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Road to Rome 2020

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

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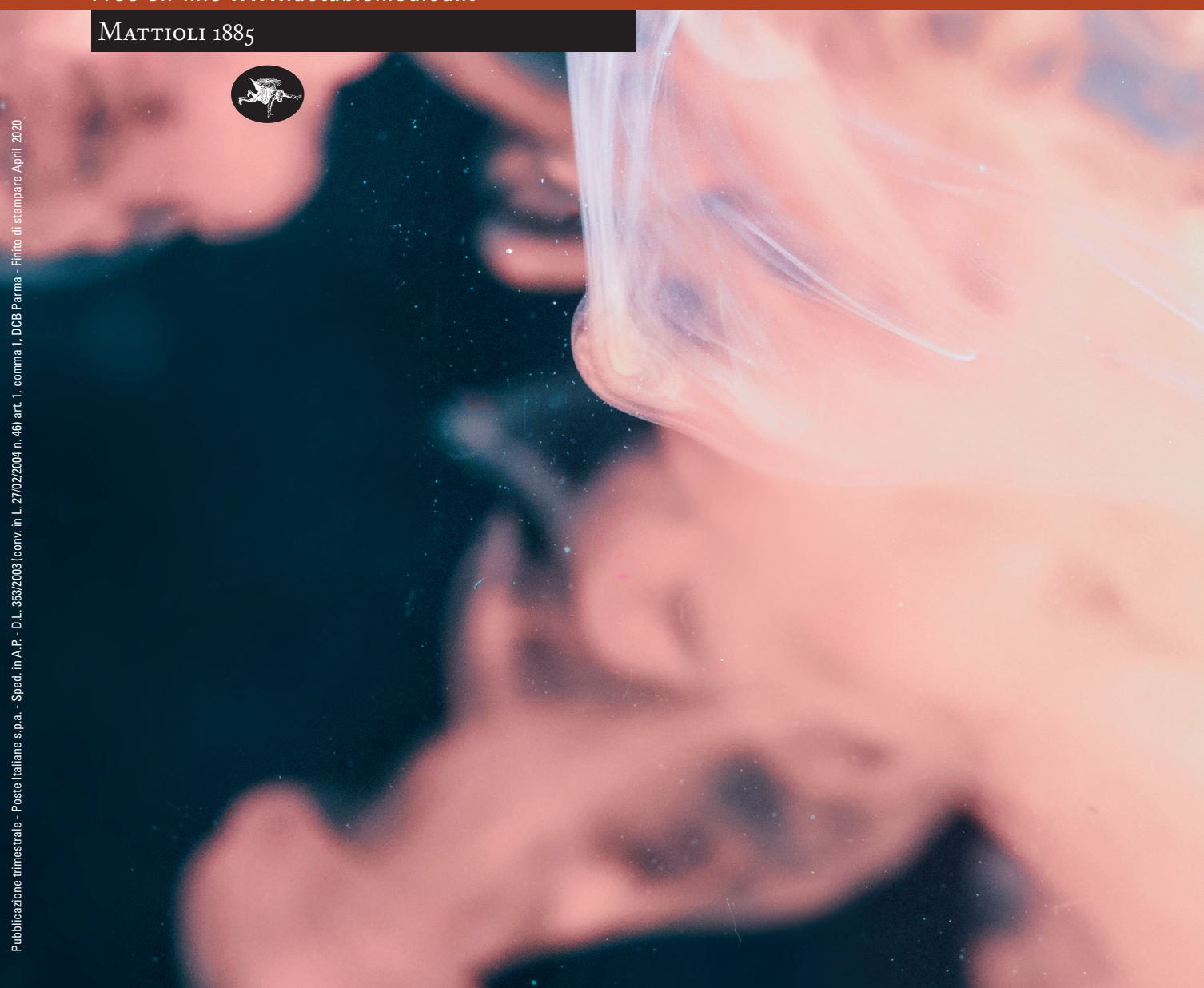

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Short papers

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COVID-19: Hygiene and Public Health to the front

Public Health professionals and academics have been on the frontline of Italian history during the COVID-19 response like they never did before. Ancient professors of Hygiene such as Celli, Pagliani, Sclavo, Petragnani, Seppilli and Giovanardi flanked politicians in other critical moments. They helped them to manage healthcare reforms, earthquakes response, Seveso Dioxin disaster, cholera and poliomielitis epidemics and other health threats.

The ongoing COVID-19 epidemic has highlighted the paramount importance of the practical application of basic concepts of public health, which were considered so far became obsolete, such as personal hygiene, quarantine, individual protective devices or basic epidemiological measures. Hygiene and Public Health used to have a targeted audience in professionals and lecturers. Nowadays, these topics are critical and of concern of a much larger audience. Public Health women and men are now asked to act in task forces, media broadcasts, webinars and consulting activities.

In phase 2 of this epidemic - which is about to begin when this volume is to be published – the role of Public Health professionals could become even more relevant. However, this unexpected season must be managed with seriousness and intelligence, capitalizing it also for the future. If our Post-Graduate Schools of Public Health ("Igiene e Medicina Preventiva"), our scientific associations, our academic lecturers and our officers do not prove to be up to the situation, a dull future for the discipline might very well be. On the contrary, if as we all hope, we will be able to ride the wave of a dramatic health crisis, transforming it into a relevant scientific and professional opportunity, then we will be able to build on the post-COVID-19 a cutting-edge, a more attractive, relevant and modern discipline.

This Supplement of Acta Biomedica, planned before the onset of the epidemic emergency in Italy, but already successful in presenting two papers on COVID-19, is further proof of how current and lively our discipline is.

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Original article

Synergies in Design and Health. The role of architects and urban health planners in tackling key contemporary public health challenges

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Summary. *Background and aim:* Important public health improvements have been achieved over the past decades, but new challenges are emerging and progress cannot be taken for granted. Urban settlements host most of the global population, but they are also sources of several threats. The aim of the paper is to investigate the role of architects and planners in contributing to overcome these critical health challenges and propose strategic actions for collaboration with the public health workforce. *Methods:* Taking global trends and public health challenges as starting point, a scoping literature review has been conducted to illustrate the possible synergies that architecture and public health workforce should exploit to support population health improvement and tackle key public health challenges. *Results:* The built environment affects climate change and public health through the use of resources, site location, and green spaces. In architecture curricula, limited space is devoted to health and vice versa. There is an urgent need for recognition of the benefits of collaboration and cross-fertilisation between public health and planning workforce from local to global levels. *Conclusion:* Public health is evolving from a bio-medical to a socio-anthropological approach and architects/planners have fundamental roles; further collaboration, research and training are needed.

Key words: public health, urban health, workforce collaboration, climate change, noncommunicable diseases, evidence based design, urbanization, multidisciplinary, architects role

Introduction

Public health transformations and challenges

In recent years, important public health improvements have been achieved thanks to technological, social and economic evolution, but this progress cannot be taken for granted. The risk that this success can be reversed is real. In the era of increasing urbanization, globalization, digitalization, ageing population, rise of non-communicable diseases and climate changes, the nature and scale of public health challenges is rapidly evolving, and significant transformations are both necessary and urgent (1-4).

Globally, the average life expectancy at birth increased by 5.5 years between 2000 and 2016 reporting the fastest increase since the 1960s (5). Overall, it is expected to increase by 4.4 years between 2016 and 2040 and by 7.8 years for males and 7.2 years for females if more progresses are made. Nevertheless, if less progress is made, life expectancy could even decrease by 0.4 years for males and stagnate for females (6). Additionally, latest CDC data show that the U.S. life expectancy has declined over the past few years and this troubling trend is largely driven by deaths from drug overdose and suicide (7).

According to the latest Bloomberg Global Health Index, good health is still not achievable for all the countries and there are tremendous differences between the top 10 and the lowest ones (8). If a key component of achieving universal health coverage is ensuring that all populations have access to quality health care those data

appears as fairly critical. Indeed, despite substantial gains since 2000, many low and middle Socio-demographic Index (SDI, a summary measure of overall development) countries, face considerable challenges unless intense policy action and investments focus on advancing access to and quality of health care across key health services, especially Non-Communicable Diseases (NCD) (9). NCDs, such as diabetes, cancer and heart diseases, are responsible for over 70% of global deaths. The associated principal risk factors, that also exacerbate mental health issues are: tobacco use, physical inactivity, harmful use of alcohol, unhealthy diets and air pollution (5).

Emergent conceptual frameworks place a substantial focus on the built and urban environment not least because of the contribution that healthy urban design can make to the prevention and reduction of the burden of disease associated with these elements..

For example it is recognized that two sets of risk factors related to obesity such as food quality and physical activity are strictly linked to built environment characteristics in terms of physical access to local supermarkets, groceries, fast food restaurants, or convenience stores, area walkability, greenness, blue water, land use mix, and access to recreational facilities (10).

Another important topic to consider is the risks related to air pollution and the impact this has on stroke, heart disease, lung cancer prevalence, and both chronic and acute respiratory diseases, including asthma. Healthy design intervention along with sustainable policies at the urban and building level (such as supporting cleaner transport, energy-efficient homes, power generation, industry and better waste management) would reduce key sources of outdoor air pollution (11).

Finally, recent studies highlighted that good accessibility to public transport and densely built urban texture could contribute to reduce mental health risks such as depression, especially for fragile citizens (12); at the same time, poor environmental conditions and building features that include ventilation, lighting, temperature, indoor microbial, chemical and pest exposures are likely to have negative impacts (13) .

Transformations in cities and society and their impact on public health

Cities significantly contributed to increase health conditions and are also deeply linked to the aforementioned NCDs risk factors. In fact, at the beginning of 20th century only 10% of people inhabited urban settlements while in 2015 more than half (54%) of the world population lived in urban area and this figure is projected to 60% in 2030 and 66% in 2050. The United Nations estimates that more than 90% of future urban population growth will be in developing countries (14,15). Cities constitute centers of concentration of wealth, productive capability and creativity. They are best placed to satisfy population needs because basic services can be produced at a higher quality and at lower per-capita costs, and because in cities people can best organize for their rights (16). At the same time, cities are the platform of several issues that in the recent history contributed to challenging the living conditions of dweller and workers. For example, the industrial revolution radically transformed our cities and society. Whilst significantly supporting economic growth, it also gave rise to several environmental and health problems which were new at that epoch. As stated by Szreter, "*The world's first industrial revolution seemed to be having anything but obvious health benefits for the majority of the population*" (17). Today leap changes in civilizations spearheaded by technology breakthroughs and economic growth do not always automatically result in improved health, at least not for all persons from all backgrounds in society, and particularly if they harm the earth and the environment. Another example is that urban sprawl and the segregation of workplaces from housing, when incorporated with the increasing affordability of motor vehicles and the prioritization by policy makers and planners of mobility over accessibility, have led to an over reliance on the private motor vehicle increasing sedentary, pollution and other relevant NCDs risk factors (18,19). At the same time global challenges for 21st century cities emerged related to a fast-growing urban population. Foremost amongst these include, the need for expansion of affordable housing, upgrading of water and sanitation infrastructure, provision of critical services to increasing numbers of migrants to the city and meeting of the growing demand for a reliable energy supply while mitigate greenhouse gas emissions. Cities with clean air, energy-efficient infrastructure, and widely accessible green spaces can attract more investment and businesses, create more jobs, and offer more

opportunity to people from all walks of life. These issues cannot be tackled by Public Health professionals alone but there is a need for a multidisciplinary approach, stressing the social responsibility of practitioners that are directly involved into the urban planning process.

Starting from the Health in All policies and the humble recognition that health system alone can only make a limited contribution to health improvements, a more holistic intervention can support the creation of policies such as the Economy of Wellbeing, putting people and their wellbeing at the center of decision-making processes (20,21). This can improve productivity, foster gender equality and increase social protection toward a sustainable long-term economic growth (22).

In the climate change era, socially responsible urban planners need to recognize and assume a role in improving the living conditions of city dwellers, recognizing that urban development is deeply linked to politics, economics, management and health (16,23).

In March 2019 the European chapter of the International Academy for Design & Health organized the 1st European Sysmposium in "Salutogenic Hospital Design and Urban Health - Global Perspectives and Local Identities in Healthcare Architecture", as a first attempt to set up this dialogue at the international level boosting what already achieved by national associations both in health and planning field (i.e. SIti, Italian society of Public Health and CNETO, Italian Center for Healthcare Architecture) patronaging different events and multidisciplinary working groups, in line with the innovation addressed by the European Public Health Association (EUPHA). The symposium value was to bring in the keynote session high level political representatives and decision makers (Minister of Health, Regional and Municipal healthcare authorities) along with international experts in the field of Public Health, Planning and Architecture (24).

Research Objective

Therefore, starting from this exemplary event and the challenges addressed, the aim of the paper is to investigate the relationship between public health and architecture and understand the benefits that such synergy can provide to populations and urban health.

Methods

The 2019 International Academy for Design & Health 1st European Symposium "Salutogenic Hospital Design & Urban Health – Global Perspectives and Local Identities in Healthcare Architecture" offered the platform for bringing together different expertise from the public health and the built environment field and to understand the common challenges that the two disciplines are facing. In the same year World Health Organization (WHO) started its new 5-year strategic plan focusing on universal health coverage, health emergencies and promoting better health and wellbeing. Reaching these goals would include targeting the 17 Sustainable Development Goals as well and therefore will require addressing the threats to health from a variety of angles (25). A multidisciplinary approach is therefore mandated. As stressed by WHO, issues including climate change and NCDs, are not exclusively the public health workforce responsibility, but several professional fields are involved. Specifically, in recent years there is a growing awareness on the role of architects and urban planners around those issues and researchers are starting to ask themselves *"What can urban planners do to promote the health and wellbeing of people in their cities and regions?"* (26).

Therefore, the paper is developed as a scoping review, with the aim of deepening the understanding of the relationship between public health and urban/architectural planning. In particular, specific research questions are explicitly addressed hereafter:

Are there example of existing relationships between public health and architecture? Is the scientific literature addressing this topic? Which are the challenges? Are there areas or challenges for future improvement?

In order to address the research question, a literature review was conducted in the Scopus Elsevier scientific database. This database was preferentially selected because it involves most of the technical and social science disciplines that might include a substantial component of the contributions related to architecture, urban planning and engineering along with public health, health management and health policies researches. After some preliminary searches based on the keywords that emerged during the 2019 International Academy for Design & Health 1st European

Symposium "Salutogenic Hospital Design & Urban Health – Global Perspectives and Local Identities in Healthcare Architecture", the search string selected was the following:

"*architect*" OR "*urban planner*" OR "*designer*" AND "*public health*" OR "*global health*" OR "*healthcare*".

This combination searched in *Titles*, *Abstracts* and *Keywords*, without any timespan or geographically limitations yielded 1853 results.

The results were screened and several contributions were excluded because they were out of the research scope. In particular the main exclusion criteria were:

- contributions not in English language. Some papers seemed to tackle the issue in a precise manner but they were available only in original language (i.e. Portuguese) and therefore they have been excluded because of their limited audience and local scope.
- contributions with strict focus on the building scale. Some papers had a specific focus on the role of architects and planner in the design or management of building assets, especially hospital facilities. This area is very specific therefore only contributions with explicit reference to health have been considered
- contributions that used the selected terms in figurative ways or with another meaning which is out of the research scope (i.e. architecture used as a metaphor for articulated public health governance characteristics).

After title and abstract screening, 40 full text papers were read and out of these 19 were selected, analysed and further discussed according to the following 5 thematic areas:

- The impact of urban phenomena on health
- Lack of training and need of curricular cross-fertilisation
- Need for collaboration in professional life
- Individual personalities bridging the gap
- Assessment tools based on evidence, such as: Strategic Environmental Assessment (SEA), Sustainability Assessment (SE) or Health Impact Assessment (HIA).

The full Prisma flow diagram is described in Figure 1 while the complete list of papers is highlighted in Annex 1.

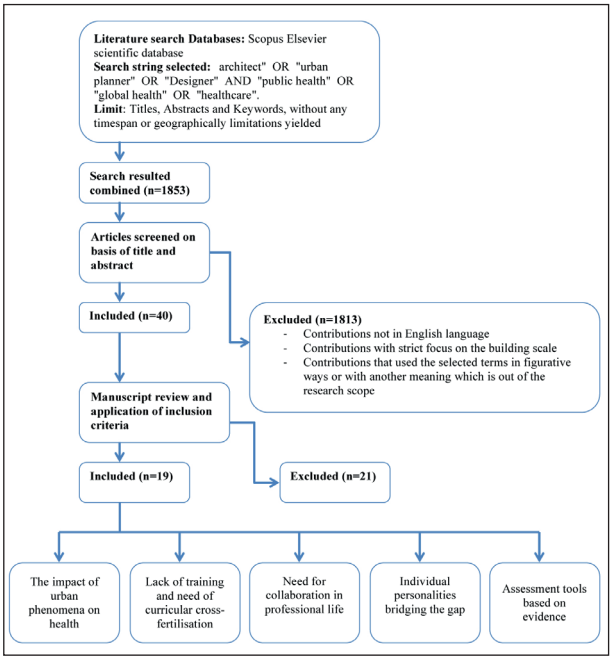

Figure 1. WHO regions of origin: distribution of subjects per year of study

Results

Descriptive analysis of the papers reviewed

Amongst the papers reviewed, the majority are primary studies (58%), 6 (32%) literature reviews and two commentaries/ editorials. Both in the primary studies as well as in the reviews, authors attempted to identify a problem or issue and propose possible frameworks to deepen the topic understanding or the systematization and conceptual elaboration. This is itself denotes a high level of novelty of the research field. Research was mostly developed in USA (47%) and UK (32%) -if considering also a case of collaboration with South Africa institution). Canada, Chile and Australia Italy and France contributed one paper each. No studies from Asian countries were found.

The topic is very recent, indeed the oldest papers included have been published in year 2000 while the newest are from year 2020.

The author affiliations are related to three main fields typically; policy, design (built environment) and health. Only two group of authors (11%) can be related to the policy-making field, 5 (26%) to the architectural, built environment and urban design field and 6 (32%) to the public health and medical field. The

remaining 32% (6 out of 19) papers have been written by co-authors that are coming from a combination of these different fields, showing a good level of collaboration.
The authors published slightly more in public health-related journals (58%) versus a 42% of the articles that are from built environment related platform. An interesting fact is that in two cases design-related authors published in health-related journals and vice-versa.

In general terms, it is noted that in the last 20 years the topic of relationship between design and health emerged, first from a policymaker point of view and then in the architectural and public health field, with a growing interest in cross-fertilisation and multidisciplinarity.

The impact of urban phenomena on health

Worldwide, the urban population has grown rapidly from 751 million in 1950 to 4.2 billion in 2018 and projections show that global trends could add another 2.5 billion by 2050 resulting in almost 70% of the total population (15). Therefore, seeking to improve public health globally requires an improved awareness of how urban life affects health and well-being (27) .

Sanitary engineering interventions importantly changed the profile of many diseases such as the case of Cholera outbreaks, where the water depuration and the improvement of sewer systems in urban areas are fundamental actions to prevent and reduce the diffusion of the bacteria (28). Indeed today several forms of engineering expertise are applied to basic public health problems, such as improving water, sanitation, and hygiene (WASH) conditions in low and middle income countries (29).

Since the mid-1990s, the European Sustainable Cities and Towns Campaign with the participation of the WHO-Healthy Cities has explored the relationship between health and planning. SDG 11 in particular aims to make cities and human settlements inclusive, safe, resilient and sustainable. Other SDGs and many of the 169 SDG targets relate closely to urban design and health planning dimension with specific regard to housing, transportation, water management, air quality, etc. (30,31). As stated by several researchers, built environment can contribute to climate change, influence transportation and affect health through the use of resources, materials, site location, availability of green space (32-35). Urban planning and public health share also common missions and perspectives. Both aim to improve human well-being, emphasize needs assessment and service delivery, manage complex social systems, focus at the population level, and rely on community-based participatory methods (36).

Urban environment, indeed, affects all aspect of life and health and therefore architects and planner play an important role in determining health and well-being (27,35).

Lack of training, need for curricular cross-fertilisation and collaboration in professional life

Nevertheless, despite health being considered in several relevant documents, (i.e. EU policies, UN and WHO reports) it does not appear to be part of the architectural profession or education at European and international level (35). Marsh et al recently showed that the Royal Society of Public Health reported that professionals related to environment (including architects and planners) are considered between the largest employment group of professionals that have impact in the wider public health realm (13%), the ones that should be most interested but the least involved into the public health agenda (1%) (4). Scholars highlighted that the profession charged with planning the urban environment currently lacks a conceptual framework for integrating health into spatial planning decision- making (32). As already mentioned, since 1992 Rio "Earth summit" and the introduction of SDGs, the official view of urban planning has shifted from a simply physical or aesthetic constructs, or manifestations of economic forces, toward providers of sustainable and healthy human habitat and ecosystems (30,32). Nevertheless, as recently pointed out by Rice, there are no requirements that stipulate that health expertise should be mandatory in the institution and agencies that have the power to mandate the scope of architectural profession, training education practice or knowledge. The current situation is that the design of built environment is undertaken by professional figures that lack sufficient exposure on health throughout their education (35,4). Despite exceptional situations in top European universities, among which is important to mention Politecnico di Milano "Design &

Health Lab" and Chalmers University of Technology "Center for Healthcare Architecture", health is rarely considered and never systematically incorporated into the architecture and planning curricula. By becoming knowledgeable about the growing body of research on health and the built environment, architects can become a positive force in the development of healthy urban centers (37,38).

Individual personalities bridging the gap and assessment tools based on evidence

Since 1854 Jon Snow's study of public water pump in London to fight cholera, toward 1960s Jane Jacobs's call for safe, walkable and non-segregating American cities, relevant personalities have overcome the disciplinary threshold between public health and urban studies (36,39). But it is now time for a call to systematic action for all the professionals and researchers, professional bodies and institutions to closely work together to face the biggest challenges for public health at global level.

Some methodologies and assessment tools, such as Strategic Environmental Assessment (SEA) and Sustainability Assessment (SA) encourage holistic, systematic projects and plans appraisal, but deeper frameworks are necessary (32,40,41). Examples of Health Impact Assessment (HIA) tools are also encouraged by the WHO and some examples are emerging (30, 42). Tools and methodologies are important in order to support the decision makers. Difficulties in basing decisions on evidence can be related to language, exploitability of data, relevancy, not willingness of listen the academic results or, not direct link of health benefits with return on investments (30). Therefore, public health evidence must be translated into actionable healthy planning principles ensuring an Evidence-Based Design process of planning at different scales, providing empirical data on design elements. While architecture itself does not necessarily provide a cure, good design can also act as a preventive tool and enhance the overall quality of life (43-45). As per the introduction of *green* and sustainable requirements into European laws, regulation and recommendation, there is the urgent need of identify also *healthy* requirements to be translated into rigorous and concrete policy interventions (46-48).

Discussion

The need for collaboration between the two fields

There is a renewed and growing recognition of the link between public health and built environment because many of the most important advancements in public health have come thanks to improvement and innovation in the built environment. Moreover, recent rising public health issues such as obesity and non-communicable diseases stressed the attention on the lifestyle and on how built environment can impact that. Unfortunately, the specialists in public health have not worked alongside built environment colleagues and the same happened with other way around. Therefore, the need for a workforce development initiative through shared learning and reflection between the two professional sectors and agendas emerges (37).

On one hand, by focusing on the health-promoting aspects of design, architects have the opportunity to contribute to find solutions to major societal challenges, to lead change, to improve the quality of life for everyone, and to grow the demand for their services (49). In the ideal world, architects and their clients will begin to consider the health-promoting aspects of design as routine and desirable as they now consider sustainable elements of design understanding that many features of sustainable design offer co-benefits of promoting health (50). To reach that stage, architecture students and health science students need to be taught consistently about the health impacts of design elements in an Evidence Based Design perspective (4,35,51).

On the other hand, among the different non-traditional careers and leadership opportunities that medical doctors have, an emerging field is the relationship between health and built environment. As highlighted by Ganske, clearly emerge the need of cross-fertilisation between the two field both in education and in practice. This shared learning approach could open up valuable and multidisciplinary career possibilities strengthening the characteristics of public health as interdisciplinary and multi-professional field (52,53).

Joint collaboration between the two field and a higher degree of contamination should be promoted and improved. Working across sectors to incorporate a health promotion approach in the design and evaluation of built environment components may mitigate

climate change, promote adaptation, and eventually improve public health (34,54). Furthermore, the engagement of professional bodies, institutions and government for significantly incorporating and better integrating health in the built environment and urban agenda is fundamental. Leadership capabilities emerged to be very important in this negotiation, in order to building bridges, enforcing the decision-making role and empowering the next generations (55). Appropriate governance is also important in terms of policies, structures, funding and services that are able to leverage and address resources in a proper way. Finally, it is important to exploit the power of contemporary communication and dissemination toward politicians, clinicians and technicians but, as well, to the general public with a wise use of new media and a narrative aligned to people's real concerns.

Both evidence and experience should support large scale decisions to solve complex problems and communicate the solutions to the wider public in order to truly implement the SDGs.

Conclusion

Recent trends in contemporary society engender new challenges for public health, including climate change, ageing population and non-communicable diseases. To face those complex issues a novel and multidisciplinary approach is required and public health workforce should be enriched and contaminated by other disciplines.

The appraisal of the literature in the area highlighted also important gaps and relevant future research agenda in terms of analysis, advocacy and actions. New strategies must be taken in the different fields of research, teaching and practice in order to improve the synergies and achieve global objectives.

The literature review conducted highlights in several ways that the built environment in which we live is a significant determinant of health. Therefore, architecture and planning should be finally considered as an instrument for creating healthy communities and contribute to tackling the emerging public health challenges at local and global level. Public health is the result of various socio-economic, cultural and environmental factors and therefore should move from a biomedical to a socio-anthropological model. Contamination between planning and health in the spheres of education, research, dissemination and governance is highly recommended for future developments.

Limitations

The search has been conducted only in Scopus Elsevier database and only scientific articles have been reviewed therefore some relevant journals from the architectural field who are not traditionally indexed in those databases might have been excluded.

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ANNEX 1. Table of Literature included

Authors, year	Authors	Year	Title	Journal	type	place	author field	journal field	Urban phenomena impacts on health	Lack of training and need of curricula contamination	Need for collaboration in professional life Need for collaboration in professional life	Individual personalities bridging the gap	Assessment tools based on evidence (SEA / SE / HIA / EBD)
Dubé, 2000	Dubé, P.	2000	Urban health: An urban planning perspective	Reviews on Environmental Health	study	Canada	policy	health	x				
De La Barra, 2000	De La Barra, X.	2000	Fear of epidemics: The engine of urban planning	Planning Practice and Research	study	Chle	policy	design	x				
Barton, 2005	Barton, H.	2005	A health map for urban planners: Towards a conceptual model for healthy, sustainable settlements	Built Environment	review	UK	design	design	x	x			x
Kochtitzky et al, 2006	Kochtitzky, C.S., Frumkin, H., Rodriguez, R., Dannenberg, A.L., Rayman, J., Rose, K., Gillig, R., Kanter, T.	2006	Urban planning and public health at CDC	MMWR. Morbidity and mortality weekly report	review	USA	health+ policy	health	x			x	
Galea et al, 2006	Galea, S., Freudenberg, N., Vlahov, D.	2006	Cities and the Health of the Public	A framework for the study of urban health	study	USA	health	health	x				
Gorman et al, 2007	Gorman, N., Lackney, J.A., Rollings, K., Huang, T.T.-K.	2007	Designer schools: The role of school space and architecture in obesity prevention	Obesity	review	USA	health+ design	health	x				x
Younger et al, 2008	Younger, M., Morrow-Almeida, H.R., Vindigni, S.M., Dannenberg, A.L.	2008	The Built Environment, Climate Change, and Health. Opportunities for Co-Benefits	American Journal of Preventive Medicine	review	USA	health	health	x	x	x		

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Plkington et al, 2008	Pilkington, P., Grant, M, Orme, J.	2008	Promoting integration of the health and built environment agendas through a workforce development initiative	Journal of the Royal Institute of Public Health	study	USA	design	design	x	x	x		
Verderber, 2012	Verderber, S.	2012	Sprawling cities and our endangered public health	Sprawling Cities and Our Endangered Public Health	study	USA	design	design	x				
Seidel et al, 2012	Seidel, A.D., Kim, J.T., Tanaka, I.B.R.	2012	Architects, urban design, health, and the built environment	Journal of Architectural and Planning Research	review	USA	design	design	x	x	x		
Ganske, 2012	Ganske, I.	2012	A different angle: Physician and architect	Physicians' Pathways to Non-Traditional Careers and Leadership Opportunities	study	USA	health	health	x	x	x		
Burton et al, 2015	Burton, A., Bambrick, H., Friel, S.	2015	If you don't know how can you plan? Considering the health impacts of climate change in urban planning in Australia	Urban Climate	study	Australia	health	design	x		x		
Exner, 2015	Exner, M.	2015	Edwin Chadwick and the public health act 1848: Principal architect of sanitary reform	Routledge Handbook of Water and Health	review	UK	health	health	x			x	

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Authors, year	Authors	Year	Title	Journal	type	place	author field	journal field	Urban phenomena impacts on health	Lack of training and need of curricula contamination	Need for collaboration in professional life Need for collaboration in professional life	Individual personalities bridging the gap	Assessment tools based on evidence (SEA / SE / HIA / EBD)
Capolongo et al, 2016	Capolongo, S., Lemaire, N., Oppio, A., Buffoli, M., Le Gall, A.R.	2016	Action planning for healthy cities: The role of multi-criteria analysis, developed in Italy and France, for assessing health performances in land-use plans and urban development projects	Epidemiologia e Prevenzione	study	Italy+ France	design	health	x		x		x
Dannenberg & Burpee, 2018	Dannenberg, A.L., Burpee, H.	2018	Architecture for Health Is Not Just for Healthcare Architects	Health Environments Research and Design Journal	comment	USA	health+ design	design	x	x	x		
Anderson, 2019	Anderson, D.C.	2019	Bricks and Morals—Hospital Buildings, Do No Harm	Journal of General Internal Medicine	comment	USA	health+ design	health	x		x		x
Carmichael et al, 2019	Carmichael, L., Townshend, T.G., Fischer, T.B., Lock, K., Petrokofsky, C., Sheppard, A., Sweeting, D., Ogilvie, F.	2019	Urban planning as an enabler of urban health: Challenges and good practice in England following the 2012 planning and public health reforms	Land Use Policy	study	UK+ South Africa	health+ design+ policy	design	x		x		x
Marsh et al, 2020	Marsh, R., Pilkington, P., Rice, L.	2020	A guide to architecture for the public health workforce(Article)	Public Health	study	UK	health+ design	health	x	x	x		
Rice, 2020	Rice, L.	2020	The nature and extent of healthy architecture: the current state of progress	Archnet-IJAR	review	UK	design	design	x	x	x		

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Original article

New competences to manage urban health: Health City Manager core curriculum

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Summary. A core curriculum is an essential step in development knowledge, competences and abilities and it defines educational content for the specialized area of practice in such a way that it can be delivered to new professional job. The Health City Manager core curriculum defines the strategic aspects of action to improve health in cities through a holistic approach, with regard to the individual, and a multi-sectoral approach, with regard to health promotion policies within the urban context. The Health City Manager core curriculum recognizes that the concept of health is an essential element for the well-being of a society, and this concept does not merely refer to physical survival or to the absence of disease, but includes psychological aspects, natural, environmental, climatic and housing conditions, working, economic, social and cultural life - as defined by the World Health Organization (WHO). The Health City Manager core curriculum considers health not as an "individual good" but as a "common good" that calls all citizens to ethics and to the observance of the rules of civil coexistence, to virtuous behaviours based on mutual respect. The common good is therefore an objective to be pursued by both citizens and mayors and local administrators who must act as guarantors of equitable health ensuring, that the health of the community is considered as an investment and not just as a cost. The role of cities in health promotion in the coming decades will be magnified by the phenomenon of urbanization with a concentration of 70% of the global population on its territory.

