichiara di dedicare un insegnamento o un modulo di insegnamento al Risk Management; la formazione è sviluppata mediante lezioni frontali (73%), se-

minari (67%), attività di progettazione (47%), attività di tirocinio (87%) e simulazioni (3%).

Discussione

Il contributo originale del presente articolo analizza la produzione scientifica internazionale sul tema della gestione del Rischio Clinico e la sua declinazione nella realtà accademica italiana, contestualmente ad un approfondimento nel merito della formazione. Dall'analisi critica dei dati ottenuti risulta evidente su scala globale l'aumento esponenziale, negli ultimi vent'anni, della produzione scientifica sui temi del risk management in ambito sanitario, soprattutto negli Stati Uniti e nel Regno Unito. Seppur questo dato non possa essere disgiunto dall' aumento generale della produzione scientifica, gli elevati tassi di crescita annuali confermano con buona approssimazione il progressivo interesse della ricerca su questi temi. In particolare, a partire dalla fine degli anni '90 e dai primi anni 2000, la pubblicazione e successiva diffusione di "*To err is human*" (2) ha segnato profondamente la crescita della cultura dell'errore in ambito sanitario, proponendo un nuovo modello di gestione del rischio. Lo stesso documento sottolineava l'importanza dello sviluppo della ricerca per produrre evidenze e conoscenze sulla sicurezza delle cure (2); non a caso in questa decade si assiste un picco di pubblicazioni di studi sperimentali. Al contempo, la pubblicazione di revisioni sistematiche/metanalisi aumenta parallelamente all'affermarsi della cultura della medicina basata sulle evidenze (EBM). Appare inoltre interessante la distribuzione dei differenti termini Mesh tra le categorie di riviste scientifiche, a sottolineare come alcuni ambiti specifici siano stati sviluppati anche dalle scienze infermieristiche in contesti multidisciplinari, mentre altri rimangano tradizionalmente di pertinenza medica.

Da sottolineare il terzo posto dell'Italia tra i Paesi europei per produzione scientifica sul rischio clinico, davanti a Francia, Spagna e Paesi del Nord Europa. Questo dato ben si accorda con i risultati emersi dall'indagine sulle attività di formazione e ricerca nelle sedi accademiche italiane, che ha fornito un quadro complessivo aggiornato al 2018. A tal proposito, appare importante e degna di nota la numerosità delle Scuole che svolge attività di ricerca (88%) e di impatto l'osservazione che quasi la metà delle sedi annovera collaborazioni con enti e istituzioni italiane (ospedaliere, territoriali, regionali e sovranazionali) ed internazionali. Non stupisce che la tematica maggiormente approfondita sia la prevenzione delle infezioni correlate all'assistenza, coadiuvate in larga parte dalle attività del GISIO della SItI.

E' importante sottolineare come nelle nostre Scuole di specializzazione il tema sia presente anche a livello didattico e, soprattutto, che trovi spazio nelle attività di progettazione e di tirocinio. Come sottolinea l'OMS, il miglioramento della sicurezza del paziente può essere conseguito comprendendo la natura dell'errore e apprendendo dall'errore osservato e analizzato, dall'errore evitato e dai successi conseguiti nel controllo degli errori stessi; questo è reso possibile da un apprendimento attivo e dal confronto all'interno di team, nel quale si sviluppi la capacità di osservazione e di comunicazione.

Il nostro studio presenta alcune limitazioni, sia nella sua *componente scientometrica*, la cui analisi consente di ottenere stime molto generali sulla produzione scientifica, senza dettagli sulla qualità degli studi e senza la possibilità di considerare altri parametri che, oltre alle pubblicazioni scientifiche, misurano altre dimensioni della ricerca (i.e. entità dei finanziamenti), sia nella sua componente di *survey,* per la quale non abbiamo avuto modo di dettagliare il grado di approfondimento delle ricerche e delle collaborazioni riportate. Tuttavia i macro elementi emersi dall'analisi scientometrica offrono interessanti spunti di riflessione sui volumi, gli ambiti e i contesti in cui si sviluppa, a livello globale, la ricerca sule tema della sicurezza delle cure, mentre la survey ha raccolto in maniera completa a sistematica lo spaccato della situazione italiana.

La ricerca è di vitale importanza per acquisire e consolidare conoscenze sul rischio clinico, e per la sua gestione. Le modalità con cui essa viene condotta, le priorità individuate e le modalità di diffusione dei risultati possono avere un significativo impatto sul miglioramento delle pratiche sanitarie nell'ottica della sicurezza del paziente (13,14). La ricerca fornisce quindi un adeguato supporto teorico evidence-based, finalizzato all'acquisizione di conoscenze e all'attuazione di strategie di studio; la ricerca infine supporta la progressiva e graduale implementazione di metodo-

logie di cambiamento. A tal proposito, l'OMS, in linea con la necessità di una politica di prevenzione e corretta gestione del rischio clinico, ha identificato specifiche aree prioritarie di ricerca, suddivise a seconda del contesto in cui esse si inseriscono (13,14), ponendo l'accento per i Paesi a basso reddito sull'area materno-infantile, sulle infezioni correlate all'assistenza (ICA), sull'acquisizione di conoscenze e competenze e sulle pratiche trasfusionali ed iniettive, mentre nei Paesi ad alto reddito il focus è posto sul miglioramento dei processi organizzativi e di comunicazione (handover), sulla diffusione della cultura della sicurezza, anche mediante l'istituzione di opportuni indicatori (14,15).

Parallelamente, una solida formazione sul tema del Risk Management - che rappresenta le fondamenta per la realizzazione di sistemi altamente efficienti- deve sia concentrarsi ed agire sul comportamento umano come fonte di errore, sia focalizzarsi sulle condizioni, sulle variabili di contesto nelle quali avviene l'errore, per far emergere le problematiche potenziali e/o latenti, al fine di "rimodellizzare" i processi, migliorandoli (15,16,17). Pertanto risulta fondamentale formare professionisti sanitari, ed in particolare nel contesto Italiano, specialisti in Igiene e Medicina Preventiva, a partire da una nuova cultura dell'errore, non più visto come evento a connotazione negativa, ma come punto di partenza di un processo di apprendimento e di miglioramento (17,18,19). La diffusione di questa visione deve iniziare ed andare di pari passo con la genesi e la maturazione di un professionista sanitario (17,18,19).

Il nostro lavoro, contestualizzando il tema della sicurezza delle cure e gestione del rischio clinico in Italia alla luce dei nuovi assetti normativi introdotti dalla Legge Gelli, suggerisce come ricerca e formazione siano elementi complementari fondamentali per la promozione di una nuova cultura di gestione del rischio clinico da sviluppare in contesti di sempre maggiore sinergia e collaborazione tra ambiti accademici, territoriali ed istituzionali.

Ringraziamenti

Per la stesura del paper e la pronta collaborazione alla compilazione della survey, si ringraziano i Professori e Direttori delle Scuole di Specializzazione in Igiene e Medicina Preventiva: Francesco Attena, Antonio Azara, Vincenzo Baldo, Aida Bianco, Paolo Bonanni, Paola Borella, Silvana Castaldi, Alessandra Casuccio, Giancarlo Cesana, Paolo Contu, Gianfranco Damiani, Marcello Mario D'Errico, Francesco Donato, Leila Fabiani, Maria Pia Fantini, Giovanni Gabutti, Giancarlo Icardi, Marina Marranzano, Gabriele Messina, Leonardo Palombi, Massimiliano Panella, Maria Parpinel, Gabriele Pelissero, Isa Picerno, Rosi Prato, Gaetano Pierpaolo Privitera, Michele Quarto, Gabriele Romano, Roberta Siliquini, Tommaso Staniscia, Fabrizio Stracci, Ida Torre, Paolo Villari. Un ringraziamento per il supporto e la collaborazione alla Direzione Sanitaria dell'I.R.C.C.S Ospedale San Raffaele, al Dott. Carlo Orlandi e alla Dott.ssa Maria Paola Garancini.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Received: 15 June 2019
Accepted: 18 July 2019
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Acta Biomed 2019; Vol. 90, Supplement 9: 87-91 DOI: 10.23750/abm.v90i9-S.8731

Il background formativo dei Direttori Generali delle Aziende Sanitarie Italiane: risultati di uno studio su otto Regioni

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The educational background of the Top Managers of the Italian Health Authorities: results of a study on eight Regions

Summary. A survey to investigate the educational background of the Health Top Managers recently appointed by Italian Regions as CEOs (Chief Executive Officer) of Local Health Authorities (ASL) and General Hospitals was performed in April 2019, approximately one year after the entry into force of the new law for their selection (D.Lgs 171/2016). The study follows a similar one carried out by Bocconi University in 2013 and focuses on 8 Italian Regions (Piedmont, Lombardy, Liguria, Umbria, Lazio, Basilicata, Sicily, Sardinia). The study examined the CVs of the 112 recently appointed CEOs: the average age is 58.7 years, with the proportion of female surprisingly low (16%). About half of them (50.5%) have a Degree in Medicine and Surgery. Among Managers with a non-medical degree (49.5%), Law (21) and Economic sciences (21) are the most common degrees. Among medical doctors, 33 (58.9%) are specialists in Hygiene and Preventive Medicine. Overall, our data are consistent with those recorded in 2013 (except a decrease in medical graduates -18.5%) and confirm the diversified backgrounds of Health Managers. The background in Public Health, acquired from the 35 Schools of Hygiene and Preventive Medicine, remains relevant among Managers of the Italian National Health Service. (www.actabiomedica.it)

Key words: Director General, top manager, academic background, curricula, Degree, Medicine and Surgery, Hygiene and Preventive Medicine

Riassunto. Dopo circa un anno dall'entrata in vigore della nuova legge per la selezione dei Direttori Generali (DG) (D.Lgs. 171/2016), è stato condotto uno studio (dati aggiornati ad Aprile 2019) che ha indagato il background formativo dei DG recentemente nominati dalle Aziende Sanitarie Locali e Aziende Ospedaliere in Italia. Lo studio, ricalcando una ricerca analoga realizzata dall'Università Bocconi nel 2013, ha preso in considerazione 8 Regioni (Piemonte, Lombardia, Liguria, Umbria, Lazio, Basilicata, Sicilia, Sardegna), esaminando i curricula dei 112 DG recentemente nominati: l'età media è di 58,7 anni, con una percentuale di donne sorprendentemente bassa (16%). Circa la metà dei DG (50,5%) ha conseguito una laurea in Medicina e Chirurgia. Tra i DG non medici (49,5%), le lauree in Giurisprudenza (21) ed Economia (21) sono le più comuni. Tra i medici, 33 (58,9%) sono specialisti in Igiene e Medicina Preventiva, altri sono specializzati in diverse aree, principalmente cliniche. Complessivamente, i nostri dati sono coerenti con quelli registrati nel 2013 (eccetto un decremento dei laureati in Medicina -18,5%), confermando i diversi background formativi dei Manager della Sanità e il fatto che il background in Sanità Pubblica (acquisito nelle 35 Scuole di Igiene e Medicina Preventiva) rimane rilevante nelle carriere dirigenziali del Servizio Sanitario Nazionale italiano.

Parole chiave: Direttori Generali, top manager, background formativo, curricula, Laurea, Medicina e Chirurgia, Igiene e Medicina Preventiva

Introduzione

La figura del Direttore Generale (DG) delle Aziende Sanitarie Italiane è stata introdotta con il D.Lgs. 502/1992 (1), che non prevedeva requisiti molto specifici, fatto salvo il possesso di una laurea, una maturata esperienza dirigenziale e la frequenza a un corso di formazione manageriale. A seguito di tale normativa, le nomine dei Manager delle Aziende sanitarie hanno investito sia laureati in Medicina e Chirurgia che altri professionisti. Il D.Lgs. 171/2016 (2) ha istituito, presso il Ministero della Salute, l'elenco nazionale (aggiornato con cadenza biennale) dei soggetti idonei alla nomina di DG delle Aziende sanitarie e di altri enti del SSN (Servizio Sanitario Nazionale) con l'intento di uniformare i requisiti di accesso e la qualità dei manager; sono anche stati ribaditi i requisiti dei candidati DG per l'inserimento nell'albo nazionale: conseguimento di una laurea, esperienza dirigenziale maturata di almeno 5 anni (se in ambito sanitario) oppure 7 anni (se in altri ambiti) e certificazione di frequenza e superamento di uno specifico corso di formazione per DG in ambito sanitario; tale requisito non può più essere conseguito dopo la nomina, come consentito in passato da alcune Regioni. Il recente Accordo stipulato il 14 maggio 2019 fra il Governo, le Regioni e le Province Autonome di Trento e Bolzano (3) ha disciplinato la strutturazione degli specifici corsi di formazione in materia di sanità pubblica, organizzazione e gestione sanitaria indirizzati ai candidati da inserire nel predetto elenco di idonei che viene aggiornato con cadenza biennale. A seguito dell'entrata in vigore del nuovo sistema, si è ritenuto pertanto di condurre uno studio che valutasse il background formativo dei DG di recente nomina (agosto 2016 – aprile 2019) nelle 8 Regioni che hanno effettuato le suddette nomine nel periodo considerato, prendendo come termine di paragone il Rapporto OASI 2013 dell'Università Bocconi (4), fino ad oggi una delle poche fonti ad aver raccolto in modo sistematico dati sul background formativo dei manager sanitari italiani.

Metodi

Sono stati esaminati i profili dei DG di Aziende USL (Unità Sanitarie Locali) e Aziende Ospedaliere (in Lombardia ASST: Aziende Socio-Sanitarie Territoriali e ATS: Agenzie di Tutela della Salute) nominati nell'ultimo triennio in Piemonte (5), Lombardia (6), Liguria (7), Umbria (8), Lazio (9), Basilicata (10), Sicilia (11) e Sardegna (12). Tutti i curricula sono accessibili online, come previsto dal D.Lgs. 33/2013 (13) emanato in attuazione di quanto previsto dalla Legge anticorruzione (L. 190/2012), secondo il quale sussiste l'obbligo di pubblicazione dei documenti e delle informazioni (compresi atto di nomina e curriculum vitae) relativi ai titolari di incarichi amministrativi di vertice e incarichi dirigenziali. Sono stati quindi estratti ed esaminati i seguenti dati: nascita, genere, lauree conseguite e, nel caso della Laurea in Medicina e Chirurgia, le eventuali Specializzazioni. Infine i profili dei medici sono stati integrati coi dati presenti nel database dell'Ordine dei Medici Chirurghi e Odontoiatri italiani (OMCeO).

Risultati

Dall'analisi dei dati relativi ai 112 DG (111 curricula esaminati, in quanto 1 DG ricopre la carica in due differenti ASL) è emerso che l'età media è abbastanza elevata, attestandosi intorno ai 60 anni (media 58.7 anni, moda 60 anni, mediana 60 anni, range 38-73 anni). La percentuale di donne è relativamente bassa (solo 18, 16%). Poco più della metà dei DG ha un background medico (56 DG, 50.5% del totale) (Figura 1). Fra i laureati in settori diversi (55 DG, 49.5%) sono maggiormente rappresentate le Lauree in Giurisprudenza (21) ed Economia (21), seguite da altre Lauree, quali Scienze Politiche (5), Ingegneria (3), Fisica (2) ed altre rappresentate singolarmente (Figura 1). Quattro DG non medici hanno conseguito doppia laurea (2 Economia + Giurisprudenza, 1 Economia + Scienze dell'informazione, 1 Scienze dell'educazione + Scienze infermieristiche).

Fra i laureati in Medicina e Chirurgia, una quota rilevante ha conseguito la Specializzazione in Igiene e Medicina Preventiva (33), seguita da altre Specializzazioni di aree principalmente cliniche, quali Medicina Interna (4), Statistica sanitaria (4), Medicina legale (4), Malattie infettive (4), Ematologia (4), Psichiatria (3), Endocrinologia (3), Farmacologia (2), Ostetricia e

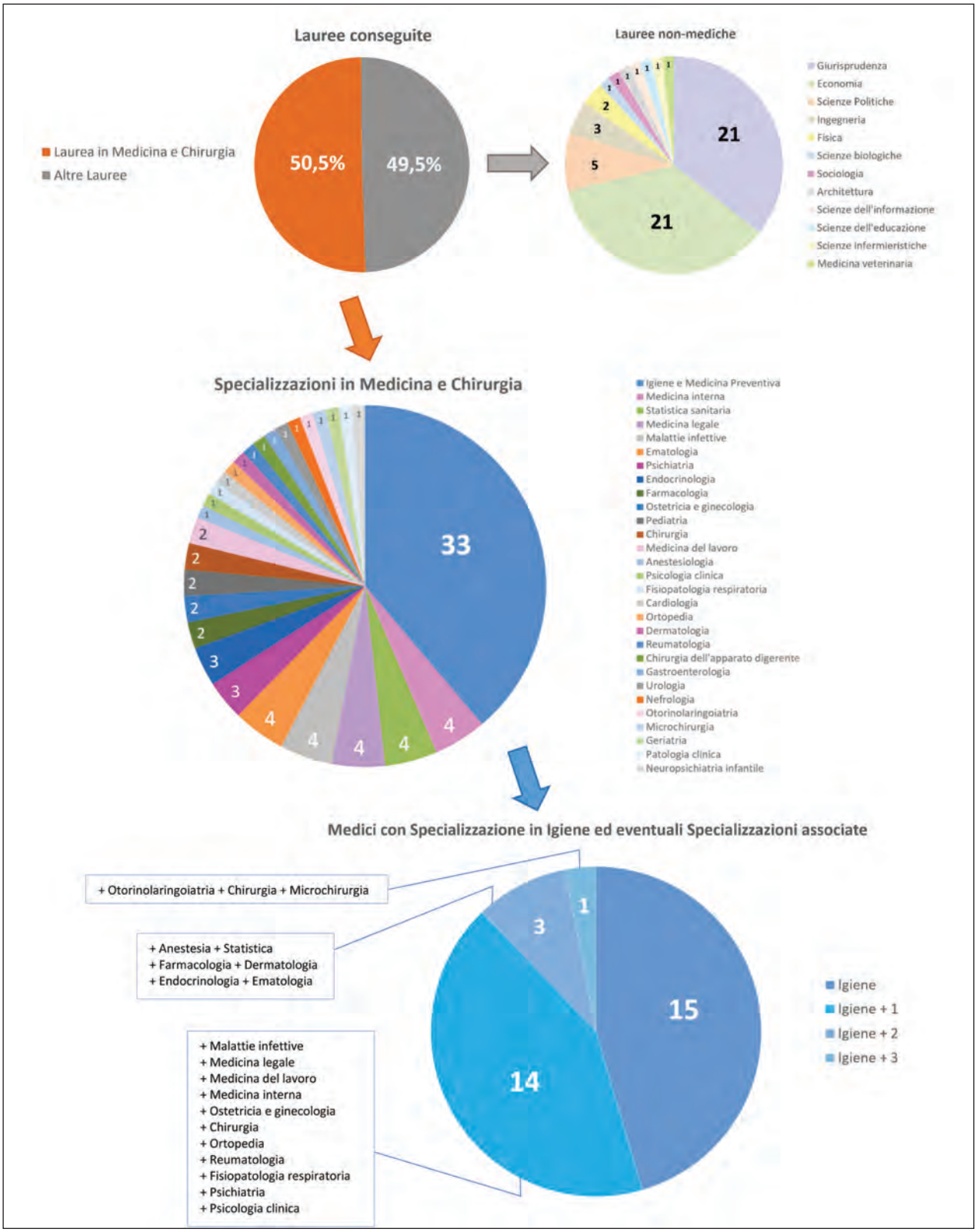

Figura 1. Ripartizione dei Direttori Generali (DG) per Lauree conseguite e Specializzazioni

Tabella 1. Riassuntivo dati da curricula: confronto Rapporto OASI 2013 – studio 2019

	Rapporto OASI 2013	Studio 2019
N° Regioni Italiane	4	8
N° CV esaminati	83	112
Età media (anni)	59	58,7
Maschi e femmine (%)	♂ 85% e ♀ 15%	♂ 84% e ♀ 16%
Laurea in Medicina e Chirurgia (%)	69%	50,5%
Specializzazione in Igiene e Medicina Preventiva (% sui Medici)	56%	59%

ginecologia (2), Pediatria (2), Chirurgia (2), Medicina del lavoro (2) ed altre rappresentate singolarmente (Figura 1). Tra i Medici non igienisti (23 DG, 41,1% sul totale dei Medici) 7 hanno conseguito una doppia specializzazione; le associazioni principali sono: 3 Medicina interna (+ Endocrinologia, + Farmacologia, + Nefrologia), 2 Statistica sanitaria (+ Chirurgia dell'apparato digerente, + Medicina del lavoro), 1 Ostetricia e ginecologia (+ Endocrinologia) e 1 Ematologia (+ Patologia clinica). Tra i Medici che hanno conseguito una Specializzazione in Igiene e Medicina Preventiva (33 DG, 58,9% sul totale dei Medici) 15 hanno una formazione esclusivamente igienistica; tra questi 4 hanno conseguito la Specializzazione in Igiene con due indirizzi e 1 con tre indirizzi (Laboratorio, Sanità Pubblica, Igiene e tecnica ospedaliera) mentre 18 hanno conseguito ulteriori specializzazioni in associazione: 14 Igiene + 1 specializzazione, 3 Igiene + 2 specializzazioni, 1 Igiene + 3 specializzazioni (Figura 1, Medici con Specializzazione in Igiene ed eventuali Specializzazioni associate). Infine un DG medico risulta non aver conseguito alcuna specializzazione.

Discussione e Conclusioni

Confrontando i curricula dei DG di recente nomina (2016-2019) con quelli presi in considerazione nel Rapporto del 2013 (4) (Tabella 1), si nota che l'età media dei DG si è mantenuta elevata con una rappresentanza di quote rosa stabile (15% *vs* 16%), su livelli bassi e inferiori alle percentuali degli iscritti all'albo nazionale degli idonei alla nomina a DG (205 donne su 761, 26,9%) (14). Risultano in diminuzione i DG con Laurea in Medicina e Chirurgia (69% *vs* 50,5%, -18,5%), mentre fra i medici è in lieve ascesa la percentuale di Specialisti in Igiene e Medicina Preventiva (56% *vs* 59%) e più in generale dell'area della Sanità Pubblica (che include oltre a Igiene la Statistica sanitaria, la Medicina Legale e la Medicina del lavoro) che raggiungono il 67,9% dei medici. Inoltre si è osservato che tra i medici igienisti con specializzazione multipla, nella maggior parte dei casi quella in Igiene è l'ultima specializzazione conseguita.