Key words: urban health, public health, Health City Manager, core curriculum

Introduction

The concept of health is essential to the well-being of a society. This concept, as defined by the World Health Organization (WHO), relates not merely to physical survival or the absence of disease, but includes psychological factors, natural, environmental, climate and housing conditions and working, economic, social and cultural life. Cities play an important role in health promotion owing to the phenomenon of urbanisation, with 70% of the world's population living in urban areas.

The EU Committee of the Regions during its 123rd plenary session, 11-12 May 2017, approved the own-initiative Opinion "Health in cities: the common good". The Opinion calls for more effective and responsive multilevel governance to improve health policy and design a fair, shared, harmonious urban system and suggest evaluating the benefits of establishing the post of a healthy city manager and it suggested that cities which do not yet have such a service should evaluate the potential benefits and costs of establishing the post of a HEALTH CITY MANAGER, who would interpret the needs expressed by the city and guide the improvement process in synergy with local authorities by aligning their policies and ensuring their implementation.

In December 2017, Italian Minister of Health and President of Italian Municipalities Association (ANCI) during the G7 side event signed the Urban Health Roma Declaration. The declaration has underlined the necessity of a strong alliance between Municipalities, Universities, Health Centres, Research Centres, Industry and Professionals to study and monitor the determinants of citizens' health at an urban level and it suggested in the same time the creation of a HEALTH CITY MANAGER figure, able to guide the process of health improvement in urban areas in synergy with local and sanitary administrations.

Health City Institute, in partnership with EUPHA-Urban Health and WFPHA, has developed a core curriculum to define the HEALTH CITY MANAGER knowledge, competences and ability.

Learning degree and professional profile

The HEALTH CITY MANAGER must have acquired transversal and interdisciplinary knowledge in:

- promotion of health and well-being, prevention through the adoption of correct lifestyles of communicable and non-communicable diseases typical of urban areas, in synergy and collaboration with the Authorities responsible for Public Health and Prevention, as well as the Health Professions of the territory;
- assessment of the social and psychological impact of urban life on the quality of life of the citizen with specific attention to situations of greater fragility and to the weak categories of the population in order to achieve improvement;
- city architecture, urban planning and territorial planning, both in terms of the functionality of the city areas and the activation and coordination of participation processes, together with the ability to read, integrate and coordinate the plans aimed at governing the territory and transforming urban contexts;
- capacity for political-administrative dialogue at the various institutional levels, in respect of mutual prerogatives, and interaction with the informal / horizontal levels for the management of the city;
- management of relations for the finalization and measurement of public policies implemented according to adequate timelines and criteria for the replicability and scalability of the project.

The Health City Manager gains professional skills in public health management, sociology and psycho-sociology of communities, urban architecture and control in reducing social and health inequalities.

Duration of the course is determined in University Educational Credits (CFU): each CFU corresponds to 25 hours of student learning. Being a highly theoretical learning, each CFU corresponds to 8 hours of lectures and 17 hours of individual study. The duration of the course will be 80 hours of frontal teaching for a total of 250 hours of student learning and 10 CFU. Degrees valid for access to the course are Master's Degree (MD) achieved in the fields pursuant to Ministerial Decree 22 October 2004, No. 270; Master's Degree (LS) obtained pursuant to Ministerial Decree of November 3rd 1999, n.109, to the previous equivalent; Diploma (DL) referred to the previous equivalent regulations; foreign equivalent qualifications equivalent. (figure 1).

Degree of knowledge
Superficial: the student has heard of it
General: the student knows how to frame the topic within the overall knowledge
Detailed: the student must know the subject in a comprehensive way in relation to training needs
Degree of competence
Mnemonic: the student remembers what he has learned
Interpretative: the student knows how to apply lessons learned to interpret data or phenomena, related to a context he has witnessed or to a problem that has been faced and solved by others
Decisional: the student knows how to apply lessons learned to solve problems personally and make autonomous decisions
Degree of ability
Not required: the student does not have to apply the knowledge or the competence
General: the student is able to carry out the activity in cooperation
Autonomous: the student has to accomplish the activity autonomously

Figure 1. Learning degrees

Knowledge, competences and abilities of the Health City Manager

The following table 1 identifies ten priority objectives on Urban Health, the related activities and the knowledge, competences and abilities to be required to the Health City Manager.

Conclusion

The function of Health City Manager is the product of a wider consideration process started by the Health City Institute think tank on the main issues of its surveys, namely health in cities and the impact of urbanization on health determinants.

What clearly emerges from this consideration is the need to adopt a new interpretation paradigm, which takes into account a multidisciplinary approach to this issue and the need to achieve a complete involvement at level of local institutions, represented by Administrations and Health Units. These institutions can have a faster and deeper impact on the quality and on the lifestyles of citizens through goal-oriented public policies. New welfare and care models should therefore be

Table 1. Health city manager – core curriculum

Objective	Activities	Knowledge	Competences	Abilities
1. Health and urban public policies: innovative models of governance, multilevel and multidisciplinary	• Knowing how to analyze the urban context from a health perspective	General	Interpretative	Not required
	• Involving citizens in choices according to the "health in all policies" approach	General	Interpretative	General
	• Engage local administrations in promoting the health of citizens by studying and monitoring the health determinants specific to their urban context, leveraging the strengths of cities and drastically reducing health risks	Detailed	Decisional	Autonomous
	• Promote public-private partnerships for the implementation of policies and consequent strategic actions	Detailed	Decisional	Autonomous
2. Literacy and accessibility to information and health education, including in schools	• Promote training courses at regional or local level addressed to social and health workers, health professions and patient associations to allow them to assess the degree of understanding of the citizen and express themselves accordingly with compatible and effective language	General	Interpretative	General
	• Allow citizens, patients and their associations to communicate easily and promptly with the health system, being able to find, understand and evaluate the information most appropriate from time to time to satisfy their own care needs, also by exploiting the potential offered by the digital technologies	General	Decisional	Autonomous
	• Promote and consolidate collaboration between healthcare, education and local communities	Detailed	Interpretative	Not required – charged to the decision maker
	• Create a network of health operators between ASL and AO and teachers of schools in order to define guidelines for correct information on health	General	Interpretative	Not required – charged to the decision maker
3. Healthy lifestyles in the workplace, in large communities and in families	• Spread good practices for health promotion in the workplace and strengthen the incentive system for socially responsible companies that invest in safety and prevention	Detailed	Decisional	Autonomous
	• Implement projects in large communities, involving families	General	Interpretative	Not required – charged to the decision maker
4. Food and nutritional culture	• Outline guidelines that take into account the different contexts and different targets of the population (appropriate school and / or companies menus)	Detailed	Decisional	Autonomous
	• Organize information events and food education projects in the territory (Gardens for Health, Zero Waste).	Detailed	Decisional	Autonomous

Table 1. Health city manager – core curriculum

Objective	Activities	Knowledge	Competences	Abilities
5. Access to sports and physical activity practices for all citizens	• Guarantee all citizens free access to infrastructure and green spaces, with particular attention to people in socio-economic difficulty according to the principle of "Sport Citizenship" and to daytime physical activity in urban travel (home to work / school)	Detailed	Decisional	Autonomous – interaction with political decision maker
	• Hypothesize new ways to protect solidarity between generations, improving the inclusion of older people in cities and promoting active aging	Detailed	Decisional	Autonomous – interaction with political decision maker
	• Encourage sports and physical activity for children and young people, in contrast to the phenomenon of adolescent dropout, also through the active involvement of families	Detailed	Decisional	Autonomous – interaction with political decision maker
6. Urban transport oriented to slow and sustainable mobility and active transport according to a Walkable City model	• Encourage the use of sustainable modes of transport, through the creation of safe and well-connected pedestrian and cycle tracks, as well as an efficient Public Local Transport system	Detailed	Decisional	Autonomous – interaction with political decision maker
	• Provide for activities to raise public awareness towards more efficient and intermodal urban mobility choices, with shared parking and transportation facilities, as well as choices in favour of active transport	Detailed	Decisional	Autonomous
	• Encourage the adoption of SUMPs, air quality monitoring plans, noise zoning, and other planning tools	Detailed	Decisional	Autonomous – interaction with political decision maker
7. Strategies for urban and architectural planning aimed at promoting and protecting health	• Contrasting urban sprawl phenomena, through actions to regenerate and re-build parts of abandoned cities, and shrinking cities on the attractiveness of historic centres	General	Interpretative	Autonomous – interaction with political decision maker
	• Realize social and functional mix on a macro scale (aggregated in a logic of clustering) and micro scale (street level, neighbourhoods' attractiveness) according to the identification of *Healthy Destinations*	Detailed	Decisional	Autonomous – interaction with political decision maker
	• Implement all possible greening strategies of the city, with particular reference to the reduction of the Heat Island Effect (HIE), to the management of adverse meteorological events, to the protection and increase of urban biodiversity, identifying the environmental, social and psycho-perceptive of the elements of Green & Blue Areas, with particular reference to urban regeneration actions	Detailed	Decisional	Autonomous – interaction with political decision maker
	• Contrasting the phenomenon of Climate Change, identifying strategies of urban resilience for the reduction of environmental and health effects on a macro scale (whole city and hinterland, city dials, etc.) and micro (district, isolated, single square, etc.)	General	Interpretative	Autonomous – interaction with political decision maker
	• Manage Urban Solid Waste according to smart collection systems aimed at improving the hygienic conditions of the urban context and the aesthetic pleasantness of outdoor and mechanized conveying spaces in landfills or in processing centres	Detailed	Decisional	Not required

Table 1. Health city manager – core curriculum

Objective	Activities	Knowledge	Competences	Abilities
8. Primary prevention and chronic diseases	• Promote information programs on prevention to integrate diagnostic-therapeutic-assistance pathways for transmissible and non-transmissible chronic diseases among municipal administrations, in collaboration with the local health authority	General	Interpretative	Not required
	• Activate study projects in the most suitable urban contexts to bring the citizen closer in the course of his daily activities (places of care, workplaces, recreational places, sports facilities, virtual places as reference websites of the administrations themselves) in which to convey - through paper or virtual material - key messages for prevention, involving municipal administrations and health authorities	Detailed	Decisional	Autonomous
9. Social Inclusion	• Adopt policies aimed at improving the social, economic and environmental conditions of degraded neighbourhoods, with interventions, also mean-tested, aimed at improving the reference urban context	Detailed	Decisional	Autonomous
	• Align the city with the highest standards of accessibility and usability of urban services and design for all, identifying the different types of disabilities, not just motor and / or cognitive, and identifying Inclusive / Universal Design strategies for the accessibility of open spaces of the city to the different categories of users	General	Interpretative	Not required
	• Promote economic and social measures aimed at improving the inclusion, integration and social aggregation of all population categories considered disadvantaged due to economic and social conditions, or due to health conditions such as illness and disability, promoting their participation also in sports and recreational activities	General	Interpretative	Not required
	• Promote policies of prevention and socio-health inclusion for migrant populations also through the cooperation of cultural mediators	General	Interpretative	Not required
10. Monitoring of health data	• Create control booths for the study and monitoring of the impact of health determinants in the urban context, providing for the joint involvement of Municipal Administrations, Health Authorities, Universities and Research Centres	Detailed	Decisional	Autonomous – interaction with political decision maker
	• Promote multi-stakeholder partnerships for urban policies that, based on studies on the impact of health determinants in cities, can create "smart" interventions aimed at reducing health risks and promoting a healthy and inclusive urban environment	Detailed	Decisional	Autonomous – interaction with political decision maker
	• Create a permanent conference of the Hospitals of the Metropolitan Areas by delegating significant skills and decision-making powers in terms of planning (objective plans) and providing hospital health services	Detailed	Decisional	Autonomous – interaction with political decision maker
	• Interact with European Union bodies and the WHO to carry out targeted projects and attract resources	Detailed	Decisional	Autonomous – interaction with political decision maker

identified and promoted within the territorial administration culture.

All institutional and decision-making levels must develop a deeper awareness of the urgency required by the issue of health in urban areas. In order for this to happen, the Health City Institute, in cooperation with EUPHA-Urban Health and WFPHA, has identified in Health City Manager the most appropriate profile

to guide cities towards a "Health City" model, contributing to increase the administrative skills of the Authorities and to develop innovative and inclusive solutions to meet the health and welfare requests by citizens.

It is a professional profile the establishment of which has been endorsed also at European level, also through the own-initiative opinion "Health in cities: common good" adopted by the EU Region Committee (May 2017) and the positive feedback by the European Health Commissioner on the occasion of the III Health City Forum of Rome (July 2018). The Health City Institute, together with the project partners EUPHA (European Union Public Health Association - Urban Public Health Section) and ANCI (National Association of Italian Municipalities), has, therefore, on the basis of this, designed the learning profile of the Health City Manager and created the relevant training course.

The aim is to train a professional in management skills in public health, in community sociology and psycho-sociology skills and in urban architecture skills as well as in skills to reduce social and health inequalities.

To this end, the methodology, which led to the development of the core curriculum of the Health City Manager, implied the participation of highly-skilled experts in each of the area of expertise and the sharing of a multidisciplinary approach which would enable to achieve a synthesis as satisfactory and comprehensive as possible.

As a matter of fact, the course is to be considered as a postgraduate course useful to develop a professional who can be part of the Mayor' staff and to develop those skills and competencies which are however limited and functional to the goals in the remit as indicated in the programming document of the Municipal Administration with which the Health City Manager shall interface. The Health City Manager perfectly integrates with political and technical colleagues there may be in the PA staff since her/his primary task will be to calculate and describe the impact on health and wellbeing of citizens of each resolution, transversally, making it explicit (in writing) and clear to policy makers and field operators. Coordination and periodic alignment of actions put in place is a main goal to be achieved through meetings from large to small scale, including external opportunities of presenting them to the public in such a way that community understands and gains in awareness. Thanks to specific competences in project management for health, plans eventually adopted by Municipalities (i.e. SUMPs, Traffic Plans, Climate Neutral Plans, PEBAs - i.e. plans to eliminate architectural barriers, Urban Planning Strategies, AI applications or data sharing plans) converge in a common shared vision to build up a "health city". The contribution and the value added provided by this figure can improve the relations and performance of local public administrations with the health units in the territory thereby reconciling and somehow overcoming the historically very deep separation in Italy between the social and the healthcare sectors.

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Original article

2019-novel coronavirus survey: knowledge and attitudes of hospital staff of a large Italian teaching hospital

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Summary. One week after the World Health Organization (WHO) declared the 2019 novel coronavirus (2019-nCoV) outbreak a global health emergency we conducted a survey to explore knowledge and attitudes on 2019-nCoV, recently renamed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), in a large cohort of hospital staff. A representative sample of 2,046 hospital staff of a large university hospital in northern Italy (54% healthcare workers and 46% administrative staff, overall response rate: 25%) was administered an online questionnaire: overall there is good knowledge on 2019-nCoV control measures. The mean of correct answers for questions on general aspects of 2019-nCoV epidemic was 71.6% for HCWs and 61.2% for non-HCWs. The mean of correct answers for questions on 2019-nCoV patient management was 57.8% among HCWs. Nevertheless, on recommended precautions, also among healthcare workers there is still much to do in order to promote effective control measures and correct preventive behaviours at the individual level.

Key words: 2019-novel coronavirus, COVID-19, healthcare workers, knowledge and attitudes, infection control and prevention measures, emergency preparedness

Background

The very first news about the emergence of a novel coronavirus, firstly named 2019-nCoV and then renamed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1), in Hubei province, China, dated back to mid-December 2019. Only during January 2020 global awareness of this potential challenge for public health raised. On January 30th, the World Health Organization (WHO) declared coronavirus outbreak a Public Health Emergency of International Concern (2).

Even the most developed economies and healthcare systems in the world could be in significant difficulty facing the same epidemic ongoing in China (3).

The WHO, Chinese Centre for Disease Control and Prevention (China CDC), Centers for Disease Control and Prevention (CDC), European Centre for Disease Prevention and Control (ECDC) were quite soon involved in the surveillance of the 2019-nCoV spreading through careful epidemiological reports and worldwide situation updates (4). Nevertheless, to deal with this threat, national and international authorities started producing several recommendations on the most different aspects of this emergency, included risk assessment guidelines (5), travel advice (6), technical guidance (7), case definition and frequently asked questions (FAQs) (8,9).

In Italy, the Ministry of Health produced circular letters on case definition, patient management and travel restrictions (10,11). According to the Italian National Health System, these documents were adopted and published by the Regions, too.

However, as long as the situation evolved, extraordinary measures of public health were adopted by Chinese authorities with an unprecedented quarantine of wholes cities and provinces and millions of citizens involved. For instance, also the Italian government forbade direct flights from and to China (11). This

administrative order was very contested but avoiding travelling in China is today the easiest way to prevent cases in other countries (6).

All these interventions, along with the extensive use of the internet and social networks, led to the massive engagement of public opinion. The participation of media to the distribution of information and updates on the evolving epidemiology and restrictions, but also on the virology, clinics and available treatments, was crucial. General population conscious involvement is quite a new element in the management of this type of events. Recently, WHO was forced to take steps in order to ensure that the coronavirus epidemic did not spark a dangerous social media "infodemic" fueled by false information (12).

In this context, healthcare workers (HCWs) and in general hospital and public services staff, even if not directly involved implementing control measures, are key target populations of health authorities recommendations on 2019-nCoV control (13,14), with particular reference to suspected case hospital management and infection control (IC) precautions in hospital and community settings.

Fully aware and well-trained HCWs and workers in public services are a unique resource to keep health systems active and tackle the potential epidemic (15,16). Most studies show that in everyday assistance HCWs do not often observe standard precautions such as hand washing or rubbing (17,18), that are the first-line measures to prevent the new epidemic, too.

As of today, no studies had yet assessed the general knowledge on this new pathogen and the awareness on case management and IC measures recommended during hospital care and everyday life.

Objective

Aim of the current study was to assess concern, general and specific knowledge (modes of transmission, clinical presentations, and IC precautions) and health-related knowledge (case management and treatment) among hospital staff of a large Italian teaching hospital on novel coronavirus 2019 in the very first phase of the world epidemic.

Specific objectives were to investigate differences in the knowledge of 2019-nCoV between HCWs and other workers.

Methods

San Raffaele Hospital (OSR) is a 2-site tertiary-care referral hospital in Milan, Lombardy, with more than 1,300-beds hosting a private University (Vita-Salute San Raffaele University) with a medical, nursing, public health and dental school, among others.

The Infection Control Unit, in collaboration with the School of Public Health, developed a 7-item questionnaire on the 2019-nCoV, its transmission and prevention, as well as on perceived attitudes on the ongoing epidemic (available as supplementary material in Appendix 1).

Along the lines of a previous Italian study on Zika virus (19), questions were developed ad hoc, starting from brainstorming ideas and selected publications from the leading international sources. Developers had been working on the matter from the very beginning of the emergency and were daily updated on the topic.

Five questions addressed all staff while two additional questions only addressed HCWs. In order to stratify responders by professional category (HCWs or not), we introduced Question 6, and we collected only surveys where the responder answered to it.

The survey was set up using SurveyMonkey® and online administered to all OSR staff through company email. The data collection lasted seventy-two hours between February 4th and 7th 2020.

Answers were collected on a voluntary basis and responses were anonymous. Hence, it was not considered necessary to seek ethical approval.

We report descriptive analysis of 2019-nCov knowledge and attitudes distribution in HCWs and other staff. Data were statistically analysed using Excel (Microsoft Corporation, Redmond, WA, USA).

Results and Discussion

A total of 2,046 OSR staff answered the questionnaire (response rate 25%), including HCPs (physician, nurses, midwives, healthcare assistant, physiotherapists, respiratory technicians, X-ray technicians), administrative and technical staff, laboratory and research staff and they included employees, as well as medical residents and consultants.

We excluded 19 surveys on the basis of unan-

swered Question 6: therefore, 2,027 responses were analyzed.

Among the total number of 2,027 responders included, 1,102 declared themselves as HCWs or HCWs in training (54%), and 924 identified themselves as non-HCWs (46%).

Numbers and percentages of responses in each group are shown in Table 1.

In terms of concern for the incoming pathogen, almost 60% of the responders showed quite enough or a lot worry about 2019-nCoV, as shown in Figure 1. There was little difference across the two groups: non-HCWs

Table 1. Survey (questions and possible answers) and relative results presented as total and divided for healthcare workers, also in training, and non-healthcare workers (numbers and percentages). Correct answers presented in bold.

Questions		Possible answers	HCW r esponse (%)	not-HCW response (%)	Total (%)
1	Are you worried about novel coronavirus?	A lot	73 (6.6)	85 (9.2)	158 (7.8)
		Quite enough	595 (54)	457 (49.6)	1052 (52)
		Little	379 (34.4)	338 (36.7)	717 (35.4)
		Not at all	54 (4.9)	42 (4.6)	96 (4.7)
2	What is the main mode of interhuman transmission of novel coronavirus?	Airborne	278 (25.3)	309 (33.5)	587 (29)
		Droplet spread	785 (71.4)	562 (61)	1347 (66.6)
		Direct contact	37 (3.4)	49 (5.3)	86 (4.3)
		It is not transmitted.	0 (0)	2 (0.2)	2 (0.1)
3	Which clinical forms are caused by novel coronavirus?	Asymptomatic form	6 (0.5)	8 (0.9)	14 (0.7)
		Flu-like form	221 (20.1)	285 (30.9)	506 (25)
		Severe pneumonia	74 (6.7)	125 (13.5)	199 (9.8)
		All the previous	799 (72.6)	505 (54.7)	1304 (64.5)
4	Nowadays, in Italy, how can you protect yourself from novel coronavirus?	Avoiding crowded places	455 (41.4)	378 (41.2)	833 (41.3)
		Not travelling in China	575 (52.3)	461 (50.3)	1036 (51.4)
		Wearing always a surgical mask	67 (6.1)	69 (7.5)	136 (6.7)
		Not going to Chinese restaurant	2 (0.2)	9 (1)	11 (0.5)
5	What should I do in common areas, if I have a cold or flu?	Coughing and sneezing covering nose and mouth (with a napkin or upper arm)	68 (6.7)	123 (14.2)	191 (10.1)
		Often washing hands	27 (2.7)	47 (5.4)	74 (3.9)
		Keeping distance from other people, if possible	4 (0.4)	15 (1.7)	19 (1)
		All the previous	916 (90.2)	683 (78.7)	1599 (84.9)
6	Are you a healthcare worker, also in training?	Yes	1102 (100)	0	1102 (54.4)
		No	0 (0)	924 (100)	924 (45.6)
7	Which precautions are recommended by the Ministry of Health?	Standard precautions	251 (24.1)		
		Airborne precautions	337 (32.3		
		Contact precautions	26 (2.5)		
		Eye protection	1 (0.1)		
		All the previous	427 (41)		
8	Which measure are available today against novel coronavirus?	Vaccine	6 (0.6)		
		Specific therapy	29 (2.8)		
		Supportive therapy	780 (74.5)		
		All the previous	6 (0.6)		
		None of the previous	226 (21.6)		

are slightly more concerned than the HCWs, probably because they are less well aware of the topic (16).

On the question relating to modes of transmission of 2019-nCoV, the latest pieces of evidence declared that droplets are involved in the virus spread (20,21), and most of the responders answered correctly. An important proportion (33.5%) of non-HCWs answered that 2019-nCoV has an airborne transmission: this can be explained with the non-medical preparation that did not allowed distinguish the subtle but relevant difference between airborne and droplets transmission. There was also significant variation in correct reply to the question between HCWs and non-HCWs: among the second ones 61% supposed a droplets transmission against the 71.4% of HCWs.

When asked about the clinical presentations of the new infection (22–24), there were essential elements of variation between the two groups: 72.6% of HCWs answered correctly to the question stressing the wide range of possible presentations of the epidemic. At the same time, non-HCWs focused on the flu-like form, that is one of the most common forms of frequent respiratory infections. Moreover, adding up those who answered "Flu-like form" and "Severe pneumonia", a proportion of 34.8% responders excluded asymptomatic form of the infection (25), which could be quite a big problem in the containment of the epidemic.

On the question about personal protection from 2019-nCoV in everyday life in Italy (Question 4), most (more than 50%) of the responders in both groups answered adequately. It must be reported that in both groups the same quite high percentage of more than 41% suggested avoiding crowded places, that is nowadays a useless prevention measure in Italy (9). As a matter of fact, on the 7th February 2020, in Italy, 2019-nCoV transmission had not yet been confirmed, and there were only three confirmed cases of infection in travellers from China (26).

On the question about cough etiquette in common areas (Question 5), a very high percentage answered accurately in both groups, even if amongst HCWs there was a higher level of awareness of all the actions suggested (9,27).

On these first five questions of the survey, there were uniform trends in the answers in the two groups. Generally, HCWs were more aware and answered correctly with higher percentages (mean of correct answers 71.6%) than non-HCWs (mean of correct answers 61.2%), as shown in Figure 2. Only in Question 4, there were tiny differences in the answers, maybe because of the relevant and frequent campaign on public media against fake news that reaches the public opinion with compelling messages (28).

Only auto-declared HCWs answered to the last two questions.

On the question regarding IC precautions recommended by the Italian Ministry of Health (Question 7), only 41% answered properly. Most of the responders missed the recommendations to adopt simultaneously standard, contact and airborne precautions plus eye protection in the management of suspected and confirmed cases, as proposed by national and international authorities (29,30). Regarding the droplets transmission of 2019-nCoV (20), the surgical mask could be the appropriate protection needed, but Italian health authorities preferred to raise the level of prevention measures.

On the last question of the survey, on available treatments, a very high percentage of HCWs answered

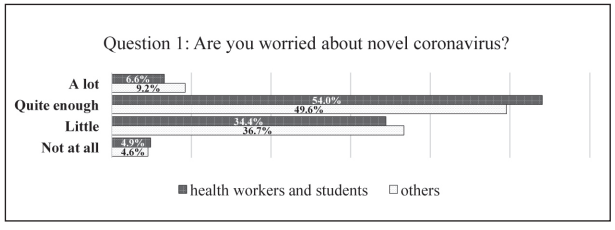

Figure 1. Answers for Question 1, presented as percentages and divided between healthcare workers, also in training, and non-healthcare workers

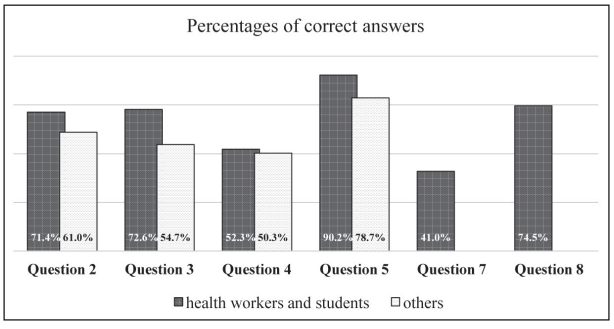

Figure 2. Percentages of correct answers for Questions 2, 3, 4, 5, 7 and 8, divided between healthcare workers, also in training, and non-healthcare workers.

correctly (74.5%), that is that only supportive therapy is now available and vaccine or specific drugs are not at disposal today (30).

The last two questions showed that among HCWs there is a generally good knowledge on the topic and the specific measures of IC recommended by health authorities and by the Chief-medical Office of OSR.

We acknowledge our study bears several limitations, including the fact that the survey was relatively short, online administered and not previously validated. Moreover, the study design was cross-sectional, and answers were exclusively self-reported and suffered from social desirability bias and voluntary enrolment.

Among conceptual limitations, there was the imprecise classification of the subjects: Question 6 allowed to distinguish only between HCWs, also in training, and non-HCWs. Another one was the lack of a specific answer on the case definition of COVID-19. It would have been quite interesting testing awareness of this topic since this is the first issue in the Emergency Department that nurses and physicians are facing. The rigorous knowledge of clinical and epidemiological criteria should lead the case management.

However, we are among the first to explore hospital staff knowledge and attitudes on 2019-nCoV, reporting data from a large study population. In the context of the ongoing public health emergency, it is of utmost importance that hospital staff and HCWs are adequately trained and informed so as to behave at their best to control infection transmission (31,32). Our data can inform the planning, implementation and evaluation of ad hoc targeted preventive interventions, as well as stimulate similar research in other settings and over time.

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Original article

Public health strategies adopted to manage the increase of accesses to vaccination services, as a result of the application of the law 119/2017

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Summary. *Background and aim of the work:* In response to the alarming reduction of vaccination coverage rates, Italian Ministry of Health approved the law number 119/2017, which has extended the number of mandatory vaccinations, for school attendance, from four to ten. The present study aims to evaluate accesses to the vaccination services of the Palermo Local Health Unit (LHU) and the variation of the vaccination coverage rates for hexavalent and measles, mumps, rubella and varicella (MMRV) vaccines, after the implementation of the law 119/2017. *Methods:* An extent of opening hours and an involvement of other health-care professionals in the vaccination services of the Palermo LHU have been adopted to manage the excess of accesses after the introduction of 119/2017 law and to limit the discomfort of general population. Vaccination accesses and coverage rates were calculated from the electronic immunization registers. *Results:* An overall increase of about 15% of single vaccination accesses was observed in the three semester after the introduction of the law in the LHU of Palermo. A peak of 35,516 accesses was observed during the second semester of 2017 (+ 30% compared to the same semesters of 2016 and 2018). From 2016 to 2018, coverage rates for full hexavalent cycle and first dose of MMRV, at 24 and 36 months, and for full MMRV cycle and fourth dose of diphtheria, tetanus, pertussis, poliomyelitis (DTPa+IPV), among 6 years old children, showed considerable increases. *Conclusions:* Law 199/2017 demonstrated a high efficacy in increase vaccination coverage rates also in Sicily. The synergy established between the LHU and the University of Palermo allowed an excellent management of the accesses to vaccination services, making it possible to respond to the public health needs of the general population.