Questo studio fotografa il background formativo di una figura unica nell'ordinamento nazionale, ossia quella del manager pubblico delle Aziende sanitarie nell'ambito di un Servizio Sanitario in evoluzione e trasformazione (15, 16); il SSN non può infatti prescindere oggi da una gestione efficiente per vincere la difficile sfida della sostenibilità (17). Si conferma, pur con proporzioni variate, la diversificata formazione di base dei manager, con la componente maggioritaria dei laureati in Medicina e Chirurgia e quella del background giuridico-economico. Tra i medici si confermano alte le percentuali degli specialisti in Igiene e Medicina preventiva (e più in generale dell'area della Sanità Pubblica), a testimonianza della validità della formazione specialistica nelle 35 Scuole italiane (18).

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Received: 15 June 2019
Accepted: 18 July 2019
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Acta Biomed 2019; Vol. 90, Supplement 9: 92-94 DOI: 10.23750/abm.v90i9-S.8725

La Laurea in Tecniche della Prevenzione nell'Ambiente e nei Luoghi di Lavoro: un corso quasi unico nel panorama europeo per i professionisti non medici coinvolti nelle attività di prevenzione

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The University Degree in Environment and workplace prevention techniques: a quasi unicum Course in the European panorama for non-medical professionals involved in prevention activities

Summary. The University Degree programme in Environment and workplace prevention techniques (Tecniche della Prevenzione nell'Ambiente e nei Luoghi di Lavoro) is a 3-year course established in Italy in 2000 by the Ministry of University to train healthcare professionals responsible for prevention activities such as environment and food controls, and workplaces prevention, operating both in the National Health Service and in private settings. Frontal teaching activities and training programmes include a background in bio-medical sciences, epidemiology, public health, social sciences and law, including the inspection and control tasks of health and safety in living and working environment, food hygiene, environmental controls and veterinary public health, which represent the field of specific competences of graduates. Currently, 38 courses have been activated in 30 Italian Universities, but relatively few similar courses are present in Europe (similar programmes were found in France, Spain, UK and Belgium) causing the lack of internalization and student exchange programmes. It is essential to identify similar training tasks in other European countries, in order to enhance cultural exchanges and the development of research activities in these strategic areas. (www.actabiomedica.it)

Key words: degree, technician, prevention, environmental, workplace

Riassunto. Il Corso di Laurea in "Tecniche della Prevenzione nell'Ambiente e nei Luoghi di Lavoro" è un corso triennale istituito in Italia nel 2000 dal MIUR (Ministero dell'Istruzione, dell'Università e della Ricerca) per formare operatori sanitari responsabili di attività di prevenzione quali il controllo dell'ambiente e degli alimenti e la prevenzione nei luoghi di lavoro, operando all'interno del Servizio Sanitario Nazionale e in contesti privati. Le attività didattiche frontali e i programmi di formazione comprendono un background in scienze biomediche, epidemiologia, sanità pubblica, scienze sociali e giuridiche, comprese le ispezioni e il controllo della salute e sicurezza negli ambienti di vita e di lavoro, igiene degli alimenti, controlli ambientali e sanità pubblica veterinaria; tutto ciò rientra nei campi di competenze specifiche dei laureati. Attualmente in Italia sono attivati 38 corsi in 30 Università, ma in Europa sono presenti relativamente pochi corsi simili (programmi analoghi sono presenti in Francia, Spagna, Regno Unito e Belgio) rendendo difficoltosi programmi di internazionalizzazione e scambio di studenti. È essenziale identificare percorsi di formazione simili in altri Paesi europei al fine di migliorare gli scambi culturali e lo sviluppo di attività di ricerca in queste aree strategiche.

Parole chiave: laurea, tecnico, prevenzione, ambiente, luogo di lavoro

Introduzione

Il Tecnico della Prevenzione nell'Ambiente e nei Luoghi di Lavoro (TPALL) è una Professione Sanitaria riconosciuta dal Ministero della Salute (1). Le Professioni Sanitarie, oltre a quelle mediche (3), sono suddivise in quattro aree professionali di riferimento (Decreto Ministeriale 509/1999 (2) e successiva modifica Decreto Interministeriale 2 aprile 2001 (1)): classe 1 delle Lauree e Professioni Sanitarie Infermieristiche e Ostetriche, classe 2 delle Lauree in Professioni Sanitarie della Riabilitazione, classe 3 delle Lauree in Professioni Sanitarie Tecniche, classe 4 delle Lauree in Professioni Sanitarie della Prevenzione. Il Corso di Laurea in Tecniche della Prevenzione nell'Ambiente e nei Luoghi di Lavoro è inserito nella IV area delle Professioni tecniche della Prevenzione.

Il profilo professionale del TPALL è stato delineato in accordo con il Decreto Ministeriale 58/1997 (5) e i successivi emendamenti ed addizioni. In particolare, la Legge 251/2000 (6) ha definito gli obiettivi della formazione professionale.

Profilo professionale e formativo

Il Tecnico della prevenzione è l'operatore sanitario responsabile di tutte le attività di prevenzione, verifica e controllo relative all'igiene e alla sicurezza negli ambienti di vita e di lavoro.

Il profilo professionale del TPALL spazia in differenti campi: aria, acqua, suolo, rifiuti, protezione della salute e sicurezza sul lavoro, sicurezza alimentare, edilizia, sistemi industriali, sanità pubblica veterinaria, legislazione in sanità pubblica, psico-sociologia, promozione della salute e di stili di vita favorevoli alla salute della popolazione.

Il Corso di Laurea in "Tecniche della Prevenzione nell'Ambiente e nei Luoghi di Lavoro" in Italia ha una durata di tre anni e prevede l'acquisizione di 180 CFU (Crediti Formativi Universitari). Il Corso ha l'obiettivo specifico di assicurare allo studente un'adeguata padronanza di metodi e contenuti scientifici generali, nonché l'acquisizione di specifiche competenze professionali.

Le attività didattiche frontali e i programmi di formazione comprendono un *background* in scienze biomediche, epidemiologia, sanità pubblica, scienze sociali e giuridiche, compresi i compiti di ispezione e controllo della salute e sicurezza negli ambienti di vita e di lavoro, igiene degli alimenti, controlli ambientali e sanità pubblica veterinaria.

Molti laureati al termine del percorso formativo trovano impiego come Tecnici della Prevenzione nelle diverse Aziende Sanitarie Locali e/o Territoriali afferenti al Servizio Sanitario Nazionale Italiano. Altri professionisti sono impiegati quali addetti/responsabili della sicurezza in aziende private o si dedicano ad attività di consulenza.

Prospettive

Ad oggi in Italia risultano attivati 38 Corsi di TPALL da 30 diverse Università (Figura 1) in 35 città.

Negli altri Paesi Europei sono presenti pochi Corsi con programmi professionalizzanti analoghi, tra cui Francia (Bordeaux – *Coordonnateur de Prévention*),

Figura 1. Corsi di Laurea in Tecniche della Prevenzione nell'Ambiente e nei Luoghi di Lavoro (TPALL) attivati in Italia e relative sedi

Spagna (Madrid – *Escuela de la Inspección de Trabajo y Seguridad Social*), Regno Unito (Inghilterra, Scozia, Galles – *Health and Safety Executive*) e Belgio (Bruxelles – *Sante Publique, Securite de la chaine Alimentaire et Environnement*) (7). Nella programmazione di questi Corsi si ritrovano molti insegnamenti comuni a quelli italiani, prerogativa che rende auspicabile nel prossimo futuro uno scambio di studenti mediante i programmi di internazionalizzazione Erasmus (8, 9).

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Received: 15 June 2019
Accepted: 18 July 2019
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Acta Biomed 2019; Vol. 90, Supplement 9: 95-97 DOI: 10.23750/abm.v90i9-S.8702

La sorveglianza ambientale per poliovirus e non-polio enterovirus a Parma nell'ambito del "Global Polio Eradication Program" (GPEI)

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Poliovirus and non-polio-enterovirus environmental surveillance in Parma within the "Global Polio Eradication Program" (GPEI)

Summary. *Background:* Environmental surveillance of poliovirus plays an essential role in GPEI both for the detection of WTP and VDPV circulation in endemic areas and for monitoring their absence in polio-free countries. *Methods:* Since 2005 to 2018, in Parma, 642 wastewater samples were collected from the two wastewater treatment plants and analyzed according to the WHO Guidelines. All isolates supposed being poliovirus were sent to ISS reference laboratory for molecular characterization while NPEV only refer to samples up to 2016. *Results:* Positivity was obtained in 68% of samples without significant difference between the two treatment plants. Six polioviruses (1.4%) were detected, all characterized as Sabin-like: 4 of them (66.7%) were type 3 and 2 (33.3%) type 1. Coxsackieviruses B mainly recurred among NPEV (85%) while residual 15% was Echoviruses. B4 was the most frequent Coxsackie serotype isolated (31%) while, among Echovirus, Echo 7 and Echo 11 prevail (both 23%). *Conclusion:* As OPV isn't used in Italy since 2002, recovery of Sabin-like polioviruses indicates the possibility of poliovirus reintroduction, considering also the important exposure to migratory flows. Finally, monitoring the environmental circulation of NPEV, could compensate for the lack of a surveillance system of the infections they cause. (www.actabiomedica.it)

Key words: poliovirus, enterovirus, environmental surveillance

Riassunto. *Introduzione:* La sorveglianza ambientale per poliovirus svolge un ruolo essenziale nell'ambito del GPEI sia per il rilevamento della circolazione WTP e VDPV in aree endemiche sia per il monitoraggio della loro assenza nei paesi "polio-free". *Metodi:* Dal 2005 al 2018, 642 campioni di acque reflue sono stati raccolti dai due impianti di trattamento di Parma, ed analizzati secondo le Linee Guida dell'OMS. Tutti i "sospetti poliovirus" isolati nel periodo sono stati caratterizzati presso il laboratorio di riferimento dell'ISS; invece la tipizzazione dei NPEV si riferisce solo al 2005-2016. *Risultati:* Il 68% dei campioni è risultato positivo senza differenze significative tra i due impianti. Sono stati rilevati 6 poliovirus (1,4%), tutti caratterizzati come Sabin-like: 4 polio 3 (66,7%) e 2 polio 1 (33,3%). L'85% dei NPEV sono risultati Coxsackievirus B di cui B4 il sierotipo più frequente (31%); tra gli Echovirus (15%) prevalgono Echo7 ed Echo11 (entrambi 23%). *Conclusione:* Poiché l'OPV non è utilizzato in Italia dal 2002, l'isolamento di poliovirus Sabin-like indica la possibilità di reintroduzione del poliovirus, considerando anche l'importante esposizione ai flussi migratori. Infine il monitoraggio della circolazione ambientale di NPEV potrebbe supplire alla mancanza di un sistema di sorveglianza delle infezioni da essi sostenute.