Key words: vaccination coverage, immunization programs, vaccination policies, mandatory vaccination, National Immunization Plan

Introduction

Vaccination is the most effective and efficient preventive measure for the control, elimination or eradication of several infectious diseases (1).

The Italian National Immunization Plan (NIP) 2017-2019 identified, within the National Health System, vaccines that are offered actively and free of charge to at risk populations (2). Despite this, similarly to other European countries, Italian health-care professionals had to face the re-emerging phenomenon of the vaccine hesitancy, that contributed to alarming decreasing trends in childhood vaccination coverage (3). Recently, the general positive attitude of the population to vaccination has been undermined by "fake" news easily spread on the internet and social media, reports on suspected side effects after vaccination, increase of anti-vaccination movements actions (4 - 6).

The decrease of vaccination coverage rates led to a resurgence of vaccine preventable diseases. In particular, a significant increase of measles cases recorded in Italy from 1 January 2017 to 31 December 2018 was observed, with 7,854 cases notified by Italian Ministry of Health (7).

Of note, Sicilian Health Department reported 1,111 cases of measles in 2018 (44% of the total Italian cases), making Sicily the administrative Italian region with the highest incidence (222 cases per million inhabitants) (8).

In response to the alarming reduction of vaccination coverage rates, Italian Ministry of Health approved in July 2017 the law number 119, which has extended the number of mandatory vaccinations, for school attendance, from four to ten (9).

In particular, vaccination against poliomyelitis, diphtheria, tetanus, pertussis, hepatitis B, *Haemophilus influenzae* type B disease, measles, mumps, rubella and varicella (chicken-pox) became compulsory for kindergarten attendance (9).

For children and adolescents attending primary and secondary schools (6-16 years), monetary fines for families of unvaccinated children were imposed (9).

In order to further improve vaccination adherence among school-age children and other at-risk categories, the Sicilian Health Department has issued two directives, mainly focused on health-care professionals and staff, in order to make uniform both the vaccination offer and the application of the law n.119/2017 (10, 11).

After the adoption of the law, a significant raise of catch-up appointments and accesses to vaccination services were observed for mandatory but also for recommended vaccination (such as meningococcal and pneumococcal vaccination) (12). Several extraordinary measures have been therefore adopted by the LHU of Palermo, to manage the accesses to vaccination services and to limit the discomfort of general population and the increase in the workload of healthcare workers (HCWs) (10).

Specifically, an extent of vaccination services' opening hours (on late afternoon and on Saturday) was accompanied by an involvement of other health-care professionals working in the continuity care services, such as general practitioners (GPs) and family pediatricians (FPs) trainees (11).

Moreover, a collaboration between the LHU of Palermo and the Hygiene and Preventive Medicine post-graduate medical school of the University of Palermo was launched, with a direct contribution of medical residents in the activities of vaccination services.

The aim of the study was to evaluate the accesses to the vaccination services of the Palermo Local Health Unit, during the three semesters before and after the implementation of the national law 119/2017, with a particular focus on the variation of the vaccination coverage rates for hexavalent (diphtheria, tetanus, pertussis, poliomyelitis, hepatitis b, *Haemophilus influenza* type b) and MMRV (measles, mumps, rubella and varicella) vaccines.

Material and Methods

Sicily is the fourth most populous Italian administrative Region, with 4,999,891 inhabitants (13). The Region is divided into 9 Local Health Units (LHUs), one for each Province: Agrigento, Caltanissetta, Catania, Enna, Messina, Palermo, Ragusa, Siracusa and Trapani. In particular, the Province of Palermo, accounting for 1,252,588 inhabitants resident in 82 municipalities including three minor islands, is the most populous (13). The Local health Unit of Palermo consists of 10 Sanitary District and 65 vaccination services.

The Territorial Unit of Public Health, Epidemiology and Preventive Medicine of the Local Health Unit of Palermo, throughout electronic immunization registers available in every vaccination service, collected data on vaccination coverage rates, included in the Regional vaccination schedule.

Data collected by single Sicilian LHUs were annually recorded into a digital Regional immunization registry and, within February 28th of the following year were checked, verified and sent by the Regional Health Department in aggregate form to the Ministry of Health, to estimate the national vaccination coverage (14).

A descriptive analysis of the accesses to vaccination services in the three semesters before (from 1st of January 2016 to 30th of June 2017) and after (from

Table 1. Accesses to vaccination services of the Palermo LHU, in the three semesters before and after the introduction of the law 119/2017

Before law 119/2017 introduction (from 1st of July 2017 to 31st of December 2018)			After law 119/2017 introduction (from 1st of January 2016 to 30th of June 2017)			Overall single accesses percentage change (%)
Observation period	Number of single accesses	Overall single accesses	Observation period	Number of single accesses	Overall single accesses	
1st semester 2016	23,591	76,165	2nd semester 2017	35,516	89,442	+14.8
2nd semester 2016	24,833		1st semester 2018	29,578		
1st semester 2017	27,741		2nd semester 2018	24,348		

1st of July 2017 to of 31st December 2018) the implementation of the law 119/2017, and the corresponding percentage increase, were performed.

Moreover, vaccination coverage rates over the last three years (2016, 2017, 2018) were analyzed using crude rates at 24 and 36 months (for full vaccination cycle of hexavalent and first dose of MMRV) and at 6 years of age (for fourth dose of diphtheria, tetanus, pertussis, poliomyelitis - DTPa + IPV - and full vaccination cycle of MMRV).

All data were collected in a database using software EpiInfo 3.5.1 (Epi Info™, CDC, Atlanta) and were analyzed using statistical software package STATA v14.2 (StataCorp LP, College Station, TX, USA).

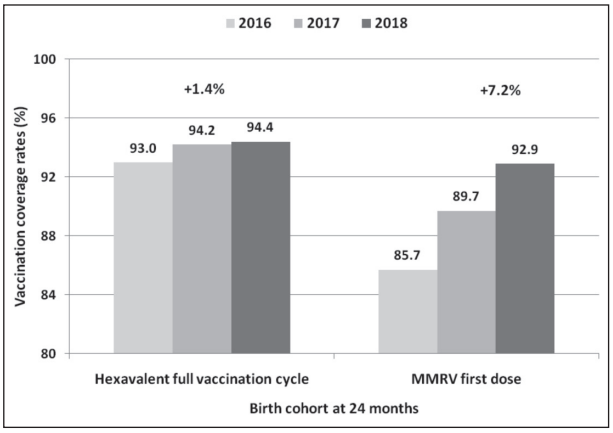

Figure 1. Vaccination coverage rates for hexavalent full vaccination cycle and first dose of MMRV, among 24 months children of the Palermo LHU.

Results

In table 1, the total number of accesses to vaccination services of the Palermo LHU, in the three semesters before and after the introduction of law 119/2017, are showed. In particular, before the introduction of the law from the 1st of January 2016 to the 30th of June 2017, 76,165 accesses were registered, while from the 1st of July 2017 to the 31st of December 2018 an overall increase of about 15% of single vaccination accesses (n=89,442) was observed.

In particular, a peak of 35,516 single accesses to the vaccination services was observed during the second semester of 2017 (+ 30% compared to the same semesters of 2016 and 2018). Also during the first semester of 2018 an increase of accesses was observed (n=29,578) in comparison with first semesters of 2016 (n=23,591; +20%) and of 2017 (n=27,741; +7%).

In figure 1 and 2 coverage rates from 2016 to 2018 for full hexavalent vaccination cycle and for the

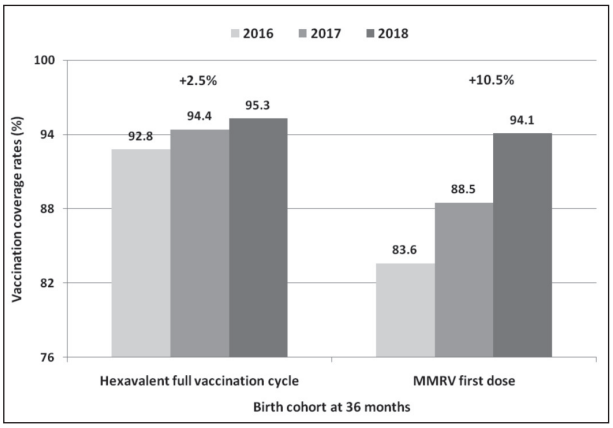

Figure 2. Vaccination coverage rates for hexavalent full vaccination cycle and first dose of MMRV, from 2016 to 2018, among 36 months children of the Palermo LHU.

first dose of MMRV observed in the LHU of Palermo, were reported by the birth cohorts at 24 and 36 months.

Full cycle hexavalent coverage rates showed an increase of 1.4% and 2.5% at 24 and 36 months respec-

tively, from 2016 to 2018. Moreover, in the same period, a 7.2% and a 10.5% increase of adherence to first dose of MMRV were observed at 24 and 36 months, respectively.

Finally, as reported in figure 3, vaccination coverage rates for full vaccination cycle of MMRV in the Palermo LHU, among 6 years old children, showed an increase from 61% to 89.7% (+28.7%) from 2016 to 2018.

Moreover, in the same time interval, a considerable increase of vaccination coverage rates for the 4th dose of DTPa+IPV at 6 years of age was observed (from 43% to 94.2%; +51.2%).

Discussion

In Italy, all vaccinations recommended in the National Immunization Plan are actively and freely offered to general population and are usually administered by vaccination services (2).

Moreover, all these vaccines is considered part of the so-called "minimum level of healthcare services" that the Italian regional public health authorities must provide to citizens free of charge (2).

Nevertheless, the debate about vaccine efficacy and safety, occurred in the last decade at national and international levels, caused a reduction of vaccination coverage rates and a consequent reemergence of outbreaks due to vaccine preventable diseases (8, 15, 16).

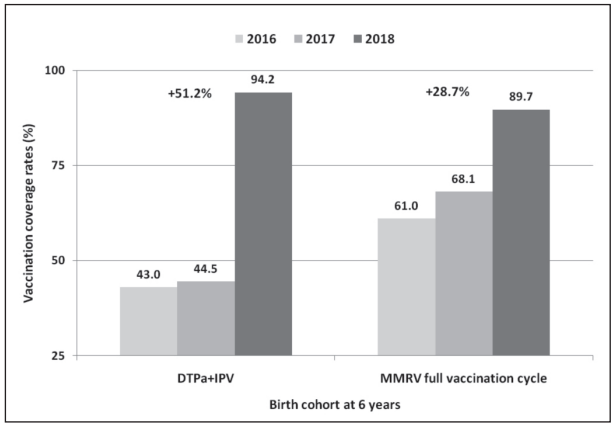

Figure 3. Vaccination coverage rates for fourth dose of DTPa+IPV and full vaccination cycle of MMRV, from 2016 to 2018, among 6 years old children of the Palermo LHU.

For all these reasons, the Italian Ministry of Health, after expressing concerns about increasing numbers of parents refusing to vaccinate their children, introduced the law 119 for compulsory vaccination of all children against ten vaccine-preventable diseases in case of kindergarten attendance (17).

Similarly to Italy, also France and other non-European Countries recently opted for mandatory childhood vaccination (18, 19).

On the other hand, Greece Ministry of Health, in the same period (end of May 2017), proposed that all parents could choose if vaccinated their children, moving from a paternalist to a more free approach to infant vaccination (20).

The law 119/2017 showed a rapid increase of vaccination coverage not only for mandatory vaccines, but also for those recommended among Italian children (21).

Also in the LHU of Palermo, an increase of more than 13 thousands single access to vaccination services was observed during the three semesters after the implementation of the law 119/2017, with a peak in the second semester of 2017, concomitantly with the beginning of the first school year (in September 2017) with a vaccination mandate for attendance of school age children.

To manage the excess of workload of each vaccination services of the Palermo LHU, an organizational effort involving Academic and Territorial Public Health Authorities was carried out.

The extension of the opening days (on saturday morning) and hours (on the late afternoon) has made it possible to better support the increase of vaccination accesses reducing waiting times for general population.

Because of the increase activity of vaccination centers, vaccination coverage rates at 24 months, 36 months and at 6 years of age, for all the vaccines involved in the law 119/2017, have risen.

A greater increase was observed for MMRV vaccination coverage rates in any birth cohort analyzed, similarly to what observed in Emilia-Romagna Region (22).

Before the introduction of the law 119, the MMRV vaccination was affected by a considerable coverage rates reduction from 2012 to 2017 (16).

In particular, in Italy coverage rates have been decreasing since 15 March 2012, in correspondence with

the Rimini Court judgment that supported, extensively sustained by mass media, the possible association between vaccine and autism (23).

The Rimini sentence was overturned only three years later by the Bologna Appeal Court, allowing to no-vax movements and their correlated web and social media pages to increase mistrust and fear into general population during this period (24, 25).

In general, among European parents, several factors such as misleading knowledge, beliefs and perceptions on MMRV vaccine and a limited knowledge of HCWs on this vaccination were significantly associated with lower vaccination uptake rates (26, 27).

The involvement of general practitioner, pediatricians trainees and of medical residents in Preventive Medicine in the strategies adopted to manage the emergency, could lead to a more conscious and proactive adherence to immunization campaigns of future healthcare professionals, in order to contrast the phenomenon of vaccine hesitancy (28).

Furthermore, the implementation or the strengthening of National and Regional immunization registries should be ensured in order to allow an updated monitoring of vaccination coverage and to quickly organize vaccination strategies tailored to areas or at risk groups.

Specifically, among children of 6 years of age, low vaccination coverage rates were observed for the fourth dose of DTPa + IPV (below 45%) and for the full MMRV cycle (below 70%).

After the introduction of the 119/2017 law, probably supported by the introduction of monetary fines for families of unvaccinated children at primary school, a considerable increase of vaccination coverage for these two vaccination booster was observed.

In future, although the Italian law on mandatory vaccination demonstrated high efficacy, tailored communicative strategies should be promoted by Public Health Authorities, in order to educate general population in a more conscious adherence to vaccinations (29 - 31).

Preventive Medicine issues suffering for ineffective communication or influential interactions with health care providers (32). In Italy other 5 vaccines were strongly recommended and freely offer to general population under 18 years old and, without a strong physician's recommendation that represent a major significant predictor for vaccination adherence, these vaccinations may not reach the minimum level of coverage rates requested by National Immunization Plan (2, 30). This topic could play a role in a lower adherence to vaccinations in particular among the more vulnerable segments of the population, such as Sicilian population with low socio-economic level and particular cultural characteristics (27, 33).

In conclusion, law 199/2017 demonstrated a high efficacy in increase vaccination coverage rates also in Sicily. The synergy established between the LHU and the University of Palermo allowed an adequate management of the accesses to vaccination services, making it possible to respond effectively to the public health needs of the general population.

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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Original article

Knowledge and attitudes of parents after the implementation of mandatory vaccination in kindergartens of Palermo, Italy

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Summary. *Background and aim of the work:* Even though vaccination is easy to access in Europe, it has been facing several outbreaks caused by vaccine preventable diseases. Trying to balance the right to health of the community with individual self-determination, in Italy was mandate vaccination for ten vaccine preventable diseases in 2017. The project "Sportello Vaccinale" provided a counseling service to parents in kindergarten of Palermo. The main objective of the study was to investigate knowledge and compliance on vaccination by children's parents after the implementation of mandatory vaccination. *Methods:* A cross sectional study was conducted among parents accessing to the "Sportello Vaccinale" using a questionnaire. The questionnaire consisted of 34 items divided into three sections: socio-demographic data; knowledge and attitude on mandatory vaccination using Health Belief Model (HBM); Health Literacy (HL) level. *Results:* A total of 95 questionnaires were garnered in the kindergartens from respondents with a mean age of 36 (±SD=6) years. The respondents who delayed hexavalent or Measles, Mumps, Rubella and Varicella (MMRV) vaccinations were 8 (8%) and the more frequent cause was fear of adverse reaction (87%). The sample had more often high level of health literacy (37%), and 55% had higher HBM score. The factor significantly associated with higher HBM score was the age of respondents (OR= 1.14, p=0.006) after controlling for other variables. *Conclusions:* Consent to vaccination practice was widely represented, but the results of the study highlighted the need for parents to have more information and more time devoted to the practice of vaccination counseling. Implementing counseling activities at school or at the vaccination service, could support an aware decision process of the parents on vaccination topic.

Key word: mandatory vaccination, vaccine adherence, parent age, MMRV vaccine, hexavalent vaccine, Health Belief Model, Health Literacy, Safety, Accessibility, Sicily

Background

The Strategic Advisory Group of Experts on Immunization (SAGE) of the World Health Organization (WHO) defined with the term "vaccine hesitancy" the delay in the acceptance or the refusal of the vaccine despite the availability of vaccination services (1). Vaccine hesitancy represents a complex topic, context-specific and very variable depending on the country, the age of the subject and the type of vaccine. It is influenced by factors such as information on vaccine-preventable diseases, efficacy and safety (1). Indeed, the lack of right information on the risk of contracting the disease, the mistaken belief that vaccines are unsafe or the lack of confidence in the efficacy of the vaccine can be obstacles to vaccination adherence (2).

Even though vaccination is easy to access in more developed countries, Europe has been facing several outbreaks caused by vaccine preventable diseases such as measles (3). This can be due by different measles vaccination coverage rates observed in countries, ranging from 85% in Italy to 99% in Luxembourg, with an average coverage for the EU of 93.6% in 2016 for the first dose (4).

Nowadays, the Italian vaccination schedule offer, as reported in the National Vaccine Immunization Plan (PNPV) 2017-2019, provides universal mass vaccination for 18 vaccine preventable diseases (5).

Notwithstanding, in Italy, 4,991 measles cases were reported in 2017 (including over 300 healthcare workers), with 4 deaths and 95% of the cases that were unvaccinated or vaccinated with a single dose (6). Other 2,526 cases of measles were reported in 2018. During this period, the highest incidence was recorded in children under one year of age. Furthermore, 47% of cases reported at least one complication and 8 deaths occurred (7). In Sicily, one of the four most populous Italian administrative region, before 2017 was showed vaccination coverage rates against measles far below 95%, the minimum level reccomended to eliminate virus circulation (8).

Trying to balance the right to health of the community with individual self-determination, the Italian Ministry of Health has decided to mandate vaccination for ten vaccine preventable diseases, adopting the law 119/2017 (9). Furthermore, the Italian government considered essential to focus on a better communication strategy aimed at the active and informed participation of the citizen in the public health program (9).

The new Italian mandatory law has showed an increase of vaccination coverage for the hexavalent and Measles, Mumps and Rubella (MMR) vaccines, but also for those vaccines which has been only recommended, such as the anti-pneumococcal and the antimeningococcal C vaccine (10). Although other factors on this phenomeon cannot be quantified and remain undefined, they may have a role as: the better information of healthcare workers, the judgment announcement of lack of causation between vaccination and suspected adverse reactions and the increase of web scientific information and social media debate by vaccinology experts (11).

A project called "Sportello Vaccinale" was conducted from March to April 2018 in 19 kindergarten of Palermo. The main aim of the project consisting in providing a counseling service to parents, giving information about vaccines of the Sicilian Immunization Schedule and the new regulations on vaccination in Italy after the introduction of the law 119/2017.

The main objective of the study was to investigate knowledge and compliance on vaccination by children's parents attending kindergarten in Palermo after the implementation of mandatory vaccination.

Materials and methods

A cross sectional study was conducted among parents accessing to the "Sportello Vaccinale" using a questionnaire. It was filled in after collecting the written consent form by the children's parents. The anonymity of the questionnaire was guaranteed by assigning an alphanumeric code, and after filling in the questionnaire an individual counselling with a Public Health physisician was held, to clarify any doubt and give information on mandatory vaccination law and Regional Vaccination schedule.

The questionnaire consisted of 34 items divided into three sections: socio-demographic data; knowledge and attitude on mandatory vaccination using Health Belief Model (HBM); Health Literacy (HL) level.

The second section of the questionnaire used one of the most validated and widely implemented model to explain vaccination adherence, the HBM. HBM was developed in the 1950s to explain and predict behavior in a population that adhere to preventive practices (12). It is structured in 4 main domains: susceptibility and perceived seriousness of disease, perceived advantages of preventive strategy and barriers to reach preventive services (12). The questionnaire contained 21 questions using a five points Likert scale (1 = not at all, 2 = little, 3 = enough, 4 = very and 5 = very much), that investigated the following items: perceived advantages on vaccinations; perceived advantages on hexavalent and Measles, Mump, Rubella and Varicella (MMRV) vaccinations; perceived barriers on vaccinations; perceived obstacles on hexavalent and MMRV

vaccinations; perceived susceptibility to diseases prevented by vaccines; perceived severity of vaccine preventable disease.

A score was assigned to each answer, assigning 0 to the replies considered negative and 1 to the positive ones. High scores reflect a greater awareness of vaccination issue, its importance and the need to carry out available vaccinations. On the other hand, the lower scores were indicators of a lower awareness of vaccination and adherence to the vaccination programs.

HL allows to assess the ability to obtain, understand and manage health information and make appropriate health decisions using the offered services (13). For the evaluation of the HL, an examination based on the Medical Term Recognition Test (METER), adapted to the Italian language, was used (14) (15). The proposed test provides a list of 70 terms, 40 of medical use and 30 non-words or words not referable to medical use, requiring to mark only the words recognized as medical terms. The score is established by calculating the number of correctly recognized words and the results are then classified according to the scale: 0-20 = low level, 21-34 = medium level, 35-40 = high level.

Finally, to assess the reasons that led the parents to delay or refuse mandatory vaccinations, an open-ended questions was included "What was main reason of vaccine delay?". The ethical committee Palermo 1 approved the study during the session 06/2017.

Statistic analysis

The normality of the distribution of quantitative variables was assessed with the Skewness and Kurtosis test. The quantitative variables distributed normally have been summarized as mean (standard deviation) and those distributed not normally as median (interquartile range). For the qualitative variables the absolute and relative frequencies have been calculated. Subsequently the whole population was divided in higher and lower HBM level according to median HBM score. The association of the quantitative variables normally and not normally distributed with higher scores achieved at the HBM was evaluated with the student's T and with the Wilcoxon and Mann Withney test respectively; while for the qualitative variables the Chi2 test was used. All the variables associated with a p-value<0.5 with higher HBM scores were included in a multivariate logistic analysis model to analyze their effect. All the data collected were analyzed using the Stata MP 14.2 statistical software. For all analyses, a P-value of 0.05 was assumed to indicate significance (two-tailed).

Results

A total of 95 questionnaires were garnered in the kindergartens. Table 1 shows characteristics of interviewed parents, univariate and multivariate analysis. The questionnaire was filled in more frequently by mothers (89%), followed by fathers (7%), and by both parents (3%). The respondents had a mean age of 36 (±SD=6) years, their families were composed by 4 (±SD=1) members and they were more frequently Italian (93%). The most frequent civil status was married (81%) followed by cohabiting parents (14%) and the most prevalent education level was middle school (49%), followed by high school (35%) and university (11%). Only 5% of the sample worked in the health sector (social health assistant, pharmaceutical salesman and nurse). The main source of information regarding vaccinations was more frequently pediatrician (94%) followed by Local Health Unit vaccinating physician and book/newspaper (2% each). The sample had more often high level of health literacy (37%), followed by low (35%) and medium level (28%). The median score for HBM answer was 16 and according to this cut-off 52 (55%) respondents had higher and 43 (45%) lower HBM score. The respondents who delayed hexavalent or MMRV vaccination were 8 (8%).

The age of respondents was the only characteristics that significantly differ between respondents with higher and lower HBM scores (38 vs 34 years old, p=0.002).

A multivariate analysis was performed in order to assess the association of demographic characteristics and HL level with the HBM scores. The age of respondents was significantly associated with higher score of HBM (OR= 1.14, p=0.006) after controlling for variables with p-level < 0.5 at univariate analysis (working as healthcare worker; country; number of family members; vaccination information source; HL level).

Table 1. Characteristics of sample and difference between Low and High HBM score.

		Total n=95	Low HBM n=43	High HBM n=52	p	Crude OR	p	Adjusted OR	p
1) Questionnaire compiler, n (%)	Mother	80 (89%)	37 (91%)	43 (88%)		ref			
	Father	6 (7%)	3 (7%)	3 (6%)	0.782	0.86	0.859		
	Both Parents	3 (3%)	1 (2%)	2 (4%)		1.72	0.663		
	Grandparents	1 (1%)	0 (0%)	1 (2%)		1			
2) Civil state, n (%)	Married	66 (81%)	30 (79%)	36 (84%)		ref			
	Cohabiting	11 (14%)	6 (16%)	5 (12%)	0.644	0.69	0.577		
	Divorced	1 (1%)	1 (2%)	0 (0%)		1			
	Single	3 (4%)	1 (2%)	2 (4%)		1.67	0.683		
3) Respondent age, mean (±SD)		36 (6)	34 (6)	38 (6)	0.002	1.12	0.004	1.14	0.006
4) Education level, n (%)	Nothing	1 (1%)	0 (0%)	1 (2%)		ref			
	Primary school	4 (4%)	2 (5%)	2 (4%)		1			
	Middle school	43 (49%)	18 (46%)	25 (50%)	0.896	1.39	0.641		
	High school	31 (35%)	14 (36%)	17 (34%)		1.21	0.79		
	University	10 (11%)	5 (13%)	5 (10%)		1			
5) Healthcare worker, n (%)	Yes	5 (5%)	3 (7%)	2 (4%)	0.479	ref			
6) Country, n (%)	Other	6 (7%)	1 (2%)	5 (10%)	0.148	0.52	0.485	0.57	0.595
	Italian	85 (93%)	40 (98%)	45 (90%)		ref			
7) Number of family members, mean (±SD)		4 (1)	4 (1)	4 (1)	0.115	0.22	0.182	0.26	0.261
8) Information source, n (%)	Pediatrician	88 (93%)	40 (95%)	48 (92%)		1.51	0.12	0.96	0.900
	Local Health Unit Vaccination Service	2 (2%)	0 (0%)	2 (4%)		ref			
	Book/newspaper	1 (1%)	0 (%)	1 (2%)	0.220	1			
	Other physician	2 (2%)	2 (5)	0 (0%)		1			
	Social network	1 (1%)	0 (0%)	1 (2%)		1			
9) Health Literacy level, n (%)	Low	33 (35%)	11 (26%)	22 (42%)		1			
	Medium	27 (28%)	16 (37%)	11 (21%)	0.133	ref		ref	
	High	35 (37%)	16 (37%)	19 (37%)		0.34	0.047	0.31	0.067
10) Did you delay in exavalent/MMRV vaccination uptake?	Yes	8 (8%)	4 (9%)	4 (8%)	0.540	0.59	0.30	0.50	0.245
Missing answer: question 1=5 , question 2= 14, question 4=6, question 6=4, question 8=1									

The reason for delay hexavalent or MMRV vaccination by parents were reported in Figure 1. The more frequent cause declared was fear of adverse reaction (87%), while only one parent expressed difficulties in vaccination services access (13%).

Discussion

The "Sportello vaccinale" project demonstrated that vaccination is a widely accepted and a shared practice among parents with children attending kindergarten in the city of Palermo. Indeed, the majority of parents did not express doubts about the need to

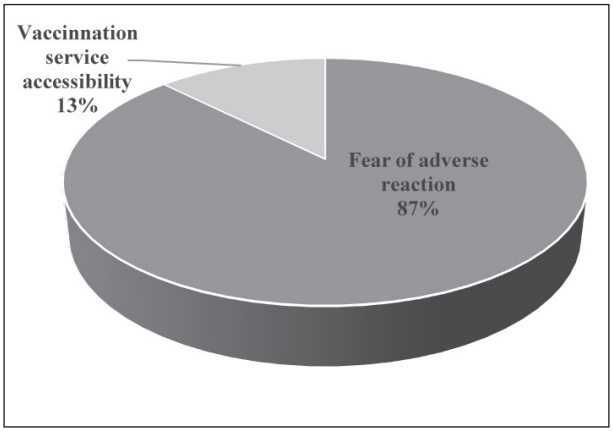

Figure 1. Reason of parents who delayed hexavalent and MMRV vaccination in kindergarten of Palermo.

carry out all the available vaccinations.

Notwithstanding, the parents' concerns, in our sample, were largely aimed at the possible adverse reactions that could arise: the doubt on vaccines was induced from uncertainty about its safety, rather than doubts about its efficacy. A recent American review on the vaccine beliefs of parents had similarly demonstrated that concerns about vaccines safety were the most commonly reported by parents (16). In another study conducted in 67 countries, although the opinion on vaccination is generally positive, confidence in them is very fragile. The highest levels of mistrust have been recorded in Europe, specifically in France, where 41% of respondents said they did not consider vaccines a safe medical device (17). In the sample of parents enrollend in the study, there was the opinion that vaccination is often performed following the advice of the pediatrician, or to fulfill the obligation, but without a real awareness of the benefits deriving from it. As evidenced by an American study (18) on the "vaccine hesitancy" and by a Cochrane review (19) about the importance of vaccination counselling for parents, the interventions in this area should not only be aimed at parents who totally postpone or reject vaccinations, but must also they aim to reassure and resolve the concerns of those families who, although they have decided to carry out all the vaccines, they have doubts about it. This category of subjects is susceptible to misinformation often conveyed by the media and social networks which, by giving partial or incorrect information, lead to a lack of confidence in vaccinations and institutions (20-22).

Among the safety doubt that led to delay vaccination, the false association between vaccines and autism insurgence, despite the study by Wakefield has already been withdrawn and widely denied for years, was reported in our sample (23). Moreover, also precautionary measures adopted by the Italian Health Ministry were often misunderstood by general population, as observed with the "Fluad" case. It occurred during the influenza season 2014-2015, when two batches of influenza vaccine were withdrawn following the report of three death of elderly a few days after vaccination. Although the withdrawal was just a preventive measure, and then the batches proved to be perfectly compliant, the vaccination campaign marked a dramatic drop in adherence (24, 25). In that case, the refusal of influenza vaccination was independent of the Health Literacy profile, the level of schooling or medical knowledge, but mainly due to the incorrect information given by Public Health Authorities following the withdrawal of the vaccine and the media coverage attention reserved for the event (24).

The main result of the study was the strong correlation between a high degree of HBM and older people. This is a topic widely reflected in the literature with preventive strategies or medications adherence, as a study carried out on antiretroviral therapy compliance in HIV + subjects, where the rate of low treatment adherence in the sample of the youngest people was almost double than recorded in the older patients (26). In a recent Chinese study, older parents performed significantly better on knowledge ($p < 0.001$) and awareness ($p < 0.001$) about papillomavirus vaccination than younger (27). It is likely that a greater age is related to higher responsibility and awareness of what the diseases covered by the vaccine have involved in the past. Today, that the relationship with the doctor has often become conflicting and the trust towards healthcare is always lower, it is necessary to find a meeting point with families, to provide clear and complete information to anyone who is hesitant and, above all, to demonstrate how vaccination represents a safe practice (28, 29).