Parole chiave: poliovirus, enterovirus, sorveglianza ambientale

Introduzione

Accanto alla sorveglianza dei casi di paralisi flaccida acuta (PFA), la sorveglianza ambientale (environmental surveillance ES) della circolazione di virus polio e non-polio rappresenta un utile strumento per misurare l'efficacia delle strategie adottate dall'Organizzazione Mondiale della Sanità (OMS) nel programma globale di eradicazione della poliomielite (1,2).

Condotta su acque reflue provenienti da insediamenti civili, svolge un ruolo fondamentale sia in condizioni di attiva circolazione di virus che di assenza della medesima. Nel primo caso infatti consente di evidenziare una trasmissione in atto sia di poliovirus selvaggi (WPV) sia di ceppi vaccino-derivati (VDPV), anche in assenza di casi di malattia (3); inoltre supporta la sorveglianza PFA in aree endemiche o a rischio di introduzione di poliovirus, soprattutto là dove il livello di immunizzazione della popolazione non è ottimale o la sorveglianza PFA è assente o insufficiente (4,5).

D'altro canto, confermando l'assenza di circolazione virale, contribuisce alle certificazioni "polio-free" e consente di verificare l'efficacia del processo di contenimento previsto dall'OMS e in atto già dal 2015.

Inoltre l'ES rileva la diffusione ambientale degli enterovirus non polio (NPEV) responsabili di diverse forme patologiche, anche gravi, nella popolazione.

L'Unità di Sanità Pubblica dell'Università di Parma dal 2005 è inclusa nella rete di laboratori sub-nazionali di riferimento coinvolti nell'ES e si inserisce nel contesto nazionale coordinato dall'ISS e, a livello mondiale, dall'OMS (6-9).

Materiali e metodi

Nel periodo 2005-2018, dai due impianti di trattamento dei reflui di Parma (est e ovest) sono stati prelevati due campioni/mese da 1 litro di reflui in ingresso (medio delle 24 ore). I campioni raccolti e concentrati sono stati sottoposti ad indagine virologica colturale secondo il protocollo e l'algoritmo previsti dall'OMS (10). Gli isolati ottenuti, distinti in "sospetti poliovirus" e NPEV, sono stati inviati al Laboratorio di Riferimento Nazionale presso l'ISS per la caratterizzazione biomolecolare. In particolare i campioni sospetti polio vengono inviati immediatamente dopo l'isolamento per l'identificazione, la differenziazione intratipica e il saggio di identificazione di VDPV (10). L'invio degli isolati NPEV invece avviene periodicamente. Per questo, i dati relativi agli isolamenti di poliovirus sono costantemente aggiornati mentre quelli riguardanti i NPEV sono confermati e caratterizzati solo relativamente al periodo 2005-2016.

Risultati

Dei 642 campioni analizzati il 68% è risultato positivo, senza differenze significative fra i due depuratori, anche se la percentuale di positività è leggermente maggiore nell'impianto Parma ovest (70% contro il 66% dell'est).

Dal 2005 fino ad oggi sono stati isolati 6 virus polio (1.4%), di cui 4 (66.7%) di tipo 3 e 2 (33.3%) di tipo 1, tutti Sabin-like. In tabella 1 sono riportati gli anni di isolamento: interessante la presenza di poliovirus 3 in due campionamenti consecutivi del 2015 che sembrerebbe indicare un protrarsi, se pur per tempi contenuti, della circolazione del virus.

La circolazione di NPEV ha evidenziato, in generale, una netta prevalenza di Coxsackievirus tutti di tipo B (85%), mentre gli isolati caratterizzati come Echovirus sono stati mediamente il 15% con andamento molto variabile e un aumento di isolamenti soprattutto negli ultimi due anni di indagine (2015-16); in particolare, quando presenti, sono passati da un minimo del 2.4% nel 2013 ad un massimo del 72% nel 2016, anno in cui si è osservata un'inversione di frequenza rispetto ai Coxsackievirus.

I sierotipi di Coxsackievirus più frequenti sono risultati il B4 (31.1%) e il B5 (23%), il primo con una presenza praticamente costante ad eccezione di un solo anno (2014). Fra gli Echovirus prevalgono i sierotipi Echo 7 ed Echo 11 (23.1% per entrambi) e gli Echo 6 (21.2%).

Tabella 1. Isolamenti di poliovirus dalle acque reflue di Parma 2005-2018

Data	Poliovirus	ITD/VDPV
giu-05	poliovirus 3	SL
ago-11	poliovirus 1	SL
apr-15	poliovirus 3	SL
mag-15	poliovirus 3	SL
feb-16	poliovirus 1	SL
ott-17	poliovirus 3	SL

Discussione

Nel periodo considerato e fino ad oggi, gli isolamenti di poliovirus a Parma sono stati sporadici, in accordo con quanto riscontrato anche a livello nazionale (8). In particolare, tutti gli isolati polio sono risultati essere Sabin-like e quindi privi di mutazioni responsabili della comparsa di VDPV; ciò indica una circolazione nella popolazione estremamente contenuta nel tempo. L'assenza di ceppi selvaggi a Parma, come nel resto dell'Italia, conferma il mantenimento della condizione di "polio-free" nel Paese (11).

Tuttavia anche se saltuari, questi rilievi rappresentano dei significativi indicatori di una possibile reintroduzione di poliovirus nel nostro territorio giustificata anche dell'importante esposizione ai flussi migratori visto che l'Italia non utilizza più il vaccino orale di Sabin (OPV) dal 2002.

Fra i NPEV, i Coxsackievirus B4 sono i più rappresentati (26%) diversamente da quanto riportato a livello nazionale dove risultano più frequenti i B5. In linea invece la maggiore frequenza degli Echo7 (11).

Dal momento che in Italia manca un sistema di sorveglianza per le patologie sostenute da NPEV (sia a livello ospedaliero che di comunità), anche il monitoraggio della circolazione di altri enterovirus nell'ambiente rappresenta un utile strumento epidemiologico, alla luce dell'aumentato numero di episodi epidemici sostenuti da questi virus e rilevati a livello mondiale (12-15).

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Received: 15 June 2019
Accepted: 18 July 2019
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Acta Biomed 2019; Vol. 90, Supplement 9: 98-107 DOI: 10.23750/abm.v90i9-S.8707

Il contributo degli igienisti universitari al progresso e allo sviluppo della sanità pubblica in Italia: cento anni di storia*

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The contribution of professors of Hygiene to the progress and development of public health in Italy: one hundred years of history

Summary. In 1917 Achille Sclavo, a distinguished researcher and founder of the Italian Society of Hygiene, ended up the first term as Rector of the University of Siena. Since then, the contribution of professors of hygiene in Italian universities has ranged over several relevant topics including vaccinations, environmental hygiene, hospital hygiene, healthcare organization and management, with an important contribution to the health reform of 1978 by Augusto Giovanardi and Alessandro Seppilli. Several Academic Schools (Roman, Neapolitan, Genoese, Sicilian, Venetian, Lombard, etc.) have produced excellent researchers, teachers and mentors who have also occupied important positions in the panorama of the Italian health system. This note analyzes the main research topics, the most famous institutes and departments of hygiene and public health and the contributions of the most famous professors for the development of the discipline, the management of the post- graduated Schools in hygiene and preventive medicine, the commitment in scientific associations and the role of some of them in important institutional positions. Even through its contribution and constant commitment to the institutions, Italian public health has achieved the reputation of being one of the best known and appreciated in the international scientific community.(www.actabiomedica.it)

Key words: hygiene, public health, university, Italy

Riassunto. Nel 1917 Achille Sclavo, insigne ricercatore e fondatore della Società Italiana di Igiene, concludeva il primo mandato di Rettore dell'Università di Siena. Da allora il contributo dei docenti d'igiene nelle università italiane ha spaziato tra diversi temi rilevanti, tra cui le vaccinazioni, l'igiene ambientale, l'igiene ospedaliera, l'organizzazione sanitaria ed il management, con l'importante contributo alla riforma sanitaria del 1978 da parte di Augusto Giovanardi ed Alessandro Seppilli. Diverse Scuole igienistiche (romana, napoletana, genovese, siciliana, veneta, lombarda, ecc.) hanno sfornato eccellenti ricercatori, docenti e maestri che hanno occupato anche posizioni rilevanti nel panorama del sistema sanitario italiano. Questa nota analizza i principali filoni di ricerca, i più noti istituti e dipartimenti d'igiene e i contributi dei più noti docenti per lo sviluppo della disciplina, la gestione delle Scuole di specializzazione in igiene e medicina preventiva, l'impegno nelle società scientifiche ed il ruolo di alcuni di loro in rilevanti posizioni istituzionali. Anche attraverso il loro contributo ed il costante impegno a fianco delle istituzioni la sanità pubblica italiana ha raggiunto la fama di essere una delle più note e apprezzate nella comunità scientifica internazionale.

Parole chiave: igiene, sanità pubblica, università, Italia

* Adattamento della relazione presentata al Convegno "La prevenzione nella popolazione ed in ambiente ospedaliero alla luce dei nuovi LEA", Taormina, 6-7 ottobre 2017

Introduzione

L'Igiene si è andata affermando come disciplina sperimentale, a livello universitario, già nella seconda metà dell'Ottocento. Luigi Pagliani (1847-1932) ne fu il più noto rappresentante, essendo stato chiamato dall'allora primo Ministro Francesco Crispi dall'Università di Torino a Roma, dove guidò la nuova Direzione Generale della Sanità presso il Ministero dell'Interno e diede un significativo contributo alla legge 22 dicembre 1888, n. 5849 (Legge sulla tutela dell'igiene e della sanità pubblica, più nota come Legge Crispi-Pagliani). Tra gli allievi di Pagliani ci fu Achille Sclavo (1861-1930), che nel 1904 fondò l'"Istituto Siero e Vaccino Produttore" nella sua villa di campagna alla periferia di Siena, nella cui Università fu professore di Igiene ed anche Rettore per tre mandati (1914-17; 1924-26; 1927-29) (1).

Oggi l'Igiene universitaria è una delle dieci discipline dell'area sanitaria con il maggior numero di docenti, gestisce 35 Scuole di Specializzazione in Igiene e Medicina preventiva (2) e vanta 84 professori ordinari, 88 professori associati e 93 ricercatori, di cui 36 a tempo definito *ex Lege* 240/2010 (17 di tipo A e 19 di tipo B), distribuiti in numerosi Corsi di laurea di diversa affiliazione (medicina e chirurgia, odontoiatria, scienze motorie, scienze umane, agraria, biologia, farmacia, architettura, ingegneria, oltre a quasi tutte le professioni sanitarie). La disciplina - che ha conservato l'antica denominazione ma che, a tutti gli effetti si riconosce nella *Public Health*, così come intesa a livello internazionale – s'interessa di svariati temi di ricerca, alcuni dei quali all'avanguardia, ma senza aver abbandonato, o meglio avendo recuperato in chiave moderna, quelli che si riconoscono nelle antiche tradizioni degli istituti accademici (la *Urban Health* ha rifondato la tradizionale Igiene edilizia, l'approccio integrato all'antibioticoresistenza ha continuato la tradizione dell'igiene ospedaliera, ecc).