Despite the fact that usually population with a high level of HL correlates better with adherence to preventive strategies, considering vaccination topic it was often observed a paradox with parents with higher

HL levels that not vaccinate their children (30, 31). Also, in our study there is no evidence of a correlation between HL levels and a higher propensity towards preventive strategies, probably because there are many factors to consider and the HL alone does not guarantee reassurance for the numerous questions presented by families (32). A review of 2018 shows that HL in vaccination choices seems to be influenced by various factors such as the country of origin, age and type of vaccine (33). Therefore, it seems appropriate to support parents in making vaccination a voluntary and conscious choice with deepening counselling activities conducted with the first time younger parents (34).

The main limitations of the study is the low sample of people recruited in the project and missing answer in the questionnaire. Notwithstanding, the study threats knowledge and attitude of people about vaccination a year after the introduction of mandatory vaccination introduction in Italy, that is a topic rarely treated in the literature.

This study gave the opportunity to explore parents' beliefs about vaccinations using the HBM methodology. Consent to vaccination practice was widely represented, but at the same time the results highlighted the need for parents to have more information and more time devoted to the practice of vaccination counseling. Moreover, significantly positive association emerged between the age of the parents and a higher grade of HBM. While no correspondence was found between the level of Health Literacy and the propensity towards vaccination.

The project carried out in the kindergartens, which also included a large part of counseling activities, was pleasantly received by the parents. Implementing counselling activities at school or at the vaccination service, could support an aware decision process of the parents on vaccination topic.

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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Original article

Burden of measles using disability-adjusted life years, Umbria 2013-2018

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Summary. *Background and aim:* The low measles vaccination coverage contributes to the re-emerging of measles in Italy. This study aimed to estimate the measles burden, expressed in Disability Adjusted Life Years (DALYs), in Umbria, for the period 2013-2018. *Methods:* Data on measles cases in Umbria were obtained from the MoRoNet. While data related to the resident population, were obtained from the website of the National Institute of Statistics. The estimated DALYs was calculated using the Burden of Communicable Diseases in Europe toolkit. The results are expressed in DALYs per year, per case and per 100,000 subjects, for acute illness and for sequelae. *Results:* The estimated incidence in mean for the entire period was 52.50 cases per year. Resulting in an average loss of 3.10 DALYs per year. *Conclusions:* The data obtained from this analysis provide important information on the impact of measles in the Umbria region, and offer useful data to the Health Authorities that can be used to reduce measles incidence in the region.

Key words: measles, burden of disease, Italy, vaccination, disability-adjusted life years

Background

Measles is an acute (RNA) viral, vaccine-preventable disease, transmitted by droplets, and still responsible of recurrent epidemics (1). Measles is an important cause of death and disability among children worldwide , responsible of 100 million of acute infections and 6 millions of deaths per year all over the word. Immunisation against measles started in the 1960s and dramatically changed the epidemiology of the disease, preventing 99% of cases in many industrialized countries. Considering the several efforts adopted, measles appears eliminated in 43 out of 53 WHO European Region member states (2), but not in Italy where the last epidemic outbreak started at the end of 2016 and it is still ongoing (2019), counting for more than 9,000 cases. In Italy, the first measles vaccine (mono-component, single-dose) was introduced in late 1970s, and later replaced in 1980s with the trivalent vaccine (measles-mumps-rubella, MMR) (3). However, despite the high vaccine effectiveness (95%), which is able to induce a life-long immunity (4), measles vaccine coverage in Italy remained very low (approximately 40%) for several decades, until the early 1990s (5). However, the rate highly improved after the reinforcement of mandatory vaccination law, which increased by 6% points the coverage (6).

Considering the re-emerging of measles, and its related health outcomes, it is important for Health Authorities and policy makers to have the best possible evidence in order to identify the most cost-effective interventions able to promote and guarantee the health of citizens. In order to do so, it is necessary to identify mixed measures, able to measure the loss of health

in terms of years, thus allowing to make quantitative comparisons between the various phenomena, and that are also representative of the complex phenomena related to human health. In other words, it is necessary to estimate the burden of infectious diseases, so that an effective public health planning can be carried out (7). Regarding measles, even though the infection is mainly acute and mostly evolves into a resolution, it is also associated with both short and long-term complications, impacting on health and quality of life. However, the burden of disease of measles is not entirely known yet, and no studies aimed to estimate the measles burden during an epidemic have been conducted so far. Furthermore, there are no studies available to evaluate the burden at a national level in Italy, and above all there are no regional assessments. This information is largely needed in order to support public health policies (8). In this perspective, this work aimed to: i) describe the epidemiology of measles in Umbria for the period 2013-June 2019; ii) assess the burden of measles, expressed in Disability Adjusted Life Years (DALYs), in Umbria, in different age groups, for the period 2013-2018.

Methods

Data source

Data on measles cases in Umbria were obtained from the MoRoNet (Measles and Rubella Network) notification system for the period 2013-June 2019 (last update July 2019). While data related to the resident population, were obtained from the website of the National Institute of Statistics (9).

Estimation of the burden

DALYs is a composite measure that considers the years of life lost to disabilities (YLD), and the years of life lost due to premature death (YLL). The YLD is calculated considering the impact of the disease on the quality of life, while the YLL is calculated considering the years of life lost due to premature death, according to the life expectancy. The information needed to build the mathematical model are related to disease progression, rate of sequelae and underreporting. However, since a mathematical model is based on some assumptions, and in order to express the uncertainty in the outputs, given the random nature of its inputs, the Monte Carlo simulation was recommended (10).

In order to assess the burden, only data referring to the 2013-2018 were considered. The analysis was divided in three sub-analysis: the pre-epidemic period (2013-2016), then the epidemic year (2017), and lastly the entire 2013-2018 period. The analyses for the 2013-2016 and 2013-2018 were carried out considering both the cumulative incidence recorded in the two periods and the average incidence per year. The estimated DALYs was calculated using the Burden of Communicable Diseases in Europe (BCoDE) toolkit, a software developed by the European Centre for Disease Prevention and Control (ECDC) (11).

In our analysis a standard life expectancy was considered (maximum age 85 years). The mathematical model used for the current analysis was developed by the ECDC through a literature review and expert consultation. Regarding the multiplication factor (MF) used to correct for the underreporting, this should ideally be sex, age group, and country specific (depending on the type of notification systems) (11). However, in literature, these data are not often reported. A previous study conducted in Germany, aimed to estimate the measles burden, used a single MF of 2.5 for each age group and sexes (12). It was identified by literature search and estimating a low rate of underreporting, considering that measles notification systems, as well as diagnosis, reached a high-quality level in Europe.
For each sub-analysis the DALYs are reported per year, per case and per 100,000 subjects (each of which is specified on the total), for acute illness and for sequelae. Finally, the DALYs per year and per case are presented in both aggregated and disaggregated forms (YLL and YLD). Values are expressed as medians with 95% uncertainty interval (95% IU) quantified by performing a Monte Carlo simulation (10,000 iterations).

Statistical analysis

Descriptive analysis of measles cases was reported either as a percentage or as an average with standard deviation (SD). The cumulative incidence was calculated considering all notified cases in the 2013-2018 period referring to the average of the resident population in the same period. Resident population was stratified by sex and age.

Ethical approval

This study has been conducted using data routinely collected within the Italian Ministry of Health mandate; no ethical approval was needed.

Results

126 cases were reported in Umbria in the period January 2013-June 2019, with a cumulative incidence of 14 measles cases per 100,000 residents, 58% of which occurred in females. The mean age was 29±16.3 years, and 15.3% cases were reported in children aged ≤5 years. Laboratory confirmation was performed in 75.6% of cases, 93.9% of which were positive for measles (PCR or IgM). The vaccination status was known for 97% of the cases, 79%of which were not vaccinated, while the remaining had received only one dose. One case was recorded in a pregnant woman, and 16% occurred among health care workers (HCW). The most observed complications were diarrhoea (18%), stomatitis (11.7%), pneumonia (9.4%), keratoconjunctivitis (7.8%), hepatitis (6.3%) and thrombocytopenia (5.5%). Hospitalization (or at least emergency room access) occurred in 57% of the cases, and the mean length of stay was 4 days (range 1-12 days).

Burden of measles

Considering the pre-epidemic period 2013-2016, a cumulative incidence of 23 notified measles cases was observed, 47.8% of which in females. After correction for underreporting, the estimated number of new cases was 57.5. Modelling the long-term sequelae, the expected rates were 0.02 cases of permanent disability due to encephalitis, 0.004 cases of post-infectious encephalitis, 0.04 deaths and 0.002 cases of subacute sclerosing panencephalitis (SSPE). Considering the pre-epidemic period 2013-2016 as a mean, 5.75 cases occurred on average per year. After correction for underreporting, the estimated number of new cases was 14.38 per year. Modelling the long-term sequelae, the expected rates are 0 cases of permanent disability due to encephalitis, 0.001 cases of post-infectious encephalitis, 0 deaths and 0.001 cases of SSPE. Considering the epidemic year (2017), 91 new cases occurred, 64.8% of which in females. After correction for underreporting, the estimated number of new cases was 227.50. Modelling the long-term sequelae, the expected rates were 0.06 cases of permanent disability due to encephalitis, 0.15 cases of post-infectious encephalitis, 0.004 deaths and 0.004 cases of SSPE. Considering the period 2013-2018, a cumulative incidence of 131 notified cases was observed, 59.5% of which in females. After correction for underreporting, the estimated number of new cases was 315. Modelling the long-term sequelae, the expected rates were 0.08 cases permanent disability due to encephalitis, 0.21 cases of post-infectious encephalitis, and 0.003 cases of SSPE. Lastly, considering the pre-epidemic period 2013-2018 as a mean, 21 cases occurred on average per year. After correction for underreporting, the estimated number of new cases was 52.5 per year. Modelling the long-term sequelae, the expected rates were 0.01 cases of permanent disability due to encephalitis, 0.03 cases of post-infectious encephalitis, 0.001 deaths and 0.001 cases of SSPE. The estimated DALYs are reported in Table 1. The DALYs – in both aggregated and disaggregated forms – per year by sex and age groups are depicted in Figures from 1 to 3.

Conclusion

The most recent epidemic outbreak faced by Umbria, as well as by Italy, started at the end of 2016 and mainly occurred during 2017. The mean age of the cases notified during the whole period 2013-2018 was 29±16.3 years, with 58% recorded among children ≤5 years old. These results highlight the need for new vaccination strategies as the catch up policy, or offering the anti-MPR(V) vaccination during all possible occasions, and in particular in women of child-bearing age (13).

In this perspective, and considering the restricted resources for health (14), a crucial role is played by counselling and communication (15), especially for measles vaccination, to which a large population distrust is associated, mainly due to the alleged and false association with autism (16). In Italy, the reasons for missed measles vaccination are routinely collected, and show a decreasing trend during the last three years

Table 1. Overview of the measles burden, Umbria 2013-2018. Disability-adjusted life years (DALYs), Years Lived with Disability (YLD), Years Life Lost due to premature death (YLL).

	2013-2016 cumulative	2013-2016 average per year	2017	2013-2018 cumulative	2013-2018 average per year
DALYs per year, total	3.63 (3.25-4.00)	0.91 (0.81-1.00)	13.17 (12.09-14.24)	18.58 (17.01-20.13)	3.10 (2.84-3.36)
YLD	0.91 (0.71-1.13)	0.23 (0.18-0.28)	3.34 (2.74-3.97)	4.69 (3.92-5.49)	0.78 (0.65-0.93)
YLL	2.72 (2.41-3.03)	0.68 (0.61-0.75)	9.84 (8.88-10.78)	13.88 (12.54-15.17)	2.32 (2.10-2.53)
DALYs per year, acute disease	2.74 (2.43-2.94)	0.69 (0.61-0.76)	10.08 (9.15-11.02)	14.19 (12.85-15.46)	2.37 (2.15-2.58)
YLD	0.12 (0.11-0.13)	0.03 (0.03-0.03)	0.48 (0.46-0.51)	0.67 (0.63-0.71)	0.11 (0.11-0.12)
YLL	2.62 (2.32-2.94)	0.66 (0.58-0.73)	9.60 (8.65-10.54)	13.52 (12.17-14.80)	2.26 (2.03-2.47)
DALYs per year, sequelae	0.88 (0.69-1.11)	0.22 (0.17-0.28)	3.09 (2.51-3.72)	4.39 (3.63-5.17)	0.73 (0.60-0.87)
YLD	0.78 (0.58-1.01)	0.20 (0.15-0.25)	2.85 (2.27-3.47)	4.02 (3.27-4.82)	0.67 (0.54-0.81)
YLL	0.10 (0.09-0.11)	0.02 (0.02-0.03)	0.24 (0.22-0.26)	0.37 (0.33-0.40)	0.06 (0.06-0.07)
DALYs per case	0.06 (0.06-0.07)	0.06 (0.06-0.07)	0.06 (0.05-0.06)	0.06 (0.05-0.06)	0.06 (0.05-0.06)
DALYs per case, acute disease	0.05 (0.04-0.05)	0.05 (0.04-0.05)	0.04 (0.04-0.05)	0.05 (0.04-0.05)	0.05 (0.04-0.05)
DALYs per case, sequelae	0.02 (0.01-0.02)	0.02 (0.01-0.02)	0.01 (0.01-0.02)	0.01 (0.01-0.02)	0.01 (0.01-0.02)
DALYs/100.000	0.41 (0.36-0.45)	0.10 (0.09-0.11)	1.48 (1.36-1.60)	2.09 (1.91-2.26)	0.35 (0.32-0.38)
DALYs/100.000 acute disease	0.10 (0.08-0.12)	0.08 (0.07-0.09)	1.13 (1.03-1.24)	1.59 (1.44-1.74)	0.27 (0.24-0.23)
DALYs/100.000 sequelae	0.31 (0.27-0.34)	0.02 (0.02-0.03)	0.35 (0.28-0.42)	0.49 (0.41-0.58)	0.08 (0.07-0.10)

(17). This achievement is mainly due to the approval of the new Immunisation Plan 2017-2019 (13), the reinforcement of a mandatory vaccination law (18), and the implementation of the immunization information system (IIS), a useful instrument to counter vaccine hesitancy and to identify subjects under or unimmunized (19). The Umbria region has an advanced IIS, considering that all the Local Health Units use the same shared software, and data are individual-based (20). However, until now, electronically stored data are mainly related to infants' vaccinations, while older data that had been recorded on paper in the past decades have not been digitalized yet. Considering our results, future efforts in electronically recording immunization data of older cohorts is needed (21). Moreover, a higher percentage of cases notified in HCWs has been recorded in Umbria compared to national data (16% vs 5% in Italy) despite measles vaccination is one of the highly recommended vaccinations for HCWs. Measles vaccination among HCWs is extremely important for several reasons. Firstly, to avoid potentially causing

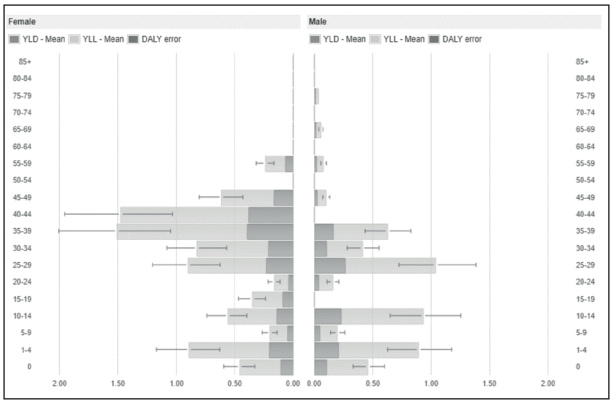

Figure 1. Disability-Adjusted Life Years (DALYs), Years Lived with Disability (YLD) and Years of Life Lost (YLL) per year and by sex and age group of measles cases, Umbria 2017.

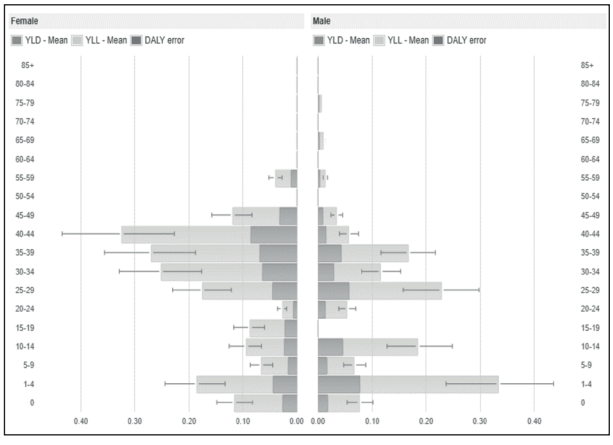

Figure 2. Average Disability-Adjusted Life Years (DALYs), Years Lived with Disability (YLD) and Years of Life Lost (YLL) per year and by sex and age group of measles cases, Umbria 2013-2018.

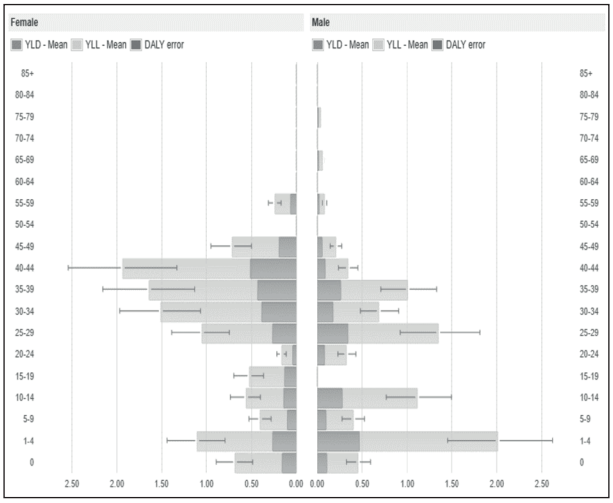

Figure 3. Disability-Adjusted Life Years (DALYs), Years Lived with Disability (YLD) and Years of Life Lost (YLL) per year and by sex and age group of cumulative measles cases, Umbria 2013-2018.

nosocomial outbreaks and secondly because HCWs represent a positive model. Indeed, even though health-related information are often searched on the Internet (22-27), HCWs are still the most trusted and most consulted source of information (28). Nevertheless, despite these aspects and the high efficacy and safety of vaccinations, vaccination coverages are still below the threshold (29). HCWs' immunization, as well as for the general population, is another crucial strategy to reach elimination goal (30). The hospitalization rate was slightly lower in Umbria compared to the national data, but in both cases approximately 60% of the affected people were treated at the hospital. On one hand, these data confirm that measles can have severe manifestations requiring hospitalization. On the other hand, this high rate of hospitalization might be since the surveillance system is much more precise in the identification of hospitalized patients, compared to people treated in primary care. As a matter of fact, under-reporting is an intrinsic issue of surveillance systems, even in industrialized countries. In particular, under-reporting highly affects primary care mainly due to underdiagnosis. Considering this, we applied a MF to our measles burden estimation. Using both the MF and the notified cases of measles, we observed an estimated incidence of 52.50 cases per year. The estimated cases resulted in an average loss of 3.10 DALYs per year, whose major component is the YLL (75%). This is mainly due to the intrinsic characteristics of measles, resulting in a low rate of complicated infections but with a high fatality rate.

The DALY for 100,000 estimated confirmed results shown in a previous European study (period 2009-2013) (31). However, in our study, the DALYs per 100,000 considering only 2017, is twice higher compare the entire period. However, it should be kept in mind that the burden of measles could be completely avoided, thanks to the effective and safe vaccine. According to previous study estimated the measles burden in Germany, referring to the period 2005-2007, the most affected age group in term of burden was the 0-19 years old subjects, without gender differences (12). This was not confirmed in our study, in which the most affected age group was the 20-44 years old subjects, and mainly females. While the 0-19 age group ranked second, without gender differences. These differences might be explained considering the historical low measles vaccination coverage obtained in Italy. Indeed, measles vaccination coverage was around 40% from 1976 (when the measles vaccination was first introduced in Italy) to the end of the 1980s. Moreover, the second dose was introduced in the vaccination schedule in the year 2013 (5). Considering these aspects, it is extremely important to know both coverage and burden data to effectively plan interventions aimed to eliminate measles. In fact, identifying the most affected age group is mandatory to reduce the measles burden during potential future epidemic outbreaks, as recommended by the WHO (32).

This study has some limitations. Firstly, the measles incidence was calculated using the total population and not the susceptible population, potentially contributing to an underestimation of the burden. Secondly, the selected MF, although previously used in similar analysis, it must be noted that they were European studies, and therefore it may not be perfectly applicable to the Umbrian situation. However, it was relatively low, and this may have led to an underestimation of the burden. Indeed, surveillance systems are affected by a certain rate of under-reporting, which cannot be ignored. Lastly, we did not modify any parameters set in the software. These parameters are based on simplified generalizations of the disease evolution that, in the real world, might highly be heterogeneous. Moreover,

they had been set based on the European context that, even though it could be representative of the Umbria region as well, it could also be partially different.

Despite the mentioned limitations, the study has important strengths. This is the first study presenting epidemiology and measles burden in Umbria, in both epidemic and non-epidemic periods. Another strength is the pathogen-based approach used to estimate the burden. This method is more precise compared to the disease-based approach, allowing to include all possible clinical manifestations of the disease, instead of considering only one (33). Furthermore, the pathogenic-based approach ensures greater comparability of results between various infectious diseases, as well as between different populations (12). Moreover, in this study data form the national surveillance system has been used, representing the most reliable and trustful source. Lastly, in order to estimate the burden we used the BCoDE toolkit, an intuitive software, listed by the European Food Safety Authority (EFSA) among the risk ranking tools (34).

The data obtained from this analysis provide important information on the impact of measles in Umbria, and offer useful data to the Health Authorities that can be used to reduce measles incidence in the region, thus contributing to the achievement of the elimination goal.

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Original article

Vaccines are underused in pregnancy: what about knowledge, attitudes and practices of providers?

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Summary. *Introduction.* To investigate actual knowledge of official recommendations towards seasonal influenza (SID), and Tetanus-diphtheria acellular-pertussis (Tdap) vaccines in obstetrics/gynecologists (OBGYN). *Methods.* PubMed and EMBASE databases were searched. A meta-analysis was performed to calculate odds ratio (OR) and 95% confidence interval (CI) among case controls, cross-sectional studies, either questionnaire or laboratory exams based. *Results.* A total of 6 studies met inclusion criteria, including 1323 OBGYN from 5 different countries. Overall, around 99% of sampled professionals were aware that official recommendations towards SID in pregnancy do exist, compared to 92% for Tdap, with significant heterogeneity (I^2 > 95%, p < 0.001). Concerns about vaccine safety was reported by 10% of respondents for Tdap, and by 6.0% for SID, but again available studies were substantially heterogenous (I^2 = 86.7% and 86.0%, p < 0.001). Eventually, 93% of respondents actively recommended SID in pregnancy, compared to 88% for Tdap (I^2 98.8% and I^2 95.9%, respectively p < 0.001). The evidence of significant publication bias was initially subjectively identified from the funnel plot, and then objectively confirmed through the regression test for all analyses. *Conclusions.* These results suggest an appropriated understanding of official recommendation among sampled OBGYN, with high shares of professionals actively promoting vaccination practices among their patients. Despite the high heterogeneity and the significant publication bias we identified, our results also hint towards extensive knowledge gaps of OBGYN, and particularly regarding unmotivated concerns about vaccine safety. As a consequence, appropriate information and formation campaigns should be appropriately tailored. (www.actabiomedica.it)

Key words: vaccination, pregnancy, influenza vaccines, Pertussis vaccine, Diphtheria-Tetanus-Pertussis Vaccine

Introduction

Pregnant women and infants under 6 months are at higher risk for adverse outcomes from seasonal influenza (SID) and pertussis (1–6)and opinions concerning potential barriers to immunization, among obstetrician-gynecologists. Methods: In 2007, surveys were sent to Collaborative Ambulatory Research Network members, a representative sample of practicing Fellows of the American College of Obstetricians and Gynecologists; 394 responded (51.2%. Therefore, maternal immunization has been proposed as an evidence based strategy to prevent or mitigate the severity of infections in pregnant women and their newborn in-

fants through transplacental antibody transfer (7,8). However, CDC have recently reported that around 65% of American women do not receive influenza Tetanus-diphtheria acellular-pertussis (Tdap) vaccines, as otherwise recommended by available guidelines since 2011 (9).

Root cause analyses for inappropriate vaccination rates usually focus on knowledge, attitudes and practices (collectively, KAPs) of the target populations (ie pregnant women) (10–12), but also knowledge gaps and misbeliefs of healthcare providers may actively contribute (13–15). In particular, a certain base of evidence points towards the lack of understanding of obstetrics-gynecologists (OBGYN) of official recommendations for SID/Tdap vaccines, that associated with their potential overstating of potential health effects of immunizations, may collectively contribute to restrain pregnant women from appropriate vaccinations (14–16).

Therefore, this systematic review will assess the available base of evidence about KAP of OBGYN towards SID/Tdap vaccines.

Materials and Methods

This systematic review has been conducted following the PRISMA (Prepared Items for Systematic Reviews and Meta-Analysis) guidelines (17). We searched into two different databases (PubMed and Embase) for relevant studies published from 2011 (ie inclusion of SID/Tdap among recommended vaccinations for pregnant women) to 31/12/2019, without any chronological restriction. The search strategy was a combination of the following keywords (free text and Medical Subject Heading [MeSH] terms): *"knowledge, attitudes, practices", "obstetric*", "gynecologist*", "vaccin*", "immunization"* (**Figure 1**). 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. Only articles reporting the actual number of OBGYN included in the study, and deliberately assessing knowledge of official recommendations towards Tdap and/or SID, 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 (ie the year of study); (4) reports including OBGYN alongside other healthcare providers lacked discrete figures for OBGYN.

Two independent reviewers reviewed titles, abstracts, and articles. Titles were screened for relevance to the subject. Any articles reporting original studies, 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. Total number of OBGYN participating into the study;
2. Settings of the study, including the characteristics of the sampling strategy and whether a power analysis had been preventively performed in order to ascertain the appropriate sample size;
3. Share of respondents aware of official recommendations towards Tdap and/or SID vaccinations in pregnancy;
4. Share of respondents exhibiting concerns towards Tdap and/or SID vaccinations in pregnancy;
5. Share of respondents reportedly recommending Tdap and/or SID vaccinations in pregnancy.

We first performed a descriptive analysis to report the characteristics of the included studies. The pooled prevalence of the reported KAP were initially calculated, and I^2 statistic was then calculated to quantify the amount of inconsistency between included studies; it estimates the percentage of total variation across

studies that is due to heterogeneity rather than chance. I^2 values ranging from 0 to 25% were considered to represent low heterogeneity, from 26% to 50% as moderate heterogeneity and above 50% as substantial heterogeneity, being pooled using a fixed-effects model because of the reduced number of samples eventually included. To investigate publication bias, contour-enhanced funnel plots were generated, and regression test for funnel plot asymmetry were ultimately performed with calculation of correspondent Z value with their p value. All calculations were performed by means of *metafor* package with R (version 3.4.3) and RStudio (version 1.1.463) software.

Results

Initially, 683 entries were identified. After applying the inclusion and exclusion criteria (**Figure 1**), 6 articles were included in the analyses and summarized (**Table 1).**

The studies reported KAP of obstetrics and gynecologist from USA (2 studies) (2,18), Italy (in table 1, 14 was reported), Lebanon (19), Israel (20), and Germany (21), for a pooled population of 1323 healthcare providers, and 65.53% of them were from a single German study (21).

As shown in Table 1, in 5 studies, sampling was performed by convenience (2,15,18,19,21), and only in three cases a preventive power analysis was performed (19–21). Even though 4 studies were reportedly multicenter ones, only three of them eventually included professionals from various geographical areas (19–21). All studies employed a structured questionnaire, that in the majority of cases was self-administered (2,15,18,19,21), also as online surveys (15,21), while in 1 study it was compiled through a face-to-face interview.

Based on the fixed-effect model, as shown in **Figure 2**, around 99% (95%CI 98-99%) of professionals were aware that official recommendations towards SID in pregnancy do exist (range 57 to in figure 2, 99 was reported), compared to 92% for Tdap (range 24% to 95%), with I^2 of 96.4% ($p < 0.001$) and 98.9% ($p < 0.001$). Interestingly enough, excluding the study of Böhm et al (21) from the pooled analyses, the respective shares would drop to 78.3% and 65.8%.

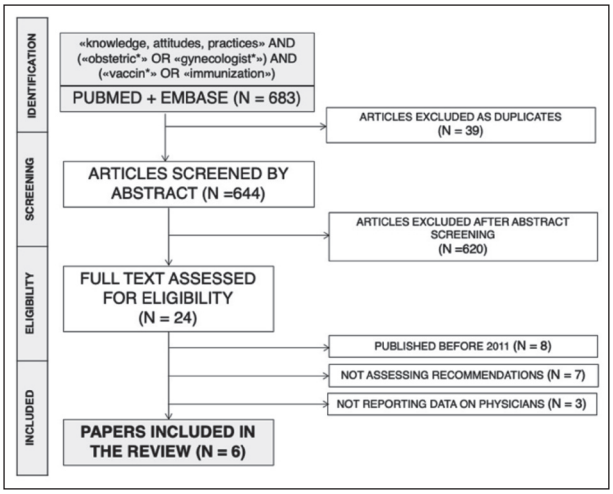

Figure 1. PRISMA flow diagram including keywords employed for the inquiry (ie «knowledge, attitudes, practices» AND («obstetric*» OR «gynecologist*») AND («vaccin*» OR «immunization»).

Table 1. Summary of reported evidence about knowledge, attitudes and practices of obstetrics-gynecologists towards diphtheria-tetanus-pertussis (Tdap) and influenza (Flu) vaccine in pregnant women.

Reference	Country	Sampled practitioners, No./TOT, %	Sampling strategy	Multicenter?	Multiple area?	Preventive Power Analysis?	Self-administered questionnaire?
Bonville et al. (2)	USA	68, 5.14%	*Convenience*	YES	NO	NO	YES
Gesser-Edelsburg et al. (20)	Israel	150, 11.34%	*Quantitative multistage*	YES	YES	YES	NO
Hobeika et al. (19)	Lebanon	114, 8.62%	*Convenience*	YES	YES	YES	YES
Panda et al. (18)	USA	56, 4.23%	*Convenience*	NO	NO	NO	YES
Riccò et al (14)	Italy	68, 5.14%	*Convenience*	NO	NO	NO	YES
Böhm et al. (21)	Germany	867, 65.53%	*Convenience*	YES	YES	YES	YES
POOLED		1323, 100%		4, 66.67%	3, 50.00%	3, 50.00%	5, 83.33%

A certain degree of concern about vaccine safety was reported by 10% of respondents for Tdap (95%CI 9-12%; range 9 to 27%), and by 6.0% for SID (95% 5-8%; range 3 to 21%). In both cases, available studies were substantially heterogenous (I^2 = 86.7% and 86.0%, $p < 0.001$ for both analyses). Still, exclusion from the pooled analyses the single German study would nearly double the share of respondents exhibiting concerns towards assessed immunization (ie 14.3% for SID and 21.1% for Tdap).