1. Gli igienisti italiani e la malaria

Uno degli apporti storici più importanti dell'igiene italiana è sicuramente aver contribuito in modo decisivo alla scoperta del ruolo della zanzara nella trasmissione della malaria. Per fare due nomi, i primi della lista, ecco quelli di Giovanni Battista Grassi e di Angelo Celli, esponenti della Scuola romana di malariologia (3). Il primo ebbe una competizione clamorosa, senza esclusione di colpi, con l'inglese Ronald Ross circa il primato nella scoperta della trasmissione del plasmodio da parte della zanzara anofele; la spuntò Ross, che ottenne il premio Nobel con grande scandalo dei ricercatori italiani (4); ma, successivamente, gli stessi inglesi (London School of Hygiene and Tropical Medicine) riconobbero la contemporaneità della scoperta, tanto che per simbolico risarcimento conferirono negli anni '90 la prima "Ross medal" ad un brillante erede di Grassi, il parassitologo della Sapienza Caio Mario Coluzzi. Il secondo, che fu anche parlamentare, rimane famoso per la battaglia vinta per la distribuzione del "Chinino di Stato" a prezzo controllato, il che permise la cura di un numero infinito di malati. Insieme alla moglie, Anna Fraentzel, tedesca e ben introdotta nell'alta società per il matrimonio della sorella con un nobile romano, creò una rete di assistenza sanitaria ma anche di scolarizzazione (scuole rurali) in tutto l'agro romano, per acculturare gli abitanti più indigenti, renderli più attivi nella lotta antimalarica, ma anche per reinserirli in quella vita di lavoro che la malaria impediva.

2. L'organizzazione sanitaria e la Riforma del 1978: Giovanardi e Seppilli

L'impegno della disciplina igienistica nell'organizzazione sanitaria si è tramandata nei decenni dopo Pagliani. Augusto Giovanardi (1904-2005), nel suo periodo padovano durante la II guerra mondiale, fu attivo nel CLN delle Tre Venezie; insieme ad *Egidio Meneghetti* e *Concetto Marchesi* (entrambi Rettori a Padova, entrambi attivi nella Resistenza, farmacologo il primo e latinista il secondo), preparò un modello di riforma sanitaria "regionalizzato" che – insieme alle proposte del perugino Alessandro Seppilli (1902-1995) - fu alla base della discussione che portò ben più tardi, nel 1978, all'approvazione della legge 833. Seppilli fu molto attivo sul tema, dopo il ritorno in Italia dall'esilio brasiliano cui l'avevano costretto le leggi razziali. In coppia con Giovanni Berlinguer di-

resse la collana "Società e Salute" del Pensiero Scientifico Editore, ove pubblicarono il volume "La Riforma Sanitaria". Ci sono stati nei decenni diversi professori di igiene impegnati a livello nazionale e regionale in attività di collaborazione con le istituzioni per norme e iniziative nel settore emergente della prevenzione, come Gaetano Maria Fara (Milano e Roma Sapienza), Giovanni Berlinguer (Roma Sapienza), Luigi Petrilli e Pietro Crovari (Genova), Bruno Angelillo (Napoli). Oggi possiamo attribuire a Walter Ricciardi (Presidente dell'Istituto Superiore di Sanità dal 2014 al 2018) ed a numerosi altri colleghi il merito di continuare l'impegno in questo ambito.

3. L'educazione sanitaria: dalla Scuola di Perugia all'Health Promotion

Su invito dell'OMS, Alessandro Seppilli fonda a Perugia il CESPES (Centro Sperimentale di Educazione Sanitaria), che - insieme con l'Istituto di Medicina Sociale di Roma da lui a lungo presieduto - ha sviluppato i diversi capitoli dell'educazione sanitaria, diffondendo i risultati di ricerca attraverso due riviste, *Educazione sanitaria* e *La salute umana,* e creando con Maria Antonia Modolo una Scuola di formazione in Educazione Sanitaria. Oggi, accanto alla scuola perugina che continua nel filone ed ai tanti che studiano ed applicano modernamente il tema (ricordiamo per tutti Gianfranco Tarsitani), dobbiamo citare il collega Paolo Contu di Cagliari, che ha assunto importanti cariche a livello internazionale (International Union for Health Promotion and Education) e Giuseppe Masaniotti di Perugia, attualmente coordinatore del Gruppo di lavoro istituito dalla SItI su questo tema.

4. I vaccini e le politiche vaccinali

Gli igienisti italiani sono stati tra gli antesignani delle vaccinazioni. Il dottor Luigi Sacco, lombardo, fu seguace entusiasta di Jenner e grande e convinto diffusore del suo vaccino antivaioloso. Presto divenne un'autorità internazionale sulla vaccinazione, ed ebbe il merito di riuscire ad inviare il vaccino fino in Australia, imbarcando su di una nave una serie di orfani e passando il vaccino da uno all'altro fino a che non raggiunse la meta!

Un altro igienista fu invece tra gli antesignani del vaccino antirabbico. Fu Claudio Fermi, che utilizzò il vaccino di Pasteur, ma lo attenuò mediante un'operazione di fenicatura praticata addizionando il fenolo all'emulsione di virus fisso. Aggiungiamo il successo del vaccino antitifico all'acetone di Giovanardi, a lungo utilizzato dalle Forze Armate italiane.

Ma in seguito ancora gli igienisti italiani furono protagonisti con successo dell'adozione di due vaccini, con cui le relative malattie furono eliminate (poliomielite) o drasticamente ridotte (epatite B). Giovanardi, Petrilli ed altri si batterono a favore del vaccino Sabin, svolgendo ricerche che ne dimostrarono la superiorità rispetto al vaccino Salk, e ne guidarono l'adozione a livello nazionale attraverso l'obbligo, che portò alla sparizione in pochi anni di tutti i casi. Storia analoga quella del vaccino anti epatite B, con l'Italia in testa all'Europa nell'adottare la vaccinazione di massa (5).

Diversi Istituti di Igiene universitari hanno continuato la tradizione, tra cui quelli di Genova (Petrilli, Crovari, Gasparini, Icardi, et al.), Milano (Grosso, Bergamini, Profeta, Zanetti, E. Tanzi, et al., Roma (D'Arca, Simonetti, Mastroeni, Fara, Franco, Ricciardi, Panà, Boccia, Villari, et al), Torino (Moiraghi, Zotti, Siliquini et al.), Sassari (Maida, Mura, Castiglia, et al.), Firenze (Davoli, Signorini, Bonanni et al.), Siena (Sclavo, Petragnani, R. Gasparini, Montomoli et al.), Bari (Barbuti, Germinario, Prato, Chironna, Lopalco et al.), Catania (Giammanco, Sciacca, Agodi, Ferrante et al.), Palermo (D'Alessandro, Dardanoni, N. Romano, Vitale et al.), Messina (De Blasi, Calisto, Squeri), Triveneto (Campello, Baldo et al.), Parma (Bellelli, Nardi, M. Tanzi, Signorelli) e molti altri ancora. La pubblicistica appare numerosa e significativa, facendo dell'Italia un paese leader non solo negli aspetti legati alla sperimentazione ed all'utilizzo dei vaccini ma, più recentemente, anche nelle politiche vaccinali (6-8).

5. Ambiente e salute ed emergenze ambientali

L'ambiente è un tema che ha coinvolto numerosi istituti (dipartimenti) di igiene nel passato e nel presente, tanto che ben presto la SItI ha sentito l'oppor-

tunità di creare un apposito gruppo di lavoro, da allora sempre molto attivo. Possiamo ricordare le ricerche pionieristiche di Giovanardi, che ebbe la "fortuna" di trovarsi nella città con il più elevato inquinamento atmosferico d'Italia negli anni '50-60 e, contemporaneamente, con l'acquedotto urbano inquinato in successione da cromo esavalente e da organo-clorurati.

Numerosi istituti e poi dipartimenti hanno affrontato ed affrontano tutti i temi dell'inquinamento ambientale e del suo rapporto con la salute: aria, acqua potabile, acque superficiali, rifiuti liquidi, rifiuti solidi, rifiuti speciali sanitari. Ricordiamo a questo proposito il Prof Pitzurra di Perugia, che presiedette il primo gruppo di lavoro SItI denominato GISSO (Gruppo Italiano di studio sulle Sale Operatorie), trasformatosi poi in GISIO (Gruppo italiano di Studio di Igiene Ospedaliera), che ha avuto il merito di internazionalizzarsi, partecipando ad importanti reti di ricerca (9).

Ma nella storia dell'Igiene italiana restano memorabili anche alcuni esempi di contaminazione ambientale, di natura chimica, caratterizzati da eventi catastrofici:

Anzitutto la vicenda di Seveso del 1976 e della contaminazione da diossina, che fu una chiamata alle armi per tantissimi igienisti italiani che vi furono coinvolti per anni: a parte ovviamente i milanesi Giovanardi, Fara e Ziglio, lavorarono a Seveso Dardanoni, Paccagnella, Giambelluca, Favaretti, D. Greco (10).

Quando, nel 1986, l'incidente atomico di Chernobyl inquinò i cieli d'Europa, tutti gli igienisti del nord Italia furono coinvolti nelle attività di analisi e bonifica. Ma toccò più tardi agli igienisti del sud occuparsi delle grandi contaminazioni di Bagnoli, Priolo, Taranto, Gela, Caserta, eventi non ancora tutti conclusi.

Tra i problemi ambientali che in vari anni hanno coinvolto gli igienisti possiamo ancora citare i **terremoti** del Belice (1968), del Friuli (1976), della Campania e Basilicata (1980), di Abruzzo, Umbria e Marche (1997), ancora dell'Abruzzo (2009), di Emilia e Romagna (2012), del Centro Italia (2016 ed ancora 2017). Il 52° Congresso Nazionale di Igiene, in programma a Perugia nell'Ottobre 2019, organizzato dalle Sezioni Umbria, Marche ed Abruzzo, avrà tra i temi principali l'esperienza emergenziale vissuta dai Dipartimenti di Igiene e dalle istituzioni sanitarie di quelle tre regioni così duramente colpite dai terremoti più recenti.

Più recentemente si è diffusa l'attività di ricerca in settori chiave, come la sicurezza nei cantieri, il rapporto tra inceneritori e salute (11), l'Urban Health, l'inquinamento indoor, le politiche ambientali, con l'attiva azione di nuclei di medici ed architetti afferenti alle Cattedre di Igiene ambientale del Politecnico di Milano (Stefano Capolongo) e dell'Ingegneria di Roma Sapienza (Daniela D'Alessandro) (12). .

6. Il ruolo nelle università, negli enti e nelle associazioni scientifiche

Il ruolo degli igienisti nelle università continua ad essere rilevante, risultando - quello dell'igiene generale ed applicata (MED/42) - il quinto settore più numeroso nell'area scientifico-disciplinare di Medicina e Chirurgia. D'altronde i corsi di pertinenza igienistica (igiene, epidemiologia, organizzazione sanitaria, igiene ambientale, global health, ecc.) si sono progressivamente moltiplicati negli ultimi decenni, anche in corsi di laurea diversi da quelli medico-biologici e sanitari: Scienza dell'Educazione, Ingegneria, Architettura, Giurisprudenza. L'igiene è inoltre presente praticamente in tutti i corsi di laurea delle professioni sanitarie ed in molte scuole di specializzazione.