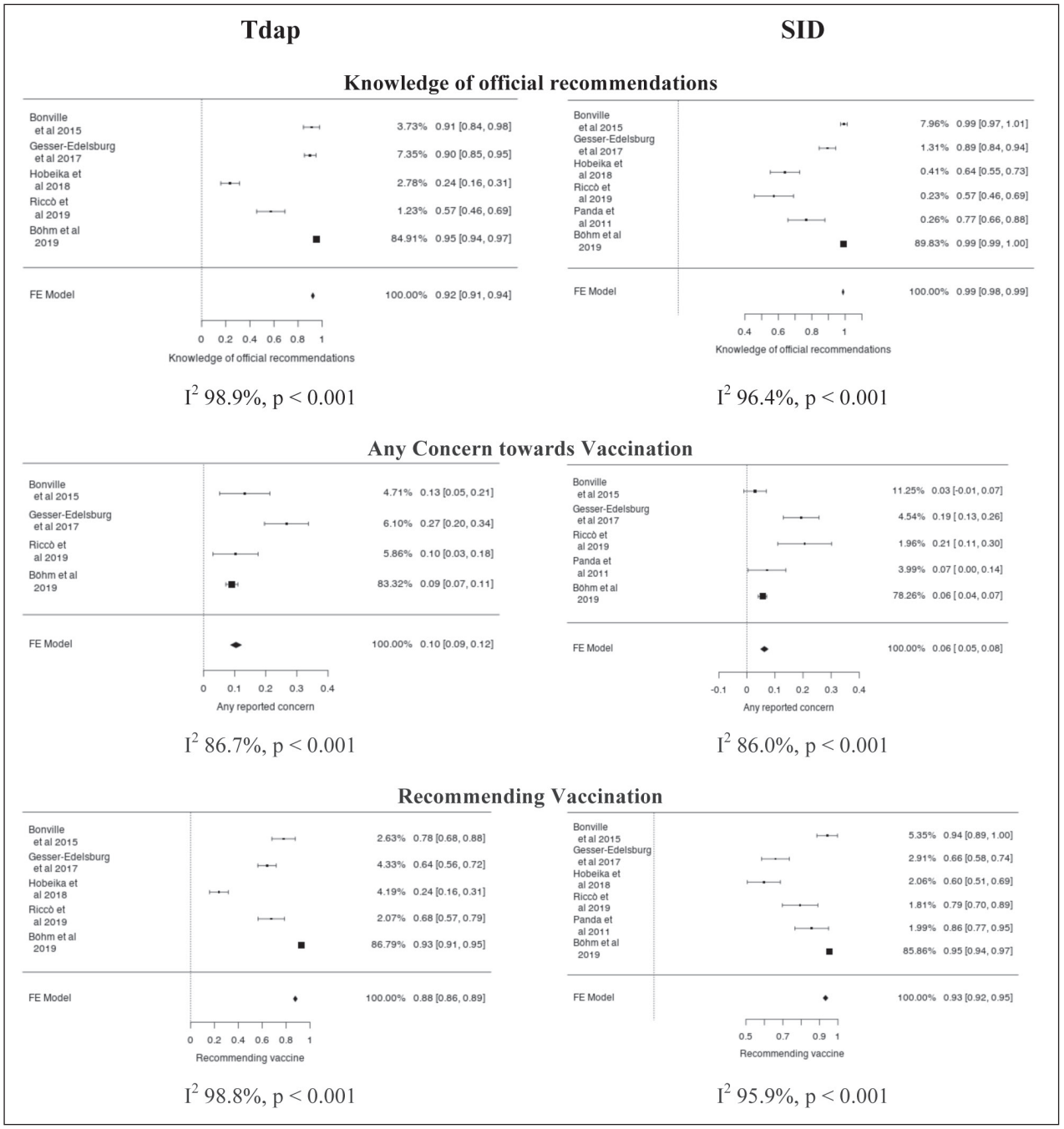

Figure 2. Forest plots reporting raw proportions with correspondent 95% confidence intervals (95%CI) of participants aware of official recommendations for Tdap and/or SID vaccine in pregnancy, reporting any concern towards Tdap and/or SID, and recommending Tdap and/or SID in pregnant women

Eventually, 93% of respondents actively recommended SID in pregnancy (95%CI 92-95), compared to 88% for Tdap (95%CI 86-89%). Again, the reports were strikingly heterogenous, with rates ranging from 24% to 93% for Tdap (I^2 98.8%, $p < 0.001$), and from 60% to 95% for SID (I^2 95.9%, $p < 0.001$). However, as better shares for both SID and Tdap were again referred from the German study of Böhm et al (21), eliding such report would shrink average figures to 73.3% for SID and 55.5% for Tdap.

The presence of publication bias was evaluated using contour-enhanced funnel plots and regression test for funnel plot asymmetry. Each point in funnel plots represents a separate study and asymmetrical distribution indicates the presence of publication bias. First, studies' effect sizes were plotted against their standard errors and the visual evaluation of the funnel plot suggested a significant publication bias, as all the 6 graphs appeared largely asymmetrical (**Figure 3**). The subjective evidence from the funnel plot was objectively confirmed using the regression test.

Conclusions

Despite a growing interest towards immunization KAPs in gynecologists/obstetrics, few studies of inconsistent quality have actually inquired their understanding of official recommendations for Tdap and/or influenza vaccines in pregnancy. More interestingly, only 4 studies have been performed in high-income countries, and 2 of them are USA based. Unfortunately, not only available studies are mostly underpowered, with around 65.53% of participants from a single research (21), but participants are often sampled by convenience (eg participant to conferences/formation courses; members of a certain health center), with subsequent concern on their actual representitivety (20). Moreover, only three studies collected participants at a national level (19–21): as a consequence, results are doubtfully generalizable.

Actually, even though available evidence seemly suggests that OBGYN are extensively aware of official recommendations towards SID and Tdap, the heterogeneity among available studies means that significant uncertainties and knowledge gaps are actually reported for both immunizations, and particularly for Tdap, with actual figures that may peak to 42.6% (15) and 76.3% (19), respectively.

Interestingly, while the majority of sampled OBGYN recommended Tdap and/or SID, a significant share of sampled medical professionals still reported unmotivated concerns on vaccine safety, particularly on Tdap. As a consequence, available estimates are only limitedly compatible with the usual health belief model, in which a particular protective action is directly influenced by the perceived susceptibility to a health threat, its severity, and perceived benefits and/or barriers (22–24). More probably, our results suggest that OBGYN, while formally coping with official recommendations, still harbor significant and unsolved misconceptions towards Tdap / SID (13,14): similarly to similar reports in vaccinations performed by General Practitioners (25,26), in the school settings (13,27) attitudes and prac-tices of STs towards vaccination are otherwise lacking. Objectives. The aim of this study was therefore to evaluate knowl-edge and attitudes of STs regarding vaccinations in a sample from North Italy. Material and methods. In this cross sectional study, 154 STs from Lombardy region (Northern Italy, and in the occupational settings (14,16,28–32)Legislative Decree n.81/2008, it is reasonable that such uncertainties in critical providers may contribute in compromising vaccination rates subjects referring to them for information and counseling, as pregnant women for OBGYN (9).

In summary, while patients and their possible vaccine hesitancy are usually identified as the main target for specifically targeted tailored information campaigns (12,33–35)even though immunization is recommended since many years and still remains the fundamental tool for its prevention. Healthcare workers (HCWs, our results suggest that also healthcare providers, and more specifically OBGYN should be specifically targeted in order to overcome the significant share of concerns and misconceptions they otherwise exhibited, eventually improving the safety profile of both mothers and children (1-4, 36-37).

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

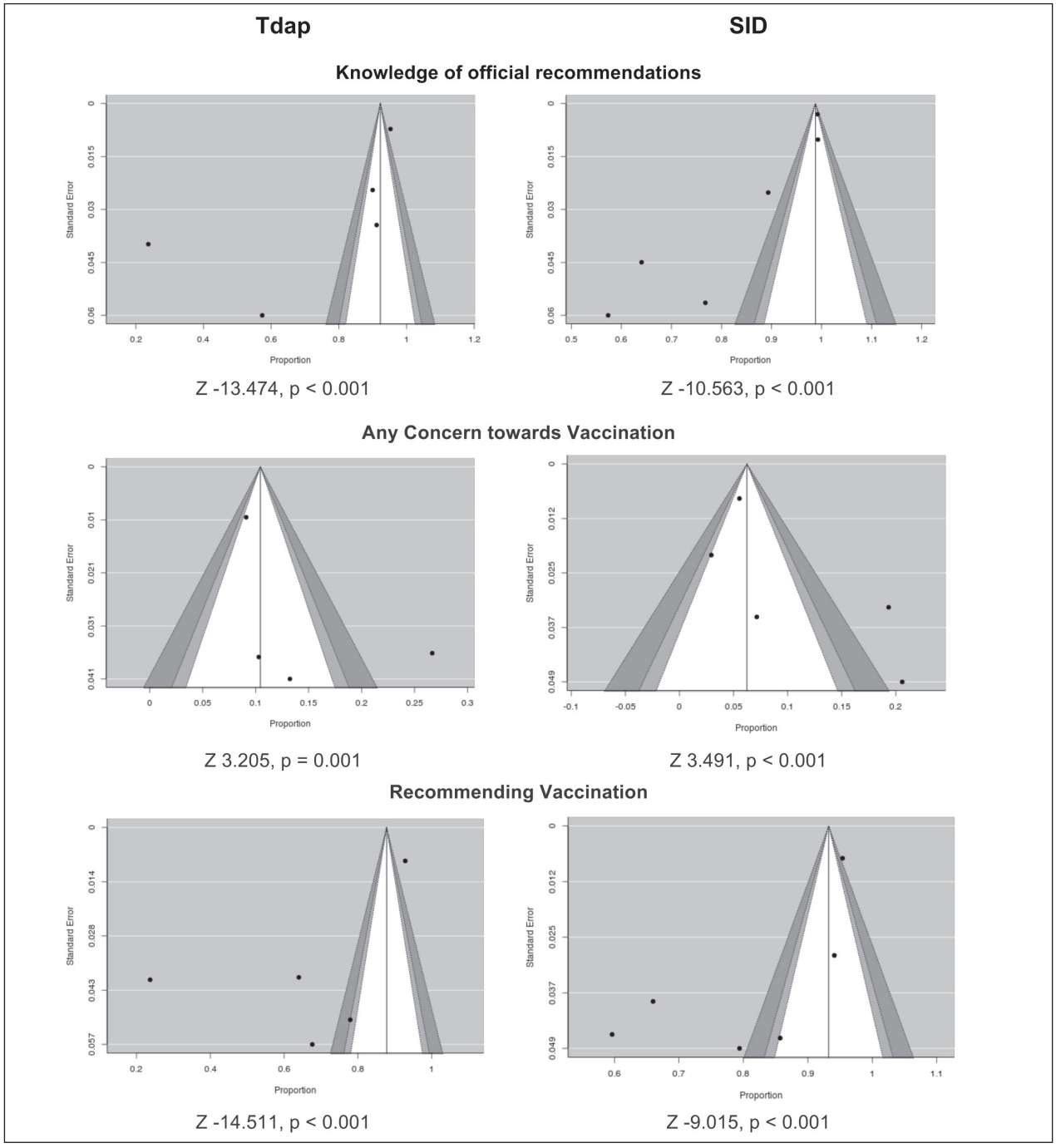

Figure 3. Contour-enhanced funnel plots of the participants aware of official recommendations for Tdap and/or SID vaccine in pregnancy, reporting any concern towards Tdap and/or SID, and recommending Tdap and/or SID in pregnant women.

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Original article

Influenza vaccine effectiveness in children: a retrospective study on eight post-pandemic seasons with trivalent inactivated vaccine

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Summary. *Background and aim of the work*: The global burden of disease attributable to seasonal influenza virus in children is difficult to quantify. Children with chronic medical conditions and healthy children may experience severe or fatal complications. Aim of the study was to estimate the influenza vaccine effectiveness (VE) in a cohort of outpatient children. *Methods:* From 2010 to 2018, a Pediatrician of Parma from the InfluNet network of Emilia-Romagna Region, performed nasal/throat swabs on every child with Influenza-like illness at least 14 days from the vaccination with trivalent vaccine. VE estimates against influenza season, virus type and subtype and age group were evaluated using a test-negative design. *Results:* 2,480 swabs were performed. The 57.6% of the analyzed swabs were positive for influenza viruses. Type A (57%) and type B viruses (43%) co-circulated. The 37.1% of type A viruses belonged to subtype A(H3N2), 19.4% to subtype A(H1N1)pdm09. The subtype A(H3N2) was prevalent among children up to 23 months (42.4%) while the type B in the 2-4 (40.7%) and 5-16 year old age groups (49.4%). Overall, 19.9% of the children were vaccinated. The highest prevalence of vaccinated subjects was found in children aged 5-16 (30.5%). The VE against subtype A(H1N1)pdm09 was 63% (95%CI 42.6-76.0), against type B 27.5% (95%CI 7.9-42.9) and against subtype A(H3N2) -14.3% (95%CI - 46.0-10.7). *Conclusions:* Our findings represent a useful contribution to the ongoing debate about the appropriateness of including influenza vaccination for healthy children, 6 months and older, in the updating National Vaccine Prevention Plan (PNPV).

Key words: influenza, children, outpatient, virological surveillance, vaccine effectiveness, test-negative design.

Introduction

The global burden of disease attributable to seasonal influenza virus (SIV) is difficult to quantify, particularly in children younger than 5 years, as pediatric hospitalization rates and SIV-related deaths vary by the predominant circulating strain, and from season to season. For instance, a study conducted by Poheling et al. (1), underlined as among young children, outpatient visits associated with influenza were 10 to 250 times as common as hospitalizations. Moreover, children with chronic medical conditions, as well as healthy children, may experience severe or fatal complications, with a substantial number of excess hospitalizations, medical visits, antibiotic use and deaths (2).

Nair et al., in a sistematic review (3), estimated that, in 2008, 90 million new cases of influenza, 20 million cases of influenza-associated ALRI (acute, lower respiratory infections) (13% of all cases of paediatric ALRI), and 1 million cases of influenza-associated severe ALRI (7% of cases of all severe paediatric ALRI) occurred worldwide in children younger than 5 years. They estimated there were 28,000–111,500 deaths in children younger than 5 years attributable to

influenza-associated ALRI in 2008, with 99% of these deaths occurring in developing countries.

Lafond et al. (4) in 2016, with a different survey methodology, confirmed the great impact of influenza on pediatric hospitalizations and estimated that influenza was associated with 10% of respiratory hospitalizations in children <18 years of age worldwide, ranging from 5% among children <6 mounths to 16% among children 5–17 years, with 374,000 hospitalizations in children <1 years and 870,000 hospitalizations in children <5 years annually.

According to American Academy of Pediatrics (5), during 2018/2019 influenza season, 51% of deaths attributable to influenza occurred in children who had at least 1 underlying medical condition; therefore, nearly half had unknown underlying medical conditions. Among the children hospitalized with influenza, 45% had no recorded underlying condition, and 55% had at least 1 underlying medical condition (asthma or reactive airway disease (27.1%)).

Nonetheless, children play a central role in the transmission of influenza virus infection to household and other close contacts (6). As shown by Principi et al., (7) the number of medical visits, and the number of missed working or school days, were all significantly greater among the household contacts of influenza positive children than those of children infected by other agents. On the other hand, children have often the highest attack rates in the community during seasonal influenza epidemics (20%-30% in children vs 5%-10% in adults) (8).

Universal seasonal vaccine administration to everyone 6 months and older is the best available strategy to prevent SIV complications (9-10), but studies focusing on estimates of vaccine effectiveness (VE) are still required (11-19). In order to contribute to a better understanding of such topic, we performed a retrospective study on eight post pandemic influenza seasons (2010-2018). More specifically, in order to produce seasonal influenza VE estimates, we established a test-negative (TN) study design in a cohort of outpatient children within the context of integrated virological and epidemiological surveillance, coordinated by the Istituto Superiore di Sanità (ISS) and conducted in Emilia-Romagna (Northern Italy), at the Regional Reference Laboratory of Parma.

Methods

Subjects in study

From 2010/2011 to 2017/2018, a Pediatrician of Parma, from the InfluNet network of Emilia-Romagna Region, with an average number of 1,149 assisted (4% of all pediatric residents of the Province of Parma) performed nasal or throat swabs, on every child who went to his medical clinic with body temperature > 37.5 °C and at least one symptom among those included in the definition of pediatric ILI (Influenza-Like Illness) (20), (i.e. dry or productive cough, pharyngodynia, nasal/cold congestion, conjunctivitis, chills, asthenia, muscle and osteoarticular pain, irritability, crying, loss of appetite) within 4 days from the beginning of the symptoms and at least 14 days from the vaccination. Each biological sample, marked with a code, was accompanied by a data collection card that reported: the date of birth, sex, the date of the beginning of the symptoms, and the vaccination status. The study was approved by the Provincial Ethical Committee (CEP) as an observational study and a written informed consent document was collected for each subject both for the execution of the swab and for the collection of data.

Virological investigation

The "Virocult" diagnostic kit (MWE, England) was used to collect the clinicals samples. Each sample was delivered into refrigerated box to the Laboratory and was analyzed within 24 hours of arrival. 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, according to CDC (Centers for Disease Control and Prevention) and WHO (World Health Organization) protocols (21-22). Viral nucleic acid was extracted from respiratory specimens using the QIAamp Viral RNA Mini Kit (Qiagen, Hilden, Germany). A rRT-PCR was performed with Quantifast Pathogen+IC Kit, (Qiagen, Hilden, Germany). From 2013/2014 season, genetic lineage of type B (B Yamagata/Victoria lineage) was also determined. All assays were performed using the Rotor Gene 6000 (Corbett).

Statistical analysis

The results were summarized in tables of frequency and the differences in the proportions were compared by the use of Chi square test, with Yates's correction of continuity when appropriate. The distribution of subjects'age was summarized by mean, standard deviation (SD) and median, and tested with Anova.

In relation to the epidemiological trend and according to the viral circulation monitored by the Italian InfluNet network (23), every influenza season was divided into three phases: first one ascending from the 46th week, a peak phase corresponding to the week with the highest number of positive samples more or less 2 weeks, and a downward phase. Children were stratified into three age groups: 0-23 months, 2-4 year of age, and 5-16 year of age.

Under the TN design, subjects who seek medical care for ILI and tested positive for influenza virus infection by RT-PCR are cases, subjects who seek medical care for ILI and tested negative by RT-PCR for influenza virus infection are controls (24-26).

We estimated the VE as 1-OR*100 with the relative confidence intervals of 95%. A logistic regression model was used to calculate the adjusted VE (i.e. outcome variable) for sex, age group and epidemic period (i.e. covariates). In particular, were estimated: the overall influenza VE (8 years) (adjusted for epidemic period, age group and sex); the VE against every influenza season (adjusted for epidemic period, age group and sex); the VE against subtype A(H1N1)pdm09, subtype A(H3N2) and type B (adjusted for epidemic period, age group and sex); the VE against age group (adjusted for epidemic period, and sex).

P-values equal to or less than 0.05 were considered statistically significant. All statistical analyses were performed with SPSS 25.0 (IBM SPSS Inc., Chicago – IL).

Results

During the 8 influenza seasons, a total of 2,480 nasal or throat swabs were performed; the highest number of samples was analyzed in the 2012/2013 season (368, 14.8% of all samples), the lowest in the 2013/2014 season (145, 5.8 % of all samples) (Table 1). Study population had a mean age of 4.7 years (SD 3.5), a median age of 4 years (range: 3 months to 16 years), with a male/

Table 1. Subjects in study by influenza season.

Influenza Season	Subjects	Sex				Age		Age group			
	(No.) *(%)*	Male (No.) *(%)*	Female (No.) *(%)*	Missing (No.) (%)	Ratio M/F	Mean *(SD)*	Median	0-23 mounth (No.) *(%)*	2-4 years (No.) *(%)*	5-16 years (No.) *(%)*	Missing (No.) *(%)*
2010/2011	276 *(11.4)*	141 *(51.1)*	134 *(48.6)*	1 *(0.3)*	1.05	5.0 *(3.5)*	5.0	52 *(18.9)*	84 *(30.4)*	137 *(49.6)*	3 *(1.1)*
2011/2012	364 *(14.7)*	183 *(50.3)*	181 *(49.7)*	0 *(0)*	1.01	4.0 *(3.1)*	3.0	84 *(23.1)*	156 *(42.8)*	124 *(34.1)*	0 *(0)*
2012/2013	368 *(14.8)*	179 *(48.7)*	183 *(49.7)*	6 *(1.6)*	0.98	4.4 *(3.2)*	4.0	70 *(19.0)*	148 *(40.2)*	150 *(40.8)*	0 *(0)*
2013/2014	145 *(5.8)*	79 *(54.5)*	63 *(43.4)*	3 *(2.1)*	1.25	4.8 *(3.8)*	3.0	32 *(22.1)*	52 *(35.9)*	61 *(42.0)*	0 *(0)*
2014/2015	339 *(13.6)*	176 *(51.9)*	163 *(48.1)*	0 *(0)*	1.08	4.7 *(3.5)*	4.0	75 *(22.2)*	115 *(33.9)*	149 *(43.9)*	0 *(0)*
2015/2016	348 *(14.0)*	183 *(52.6)*	165 *(47.4)*	0 *(0)*	1.11	4.9 *(3.5)*	4.0	73 *(21.0)*	106 *(30.4)*	169 *(48.6)*	0 *(0)*
2016/2017	305 *(12.2)*	178 *(58.4)*	127 *(41.6)*	0 *(0)*	1.40	5.4 *(4.0)*	4.0	45 *(14.8)*	122 *(40.0)*	138 *(45.2)*	0 *(0)*
2017/2018	335 *(13.5)*	217*(64.8)*	118 *(35.2)*	0 *(0)*	1.84	4.3 *(3.5)*	3.0	73 *(21.8)*	144 *(43.0)*	118 *(35.2)*	0 *(0)*
Total	**2480 *(100)***	**1336 *(53.9)***	**1134 *(45.7)***	**10 *(0.4)***	**1.18**	**4.7** *(3.5)*	**4.0**	**504 *(20.3)***	**927 *(37.4)***	**1046 *(42.2)***	**3 *(0.1)***

female ratio of 1.18. Overall, 19.9% of the children were vaccinated with inactivated trivalent vaccine (Table 2). The 57.6% of the analyzed swabs were positive for influenza viruses (range 27.6% to 71.2%; Table 2).

During the 8 considered seasons, type A (57%) and type B viruses (43%) co-circulated. The 37.1% of type A viruses belonged to subtype A(H3N2), 19.4% to subtype A(H1N1)pdm09, and the remaining 0.5% was not subtyped. The highest number of samples was collected between the 4th and 6th week of each season in the first 5 epidemic seasons, during the 7th week in the 2015/2016 season, during the 51st week in the 2016/2017 season (3rd week of December 2016) and during the 3rd week of 2018 in the 2017/2018 season (Figure 1).

The season with the highest percentage of the viral isolations was 2012/2013 (71.2%), characterized by the co-circulation of subtype A(H1N1)pdm09 (20.2%) and type B (79.4%), followed by the 2011/2012 season (70.6%) during which subtype A(H3N2) circulated almost exclusively (98.4%). The most evident co-circulation of the 2 subtypes A(H1N1)pdm09 (40.0%) and A(H3N2) (52.8%) was observed in 2014/2015 season

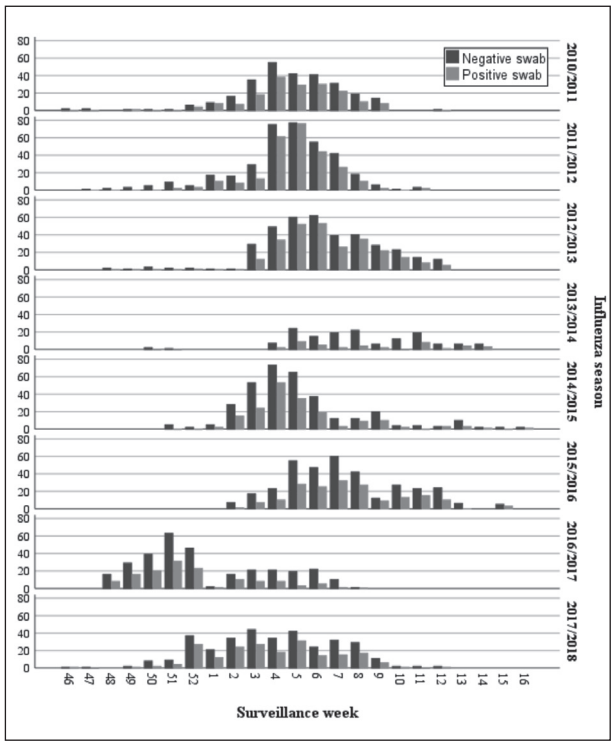

Figure 1. Number of negative and positive swabs by influenza season and surveillance week

Table 2. Influenza virus type/subtype and vaccination status by influenza season.

Influenza Season	Vaccination status		Positive samples/ total swabs	Influenza virus type or subtype					
	Vaccinated (No.) (%)	Unvaccinated (No.) (%)	(No.) (%)	A unsubtyped (No.) (%)	A(H3N2) (No.) (%)	A(H1N1)pdm09 (No.) (%)	Influenza B (No.) (%)	Lineage B/Vic (%)	Lineage B/Yam (%)
2010/2011	101 *(36.6)*	175 *(63.4)*	175/276 *(63.4)*	4 *(2.3)*	3 *(1.7)*	55 *(31.4)*	113 *(64.6)*	-	-
2011/2012	117 *(32.1)*	247 *(67.9)*	257/364 *(70.6)*	3 *(1.2)*	253 *(98.4)*	0 *(0)*	1 *(0.4)*	-	-
2012/2013	57 *(15.5)*	311 *(84.5)*	262/368 *(71.2)*	0 *(0)*	1 (0.4)	53 *(20.2)*	208 *(79.4)*	-	-
2013/2014	41 *(28.3)*	104 *(71.7)*	40/145 *(27.6)*	0 *(0)*	33 *(82.5)*	6 *(15.0)*	1 *(2.5)*	*0*	*100*
2014/2015	66 *(19.5)*	273 *(80.5)*	180/339 *(53.1)*	0 *(0)*	95 *(52.8)*	72 *(40.0)*	13 *(7.2)*	*0*	*100*
2015/2016	53 *(15.2)*	295 *(84.8)*	180/348 *(53.1)*	0 *(0)*	11 *(6.1)*	7 *(3.9)*	162 *(90.0)*	*98.8*	*1.2*
2016/2017	28 *(9.2)*	277 *(90.8)*	134/305 *(43.9)*	0 *(0)*	132 *(98.6)*	1 *(0.7)*	1 *(0.7)*	*0*	*100*
2017/2018	31 *(9.2)*	304 *(90.8)*	201/335 *(60.0)*	0 *(0)*	2 *(1.0)*	83 *(41.3)*	116 *(57.7)*	*0.9*	*99.1*
Total	**494 *(19.9)***	**1986 *(80.1)***	**1429/2480 *(57.6)***	**7/1429 *(0.5)***	**530/1429 *(37.1)***	**277/1429 *(19.4)***	**615/1429 *(43.0)***		

(Table 2). The subtype A(H1N1)pdm09 frequently co-circulated with type B, while the circulation of the other strains was substantially residual in 3 out of the 4 seasons in which the subtype A(H3N2) was prevalent.

The prevalence of sampled vaccinated children decreased during the study: 36.6% in the immediate post-pandemic season, 9.2% and 9.2% in the 2016/2017 and 2017/2018 influenza seasons (Table 2). The percentage of influenza-positive samples was significantly different in the three age groups: 43.0% among children up to 23 month of age, 55.3% in 2-4 year old children, and 66.6% in older children (p<0,001) (Table 3). The subtype A(H3N2) was prevalent among the youngest children up to 23 months (42.4% of viruses isolated in this age group), while the type B was prevalent in the 2-4 year-old age group (40.7%) and in the 5-16 year-old age group (49.4%). Overall, in the 8 seasons, the highest prevalence of vaccinated subjects was found in the group of children aged 5-16 (30.5%), without differences between males and females (Table 3).

VE analysis.

Table 4 shows the VE estimates by epidemic season, by viral type or subtype and by age group. Briegly, considering the 8 epidemic seasons, the overall VE was 37.1% (95% CI 22.2 - 49.2). In 5 of the 8 analyzed seasons, the VE exceeded 50%, ranging from 56% (95% CI 21.1 - 75.5) in 2011/2012 season to 68.9% (95% CI 21.9 - 87.6) in the 2016/2017 season. In 3 seasons, i.e. from 2013 to 2016, the VE was moderate. Specifically, in 2014/2015 season, characterized by the co-circulation of the subtypes A(H1N1)pdm09 and A(H3N2), the VE was 38.2% (95% CI -13.5 - 66.3), while in 2015/2016 season, characterized by the predominant circulation of the B virus (90%), specially B/Victoria lineage (98.8%), VE showed negative values. In the 2013/2014 season, the low number of positive samples made VE estimates unreliable. Overall, the VE against subtype A(H1N1)pdm09 was 63% (95% CI 42.6 - 76.0), against type B 27.5% (95% CI 7.9 - 42.9) and against subtype A(H3N2) -14.3% (95% CI - 46.0 - 10.7). Among the age groups, the VE estimates against younger children under 23 months, were comparable with those aged 5-16, although VE estimates were statistically significant only in this class: 43.1% (95% CI -90.2 – 83.4), and 42.9% (95% CI 23.4

Table 3. Vaccination status and influenza virus type/subtype by age group.