Senza risalire al lontano passato – d'altronde già citato - si ricordano Rettori come D'Alessandro e Gullotti (Palermo), Paccagnella (Verona), Bo (Sassari), Maida (Sassari) e Di Orio (L'Aquila). Molti di più i Presidi come Bo e Meloni (Pavia), Paccagnella (Padova), Mura (Sassari), Aggazzotti (Modena), Vitale (Palermo), Capelli (Cassino) moltissimi i presidenti di corsi di laurea e, più recentemente, i Direttori di Dipartimento; ricordiamo, perché unica nel panorama italiano, la direzione di un Dipartimento di Ingegneria, il DICEA della Sapienza di Roma, attualmente affidata ad un Ordinario medico, Daniela D'Alessandro, MED/42.

La Scuola di Specializzazione in Igiene e Medicina preventiva (IMP) è stata inserita dal MIUR tra le dieci irrinunciabili del SSN ed ha avuto importanti incrementi dei contratti per l›ammissione al primo anno, pur in un contesto di restrizioni economiche. Oggi, con la Specializzazione in IMP, si accede alle direzioni mediche di Presidio ospedaliero e sanitarie di Azien-

da sanitaria ed ospedaliera, alla direzione di Distretto, dei Servizi di igiene pubblica (SIP) e di alimenti e nutrizione (SIAN), oltre che alle carriere universitarie, a quelle nella Sanità privata ed alla posizione libero professionale di medico competente.

I vecchi corsi di perfezionamento della fine anni '80 – primi anni '90 in Epidemiologia ed in Management sanitario della Sapienza e della Cattolica ebbero un notevole successo, ed oggi proseguono come Master. Diversi i programmi di Master oggi erogati in numerosi atenei italiani e coordinati da professori di Igiene.

Una particolare menzione merita il ruolo degli igienisti italiani nel passaggio della formazione infermieristica da regionale ad universitaria. Gli igienisti di Roma Cattolica (Vanini), Roma Sapienza (Puntoni, D'Arca e Fara) e Milano (Giovanardi e Fara) hanno aperto e gestito le prime Scuole universitarie a fini speciali per Dirigenti e Docenti di Scienze infermieristiche (che richiedevano per l'accesso, oltre al Diploma regionale di Infermiere Professionale, un Diploma quinquennale di scuola media superiore, e fornivano una preparazione biennale nel campo della dirigenza, della docenza e della ricerca infermieristica); successivamente sono stati realizzati i corsi di laurea di primo e secondo livello per infermieri. Fu la Sapienza a bandire il primo concorso per professore associato di scienze infermieristiche, con Renga e Fara in commissione. Le prime Cattedre nacquero alla Sapienza (Sansoni), a Torino (Di Giulio) ed a Verona (Saiani, oggi professore ordinario). Attualmente la disciplina conta 4 posti di Professore Ordinario, 22 di professore associato e 13 di ricercatore.

Tra i molti meriti di Giuseppe D'Alessandro, Rettore a Palermo, c'è quello di aver accettato l'invito di Antonino Zichichi, trapanese e fisico di rilievo internazionale, di attivare una Scuola di Epidemiologia e Medicina Preventiva nell'Ambito del Centro di Cultura Scientifica (oggi Fondazione) "Ettore Majorana", da lui creato negli anni '60 ad Erice, ed inizialmente dedicato a studi di alta Fisica, poi allargato alla Medicina. Scomparso di lì a poco D'Alessandro, fu il suo allievo Luigi Dardanoni, insieme a Moises Szklo, epidemiologo della Johns Hopkins, ad attivare nel 1974 il primo corso "Le basi epidemiologiche della medicina preventiva", cui altri seguirono negli anni fino ad oggi, al ritmo di 1-3 l'anno. Alla sua direzione Luigi Dardanoni affiancò Gaetano Maria Fara, ed alla scomparsa di Dardanoni subentrò Giuseppe Giammanco di Catania. Carlo Signorelli e Francesco Vitale sono stati di recente cooptati come co-direttori della Scuola, che ha totalizzato sinora 56 corsi, tutti assai apprezzati, e nella primavera del 2019 ha ospitato la Deans' and Directors' Retreat dell'Association of the Schools of Public Health of the European Region (ASPHER).

La designazione nel Consiglio Superiore di Sanità (CSS) è sempre stata un ambìto riconoscimento delle competenze igienistiche, tanto che vi sono state presidenze di Sezione affidate a docenti di igiene (Augusto Giovanardi, Fernando Luigi Petrilli, Bruno Angelillo, Gaetano Maria Fara, Alessandro Maida, Bruno Paccagnella, Pietro Crovari, Walter Ricciardi) fino alla presidenza CSS di Roberta Siliquini nel 2014, prima donna a presiedere il principale organo di consulenza tecnica del Ministero.

Quanto a ruoli ricoperti da igienisti nell'organizzazione sanitaria nazionale, a partire dalla Direzione Generale di Sanità coperta in epoche diverse da Pagliani e da Petragnani, dobbiamo ricordare la lunga presidenza Seppilli dell'Istituto italiano di Medicina Sociale, la breve presidenza ISPESL, subito interrotta dalla sua scomparsa, di Floriano Ghezzo, la presidenza INRAN di Ferdinando Romano, le presidenze ISS consecutive di Walter Ricciardi e di Silvio Brusaferro, la Presidenza Gilli della Società Metropolitana Acque di Torino.

La vitalità della disciplina nell'associazionismo scientifico nazionale ed internazionale è testimoniata dai ruoli rivestiti da alcuni docenti in società ed associazioni scientifiche nel recente passato: Gaetano Privitera (Presidente SIMPIOS), Maurizio Marceca (Presidente SIMM), Ida Mura (Commissione Scientifica ANMDO), Silvio Brusaferro (Presidente SIMPIOS e Coordinatore EUNEPTIS), Paolo Contu (Vicepresidente IUHPE), Carlo Signorelli (Tesoriere EUPHA e componente Board ASPHER), Walter Ricciardi (Presidente EUPHA per due mandati ed incoming President WFPHA) ed altri ancora. Continua e importante la partecipazione dei professori di igiene nella SITI (13) mentre, più recentemente, ai docenti di igiene delle università romane si ascrive la creazione dell'Accademia Romana di Sanità Pubblica (2012)

e agli igienisti universitari degli Atenei lombardi la nascita dell'Accademia Lombarda di Sanità Pubblica (2017). Numerose le manifestazioni scientifiche internazionali organizzate in Italia (14), tra cui citiamo il Congresso Europeo di Sanità pubblica (EPH Conference) del 2015 (15) ed il prossimo Congresso mondiale di sanità pubblica del 2020, assegnato a Roma.

Conclusioni

Questa ricostruzione (che non ha la presunzione di essere né completa né esaustiva) di cento anni di storia di una disciplina universitaria rilevante nel panorama nazionale fa trasparire come l'igiene abbia, nell'ultimo secolo, rivestito un continuo e rilevante ruolo tecnico di supporto alle istituzioni sanitarie. Dalle prime leggi di polizia sanitaria fino al recente rilancio in emergenza dell'obbligo vaccinale, la disciplina ha saputo sempre prevedere e indirizzare i cambiamenti, aggiornandosi e sviluppandosi. Conquiste culturali negli ultimi decenni sono state le aree della metodologia epidemiologica, del management sanitario, dell'igiene ospedaliera e più recentemente dell'Health Technology Assessment (HTA), della leadership in sanità, della genetica in Sanità Pubblica e della digitalizzazione della sanità, (e-Health), tutti settori multidisciplinari in cui illustri colleghi hanno portato contributi culturali importanti.

C'è ancora molto da fare, soprattutto in alcuni ambiti dove il peso scientifico dell'igiene e della sanità pubblica accademica non ha ancora espresso tutti i suoi notevoli potenziali: la valutazione d'impatto sanitario, l'igiene degli alimenti e della nutrizione, il risk management, gli studi di valutazione sui servizi sanitari, la Urban Health. Tuttavia il background culturale multivariato dell'igiene, le notevoli esperienze operative, la versatilità della coabitazione in ambiti scientifici dove gli accademici si sono sempre confrontati con i colleghi del servizio sanitario nazionale, degli enti di ricerca, delle istituzioni sanitarie nazionali e internazionali, rende ottimisti per un futuro di ulteriore, grande sviluppo della disciplina.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

Appendici

1. La nascita e lo sviluppo dell'Igiene Siciliana: dagli Istituti alla Scuola Siciliana.

L'igiene come materia autonoma nasce a Messina nel 1902 con l'avallo del professor **Ziino** titolare della cattedra di medicina legale e di igiene e viene chiamato a ricoprire una cattedra di igiene, per primo, il professor **Francesco Sanfelice**, proveniente da Cagliari ma siciliano purosangue, la cui linea di ricerca verte soprattutto sull'eziologia dei tumori, anticipando in tal modo quello che alla fine del secondo millennio ed all'inizio del terzo e ritenuto il problema dei problemi. È in questo periodo che l'igiene comincia a conquistarsi spazi di intervento e di ricerca in tutta la Nazione compresa la Sicilia, tant'è che il Consiglio superiore della Pubblica Istruzione decretò che "nelle università presso le quali l'insegnamento di igiene sia provvisto di sufficienti mezzi dimostrativi e sperimentali potrà essere istituito un corso complementare di igiene pratica, sotto la direzione del professore di detta disciplina". Tale corso durerà almeno due mesi e sarà fatto in tempo, da fissarsi ogni volta dal rettore della Università.

Qualche anno prima, nel 1890, **Eugenio di Mattei** aveva vinto la cattedra di igiene a Catania dove rimase per un anno. Infatti nel 1891 vinse la cattedra di igiene a Palermo dove si trasferì per un anno per tornare poi, definitivamente, a Catania dove ha retto l'Istituto di igiene fino al 1935. Egli dev'essere ricordato per le sue ricerche sulla rabbia nel lupo, sulla malaria e la peste. Infatti il professor Di Mattei, allievo di Pettenkofer, studiò i risvolti sociali di malattie come la malaria e volle impegnarsi sul campo svolgendo per oltre 35 anni una intensa attività sul territorio, distinguendosi per l'abnegazione con cui si prodigò nell'epidemia colerica nel 1911 e negli episodi di peste del 1914 e degli anni 1920/21. Fu anche il primo a istituire in Sicilia i corsi annuali di igiene pratica per ufficiali sanitari frequentati dai medici di tutte le province dell'isola e della Calabria. Era la Catania di Verdi e De Roberto, che Di Mattei frequentava personalmente ed ebbe anche in cura, ma accanto alla

meravigliosa isola degli aranci e dell'Etna c'era anche quella della malnutrizione, della povertà e delle malattie a cui Eugenio Di Mattei, con quel senso del dovere, dedicò generosamente tutta la propria vita.