Age group	Vaccination status		Positive samples/total swabs	Influenza virus type or subtype			
	Vaccinated (No.) *(%)*	Unvaccinated (No.) *(%)*	(No.) *(%)*	A unsubtyped (No.) *(%)*	A(H3N2) (No.) *(%)*	A(H1N1)pdm09 (No.) *(%)*	Influenza B (No.) *(%)*
0-23 mounths	13 *(2.6)*	491 *(97.4)*	217/504 *(43.0)*	1 *(0.5)*	92 *(42.4)*	63 *(29.0)*	61 *(28.1)*
2-4 years	160 *(17.3)*	767 *(82.7)*	513/927 *(55.3)*	4 *(0.8)*	182 *(35.5)*	118 *(23.0)*	209 *(40.7)*
5-16 years	319 *(30.5)*	727 *(69.5)*	697/1046 *(66.6)*	2 *(0.3)*	256 *(36.7)*	95 *(13.6)*	344 *(49.4)*
Missing	2 *(66.7)*	1 *(33.3)*	2/3 *(66.7)*	0 *(0)*	0 *(0)*	1 *(50.0)*	1 *(50.0)*
Total	**494**	**1986**	**1429/2480 *(57.6)***	**7/1429 *(0.5)***	**530/1429 *(37.1)***	**277/1429 *(19.4)***	**615/1429 *(43.0)***

Table 4. Adjusted vaccine effectiveness estimates (VE) against influenza seasons, influenza type and subtype, and age group.

	P	Adjusted VE %	Adjusted 95% CI	
			Lower	Upper
Overall	< 0.001	37.1	22.2	49.2
VE= (1- ORadj) x 100		OR adjusted for epidemic period, age group and sex		
Against Influenza season				
2010/2011	< 0.05	62.0	30.7	79.2
2011/2012	< 0.05	56.0	21.1	75.5
2012/2013	< 0.05	60.5	24.8	79.2
2013/2014	n.s.	2.7	- 137.2	60.1
2014/2015	n.s.	38.2	- 13.5	66.3
2015/2016	n.s.	- 9.9	- 112.7	43.1
2016/2017	< 0.05	68.9	21.9	87.6
2017/2018	< 0.05	60.5	13.6	81.9
VE= (1- ORadj) x 100		OR adjusted for epidemic period, age group and sex		
Against Influenza type and subtype				
A(H1N1)pdm09	< 0.001	63.0	42.6	76.0
A(H3N2)	n.s.	- 14.3	- 46.0	10.7
B	< 0.05	27.5	7.9	42.9
VE= (1- ORadj) x 100		OR adjusted for epidemic period, age group and sex		
Against age group				
0 - 23 mounths	n.s.	43.1	- 90.2	83.4
2 – 4 years	n.s.	27.5	- 3.8	48.2
5 – 16 years	< 0.001	42.9	23.4	56.7
VE= (1- ORadj) x 100		OR adjusted for epidemic period and sex		

– 56.7) respectively. The lowest value was found in the intermediate age class (2-4 year-old) in which the VE was 27.5% (95% CI -3.8 – 48.9).

Conclusions

The eight epidemic seasons considered in our study were characterized by the frequent co-circulation of influenza A and B viruses. Although the percentage of vaccinated children decreased during the course of the study, the coverage rate of our children remained widely above the regional average coverage (1.85%) (27). This permitted to obtain robust VE estimates. Overall, the effectiveness of the vaccination was good but, as already observed in other studies and in different age groups (28), it was high against the subtype A(H1N1)pdm09 (63%) and substantially lower against the subtype A(H3N2) and towards the type B.

In particular, in 2014/2015 season, characterized by the co-circulation of the two subtypes A, the low VE value (38.2%; 95% CI -13.5 - 66.3) was supported by an important mismatch of the circulating A(H3N2) strain, genetically and antigenically different from the vaccine strain; in the following season (2015/2016), locally characterized by the intense circulation of type B virus, the presence in the trivalent formulation vaccine of the lineage B/Yamagata, different from the circulating lineage B/Victoria, may have determined the low VE value (27.5% ; 95% CI 7.9 - 42.9).

Interestingly in both seasons the relative prevalence of locally circulating strains was different from that observed at National level: in fact, in Italy in 2014/2015 the subtype A(H3N2) represented 41% of the viruses against 52.8% of our study, and in 2015/2016 the type B in Italy represented 57% of the viruses against 90% of our study (29-30).

This could account the lower protection of the tri-

valent vaccine observed in our paediatric population compared to that observed in other studies (31) and underlines the relevance of local surveillance systems that can provide more appropriate data and information in specific population groups (32-35).

Our 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 (36). We adjusted the VE estimates for age, sex and epidemic season period. However, for accurate VE estimation, it will be necessary to consider, in the future, also a severity score, based on the clinical symptomatology of the disease for each patient; furthermore, the low number of vaccinated children under two year old, did not allow to calculate reliable VE estimates, exactly in this age group, where the greatest questions remain in terms of cost-effectiveness of vaccination, a common theme in many diseases (37), and one of the major drivers in public health decisions. However, the scenario could change quickly: the recent indication to propose vaccination in all pregnant women could determine, in addition to protecting themselves, an increase in protection in newborns as for other vaccine preventable diseases (11,38). Furthermore, in Emilia-Romagna Region, as well as in Italy, the trivalent vaccine has been recently replaced by the quadrivalent vaccine, which should show greater efficacy against B strains, in particular in children. On the other hand, influenza vaccination in Italy in children from 6 months of age, is still voluntary and provided only with payment.

In conclusion, our findings represent a useful contribution to the ongoing debate about the appropriateness of including influenza vaccination for healthy children, 6 months and older, in the updating National Vaccine Prevention Plan (PNPV).

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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Original article

Trends in childhood vaccinations coverage in Lombardy Region after the National Vaccine Prevention Plan (2017-19) and the new law on mandatory vaccinations

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Summary. In Italy, over the last decade, the spread of vaccine hesitancy has caused a steep decrease in vaccination coverage rates, both at the national and regional level. In this study, we pool and critically analyze childhood immunization coverage rates (2011-2018) in Lombardy, Italy's most populated region, and compare them to national trends. Overall, childhood vaccination coverage in Lombardy is slightly higher the Italian national average. In 2017, the law on mandatory vaccinations came into force, acting as a powerful tool for coverage increase.

Key words: immunization, vaccines, vaccination coverage, law, obligation, Italy, Lombardy

Introduction

Over the last decade, *vaccine hesitancy*(1) has imposed itself in Italy as a new, alarming phenomenon(2-4), causing a decline of immunization coverage rates. Vaccine coverage for critical pathogens dropped below the World Health Organization (WHO)-recommended herd immunity threshold(5, 6).

In July 2017, after a previous Governmental Decree-Law (n.73, June 2017)(7), the Italian Parliament approved law No. 119(8), extending free mandatory vaccinations.

The schedule currently includes a total of ten mandatory (poliomyelitis, diphtheria-tetanus-pertussis DTP, measles, mumps, rubella-varicella- MMR-v, Hepatitis B, *Haemophilus influenzae* type b) and five recommended vaccines (Human Papilloma Virus-HPV, Rotavirus, Pneumococcus, Meningococcal B, Meningococcal $ACW_{135}Y$).

The law imposed fines on families who refused to comply and gave the basis for turning away unvaccinated children from nurseries and primary schools.

For the first time in Italian legislation, law No. 119 has taken a life-course approach to immunization, to tackle the epidemiological priorities of the National Vaccine Prevention Plan (2017-2019)(9).

The path towards a nationwide Italian immunization registry is still long. A possible roadmap has been devised by D'Ancona *et al.* (10), while other authors offer a complete overview of Italy's vaccination data reporting system (11, 12).

A recent national survey elaborates on the detrimental health impact of the Italian economic crisis(13).

The current study addresses unmet research needs. Indeed, to the best of our knowledge, no single paper has performed a complete report and assessment of vaccine coverage trends in Lombardy from 2011 onwards.

A broad literature scan on PubMed and Embase just offered one relevant paper on the subject, featuring Lombardy coverage data for measles and rubella (14).

A second source is the "Regional Vaccine Prevention Plan" (15), a document issued by Lombardy Regional Council in response to the Italian National Plan (9). As a piece of grey literature meant to inform policymakers, it describes regional and Italian-level vaccination coverage data (2000-2016) using graphs only.

Aim of this study is to monitor regional-level coverage data for childhood vaccinations in Lombardy and to assess the overall impact of the post-2017 legislative framework on regional immunization coverage rates.

The analysis was focused on the ten compulsory vaccinations, with a separate discussion of two representative recommended ones. Immunizations against HPV and Rotavirus were deliberately excluded, as the former is often administered in adolescence, and the latter is too recent to allow a meaningful retrospective analysis.

Methods

We collected, analyzed and critically interpreted Lombardy regional-level coverage rates for childhood immunizations (2011-2018) and compared them to Italian national averages.

We reported data for 24-months old children, as this cohort seemed more representative of recent epidemiological trends.

Data on childhood immunizations were retrieved from the Italian Ministry of Health (MoH) yearly reports(16).

Coverages for 2011-2012 were grouped per vaccine (e.g. M-MMR-MMR-v/DT-DTP). All subsequent data (2013-2018) were collected per single antigen.

Immunization coverage rates were expressed as the proportion of immunized subjects by resident target population, in percentage.

Results

Mandatory vaccines

MMR-v quadrivalent vaccine coverage showed an encouraging starting point in 2011 in Lombardy (94,6%), while the Italian data was not as favourable (90,1%). Considering measles as the most critical antigen for this group of immunizations, a constant fall in coverage rates can be noticed after 2011, with lowest coverages below 90%.

Afterwards, rates started an increasing path, which still lasts. In 2018, measles vaccine coverage in Lombardy is still slightly below 2011 (94,16%), while Italy had a better crude improvement (+7,93%; Lombardy +4,67%), but since the starting point was lower, is still lagging. (Figure 1, Tables 1 and 2)

Data paucity about the newly-introduced varicella vaccination impedes formulation of any substantial trend analysis. Nevertheless, 2018 coverage is <75% (Table 1).

As for diphtheria-tetanus-pertussis (DTP) vaccine, 2011 data were optimal both in Lombardy (97,1%) and Italy (96,3%). In the following years, rates have declined, though always stably above 90%, with lowest values in 2015 and excellent recovery after 2017 (>95% in 2018, Table 1). Nevertheless, 2011 levels are yet to be reached.

Hepatitis B (Hep B) and *Haemophilus influenzae* type b (Hib) experienced a similar trend (Table 1). Of note, in 2018, Italy had average rates slightly below 95% for both antigens, while Lombardy is slightly above the threshold.

Recommended vaccines:

Data availability is restricted to 2013 - 2018.

Anti-pneumococcal vaccine coverage has been fluctuating in the course of the observation period, the lower point being 2013 (Table 1).

In Lombardy, meningococcal C vaccination coverage has been continuously rising from 2013 to 2018.

Representative antigens:

We report immunization coverage rates for Measles (Figure 1) and Poliomyelitis (Figure 2) as vicarious antigens for the quadrivalent (MMR-v) and the hexavalent (IPV-DTP-HepB-Hib) vaccinations, respectively.

Both in Lombardy and Italy, a sharp decrease took place in coverages for measles immunization, especially in 2014-2015.

For polio, vaccination uptake in Lombardy and Italy are almost identical, with 2018 data both above

Table 1. Immunization coverage rates (%), per vaccine (2011-2012), per antigen (2013-2018). Lombardy and Italy. Twenty-four months old children.

Antigen/vaccine		Years							
		2011	2012	2013	2014	2015	2016	2017	2018
MMR-MMRV°	L	93,9	94,0	n/a					
	I	89,9	89,2						
M-MMR-MMRV°	L	94,6	94,1						
	I	90,1	90,0						
Measles°	L	n/a		92,6	89,5	90,3	93,4	93,9	94,2
	I	90,3		86,7	85,3	97,3	91,8	93,2	
Mumps°	L	n/a		92,6	89,4	90,2	93,3	93,8	94,1
	I	90,3		86,7	85,2	87,2	91,8	93,2	
Rubella°	L	n/a		92,6	89,4	90,2	93,3	93,9	94,1
	I	90,3		86,7	85,2	87,2	91,8	93,2	
Chickenpox/Varicella°	L	n/a		0,00	-	0,83	-	1,85	73,0
	I	33,2		36,6	30,7	46,0	45,6	74,2	
DTP°	L	96,9	96,5	n/a					
	I	95,8	96,0						
DT-DTP°	L	97,1	96,7						
	I	96,3	96,2						
Diphteria°	L	n/a		95,9	95,0	93,4	94,2	95,0	95,2
	I	95,7		94,7	93,3	93,6	94,6	95,1	
Tetanus°	L	n/a		95,9	95,1	93,6	94,4	95,2	95,3
	I	95,8		94,8	93,6	93,7	94,7	95,1	
Pertussis°	L	n/a		95,8	94,8	93,4	94,2	95,0	95,2
	I	95,7		94,6	93,3	93,5	94,6	95,1	
Polio°	L	97,0	96,7	95,9	95,0	93,5	92,8	94,9	95,3
	I	96,1	96,1	95,7	94,7	93,4	93,3	94,6	95,1
Hep B°	L	96,2	96,5	95,8	94,9	93,2	91,8	94,6	95,1
	I	96,0	96,0	95,6	94,6	93,2	93,0	94,4	94,9
Hib°	L	95,9	95,2	95,2	94,3	92,9	92,9	94,3	95,0
	I	95,6	94,8	94,9	94,3	93,0	93,0	94,3	94,3
Pneumo*	L	-		83,7	79,4	86,8	85,7	92,5	92,8
	I	86,9		87,5	88,7	88,3	90,9	91,9	
Men C*	L	-		69,1	79,4	85,8	88,2	92,2	92,4
	I	77,0		73,9	76,6	80,7	82,6	84,9	

95%. A seroprevalence study of poliomyelitis in a vulnerable Northern Italy cohort is described by Veronesi *et al.* (17).

Altogether, Lombardy and Italy experienced a mildly comforting rise in measles and polio coverage. In Lombardy alone, an improvement can be seen in pneumococcal and meningococcal C.

Table 2 illustrates all increments across the study period.

Conclusions

Lombardy is Italy's most prosperous and most populated region and displays a peculiar healthcare organization (18, 19). Overall, childhood vaccination coverage in Lombardy is slightly higher than the Italian national average.

Lowest coverage was seen in 2014-2015, roughly the same time of *vaccine hesitancy*'s maximal spread.

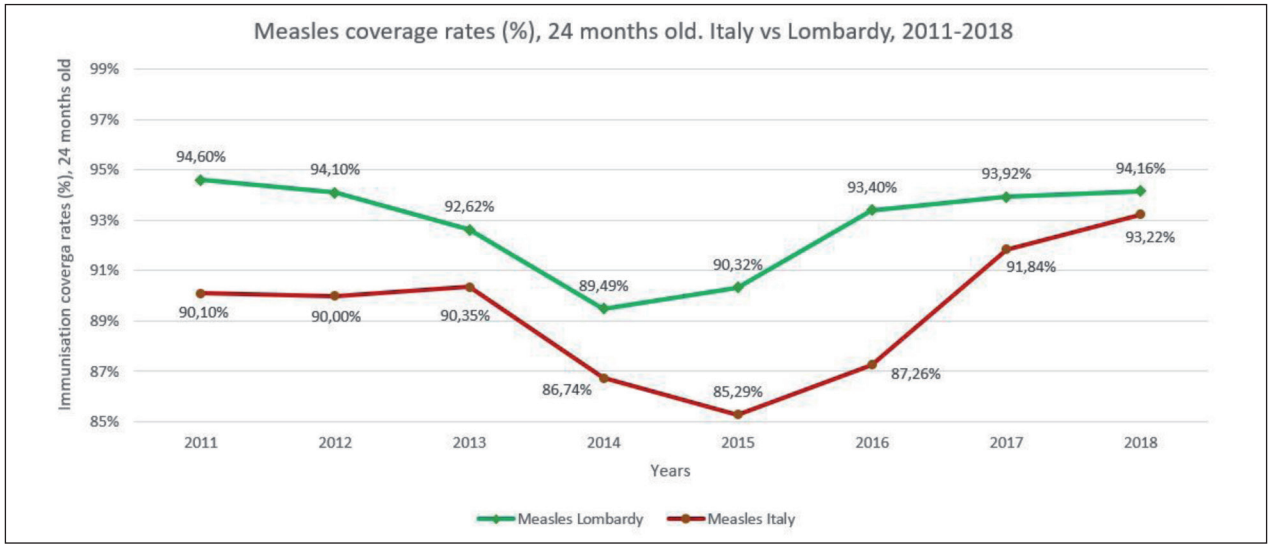

Figure 1. Immunization coverage rates (%) for measles. Twenty-four months old children, Lombardy vs Italy (2011-2018).

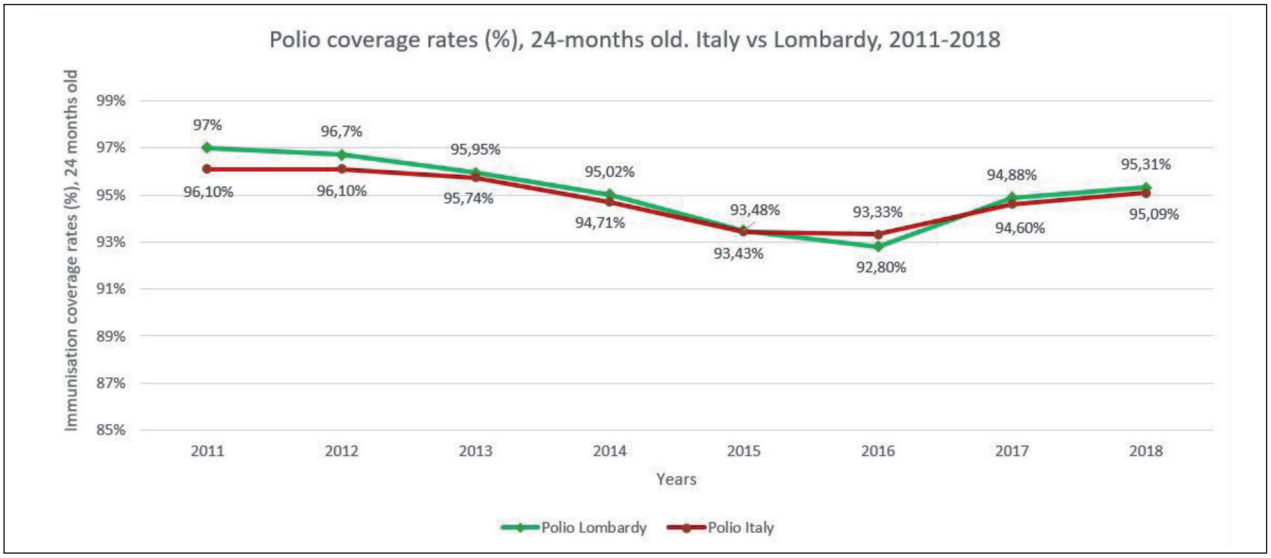

Figure 2. Immunization coverage rates (%) for poliomyelitis. Twenty-four months old children, Lombardy vs Italy (2011-2018).

Hesitancy is an international phenomenon, massively fuelled in Italy by a mixture of ideological fervour, mass media clamour, and pseudoscientific popular culture(20, 21).

In 2017, the law on mandatory vaccinations came into force, acting as a powerful tool for coverage increase – as the data show. Policy evaluation of the law's implementation efforts goes beyond this article's scope and can be retrieved in a recent *Eurosurveillance* paper(22).

The main antigen-specific findings of this study concerned the rising coverage trends of meningococcal C and pneumococcal conjugate vaccine in Lombardy (Table 2).

A recent small number of invasive meningococcal disease outbreaks in Centre-Northern Italy, which claimed conspicuous media attention(23), could be a partial explanation of the former finding. At the same time, we have no substantial hypothesis for the latter.

Different disease risk perceptions could play a role in the coverage disparity between MMR and the hexavalent vaccine (3, 24).

Table 2 – Percentage increase in immunization coverage rates. Minimal 2011-2017 coverage vs 2018 coverage (%). Lombardy and Italy.

Vaccine	Lombardy/Italy	Minimal coverage (year)	2018 coverage	Increase#
Measles-containing vaccines	L	89,5 (2014)	94,1	+4,7%
	I	85,3 (2015)	93,2	+7,9%
Polio-containing vaccines	L	92,8 (2016)	95,3	+2,5%
	I	93,3 (2016)	95,1	+1,8%
Pneumococcal Conjugate	L	79,4 (2014)	92,8	+13,4%
	I	86,9 (2013)	91,9	+4,9%
Meningococcal C Conjugate	L	69,1 (2013)	92,4	+23,3%
	I	73,9 (2014)	84,9	+11,0%

Notes to tables: L = Lombardy region; I = Italy; DTP = Diphtheria-Tetanus-Pertussis; Hep B = *Hepatitis B*; Hib = *Haemophilus influenzae* type b; Pneumo = Pneumococcal Conjugate; Men C = Meningococcal C Conjugate; MMR-v = measles, mumps, rubella, chickenpox; Polio = poliomyelitis; ° = mandatory under Law No. 119/2017; * = Recommended under Law No. 119/2017; n/a = not applicable (different data collection); - = missing data; # = 2018 coverage minus minimal coverage.

Exploring Lombardy's response to the national legislation could enable clinicians to gain a better understanding of the local epidemiological context. Furthermore, it could guide policymakers to develop tailored vaccination strategies.

Both regional and national immunization strategies should aim at reaching and maintaining optimal targets (≥ 95%) for all the vaccines included in the National Vaccine Prevention Plan 2017-2019 in all future newborn cohorts (25, 26). Conveying useful and persuasive information about vaccines is a shared duty of all healthcare personnel, and the entire scientific world (27, 28).

Stronger actions are urgently needed to fight *vaccine hesitancy* – a costly, and entirely avoidable, public health threat.

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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Original article

Immunity status against tetanus in young migrants: a seroprevalence study

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Summary. *Background and aim of the work*: Thanks to the highly effective vaccine, tetanus became sporadic in high-income countries with well-established primary childhood immunization programs, but it is common in low-income countries. The migrants, leaving countries with poor immunization programs or where vaccinations have been interrupted, may represent a new risk group for tetanus in host countries. A seroprevalence study was conducted to estimate the immunological status against tetanus in young migrants without vaccination documentation. *Methods:* After a careful assessment by vaccination services of the Local Health Authority, all migrants recently arrived in Italy were included in the serosurvey. Titers of anti-tetanus toxoid were measured using a commercial ELISA kit. Subjects were stratified by age and by WHO region. Antibody titers <0.10 IU/ml were considered to be seronegative, between 0.10 and 1.00 IU/ml as intermediate protection, and >1.00 IU/ml high protection. *Results:* From January 2004 to December 2019, 2,326 blood samples were collected. Mean age was 13.9 years with no differences between WHO regions. The percentage of the subjects without protective antibodies was 22.3%, with an intermediate level was 45.2%, with high titer was 32.5%. Among migrant coming from African and Eastern Mediterranean WHO regions, the highest percentages of seronegative titers and, at the same time, the low percentages of high protective levels were found. Titers decreased with age. *Conclusions:* The significant proportion of seronegative migrants and the decrease of protective titers increasing age, confirm the importance of the evaluation of the immunological status to employ the appropriate vaccination strategy.

Key words: tetanus**,** migrants, serological survey, seroprevalence, immunity, WHO region

Introduction

Tetanus is one of the rare diseases that is infectious but not communicable. Immunity to tetanus toxin is induced only by immunization, so the recovery from clinical tetanus does not result in protection against further attacks. On the contrary to what happens for diseases transmitted from person to person, the achievement of high vaccination coverage in children does not allow to obtain an indirect protective effect in the population. Therefore, tetanus can never be eradicated because it is impossible to eliminate spores from the soil and generally from the living environment (1-5).

The vaccine against tetanus allowed massive progress in controlling the disease. The epidemiology of tetanus has radically changed due to the availability of a highly effective vaccine since the 1930s. Tetanus became sporadic in several high-income countries, where well-established childhood primary immunization programs have made a major contribution in the drastic reduction in morbidity and deaths (6, 7). In these countries, however, most cases occur among unvaccinated elderly people (8-10).

A serosurvey study of six European countries in 2015 showed that 2–31% of people aged 65 had subprotective antitetanus toxin antibody concentrations (11).

The disease remains an important public health problem in many parts of the world, particularly in low-income countries, where most of reported tetanus cases are birth-associated, as consequence of the unclean deliveries and umbilical cord care practices (6, 7). Moreover, these cases are indicators of inequity in access to immunization and to other maternal, newborn, and child health services (12, 13). The Maternal and Neonatal Tetanus Elimination (MNTE) initiative, i.e. a reduction of the incidence below one case for 1000 live births per district, over 1 year, is the common goal in all countries of the world (14, 15).

As of September 2019, 47 out of 59 countries identified as high-risk for maternal and newborn tetanus had fully eliminated the disease and over 154 million women were immunized against tetanus between 1999 and September 2019. However, 12 countries remain to be validated, of which 11 are in the African and Eastern Mediterranean regions (16).

During 2017, 82 tetanus cases were reported in 26 countries of the European Union (EU), with a notification rate of 0.02 cases per 100,000 population that is in the range reported since 2012. Italy together with Poland accounted for 54% of all notified cases. Italy, albeit with a slow and gradual reduction over the years, remains, at European level, the country with the highest number of cases, with an annual notification rate that remained stable between 0.08-0,1 /100,000 from 2013 to 2017. Of the 231 cases reported in Italy in this period, 78% occurred in the age group 65 years old and above (8-10, 17). In Italy, tetanus toxoid vaccine was introduced in 1938 and was initially compulsory only for military personnel. In 1963, it became mandatory for two-year-old children and for workers engaged in activities considered to be at high risk of infection, e.g. construction, farming, refuse collection and animal husbandry. From 1968, tetanus vaccination became mandatory for all newborns. According to National Vaccine Prevention Plan 2017-2019, tetanus vaccination schedule consists of a primary series of three doses of tetanus-diphtheria-acellular pertussis vaccine (DTPa) at the 3th, 5th and 11th months of age, then two boosters at 6 and 12-18 years of age. Administration of additional booster doses is recommended for every 10 years of a combined tetanus-diphtheria-acellular pertussis vaccine (dTpa) (18).

In the last decades, migration flow towards Europe and Italy was highly intensified. In 2018, 30.4% of all the migrants at global level were in the European region. Within the European Union, Italy was at the third place with 8.7% of foreign legally resident citizens (19).

In 2018, the "Vaccine European New Integrated Collaboration Effort (VENICE)" survey group, conducted an extended survey among 30 countries in the European Union (EU) and European Economic Area (EEA), to map out immunization policies targeting irregular migrants, refugees and asylum seekers. The results from the survey showed that in the case of children/adolescent migrants, almost all (n.27) of the 28 countries having strategies for migrant immunization, offer all the vaccinations included in the National Immunization Programs, in line with the international recommendations (20).

In Italy, according to Law n.40/1998, regular foreign citizens are totally equated to Italian citizens as regards to all health services including preventive medical services, to safeguard individual and collective health (21).

The Italian Ministry of Health recommends to vaccine according to National Immunization Plan, based on age, all young migrants and adolescent who have insufficient documentation regarding prior vaccinations (22).

Due to its severity, tetanus poses a risk to unvaccinated or insufficiently vaccinated people. Since tetanus infection does not confer immunity, the migrants leaving countries with poor immunization programs or where vaccination series have been interrupted, can represent a new risk group for tetanus in host countries (20, 23-26).

The present study was undertaken to assess the immunity status against tetanus in young migrants who attended the Local Health Services to regularize their vaccination situation in line with the National Immunization Programme.

Methods

Study population

After a careful assessment by vaccination services of the Local Health Authority of Parma (a city with 190,000 inhabitants, in northern Italy), all migrants recently arrived in Italy, without or with incomplete vaccination documentation, were included in the serosurvey implemented between January 2004 and December 2019.

In this study, we evaluated foreign young children for quantitative determination of antibodies against Tetanus toxoid. According to the agreement "Good Clinical Practice Guidelines", all samples were treated anonymously.

The migrants came from the six WHO regions: African Region (AFR), the Americas' Region (AMR), the South-East Asia Region (SEAR), the European Region (EUR), the Eastern Mediterranean Region (EMR) and the Western Pacific Region (WPR).

Patients were reorganized into four age groups: less than 2 years, from 2 to 6 years, from 7 to 18 years and equal or more than 19 years according to Italian immunization schedule.

Serological analysis

Sterile human serum, kept at -20°C until the determination, was quantitatively analysed for antibodies IgG against Tetanus toxoid by using commercial ELISA kit (RIDASCREEN Tetanus IgG, R-Biopharm, Germany), and following the manufacturer's instructions.

Titers of anti-tetanus toxoid ELISA <0.10 IU/ml were considered as seronegative, between 0.10 and 1.00 IU/ml as intermediate protection and >1.00 IU/ml as high protection (5, 27)

Statistical analysis

The data were described in terms of mean, standard deviation (SD), median, minimum and maximum values. The results were summarized in tables of frequency and the differences in the proportions were compared using Chi square test, with Yates's correction of continuity when appropriate. The analysis of variance was applied when appropriate; otherwise, the median test was used to investigate any difference in the titers relative to the WHO region of origin or age class. P-values equal to or less than 0.05 were considered statistically significant. All statistical analyses were performed with SPSS 25.0 (IBM SPSS Inc., Chicago – IL).

Results

From January 1, 2004 to December 31, 2019, 2,326 blood samples were collected. The largest number was collected in 2011 years and the smallest in 2018 and 2019. In 176 cases, it was not possible to reconstruct the origin of the subjects. The remaining 2,150 subjects came from 85 different countries. Ten countries accounted for 65.8% of the samples. The African region, albeit with significant fluctuations over the years, provided the largest number of samples, with Senegal at 1st place (16.22%), followed by Ivory Coast and Ghana; India is at 4th place (8.48%) and the first European country was Albania at 9th place (2.5%) (Figure 1).

Overall, the AFR provided 49.4% of the samples, followed by EMR (13.4%), EUR (10.8%), SEAR (10.2%), AMR (8.7%) and WPR (7.5%). The average age was 13.19 years (SD 5.92) without statistically significant differences between WHO regions (Table 1). The median titer was 0.52 IU / ml. Overall on the WHO region of origin, 22.3% of the subjects had no protective antibodies (<0.10 IU / ml), 45.2% fell into the intermediate range and 32.5% of the subjects showed high titer of antibodies (> 1.00 IU / ml). The highest percentage of subjects without

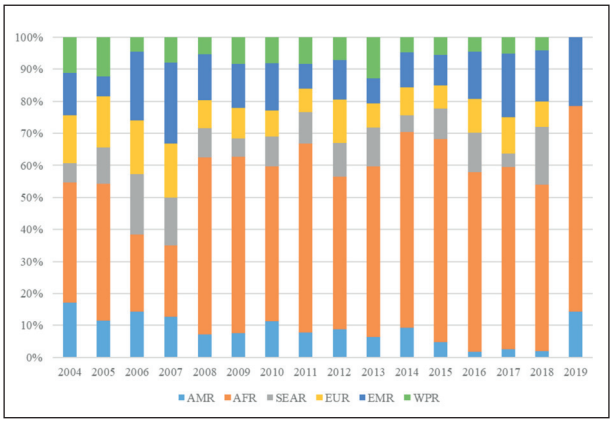

Figure 1. WHO regions of origin: distribution of subjects per year of study

Table 1. Characteristics of the study sample

WHO Region	Subjects (No.)	Age			
		Mean (SD)	Median	Min	Max
AMR	183	13.13 (5.37)	13.00	2	51
AFR	1,057	13.39 (5.88)	14.00	1	55
SEAR	217	12.36 (5.19)	12.02	2	35
EUR	229	13.67 (7.26)	14.00	1	43
EMR	286	13.10 (6.33)	13.40	1	40
WPR	160	12.52 (4.63)	13.00	0	31
Overall	2,132*	13.19 (5.92)	13.60	0	55

*Subjects with both countries of origin and age data

protective antibodies was found in the AFR (28.2%) and in subjects coming from the EMR (28.0%). In these regions, there have also been low percentages of subjects with antibodies with a high protective titer: 27.2% and 27.0% respectively. Among the subjects from SEAR, the lowest percentage of non-protective titers was found (5.9%) (Table 2).

By stratifying the subjects by age group, the median titers were higher in early childhood, decreasing in the 2 successive age groups of pre-schoolers and children and adolescents (0.60 IU / ml, 0.56 IU / ml and 0.50 IU / ml, respectively), and then up in young adults. In particular, the median antibody titers in the age group 2-6 years and 7-18 years, were statistically significantly lower than titers observed in the age group ≥ 19 years (p <0,05 with Bonferroni's Test) (Table3).

Table 2. Numbers and percentages of subjects with non-protective (0-0.1 IU/ml), intermediate (0.11-1.0 IU/ml), high (>1.00 IU/ml) tetanus antibody titers, by WHO Region

WHO Region			Tetanus Antibody Titers (IU/mL)		
			0 - 0.10	0.11 – 1.00	> 1.00
AMR	No.	186	15	92	79
	%		*8.1%*	*49.5%*	*42.5%*
AFR	No.	1,063	300	474	289
	%		*28.2%*	*44.6%*	*27.2%*
SEAR	No.	219	13	98	108
	%		*5.9%*	*44.7%*	*49,3%*
EUR	No.	232	28	96	108
	%		*12.1%*	*41.4%*	*46.6%*
EMR	No.	289	81	130	78
	%		*28.0%*	*45.0%*	*27.0%*
WPR	No.	161	43	81	37
	%		*26.7%*	*50.3%*	*23.0%*
Overall	No.	2,150	480	971	699
	%		*22.3%*	*45.2%*	*32.5%*

Conclusions

Pediatric vaccination with diphtheria-tetanus-pertussis vaccine has traditionally been the cornerstone of Expanded Program on Immunization and is often used as an indicator of how well countries are providing routine immunization services.

The vaccination schedules in low-income countries are different from those adopted in Italy in compliance with WHO indications, i.e. many more doses for diphtheria-tetanus vaccination. Many factors, such as the difficult logistical situations in which the local health services operate, the difficulty of maintaining an optimal cold chain, the low immune level of the child population for concomitant diseases and malnutrition, the organizational impossibility of reaching all children at specific ages, may be causes of incomplete immunization.

Therefore, to ensure lifelong protection against tetanus, WHO recommends that all people should receive 6 doses (3 primary plus 3 booster doses) of tetanus toxoid-containing vaccine through routine childhood immunization schedules. The booster doses

Table 3. Numbers and percentages of subjects with non-protective (0-0.1 IU/ml), intermediate (0.11-1.0 IU/ml), high (>1.00 IU/ml) tetanus antibody titers, by age class

Age	Subjects (No.)	Median Titer	Tetanus Antibody Titers (IU/mL)		
			0 – 0.10	0.11 – 1.00	> 1.00
< 2 years	21	0.60	0	19	2
			0.0%	90.5%	9.5%
2 - 6 years	266	0.56	52	134	80
			19.5%	50.4%	30.1%
7-18 years	1,701	0.50	404	752	545
			23.8%	44.2%	32.0%
≥ 19 years	144	0.99	23	53	68
			16.0%	36.8%	47.2%
Overall	2,132*	0.52	479	958	695
			22.5%	44.9%	32.6%

*Subjects with both countries of origin and age data

should be given at 12–23 months of age, 4–7 years of age and 9–15 years of age respectively.

In the EU/EEA countries, tetanus vaccination is recommended in infancy (3–4 doses in the first 2 years of life). All countries also recommend booster doses for children and teenagers after completing the priming vaccinations. Most of the Member States recommend a booster for adults who have reached 18 years of age or above.

In 2018, the global coverage rates for the third dose of the diphtheria, tetanus and pertussis (DTP3) vaccine reached 86%, up from 72% in 2000 and 20% in 1980. However, improvements have stalled over the current decade, and 83 countries have yet to achieve the Global Vaccine Action Plan target of 90% or greater coverage of DTP3 (28, 29).

Globally in 2018, 10 countries account for 11,7 of the 19,4 million under and un-vaccinated children in the world (60%). This list includes Nigeria, India, Pakistan, Indonesia, Ethiopia, the Philippines, Congo, Brazil, Angola and Vietnam, i.e. countries with moderate coverage and very large birth cohorts, and other countries with substantially lower coverage. In fact, coverage levels vary substantially across WHO regions: the gap between the best performer, the EUR, and the lowest performer, the AFR, is 18 percentage points (76% - 94% respectively) (7, 30, 31).

This epidemiological situation highlights the importance of the attention paid to foreign young population arriving in Italy without records of the main vaccine preventable diseases prior vaccinations. In particular, for tetanus, since protection is essentially based on artificially acquired immunity, the antibody dosage provides a useful indication of the immune status and can highlight any risk situation.

To our knowledge, from current literature, there is a paucity of data on tetanus immunity status of young migrants arrived in Italy, while more attention, in the epidemiological Italian context, is paid to the elderly population and to the professional categories at greater risk of tetanus infection (32-34).

Moreover, often, a limit in the interpretation of the results is represented by the differences in the laboratory tests used, in the cut-offs chosen as threshold values of effective protection (27).

From the literature, several prevalence and seroprevalence studies about the vaccine-preventable diseases immunity status of migrants, also compared with the native population, attest to the importance of this topic (10, 11, 35-55).

In this study concerning 2,150 subjects coming from the 6 WHO regions and from 85 different countries, protective tetanus antitoxin levels (>0.10 IU/ml) were found in the 45.2% of subjects, and long-protective tetanus antitoxin levels (>1.00 IU/ml) in the 32.5%. To note that a significant percentage (22.3 %) of subjects were inadequately protected.

In a seroprevalence study conducted in the past on young Italian children, the percentage of subjects without protective antibody levels is comparable with our results. The Authors explain their data supported by documentation, as the result of non-compliance with the vaccination program (56).

It is well known that tetanus toxoid is a very effective antigen, and for persons whose primary vaccination schedule is completed, the effectiveness of the vaccine is over 95% (1, 2, 5).

In Italy, since 2013, there has been a decrease in vaccination coverage in children and low levels of adherence to vaccination in adolescence (55, 57, 58). In particular, the detection of the vaccination coverage for the single tetanus antigen, for vaccinations at 5-6 years and at 16 years (cohort 2012 and 2002) (data as at 31 December 2018) shows lower percentage values than those expected as optimal in the PNPV 2017-2019 (58).

From the analysis conducted stratifying the young migrants by age group, the median titers were higher in early childhood and decreasing in the age groups of pre-schoolers and children and adolescents. This evidence must be carefully evaluated, due to the decline of tetanus immune protection, if not strengthened by booster doses. The increase of antibody titers observed in young adult, could be attributed to appropriate tetanus prophylaxis practices during accidents, traumas.
In this survey, the largest number of migrant (49.4 %) came from the African countries.

The highest percentage of migrants without protective antibodies and, at the same time, the low percentages of subjects with high protective levels come from AFR and EMR. Paxton et al. have also reported these results for east African immigrant children in

Australia (59). WHO estimates 8,5 million un-and unvaccinated children live in the AFR, almost as many as in all other regions combined (31).

In a wider European and global context, it is important to take this epidemiological situation into account, regarding risk of exposure and susceptibility of young migrants. The availability of serological investigations to assess the immunity status against many vaccine preventable diseases is an important tool for Public Health worldwide.

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Original article

Reorganization of Active Surveillance of Acute Flaccid Paralysis (AFP) in Emilia-Romagna, Italy: a two-step Public Health intervention

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Summary. *Background and aim of the work:* The International Health Regulations Emergency Committee declared in 2014 that poliovirus circulation is a public health emergency of international concern. In 2017 and 2018 Italy was classified at intermediate risk of poliovirus reintroduction based on suboptimal poliovirus surveillance. Acute flaccid paralysis active surveillance is the gold standard in the polio eradication process. The aims of this study were to investigate the causes of reduced acute flaccid paralysis case reporting in Emilia-Romagna in the last few years (step 1) and to study a public health intervention to restore an adequate level of acute flaccid paralysis surveillance in that region (step 2). *Methods:* In the first step a context analysis was performed by analysing the 2015-2017 Hospital Discharge Registers in Emilia-Romagna with the ICD-9-CM differential diagnosis codes for acute flaccid paralysis. Data from context analysis was then used to plan a new regional collaborative network of acute flaccid paralysis active surveillance. *Results:* The active surveillance network was, at the end of the study, composed by 49 doctors from both hospital administrations and clinical wards from 4 University Hospitals and 7 Local Health Authorities throughout the Region. In 15 months, 7 acute flaccid paralysis cases have been reported; 85,7% received a full clinical and virological investigation and 83,3% completed the 60 day's follow-up. The mean response to each e-mail was 48,5% (SD 7,5%). *Conclusions:* In 2019, the Emilia-Romagna's active surveillance system reached the sensitivity, completeness of case investigation and follow-up required to achieve the minimum levels for certification standard surveillance.

Key words: poliomyelitis, poliovirus, public health practice, disease notification, active surveillance, disease eradication, acute flaccid paralysis

Introduction

As the year 2019 ends, the total number of polio cases worldwide has reached a significant number. Acute flaccid paralysis (AFP) due to wild polio virus type 1 (WPV1) counted 173 cases, the highest peak since 2014, 140 cases more than 2018 (1).

Poliovirus eradication, as stated by the 41st World Health Assembly in 1988, has been considered possible under three simultaneous circumstances: 1) Overall child vaccination till the complete interruption of poliovirus transmission, 2) Verification of cessation of transmission certified by appropriate surveillance systems, 3) Poliovirus containment in international authorized laboratories.

In 2018 the European Centre for Disease Prevention and Control (ECDC), Communicable disease Threats Report, stated that "*importation of the infection as well as of polio cases into the European Union (EU) remains* possible" (4). Furthermore, given the persistence

of endemic outbreaks and the difficulty to obtain optimal vaccination in high risk groups, the International Health Regulations Emergency Committee confirmed the statement that poliovirus circulation is a public health emergency of international concern, already declared in May 2014 (5).

In 2017 and 2018, during the 31st and 32nd meeting of the European Regional Commission for Certification of Poliomyelitis Eradication (RCC), Italy was classified as a nation with intermediate risk of poliovirus reintroduction based on suboptimal poliovirus surveillance. While AFP surveillance is recommended by WHO to maintain a clear clinical picture of poliovirus infection and circulation, in the last few years, in Emilia-Romagna Region, as well as in other Italian Regions, there has been a decrease in AFP notifications. To maintain polio-free certification, the National Surveillance System (NSS) should be able to annually detect at least one case of non-polio associated AFP per 100,000 children under 15 years of age and no cases of wild-polio occurring for three consecutive years.

AFP is defined as the detection of new onset of hypotonic weakness in a child younger than 15 years. Numerous conditions can cause AFP: paralytic poliomyelitis, West Nile virus and other enteroviruses, as well as Guillain-Barré syndrome (GBS), transverse myelitis and traumatic paralysis (6-9).

Active Surveillance System allows early AFP detection and proper sample collection for virological testing. At the same time, it is necessary to be sure AFPs are not underestimated through the zero-reporting system. The absence of reported cases is not equivalent to absence of cases. The combination of these 2 surveillance systems are crucial to be certain AFP cases are reported and tested.

The aim of this study was, in a preliminary context analysis, to study whether the lack of AFP reporting was due to a lack of AFP cases in Emilia-Romagna or due to a lack of notification and eventually to analyse any critical issue preventing doctors from notifying AFP cases. Secondly, to study a public health intervention to restore an adequate level of AFP surveillance in Emilia-Romagna region.

Methods

Step 1: Preliminary Context Analysis

In the present section we discuss the preliminary context analysis methods and results. Analyzed data refers to the years were no notification occurred and its presence in "Methods" section is functional to define the methodology used to develop Step 2: proposed Public Health Intervention.

Between January and May 2018, we analyzed the cases of pediatric AFP that were not notified in the previous three years. The Public Health and Community Prevention Service of the Emilia-Romagna Region, extracted the Hospital Discharge Register (HDR) data of patients under 15 years old in Emilia-Romagna during the period 2015-2017, which reported in the first three diagnoses "International Classification of Diseases, 9th Revision, Clinical Modification" (ICD-9-CM) codes identified in literature that frequently go into differential diagnosis with AFP (Table 1) (9-10).

The 295 selected records were then divided per year and stratified by city of the discharging hospital, by diagnosis and by ICD-9-CM codes. Data was further analyzed highlighting records with codes 357 and 323 that are the diagnosis that more frequently are reported as AFP in literature (11). The cumulative annual incidence of these two codes resulted to be 5.9 cases per 100 000 people, while incidence calculated using GBS codes resulted to be 1.1 cases per 100 000 people, the same AFP annual rate expected by WHO. Clinical areas mainly interested Pediatrics (72%), Child and Adolescent Neuropsychiatry (13%),

Table 1. ICD-9-CM codes used for extraction of the Hospital Discharge Registers

ICD-9-CM code	Description
047	Meningitis due to enterovirus
320-322	Bacterial meningitis, Meningitis due to other organisms or of unspecified cause
323	Encephalitis, myelitis, and encephalomyelitis
341	Other demyelinating diseases of central nervous system
356	Hereditary and idiopathic peripheral neuropathy
357	Inflammatory and toxic neuropathy
950-957	Injury to nerves and spinal cord

Intensive Care Unit (4%), Pediatric Oncohematology (2%), Day Surgery (2%) and Pediatric Intensive Care Unit (2%).

Based on these evaluations it appeared imperative to restore an adequate level of Active Surveillance in Emilia-Romagna through a prompt reporting of AFP. Data was discussed with Emilia-Romagna Region and the next step was planned.

Step 2: Public health Intervention

Participants and proposed intervention

The "Emilia-Romagna's Reference Centre for polio surveillance", located in the Department of Medicine and Surgery (Hygiene Institute) of the University of Parma, in collaboration with the Public Health and Community Prevention Service of the Emilia-Romagna Region, studied the reorganization of the system through 4 phases:

1. Establishment of a regional collaborative network for AFP Surveillance.
2. Review of the Surveillance protocol in use and development of an algorithm to share with the regional network.
3. Creation of a computerized system of Active Surveillance – Zero Reporting.
4. Formation meetings for the whole regional collaborative network.

Phase 1. To establish the regional collaborative network for AFP Surveillance, we recruited doctors from every clinical ward involved in Emilia-Romagna hospitals with higher AFP incidence, previously identified in the context analysis. For each selected hospital we recruited also a contact person in the hospital administration.

Phase 2. Surveillance protocol was revised to better support clinicians in case of AFP detection. A visual flowchart was created to aid clinicians through the notification process. This material was explained and distributed during the formation meetings (Stage 4) and was sent via email to the physicians belonging to the regional collaborative network.

Phase 3. A computerized system of Active Surveillance-Zero Reporting was created as follows: every 15 days, one doctor from each piece of the network would receive an e-mail with a link connecting him to a webpage with two yes/no questions asking whether they had an AFP case in the past two weeks and whether the surveillance protocol was activated. Time to fill in the form was estimated less than 30 seconds, to help compliance and not burden colleagues. Attached to the e-mail an up-to-date epidemiological report in Italian on Poliovirus or Polio-related news was sent. The report was created using mainly data from GPEI (Global Polio Eradication Initiative) website (12).

Phase 4. Two meetings where organised before starting with the Active Surveillance-Zero Reporting. The first meeting was directed to the contact person in the hospital administration, the second one to the doctors from the clinical wards. The meetings were delivered in one day and were held at the regional government headquarters in Bologna. Formation was delivered by experts in the field coming from the AFP Regional Reference Centre and the Public Health and Community Prevention Service of the Emilia-Romagna Region. Information regarding national and international AFP epidemiology, the importance of AFP Surveillance, regional context analysis was delivered. Changes and innovation in Regional AFP Surveillance System was explained (phases 1-3). Educational material was handed out to the participants (the same material was also sent via e-mail to the whole collaborative network).

The two-step public health intervention was realized with no additional expenses by identifying personnel that was already present on the territory and using free online platforms. Context analysis and the planning and realization of the public health intervention was realized by researchers, expert in the field and residents of the Public Health Residency School of the University of Parma in collaboration with the Public Health and Community Prevention Service of the Emilia-Romagna Region. Doctors selected to participate to the regional collaborative network were all employees of the public Italian Sanitary System.

Hypothesis and expected Outcomes

The main hypothesis was that by reorganizing the Regional Surveillance System alongside with the implementation of a Computerized Active Surveillance-Zero Reporting system we could restore the AFP notification system to meet WHO requirements without increasing the work-load on colleagues.

Expected Primary Outcome: achievement of WHO standards for sensitivity of AFP Surveillance, one case of non-polio AFP to be detected annually per 100,000 population aged less than 15 years, meaning 6 for Emilia-Romagna Region.

Expected Secondary Outcome: (a) achievement of the WHO standards of completeness of case investigation (all AFP cases should have a full clinical and virological investigation with at least 80% of AFP cases having 'adequate' stool specimens collected) and (b) completeness of follow-up (at least 80% of AFP cases should have a follow-up examination for residual paralysis at 60 days after the onset of paralysis). Finally, (c) a complete monitoring of active surveillance program adherence.

The present paper was reported following the TREND statement for public health intervention and its extension TIDieR-PHP for population health and policy interventions. (13-14).

Results

Participant flow

The renovated active AFP surveillance began in October 2018. At the start, 23 doctors were included in the regional collaborative network for AFP Surveillance: 11 doctors from the hospital administration and 12 doctors from the clinical wards (pediatrics, pediatric surgery, child and adolescent neuropsychiatry, neurology, infectious diseases, intensive care unit, microbiology). Of the latter, 3 never actively participated to the new surveillance system and 2 dropped the network due to retirement, naming a substitute. By the end of 2019, the regional collaborative network for AFP Surveillance was composed of 49 doctors: 14 from the hospital administration and 35 from the clinical wards.

The network included 11 facilities throughout the region: 4 University Hospitals (UH) and 7 Local Health Authorities (LHA), that directly manage Territorial Healthcare Facilities, including smaller hospitals.

No variation from protocol was detected.

Outcome

Primary outcome: In 15 months of active surveillance, 7 cases of AFP have been reported through bimonthly e-mail (6 of them in 2019) (Figure 1). Of these, only 6 correctly activated the surveillance protocol. The cases were reported by doctors of the hospital administrations, child and adolescent neuropsychiatry wards and pediatric wards. We can say that the primary outcome of 6 AFP notifications per year was achieved.

Secondary outcome: Completeness of case investigation: of the 7 AFP reported cases, 6 (85,7%) had a full clinical and virological investigation with adequate stool specimens collected.

Completeness of follow-up: of the 6 AFP cases that activated the protocol, 5 (83,3%) had a follow-up examination for residual paralysis at 60 days after the onset of paralysis.

The final diagnosis of the cases was: 3 Guillain-Barre, 1 transient polyneuritis after HAV vaccination, 1 neuromyopathy from chronic disease, 1 acute myelitis in patient with DADA2. In 2 cases the paralysis persisted after 60 days.

Active surveillance program adherence: the response rate to each surveillance e-mail varied from 63,0% (November 2018) to 35,4% (June 2019) with a mean response of 48,5% (SD 7,5%). Instead, the individual response rate varied from 0 to 100%: 7 doctors have never answered to any e-mail; 3 doctors answered to all the e-mail received; the median response rate was 53,6% (IQR 74,4%). In Figure 1 we represented the AFP surveillance adherence by each doctor of the network, specifying whether it was zero reporting or the report of a case.

Conclusions

AFP surveillance remains the gold standard in the Polio eradication process. Alongside with environmental and serological control, it represents a territorial safety system in a national surveillance network, as well as other surveillance networks (15-18), whose aim is to prevent the possibility of poliovirus circulation (19-24). With the implementation of this public health intervention, we achieved the sensitivity of the surveillance, the completeness of case investigation and the completeness of the follow-up. Completeness of reporting still appears critical: the adherence to each e-mail varied from 35% to 63% and not 80% as sug-

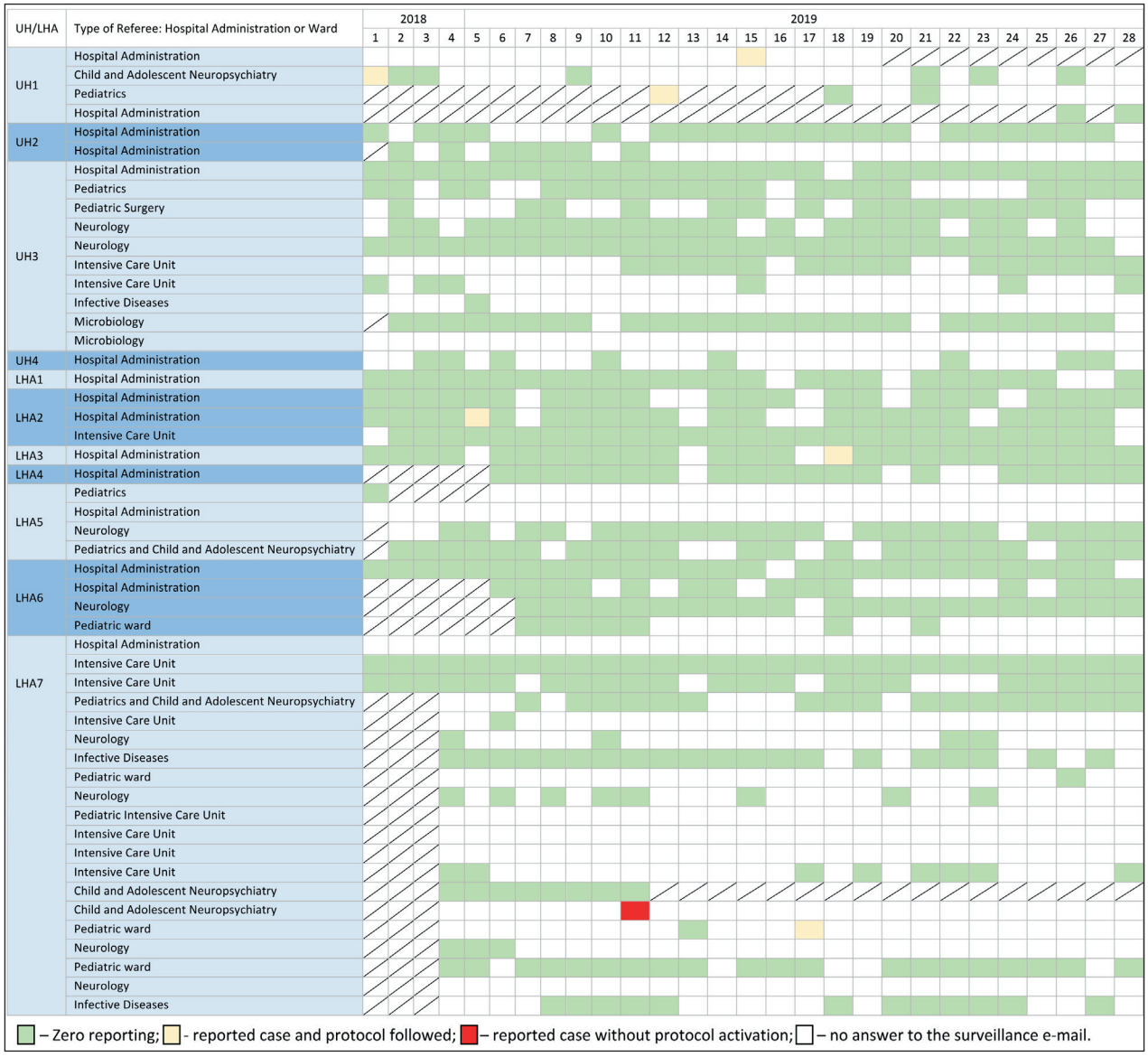

Figure 1. AFP surveillance adherence divided by type of referee of the University Hospital (UH)/Local Health Authority (LHA); - not yet part of the network;

gested by the WHO (12). However, taking into account the history of no reporting we may consider the achievement satisfactory, aiming to improve it during the years to come.

These results were influenced by the fact that the regional network met personally during the formation sessions and by the short period between the e-mails of the surveillance. Due to a direct bimonthly email contact, doctors were encouraged to express their doubts regarding AFP notification by contacting directly the Regional Surveillance Centre. The fact that the questionnaire was made of only 2 yes/no questions may have played a role in increasing the compliance. However, the fact that no polio AFP occurred for so long contributes to the lack of a proper perception of the risk by clinicians and contributes to the difficulty of implementing the zero-reporting system.

This practice is generalizable to other realities, there were no extra economic resources needed, use of human resources was limited and no extra-time load

to the clinicians was required. The collaboration of the public health residents was decisive for the success of the project, as well as representing a useful training moment on the field of real public health issues.

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Original article

Passive air sampling: the use of the index of microbial air contamination

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Summary. *Background:* Bioaerosol plays an important role in human life with potentially infectious, allergic and toxic effects. Active and passive methods can be used to assess microbial air contamination, but so far there is not a unanimous consensus regarding the indications about methods to be used and how to interpret the results. The passive method has been standardized by the Index of Microbial Air contamination (IMA). Classes of contamination and maximum acceptable levels of IMA have been proposed, related to different infection or contamination risks. The aim of this study was to provide information about the use of the passive sampling method, with reference to the IMA standard. *Methods:* We searched PubMed and Scopus for articles published until January 2020 reporting the citation of the article by Pasquarella et al. "The index of microbial air contamination. J Hosp Infect 2000". Only studies in English language where the IMA standard was applied were considered. Studies regarding healthcare settings were excluded. *Results:* 27 studies were analyzed; 12 were performed in Europe, 8 in Asia, 5 in Africa, 2 in America. Cultural heritage sites, educational buildings and food industries were the most common indoor monitored environments; in 8 studies outdoor air was monitored. *Conclusions:* This review has provided a picture of the application of standard IMA in different geographic areas and different environments at risk of airborne infection/contamination. The analysis of the results obtained, together with a wider collection of data, will provide a useful contribution towards the definition of reference limits for the various types of environments to implement targeted preventive measures.

Key words: air sampling, bioaerosol, IMA, indoor, outdoor, passive method.

Introduction

Bioaerosol plays an important role in human life with potentially infectious, allergic and toxic effects (1-5). Measuring microbial air quality is a fundamental step for risk management (6-8): it allows to confirm the presence of biological agents, identify critical situations and validate the preventive measures adopted; air sampling is also a useful tool for scientific research, quality assurance and educational purposes. So far, there is not a unanimous consensus regarding the indications for air sampling, what method should be used, and how to interpret the results in order to implement targeted preventive and control measures. Methods used for microbial air sampling can be classified in two categories: passive and active (6, 9). The active method allows the measurement of the concentration of culturable microorganisms in the air and is based on the use of some devices which collect a known volume of air, blown on to a nutrient media; the results are ex-

pressed as colony forming unit per cubic metre (CFU/m^3). Several types of devices are available, such as air impactors, impingers, centrifugal machines or filtration systems, which differ for biological and physical efficiency therefore providing different results, difficult to compare. The passive method measures the rate at which microorganisms settle on surfaces; it is based on sedimentation and relies on the use of settle plates being exposed to air for a defined period of time; results are expressed as CFU/plate/time. The passive method has been standardized by the Index of Microbial Air contamination (IMA) which corresponds to the number of CFU counted on a Petri dish (9 cm in diameter) left open to the air according to the 1/1/1 scheme (for 1 hour, 1 meter above the floor and about 1 meter away from walls and major obstacles) (10). The IMA can be expressed also as CFU/m^2 or dm^2 or cm^2/time. Five classes of IMA have been defined, representing a different increasing level of contamination: 0-5 very good; 6-25 good; 26-50 fair; 51-75 poor; ≥76 very poor. Maximum acceptable values of IMA have been proposed, related to different infection or contamination risks; these are 5, 25 and 50, in places at very high, high and medium risk, respectively (10). It is up to whoever is in charge to state the level of infection risk and adopt the corresponding maximum acceptable IMA level.

The aim of this study was to provide information about the use and diffusion of the passive sampling method for assessing the microbial air quality, with reference to the IMA standard (10). This paper deals with the results regarding non-healthcare settings.

Methods

We searched PubMed and Scopus for articles published until January 2020 reporting the citation of the article by Pasquarella et al. "The index of microbial air contamination". J Hosp Infect 2000. Only studies in English language where the IMA standard was applied were considered. Studies performed in healthcare settings were excluded and will be object of a specific paper. Only studies using nutrient media for total bacteria and/or fungi count were included. When the exposure of settle plates was longer or shorter than one hour, values measured in the sampling time considered were proportioned to one hour. The studies were analysed with reference to the Countries, settings, monitored environments and results obtained.

Results

Figure 1 shows the flow diagram of the review process. The reference "The index of microbial air contamination" was reported in n. 187 articles, 151 from Scopus and 36 from PubMed. After the screening by title, 29 duplicates were identified and removed. After the exclusion of the reviews (n. 29) and the studies performed in healthcare settings (n. 66), n. 63 articles studies performed in non-healthcare setting were considered for the review. Articles in which the citation of "The Index of microbial air contamination" was not referred to the air sampling method used, articles written in other than English language (11-16) and

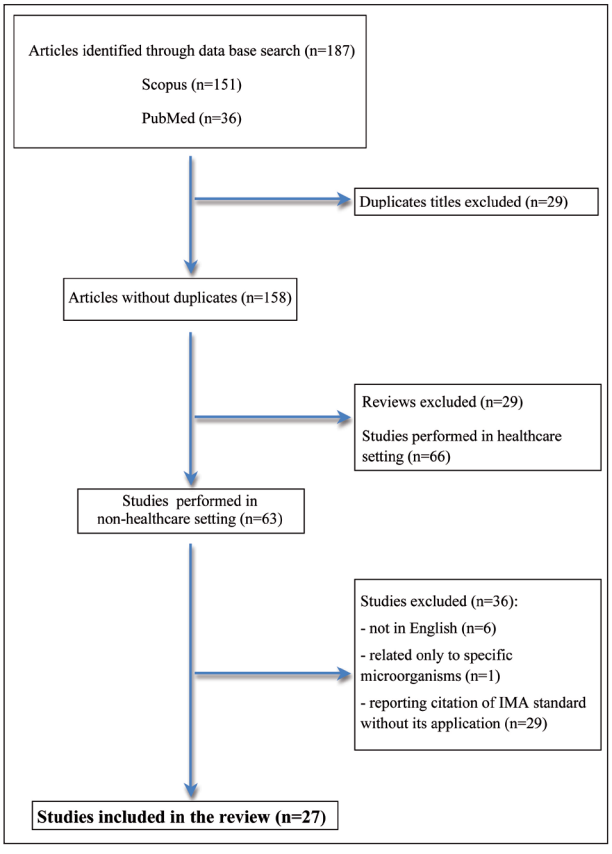

Figure 1. Flow diagram of study selection for review.

articles dealing with studies where specific microorganisms were searched (17), were excluded. A total of 27 studies were included in the review; in 25 studies quantitative or quantitative and qualitative air microbial contamination was evaluated (18-42); in 2 studies qualitative contamination only was evaluated (43,44).