Nello stesso periodo in cui Sanfelice operava a Messina e Di Mattei a Catania, a Palermo era il professor **Luigi Manfredi** che dava sostanza e corpo alla nuova igiene. Egli, può essere considerato il padre dell'Igiene Palermitana, essendosi impegnato soprattutto a trovare una sede per l'Istituto di igiene ed a dotarlo di tutte le attrezzature didattiche e scientifiche necessarie per quel tempo. Scrive

il Manfredi: "arrivato a Palermo non trovai un tetto e ricordo come l'igiene, ai suoi albori di disciplina universitaria, fosse considerata una scienza aerea" . La ricerca di locali idonei fu impegnativa fino a quando egli propose al rettore dell'Università del tempo di utilizzare i locali dell'ex monastero delle ree pentite sito in via Divisi: il vecchio, storico Istituto d'Igiene di Palermo.

Notevoli i suoi studi sull'importanza della contaminazione della superficie stradale nelle grandi città, nonché gli studi sull'inquinamento del suolo in Sicilia e in Campania.

Come si può notare le tre Facoltà ed i tre Istituti di igiene hanno iniziato il loro percorso di formazione tecnica e culturale nello stesso identico periodo 1890-92 sotto la spinta di tre grandi personalità quali erano Sanfelice, Di Mattei e Manfredi, sviluppando, ognuno di loro, un'autonoma linea di ricerca strettamente collegata alla propria formazione e ai propri interessi culturali, scevra da condizionamenti esterni di qualsiasi tipo. Si può senz'altro affermare che, fino al 1940/45, l'igiene siciliana non esisteva come scuola siciliana ma come un insieme di tre entità diverse con differenti progetti e linee di ricerca senza collegamenti e senza obiettivi comuni. Tra l'altro in quell'epoca mancava ancora il cemento unificante dei medici di sanità pubblica. Infatti l'ufficiale sanitario del tempo, figura professionale preesistente all'istituzione delle scuole di specializzazione, era formata con un corso

di soli due mesi, come già detto, ed aperto anche ad altre figure professionali quali i chimici ed i veterinari. Tale figura, evidentemente, non poteva rappresentare l'igiene del territorio in quanto carente di una cultura di base igienistica indispensabile per la gestione corretta e moderna della sanità pubblica. Mancava soprattutto la passione per la prevenzione che, nel tempo, è diventata invece la base su cui si fonda ogni interesse ed ogni atto dell'igienista.

È stato intorno agli anni 50, dopo l'attivazione delle scuole di specializzazione di igiene da parte del Prof Petragnani a Catania, del professor D›Alessandro a Palermo e del prof De Blasi a Messina, che comincia a svilupparsi il legame forte tra i tre istituti e tra essi e i territori di interesse iniziando quel percorso di collaborazione fruttuosa ed intelligente fra igienisti delle tre università e fra questi e gli igienisti del territorio che ha consentito all›igiene moderna il raggiungimento di obiettivi sicuramente non immaginabili al di fuori di questo rapporto. Ed è in questo periodo che comincia a delinearsi quella che dagli anni '50 in poi viene chiamata «Scuola siciliana» della quale, seguendo il percorso formativo dei tre istituti, è facile individuarne l›ombelico, il punto di partenza e il percorso culturale comune, e se si pone attenzione man mano agli spostamenti ed alla formazione dei principali attori, ci si accorge che i nostri istituti, e quindi anche noi, noi siciliani, iniziamo il nostro percorso nel 1939 con Giovanni Petragnani a Siena.

Petragnani è è stato il maestro di Giulio Buonomini, a sua volta maestro, a Palermo, di Giuseppe d›Alessandro e di Raffaele de Blasi; il primo dei quali nominato dapprima professore supplente a Palermo durante la guerra, in assenza di Buonomini bloccato a Pisa ed impossibilitato a ritornare nella propria sede a causa dell›invasione anglo americana della Sicilia. De Blasi, invece, immediatamente dopo la guerra si è trasferito a Pisa al seguito del suo maestro, che ivi era stato chiamato, per ritornare in Sicilia nel 1956 per ricoprire la cattedra che fino ad allora era stata di Renzo Vendramini.

Intanto dal 1945 Petragnani era stato chiamato alla cattedra di igiene di Catania. Con quest›ultimo atto il cerchio si chiude con tre insigni igienisti che, provenienti da un unico filone, iniziano da parte loro un percorso virtuoso di mutuo arricchimento scientifico e culturale che porterà la Sicilia ad un ruolo di primo piano nel mondo della sanità pubblica.

Nel 1963 esce dai ruoli il professor Petragnani e viene chiamato come titolare della prestigiosa cattedra il professor Mariano Cefalù, primo allievo del professor D›Alessandro, rafforzando ulteriormente il già forte legame fra i due istituti tanto che, alla morte del professor d›Alessandro, nel 1972, il professor Cefalù è ritornato a Palermo aprendo la strada di Catania al prof. Giammanco, mentre a Messina alla morte del professor de Blasi, al suo posto, si insediava il compianto professor Luigi Squeri.

A questo punto riteniamo che il percorso che ha portato all›unità di intenti dell'igiene siciliana sia abbastanza chiaro. Unità di intenti che nasce dall›origine culturale e dai comuni interessi ed obiettivi sia tecnico-politici che scientifici dei tre istituti; ma per approfondire questo concetto è necessario accennare ai principali temi di ricerca dei tre gruppi evidenziando la comunità d›intenti senza, tuttavia, tralasciare la specifica identità di ognuno di essi.

Il professor Petragnani ha rivolto il suo interesse soprattutto al perfezionamento di metodiche nella diagnostica delle malattie infettive ed in quest›ambito ha utilizzato per primo il terreno di cultura, per questo chiamato di Petragnani, che ha consentito l›isolamento di micobatteri della tubercolosi con le diverse «varietà s»»; la lotta antimalarica che ha fatto con grande maestria, impegnandosi nel territorio, soprattutto della Sicilia sudorientale; l›invenzione e la produzione di un vaccino antitubercolare, «L›anatubercolina integrale», ampiamente usato in tutta Europa soprattutto nel momento in cui, per un incidente avvenuto a Lubecca, il vaccino BCG è stato messo in stand-by per un lungo periodo; ha studiato ed ha utilizzato le capacità stimolanti della placenta anche per la prevenzione di malattie infettive. Gli anni '40-'70 sono molto importanti per l›igiene perché maturano indirizzi nuovi della medicina con la scoperta di nuovi farmaci e di nuove sostanze antiparassitarie che inducono alla nascita di una nuova organizzazione sanitaria. È un momento importante per la Sicilia con l›applicazione su vasta scala del DDT e degli altri insetticidi clorurati, già sperimentati dalle truppe americane, sui fronti di guerra, per la sanità pubblica nella lotta contro la malaria. L›uso del DDT contro «anofele» ed altri insetti nocivi molesti porta ad una drastica riduzione dei casi di malaria.

Memorabili restano le ricerche e gli interventi di prevenzione e di risanamento effettuati dai tre istituti in ogni angolo della Sicilia. Si distinguono in quest›opera soprattutto i due Istituti di Palermo e Catania ricaduti in zone endemiche della Sicilia mentre l›Istituto di Igiene di Messina era attivo soprattutto nella lotta antimalarica in Calabria. Si distinguono in quest›azione il prof. Petragnani, come detto, a Catania, i proff. D›Alessandro e Cefalù con l›entomologo Moriani a Palermo; il prof. Vendramini ed, a seguire, il prof. De Blasi, a Messina.

Con l›avvento del prof. De Blasi la ricerca, a Messina, subisce un›impennata soprattutto nel campo della microbiologia applicata, della parassitologia, della virologia.

L›attività del Prof De Blasi non si è limitata solo allo studio della prevenzione delle malattie infettive ma si è rivolta anche a quello delle malattie sociali, viste sotto il profilo epidemiologico e profilattico. Si deve a lui la costituzione di un Centro per le malattie cardiovascolari e di un centro di citologia cellulare per lo screening del tumore cervicale. Inoltre particolare interesse il Prof De Blasi dedicò alla immunoprofilassi e infatti fu tra i primi in Italia ad intravedere l›importanza e la necessità della vaccinazione antimorbillosa; il risultato di queste ricerche hanno contribuito alla stesura di un testo di medicina scolastica. Le ultime indagini riguardano l›isolamento e la diffusione delle infezioni da Yersinia enterocolitica.

Il Prof Luigi Squeri, succeduto al prof. De Blasi, ha dedicato il proprio impegno scientifico in modo prevalente ad indagini epidemiologiche sugli enterovirus ed in particolare sui Poliovirus. Anche lui, seguendo le linee tracciate dal suo maestro, ha rivolto il proprio interesse inizialmente alla prevenzione primaria dedicandosi alla valutazione delle prime applicazioni delle vaccinazioni antipolio, antimorbillo e antirosolia in Italia. Molto interessanti le sue ricerche sui virus influenzali , sulla circolazione degli Arbovirus nell›Italia meridionale e sull›importanza della conoscenza, del controllo e della sorveglianza delle IST.

Contemporaneamente ai due maestri operano un gruppo di ricercatori latori di esperienze diverse ma complementari a quelle dei due maestri.

Essi sono i Proff. Munaò e Grillo, grandi esperti di Igiene Ambientale e il prof. Delia che ha diversificato la sua passione scientifica soprattutto con studi sulla Legionella.

A Catania, il prof. Cefalù, avendo intuito l›importanza del supporto Igienistico per uno sviluppo sostenibile delle nuove grandi realtà industriali che in quel periodo incominciavano a sorgere nella Sicilia Orientale e Sud-Orientale, formava un nucleo di ricercatori di formazione diversa da quella medica per attivare e supportare quelle iniziative che hanno contraddistinto, in seguito l›Igiene Ambientale, nell›Istituto di Catania.

Assieme a queste nuove esperienze, il prof. Cefalù ha continuato a sviluppare a Catania l›antica matrice batteriologica, soprattutto degli enterobatteri, che a Palermo formavano ancora la principale base ed il substrato dell›Igiene.

Ci limitiamo a ricordare le grandi inchieste epidemiologiche durante le epidemie di tifo di Gela, di Piazza Armerina e di tanti altri episodi in tutta la Sicilia. Sempre in stretto contatto con l›Istituto di Igiene di Palermo e in particolare col centro per lo studio e la tipizzazione degli Enterobatteri, voluto dal prof. D›Alessandro e guidato, in quegli anni dal Prof. Giammanco, che quando il prof. Cefalù, alla morte del Prof. D›Alessandro è tornato a Palermo a dirigere l›Istituto, è stato chiamato a Catania laddove ha continuato a sviluppare i propri interessi scientifici sugli enterobatteri integrandoli con le nuove esperienze che già si erano formate in quella sede. A Palermo il prof Cefalù ha ritrovato i colleghi che avevano reso grande l›Istituto: il prof. Dardanoni eclettico ricercatore, virologo e precursore della ricerca epidemiologica, cofondatore del primo Registro dei Tumori dell›Italia centromeridionale e insulare, quello di Ragusa; il prof. Gullotti grande esperto di organizzazione sanitaria e fine politico, Preside e poi Rettore e Presidente della Siti dopo una breve avventura alla Sapienza di Roma; il prof. Nino Romano, allievo del prof. Dardanoni che, fra i primi, intuì l›importanza di nuovi filoni di ricerca virologica e particolarmente dell›HIV che studiò a fondo e fondò in un laboratorio da Lui stesso voluto e costruito con grande abilità.

E poi Laura Valentino, Giuseppe Tringali, Francesca Aiello, il compianto Nino Nastasi, trasferitosi a Firenze, e tanti altri che hanno contribuito a fare grande l›Igiene Siciliana e non solo.

Costretto dal tempo e dallo spazio alquanto brevi vogliamo ricordare, tuttavia, quello che, a nostro avviso è stato uno dei più significativi contributi offerti dalla Sicilia all›Igiene Italiana: il Congresso nazionale di Cefalù. Erano gli anni ‹70 e la dialettica fra le diverse scuole (Milanese, Genovese, Veneta, Romana, Napoletana, Siciliana) era a dir poco accesa. Il congresso di Vibo Valentia era stato complicato; non c›erano intese capaci di resistere più di qualche mese, gli interessi di «scuola» avevano sopraffatto le scelte scientifiche e culturali.

Erano gli anni ‹70 e l›atmosfera era irrespirabile, come oggi, ma i grandi maestri Siciliani di quel momento e cioè i Proff. Cefalù, Dardanoni, De Blasi, Squeri, Gullotti, riuscirono a convincere la comunità nazionale a partecipare ad un congresso straordinario solo per la rifondazione scientifica, etica e politica dell›Igiene. Riuscirono a portare avanti il progetto. Il congresso si tenne a Cefalù e l›Igiene, da allora, ha prosperato fino ai nostri tempi.

Appendice 2:
La scuola igienistica messinese

Nel 1921 **Guido Volpino** fondò l'Istituto di Igiene, da lui diretto fino al 1948; gli succedettero **Renzo Vendramini** (1949-56) e, quindi, **Raffaele De Blasi** che, dall'Università di Pisa, fu chiamato a ricoprire la cattedra di Igiene per la Facoltà di Medicina e Chirurgia. A quest'ultimo si può fare risalire l'inizio della scuola di Igiene di Messina che orientò e formò numerosi allievi nel campo della batteriologia clinica, della virologia e della parassitologia, capisaldi della ricerca igienistica di quel periodo. Egli si occupò anche di immunoprofilassi attiva valutandone l'efficacia e l'importanza nella prevenzione di malattie infettive quali la poliomielite, la rosolia e il morbillo. A tale scopo nacque il reparto di sierologia che consentì di condurre anche numerose ricerche epidemiologiche sulle pato-

logie prevalenti nel territorio (Brucellosi, Salmonellosi, Sifilide). Inoltre, il Prof De Blasi, già in epoche non sospette, ebbe l'intuizione di prevedere l'importanza della prevenzione delle patologie cronico-degenerative istituendo un centro per il controllo delle malattie cardio-vascolari e un laboratorio di citologia cellulare per lo screening del tumore della cervice uterina. Il Prof. De Blasi organizzò anche i laboratori di batteriologia e di chimica ambientale per il controllo delle acque, che in seguito furono ulteriormente sviluppati per consentire di svolgere ricerche sull'inquinamento delle diverse matrici ambientali. Sotto la sua Direzione l'Istituto, nel Maggio 1981, si trasformò in Istituto Pluridisciplinare di Scienze Igienistiche, anche grazie alle sue capacità di formare numerosi allievi che ricoprirono l'insegnamento dell'Igiene in altre Facoltà (Scienze MM, FF e NN, Scienze della Formazione, Farmacia). Questo fu da lui diretto sino al 15 Novembre dello stesso anno, giorno della sua morte. Il 24 Novembre 1981 subentrò nella direzione dell'Istituto **Luigi Squeri**, già allievo interno con Vendramini dal 1953, e dal 1959 assistente ordinario con De Blasi che da sempre lo considerò il suo naturale successore introducendolo nella scuola igienistica siciliana e nazionale.

L'attività di ricerca e di didattica di Luigi Squeri gli consentì di conseguire l'ordinariato in Igiene nel 1974. A tal proposito sono da ricordare i pionieristici studi nel campo della virologia, in particolare rivolti alla diffusione degli enterovirus nel territorio siciliano e calabrese. A questo scopo, dopo avere appreso le tecniche per l'utilizzo delle colture cellulari presso il Laboratorio di Virologia dell'Istituto di Igiene di Palermo, diretto da D'Alessandro, creò un analogo laboratorio presso l'Istituto di Igiene di Messina. In epoca successiva egli dedicò il suo interesse scientifico allo studio dei virus influenzali, alla diffusione degli arbovirus nell'Italia meridionale e, infine, introdusse la ricerca dei virus nelle acque dolci e marine, comprendendo il rischio correlato alla loro persistenza ambientale. Nell'ultimo periodo della sua attività volle affrontare, dal punto di vista della prevenzione, il tema delle Infezioni Sessualmente Trasmesse.

Contemporaneamente a quella dell'Istituto egli assunse anche la direzione della scuola di specializzazione (1981-1998, 2004-2006) di Igiene e Medicina Preventiva", precedentemente diretta dal suo maestro. Ciò gli permise di intensificare i già consolidati rapporti con la vicina Calabria favorendo l'istituzione dei primi congressi annuali interregionali della SiTI e, a tal proposito, fu Presidente per la sezione siciliana dal 1989 al 1991. Relativamente all'attività assistenziale il Prof. L. Squeri è stato direttore del Servizio di Virologia del Policlinico Universitario "G.Martino" dell'Università di Messina (1979 -1982), del I° servizio di analisi chimico-cliniche (1982-1985) e dell'UOC di Igiene Ospedaliera (1985-2003) sempre della stessa struttura.

Il Prof. L. Squeri, seguendo gli insegnamenti del suo maestro, si dedicò alla formazione di un consistente numero di allievi ai quali inculcò la dedizione e la tenacia necessarie a conseguire gli obiettivi e le finalità della ricerca sperimentale, applicando le tecniche più avanzate. Nel luglio 1986, fortemente voluto dal Prof. L. Squeri, l'Istituto Pluridisciplinare si trasformò nel Dipartimento di Igiene Medicina Preventiva e Sanità Pubblica, primo di area medica nell'Università di Messina e tra i primi dipartimenti di Igiene in ambito nazionale. Questo, intitolato al Prof Raffaele De Blasi, fu da lui diretto sino al 1992 e, in seguito, dal 1998 al 2004 data in cui, per raggiunti limiti di età, andò in quiescenza.

Nella cronologia e nella storia del Dipartimento di Igiene vanno necessariamente menzionate le due figure, rappresentate dalla Prof.ssa Calisto e dal Prof Sindoni, che per molti anni hanno affiancato e supportato sia il Prof De Blasi che il Prof L. Squeri e che sono state per gli allievi interni, poi docenti, il collegamento diretto con i due maestri. Essi hanno ricoperto a loro volta la carica di direttore del dipartimento negli anni 1992-1994 e 1996-1998 (Prof.ssa Calisto) ed in quelli 1994-1996 e 2004 -2009 (Prof. Sindoni); la prima è stata anche direttore della Scuola di Specializzazione dal 2006 al 2010. Relativamente all'attività assistenziale, il prof Sindoni è subentrato al Prof. L. Squeri nella direzione dell'UOC di Igiene Ospedaliera (2003-2009) e dal 1996 al 1997 ha ricoperto il ruolo di Direttore Sanitario dell'AOU "G. Martino", mentre la Prof.ssa Calisto ha ricoperto il ruolo di Direttore dell'UOC di Epidemiologia ed anche del DAI di Epidemiologia Igiene Medicina Preventiva e Sanità Pubblica (2003-2009). La linea seguita nella gestione e nel coordinamento delle attività di ricerca di didattica e di assistenza è stata sempre quella già segnata e profondamente inculcata dai predecessori ed entrambi hanno contribuito alla formazione di igienisti che si sono affermati anche a livello nazionale. Infine, dal 2009 al 2012, il prof Delia è stato l'ultimo direttore del Dipartimento ed ha avuto il compito di traghettare l'omogeneo Dipartimento di Igiene nel più ampio e multidisciplinare Dipartimento di Scienze Biomediche, Odontoiatriche e delle Immagini Morfologiche e Funzionali (BIOMORF). Il Prof Grillo, invece, è subentrato alla Prof.ssa Calisto nella gestione della scuola di specializzazione che ha diretto dal 2010 al 2015, ricoprendo inoltre importanti ruoli assistenziali in qualità di direttore dell'UOC di Igiene Ospedaliera e del DAI dei Servizi dell'Azienda AOU "G. Martino" dal 2009 al 2015. Relativamente all'attività di ricerca, il Prof. Delia si è occupato del controllo degli alimenti ed è stato direttore del centro regionale di riferimento per la sorveglianza ambientale e clinica della legionellosi. Sulla scia degli studi condotti dal Prof. Munaò, l'attività di ricerca del Prof Grillo ha riguardato l'Igiene ambientale. Attualmente, i filoni di ricerca seguiti dal gruppo di Igiene, inserito nella sezione di ricerca di Biotecnologie mediche e medicina preventiva del Dipartimento BIOMORF, riguardano strategie preventive in ambito ambientale, alimentare e comportamentale e la sorveglianza epidemiologica per l'individuazione dei fattori di rischio correlati alle patologie cronico-degenerative. In particolare, per quel che riguarda Il rapporto salute –ambiente, l'attività di ricerca sui meccanismi patogenetici di inquinanti ambientali è condotta con studi in vitro nel laboratorio di ricerca di Igiene ambientale diretto dalla Prof.ssa Di Pietro (16-18). Invece, i docenti inseriti nell'UOC di Igiene Ospedaliera, diretta dal Prof Raffaele Squeri, sono coinvolti in studi finalizzati al controllo del rischio infettivo in ambito ospedaliero e ai possibili interventi per il contenimento degli eventi avversi correlati (19, 20). Altro campo di ricerca di questo gruppo è quello già indicato ed ereditato dai predecessori e relativo alle vaccinazioni che vengono promosse tra gli operatori sanitari anche istituendo corsi di formazione (21-24). A tal proposito recentemente è operante all'interno di questa UOC, in collaborazione con l'ASP di Messina, un centro vaccinale che offre il servizio ai degenti e a tutto il personale sanitario. Oltre al controllo delle ICA,

nel laboratorio diretto dalla Prof Picerno, l'attività assistenziale e di ricerca è mirata alla sorveglianza epidemiologica delle infezioni da HIV sia nei soggetti con comportamento a rischio che nella popolazione generale e in quella migrante. Infine la direzione del laboratorio regionale di riferimento per la sorveglianza ambientale e clinica della legionellosi è ora affidata alla prof.ssa Laganà.

Oggi, la scuola di specializzazione in Igiene, accreditata dal MIUR, è diretta dalla Prof.ssa Picerno e continua ad essere il punto di riferimento per la formazione di medici igienisti impegnati nella sanità pubblica. Per quanto riguarda l'attività didattica, la disciplina di Igiene, ricoperta dai docenti appartenenti al vecchio nucleo del Dipartimento a cui si sono aggiunti nuovi ricercatori, è presente in 19 CdS triennali, magistrali e a ciclo unico per un numero di CFU pari a 84. Inoltre, gli stessi docenti svolgono, per il settore disciplinare di appartenenza, i corsi nelle scuole di specializzazione dell'area medica attivate nell'Ateneo di Messina.

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Received: 15 June 2019
Accepted: 18 July 2019
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