Table 1 and Table 2 list the 25 studies yielding quantitative data, with reference, in particular, to the study setting, sampling period, sampling time and environments monitored, reporting the IMA values obtained for bacteria, fungi or total count. Ten studies were performed in Europe, including eight in Italy (18- 22,24,26,31), one in Romania (39) and one in Norway (34); eight studies were performed in Asia, two in Malaysia (26,35) and one for each of the following countries: Iran (32), Israel (36), Japan (30), Thailand (33), Turkey (28), Vietnam (37); five studies were conducted in Africa, two in Ethiopia (38,41) and one for each of the following countries, Egypt (25), Nigeria (23), South Africa (29); two studies were conducted in America, one in the USA (40) and one in Cuba (42). Twenty-one studies (18-33, 38-42) evaluated indoor air contamination, mainly in cultural heritage sites, educational buildings and food processing plants; five of these studies assessed also the outdoor microbial contamination (25,31-34); three studies evaluated only outdoor air quality (35-37). In five studies (38-42), listed in Table 2, the air was sampled using the IMA standard scheme, but the results obtained (CFU/plate/time) were transformed in CFU/m^3 by using the Omelyansky's formula: $N = 5a \times 10^4 (bt)^{-1}$ where N = CFU/m^3, a = number of colonies per Petri dish, b = dish square centimeter, t = exposure time (min.) (45), based on the estimation that on the area of 100 cm^2, in 5 minutes are deposited as many microbes as there are in 10 m^3 of air. Table 2 reports both the original values in CFU/m^3 and the IMA values obtained after the conversion based on the Omelyansky's formula.

As for cultural heritage sites, six studies were performed in Italy (18-22,24) and two in Africa (Nigeria and Egypt) (23,25). Considering the Italian studies, bacterial air contamination values ranged from 0 to 35 IMA without visitors (21); fungal contamination increased during opening time up to 48 IMA (20). Higher values were found in a museum library in Nigeria, where the heaviest microbial contamination means both for fungi (73 IMA) and bacteria (30 IMA) were found during the rainy season compared with the dry season (23). Fungal contamination values found in an Egyptian museum, where six rooms were monitored, ranged from 1 to 256 IMA, with median values from 8 to 30 IMA (25); in this study also outdoor environment was monitored, and indoor /outdoor ratio confirmed that outdoor environment was the main source of indoor fungal pollution. Microbial air contamination in educational buildings was evaluated in 6 studies. Di Giulio et al. (26) performed a study in 14 University research laboratories located in three different buildings over a period of six months, in the morning and in the afternoon; the IMA values showed a seasonal fluctuation of total microbial contamination, which were always within the threshold values of 50 and 25 IMA defined respectively for the common laboratory rooms and for the bacteriology laboratory with a controlled microbial charge. An IMA value below 25 was also found in the University Tissue culture Laboratory in Malaysia by Chong et al (27); in this study the lowest bacterial mean contamination values were found in the Top Management Office, from 5.72 IMA in the morning to 3.81 IMA in the afternoon, while the highest mean IMA value (27.98) was found in the library. Other four studies, carried out in educational buildings, 2 in Ethiopia (38,41), 1 in Romania (39) and 1 in the USA (40), converted the IMA value to CFU/m^3 by using the Omelyansky's formula. Going back to CFU/plate/time values (IMA) we found in a University microbiology laboratory in Romania (39) a mean charge converted value of 13.38; about classrooms, mean fungal contamination values ranged from 11.42 to 63.25. In a University dormitory in Ethiopia (38) very high values up to 760 IMA for bacteria and 501 IMA for fungi were reached. In Cuba, Anaya et al. (42) monitored the fungal contamination for a period of nine months in two food production plants, one for artisanal chocolate and one for products for special regime plant; IMA values, calculated from the CFU/m^3 obtained by Omelyansky's formula, ranged from 0 to 125 IMA. In the study by Scholtz (29) fungal contamination was assessed along the pear export chain from South Africa to the UK over a three year period, obtaining a median range from 52 to 1725 IMA, with a median IMA value of 201. The assessment of indoor airborne fungal

Table 1. Characteristics of studies using the Index of Microbial Air contamination (IMA) standard

Country Publication year (Ref)	Study setting	Sampling period	N. of monitored environments	Sampling time/ condition	Bacteria (IMA)		Fungi (IMA)		Microbial Total Count (IMA)
					Mean (SD)/ mean range/ *median*	Range	Mean (SD)/ mean range/ *median*	Range	Mean/mean range/*median*
Indoor environments									
Cultural heritage									
Italy 2011 (18)	Museum	January	7 rooms	before opening time	2.86*	1* - 7*	0.45*	0* - 2*	
				during opening time	11.51*	3* - 21*	0.89*	0* - 3*	
Italy 2012 (19)	Library	April	8 rooms			0* - 31*		0* - 3*	
Italy 2014 (20)	Museum	May	3 rooms	during opening time				1 - 48○	
		October						0 - 10○	
Italy 2015 (21)	Library	July	1 room		*8*	3 - 35	*1*	0 - 3	
		December			*8*	4 - 15	*2*	0 - 3	
Italy 2015 (22)	Library	Spring	1 room				0 - 28*		
Nigeria 2018 (23)	Library	Rainy season			7 (2) - 30 (3)		22 (3) - 73 (4)		
		Dry season			5 (3) - 22 (4)		13 (2) - 27 (5)		
Italy 2019 (24)	Library	February	1 room		3.33	0 - 7	0.5	0 - 2	
		May			3.33	1 - 6	3.67	0 - 9	
		September			3.33	0 - 5	4.33	1 - 9	
		December			1.33	0 - 3	0.67	0 - 2	
Educational Buildings									
Italy 2009 (26)	University	April - June	14 rooms Buildings A, B, C Research laboratories	in the morning (m.) in the afternoon (a.)					A m. 1.1 - 41.8 a. 0.1 - 6
									B m. 0.5 - 3.8 a. 0.5 - 4.3
									C m. 1.1 - 20.3 a. 0.7- 29
		October - December							A m. 0 - 11 a. 0 - 45
									B m. 2.1 - 5.7 a. 0.5 - 4.2
									C m. 1.3 - 17 a.0.5 - 10.3

Table 1. Characteristics of studies using the Index of Microbial Air contamination (IMA) standard

Country Publication year (Ref)	Study setting	Sampling period	N. of monitored environments	Sampling time/ condition	Bacteria (IMA)		Fungi (IMA)		Microbial Total Count (IMA)
					Mean (SD)/ mean range/ *median*	Range	Mean (SD)/ mean range/ *median*	Range	Mean/mean range/*median*
Malaysia 2017 (27)	University		5 environments	in the morning (m.) in the afternoon (a.)					
			University Service Center		m. 12.08* a. 5.09*				
			Top Management Office		m. 5.72* a. 3.81*				
			Tissue Culture Laboratory		m. 6.99* a. 17.8*				
			Cafè		m. 22.25* a. 15.26*				
			Library		m. 27.98* a. 27.98*				
Other environments									
Turkey 2011 (28)	Morgue Department	Spring - Summer	1 autopsy room	before autopsy	Spring 9.1 (5.7)		Spring 2.7 (1.7)		
					Summer 27.4 (22.1)		Summer 16.7 (26.3)		
				during autopsy	Spring 51.1 (17.1)		Spring 117.8 (271.6)		
					Summer 60.9 (65.7)		Summer 99.3 (175.6)		
				after autopsy	Spring 21.6 (49.3)		Spring 13 (28.4)		
					Summer 19.7 (21.6)		Summer 9.2 (10.5)		
South Africa 2017 (29)	Fruit handling environments	Over three years period	11						27 - 900• *105•*
Japan 2019 (30)	Animal housing system	November - January	1		0.3•		9.3•		

Table 1. Characteristics of studies using the Index of Microbial Air contamination (IMA) standard

Country Publication year (Ref)	Study setting	Sampling period	N. of monitored environments	Sampling time/ condition	Bacteria (IMA)		Fungi (IMA)		Microbial Total Count (IMA)
					Mean (SD)/ mean range/ *median*	Range	Mean (SD)/ mean range/ *median*	Range	Mean/mean range/*median*
Indoor and outdoor environments									
Norway 2009 (34)	Dry-cured meat production facility	February, August, December	16 rooms indoor outdoor	operational			15		
Iran 2014 (32)	School dormitory and retirement home	One year period	1 1			indoor 10 - 112 outdoor 15 - 96		indoor 11 - 36 outdoor 8 - 40	
Thailand 2016 (33)	Fitness centre A (indoor)		3		2.09 (1.50)		0.97 (1.69)		
	Fitness centre B (indoor)				8.44 (5.74)		5.07 (2.34)		
	Fitness centre C (outdoor)				7.52 (3.73)		5.59 (3.57)		
Italy 2017 (31)	Buffalo farms		3 Feeding rooms (outdoor)	at rest			10 - 76		
				operational			39 - 76		
			3 Milking rooms (indoor)	at rest			6 - 76		
				operational			12 - 24		
Egypt 2020 (25)	Museum	Two years period	6 Buildings	working hours				1 - 256**	
Outdoor environments									
Malaysia 2015 (35)	Residential areas: Case study: built on dumping site		2		48•		36•		
	Control: at 20 km from case study				27•		36•		

Table 1. Characteristics of studies using the Index of Microbial Air contamination (IMA) standard

Country Publication year (Ref)	Study setting	Sampling period	N. of monitored environments	Sampling time/ condition	Bacteria (IMA)		Fungi (IMA)		Microbial Total Count (IMA)
					Mean (SD)/ mean range/ *median*	Range	Mean (SD)/ mean range/ *median*	Range	Mean/mean range/*median*
Israel 2016 (36)	Areas closeness to domestic GW-treatment systems (RVFCWs)	June - February	3	early in the morning					
				0.3 m away from GW-t systems	0.22 - 616.7**				
				1 m away from GW-t systems	0 - 15.2**				
Vietnam 2019 (37)	Ho Chi Minh City	Three years period	4	four times a day					
			road area		80.3**		4.37**		
			zoo area		33.3**		52.48**		
			residential area		42.26**		3.02**		
			rural area		99.27**		14.17**		

Legenda: *calculated from CFU/dm²/h; **calculated from CFU/m²/h; • IMA calculated for 1 h; ○only fungal count on Saburand Dextrose Agar medium was considered

Table 2. Characteristics of studies using the Index of Microbial Air contamination (IMA) standard with values expressed as CFU/m³ calculated by Omeliansky's formula

Country Publication Year (Ref)	Study setting	Sampling period	N. of monitored environments	Sampling time/ condition	Bacteria				Fungi				Microbial Total Count	
					Range		Mean		Range		Mean			
Educational Buildings														
					CFU/m³	IMA*	CFU/m³	IMA*	CFU/m³	IMA*	CFU/m³	IMA*	CFU/m³	IMA*
Ethiopia 2015 (38)	University	April, May	30 dormitory rooms	at 6 a.m.	747 - 9960	57 - 760			531 - 6568	41 - 501				
				at 7 p.m.	511 - 4010	39 - 306			730 - 6403	56 - 489				
Romania 2016 (39)	University (U) High school (Hs) Primary school (Ps)	March, April, May	5 rooms	between 12 a.m. and 5 p.m.										
			U - A3				497.3	37.94•						

Table 2. Characteristics of studies using the Index of Microbial Air contamination (IMA) standard with values expressed as CFU/m³ calculated by Omeliansky's formula

Country Publication Year (Ref)	Study setting	Sampling period	N. of monitored environments	Sampling time/ condition	Bacteria				Fungi		Microbial Total Count	
					Range		Mean		Range		Mean	
Educational Buildings												
					CFU/m³	IMA*	CFU/m³	IMA*	CFU/m³	IMA*	CFU/m³	IMA*
Romania 2016 (39)			U - A5				414	31.59•				
			U - microbiol lab				175.3	13.38•				
			Hs - classroom				829	63.25•				
			Ps - classroom				149.7	11.42•				
									March 122 -862	March 9.31 - 65.67•		
			All monitored environments						April 145 - 830	April 11.06 - 63.33•		
									May 176 - 795	May 13.43 - 60.66•		
USA 2019 (40)	High school	October - February	8 rooms								135	10
	Primary school										293	22
Ethiopia 2019 (41)	Primary school	March - April	51 classrooms	at 6:30 a.m. and at 5:00 p.m.			613.29	47	136.5 - 2164.5	10 - 164		
Food industry												
Cuba 2019 (42)	2 Food production plants:	March - November		between 1:00 p.m. and 2:00 p.m.								
	Artisanal chocolate plant		5 rooms						0 - 1507	0 - 115		
	Product for special regime plant		2 rooms						39 - 1638	3 - 125		

*IMA values calculated from CFU/m³, •IMA calculated for 1 h multiplying for 3 (20 min) or 4 (15 min)

Table 3. Fungi and bacteria isolated in the different environments

	Fungi																																
Environments Country Publication year (Ref)	***Acremonium* spp.**	***Alternaria* spp.**	***Ascochyta* spp.**	***Aspergillus* spp.**	***Aureobasidium pullulans***	***Beauveria* spp.**	***Bipolaris* spp.**	***Botryotinia* spp.**	***Botrytis cinerea***	***Candida* spp.**	***Chaetomium* spp.**	***Chrysonilia sitophila***	***Chrysosporium* spp.**	***Cladosporium* spp.**	***Cochliobolus* sp.**	***Curvularia* spp.**	***Eurotium* spp.**	***Fusarium* spp.**	***Geotrichum* spp.**	***Maya benzeri mantar***	***Microsporum* spp.**	***Monilia sitophila***	***Mucor* spp.**	***Neurospora* spp.**	***Paecilomyces* spp.**	***Penicillium* spp.**	***Phaeosphheria* spp.**	***Pithomyces* spp.**	***Pseudopestalotiopsis* spp.**	***Rhizopus* spp.**	***Rhodotorula* spp.**	***Scedosporium apiospermum***	
Cultural heritage																																	
Italy 2015 (21)		√												√												√							
Italy 2015 (22)				√					√					√												√	√						
Nigeria 2018 (23)				√												√								√		√			√				
Educational buildings																																	
Italy 2010 (26)*				√										√									√										
Poland 2013 (43)**		√		√	√				√	√	√		√	√					√		√		√		√	√				√	√		
Italy 2014 (20)*				√										√				√								√							
Romania 2016 (39)		√		√				√						√		√		√	√				√			√				√			
USA 2019 (40)		√	√	√											√											√		√			√		
Ethiopia 2019 (41)		√		√						√								√			√		√			√				√			
Food industry																																	
Norway 2009 (34)	√													√			√	√							√	√							
South Africa 2017 (29)																										√							
Portugal 2017 (44)																																	
Cuba 2019 (42)				√										√				√					√	√		√							
Autopsy room																																	
Turkey 2011 (28)	√	√		√	√		√			√		√	√					√		√		√	√		√	√				√	√	√	
Outdoor																																	
Israel 2016 (36)																																	
Vietnam 2019 (37)				√		√					√					√		√					√		√	√				√			

*Genera most frequently found; **Other isolated microorganisms: *Acanthurus blochii, Artrographis Kalrae, Arxula adeninivarans, Bipolaris spicifera, Bjerkandera adusta, Blastomyces dermatididis, Cladophiarophora boppi, Corynespora cassiicola, Cystfilobasidium informominiatum, Debaryomyces hansenii, Debaryomyces polimorphus, Debariomyces occidentalis, Debariomyces vanrijiae, Emericella quadrilineata, Emmonsia crescens, Epidermophyton floccosum, Gymnoascus dancaliensis, Hormographiella aspergillata, Hormographiella verticillata, Kluyveromyces lactis, Kluyveromyces marxianus, Kluyveromyces thermotolerans, Kluyveromyces varrowii, Kluyveromyces wickerhamii, Lipomyces starkeyi, Madurella grisea, Mrakia frigida, Nadsonnia commutata, Oosporidium margaritiferum, Phialophora bubakii, Phoma cruris-hominis, Pichia anomala, Pichia farinosa, Pichia membranifaciens, Rhizomucor pusillus, Rhodosporidium dacryoideum, Saccharomyces cerevisiae, Saccharomycopsis capsularis, Saccharomyces fructuum, Scytalidum lignicola, Yarrovia lipolytica*

														Bacteria																							
	Scopulariopsis spp.	*Sporotrichum* spp.	*Stemphylium* spp.	*Syncephalastrum* spp.	*Thielaviopsis* spp.	*Trichoderma* spp.	*Trichophyton* spp.	*Trichotecium* spp.	*Ustilago* spp.	*Verticillium* spp.	*Wallemia* spp.	*Yeasts*	*Sterile mycelia*	*Acinetobacter* spp.	*Actynomyces spp.*	*Aerococcus* spp.	*Aeromonas* spp.	*Alcaligenes faecalis*	*Bacillus* spp.	*Corynebacterium* spp.	*Cochliobolus indoltheticum*	*Curtobacterium* spp.	*Escherichia coli*	*Enterobacteriaceae*	*Enterococcus* spp.	*Klebsiella* spp.	*Microbacterium* spp.	*Micrococcus* spp.	*Mycobacterium smegmatis*	*Myroides* spp.	*Neisseria meningitidis*	*Pseudomonas* spp.	*Rathayibacterium caricis*	*Staphylococcus* spp.	*Streptococcus* spp.	*Vagococcus* spp.	*Heterotrophic*
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contamination was also performed in a dry-cured meat production facility, and outdoor in a study by Asefa et al. in Norway (34); overall, in the production rooms, the mean value of 15 IMA was observed with the heaviest contamination in the brining, smoking, and sorting processes rooms, showing the last one the highest IMA value (about 90 IMA, graphic data); the outdoor fungal contamination was about 25 IMA (graphic data). In Italy, Vella et al. (31) carried out a study in three buffalo farms, including indoor and outdoor air microbial evaluation, at rest and in operational conditions: mean IMA values for fungal contamination ranged from 6 to >76 IMA in indoor milking rooms and from 10 to >76 IMA in the outdoor areas (feeding rooms). In the study by Sonmez et al. the presence of bacteria and fungi was determined in an autopsy room, in summer and spring seasons, before, during and after autopsy. The microbial air contamination was significantly higher at the time of the autopsy than that found in pre and post- autopsy sessions, reaching the highest values of 117.8 IMA for fungi in spring and 60.9 IMA for bacteria in summer; maximum acceptable IMA values were considered 75 for bacteria and 19 for fungi. In Japan, Tasaki et al. (30) monitored, for a period of thirteen months, a cargo van rabbit housing system obtaining a mean IMA value of 0.30 and 9.30, for bacteria and fungi, respectively. Other two studies, one in Iran (32) and one in Thailand (33), monitored the indoor and outdoor microbial contamination. In the first one a school dormitory and a retirement home were monitored, and bacterial IMA values for the two environments ranged from 10 to 112, while fungal contamination from 11 to 36; outdoor bacterial and fungal IMA values ranged from 15 to 96 and from 8 to 40, respectively. The second one dealt with three fitness centers, two indoor and one outdoor, locating settle plates at 1.5 m from the floor considering this height representing the human breathing zone; indoor mean IMA values ranged from 2.09 to 8.44 for bacteria and from 0.97 to 5.07 for fungi, while in the outdoor center bacterial and fungal mean IMA values were 7.52 and 5.59 respectively. Studies dealing with only outdoor microbial air sampling were carried out in Malaysia (35) and in Israel (36), both regarding waste treatments areas, and in Vietnam (37) where air was sampled in Ho Chi Minh city. In the study by Ithnin et al. (35), air sampling was performed around a former area dumping site, the case location, and 20 kilometers away, the control location; the mean bacterial air contamination values were 48 and 27 IMA, respectively, while mean fungal contamination was the same at both sites (36 IMA). Benami et al. sampled bioaerosols emitted from domestic grey water (GW) treatment systems; low amount of bacteria, with mean values ranging from 0 to 15.2 IMA were found to aerosolized up to 1 m away from the GW treatment system, while at the 0.3 m distance the mean values reached value of 616.7 IMA. In Ho Chi Minh city, airborne bacteria and fungi in the atmosphere were assessed from 2014 to 2016, covering two wet and dry seasons, at four sites of the city (zoo, road, rural and urban areas). The highest bacterial contamination was found at rural area while the lowest at zoo (33.3 IMA), where the heaviest fungal contamination was found (52.48 IMA).

Table 3 shows bacteria and fungi isolated in the different monitored environments by using settle plates according to IMA standard; in two studies (43,44) only qualitative evaluation was performed. Studies in which both active and passive air sampling were performed, but microorganisms isolated were reported without distinguishing which method allowed their isolation were not considered (21,24,25,32). Among bacteria, *Bacillus* spp., *Staphylococcus* spp., *Micrococcus* spp., *Pseudomonas spp.* and *Enterococcus* spp., were the most frequently isolated genera, while *Penicillium* spp., *Aspergillus* spp., *Cladosporium* spp. and *Fusarium* spp. were the predominant fungi.

Conclusions

This review has provided a picture of the application of IMA standard in different geographic areas and in different environments at risk of airborne infection/contamination. The use of settle plates, whose sampling efficiency is not influenced by engineering factors, standardized with the IMA, yields comparable results wherever and whenever they were obtained, providing the basis for the definition of threshold limits towards an effective risk prevention. In some studies (26,27,28,29,31,33), the IMA threshold values initially proposed for the different environments (10) were considered, and proved to be useful for the

interpretation of results. A wide range of microbial contamination has been observed, in the same settings of several studies; a larger collection of data, recording also variables which can affect the microbial air contamination, will provide a useful contribution towards the definition of limit values referred to specific environments. In particular, exposure times and incubation temperature for fungal search need to be defined, for a complete standardization of the air sampling.

A consideration should be made regarding the use of Omelyansky's formula which was applied in order to convert the CFU/plate values (IMA) in CFU/m^3**.** Both active and passive sampling can be used for a general evaluation of microbial air quality, but they have specific aims: while active sampling measures the concentrations of microorganisms, passive sampling measures the fall-out of the biological particles, as a mirror of the airborne risk for critical surfaces (e.g. object, material, food). In any case, considering the relationship provided by the EC GGMP Guidelines to Good Manufacturing Practice (46), it can be observed that the CFU/m^3 results obtained with the Omelyansky's formula are much higher, giving an overestimation of the risk. It could be suggested to keep the IMA value without converting in CFU/m^3, and to use the EC GGMP active and passive methods relationship for a possible estimation of the CFU/m^3. However, it is questionable to assume that a predefined correspondence between active and passive sampling exists, as some Authors do when using specific formulae to obtain the number of CFU/m^3 from the number of CFU/settle plates.

In a context in which there are no generally accepted protocols for the evaluation of microbial contamination of air, the use of IMA standard, for the relevance of data providing the estimation of the airborne risk of contamination for critical surfaces and the cumulative measurements of microbial contamination, as well as for its characteristics of economy and simplicity of use, represents a valid tool in the identification of situations at risk and in the evaluation of effectiveness of prevention interventions.

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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Original article

Hepatitis A epidemic in men who have sex with men (MSM) in Milan, Italy

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Summary. *Background and aim of the work:* Hepatitis A is an infectious disease characterized by fecal-oral transmission; however, a rise in sexually-transmitted cases has been observed, particularly among "men who have sex with men". In Europe, a Hepatitis A epidemic occurred among men who have sex with men between 2016 and 2018. The aim of this study is to describe this Hepatitis A epidemic in the city of Milan and to analyze the incidence of Sexually Transmitted Diseases co-infection among Hepatitis A cases. *Methods:* Hepatitis A cases were traced and identified. Epidemiological data were collected and Hepatitis A vaccination was investigated. Cases were georeferenced, calculating incidence rates for each Milan Municipality. Viral genotypic analysis was carried out. *Results:* 353 cases were reported in Milan. Incidence rates resulted significantly higher in males (RR 18.1 CI9 5% 11.5 – 28.4). 70 cases reported foreign travel. 172 cases reported "Men who have Sex with Men" behaviour. Genotypic analysis revealed correlation with strains of the European "Men who have Sex with Men" epidemic. Georeferencing showed asymmetric case distribution. Only 12 cases reported Hepatitis A vaccination. The Relative Risk for syphilis infection among Hepatitis A cases was 133.9 (95% CI 81.7 – 219.7) and 29.7 (95%CI 9.5 – 92.7) for gonorrhea. *Conclusions:* Most genotyped cases (93.7%) correlated to the European Hepatitis A epidemic among Men who have Sex with Men. Georeferencing showed a greater incidence of Hepatitis A cases in areas characterized by the homosexual community. The higher incidence of Sexually Transmitted Diseases co-infection in Hepatitis A cases correlated to clusters responsible for the European Hepatitis A epidemic, suggests increased sexual promiscuity among Men who have Sex with Men. These data support the need for Hepatitis A vaccination programs and sensitization of Men who have Sex with Men to the adoption of safe sexual practices.

Key words: hepatitis A, epidemic, men who have sex with men

Background

Hepatitis A (HA) is an infectious disease characterized by fecal-oral transmission; however, in recent years, a constant increase in the number of sexually-transmitted cases has been observed, particularly among "men who have sex with men" (MSM) (1,2). In Europe, a HA epidemic mostly affecting the MSM category occurred between the second half of 2016 and the beginning of 2018 (3). The epidemic began in three European countries during events involving several MSM who then imported the infection to their Country (4). During the same period, the number of HA reports was higher than in previous years even in Italy, particularly within the Lombardy Region where the highest number of cases was recorded: 778 or 22.7% out of the 3,426 cases at national level (5). The aim of this study is to epidemiologically and molecularly describe the HA epidemic that occurred in the city of Milan (Lombardy, Northern Italy) in 2017, focusing on MSM population.

In addition, other sexually-transmitted disease (STD) reports were evaluated, namely syphilis and gonorrhea, in order to calculate the relative risk (RR) of STD in HA cases, compared to the general population in Milan during the same year.

Methods

Case definition and epidemiological investigation

HA cases were defined as all patients living in the city of Milan, with a confirmed HA diagnosis, and reported symptoms onset between January 1st and December 31st 2017. According to the Commission Implementing Decision (EU) 2018/945 of June 22nd 2018 on the communicable diseases and related special health issues to be covered by epidemiological surveillance as well as relevant case definitions (6), a confirmed case is identified as any person meeting clinical and laboratory criteria. The clinical criteria include any person with a discrete onset of symptoms (for example, fatigue, abdominal pain, loss of appetite, intermittent nausea and vomiting) and at least one of the following: fever, jaundice or elevated serum aminotransferase levels. The laboratory criteria include the finding of at least one of the following: detection of hepatitis A virus (HAV) nucleic acid in serum or stool, HAV specific antibody response.

Personal and epidemiological data including gender, age, address, travel abroad in previous months, MSM sexual behaviour and other HA risk factors were available for all cases. Furthermore, HA vaccination was investigated via a record linkage to the regional vaccination registry.

Cases' home addresses were georeferenced using QGIS software, mapping case distribution in the city of Milan by Municipality (n=9). Thus age- and gender-specific incidence rates were calculated overall and for each Municipality.

Genotypic characterization and phylogenetic analysis

A serum sample for each HA case was sent to the regional reference laboratory (Department of Biomedical Sciences for Health, University of Milan, Italy) for HAV genotypic characterization and phylogenetic analysis. Briefly, following nucleic acid extraction and amplification of a genomic fragment (394 nt) in the VP1-2A region, amplicons were subjected to direct sequencing (7). Using the ClustalW program implemented in the BioEdit sequence alignment editor (version 7.2.3), studied sequences were aligned with reference viral genotypes along with the three epidemic genotype IA isolates (VRD-521-2016, RIVM-HAV16-090 and V16-25801) associated with the European multi-country HA outbreak in MSM. Phylogenetic analysis was carried out using MEGA6 bioinformatics software. A phylogenetic tree was generated by means of the Neighbor-Joining method and the Kimura 2-parameter model. Nucleotide identity between studied sequences and reference viral strains for the respective epidemic cluster was computed using the Sequence Identity Matrix tool implemented in the BioEdit software. Overall, 206 HAV sequences from as many HA cases of the Milan 2017 epidemic were analyzed.

Results

Epidemiological investigation

Between January 1st and December 31st 2017 a total of 353 HA cases were reported in the city of Milan, equal to 45.4% of all cases in the Lombardy region (8). As reported in Figure 1, the peak epidemic occurred in March. Among observed cases, 333 (94.3%) were male with a median age of 35 years (mean 36 years; mode

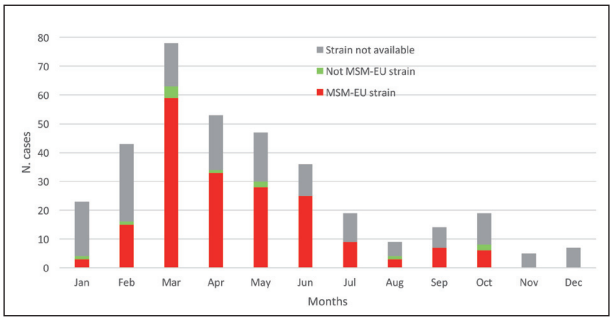

Figure 1. Distribution of HA cases from Milan, 1st January – 31st December 2017.
Red color: genotyped cases correlated to one of the European HA epidemic clusters in MSM.
Green color: genotyped cases not correlated to any of the European HA epidemic clusters in MSM.
Gray color: not genotyped cases

29 years), whereas 20 cases (5.7%) were female with a median age of 42 years (mean 37 years; mode 43 years). Regarding risk factors, 32 cases (30 males and 2 females) reported travel in Europe and 38 cases (35 males and 3 females) reported travel outside the EU; 172 cases (48.7%) reported homosexual behavior (MSM).

Georeferencing

Georeferencing of HA cases in the city of Milan showed an asymmetric distribution, with the majority of cases concentrating in easterly city areas, particularly in Municipalities 2 and 3 (Figure 2).

The total incidence rate per 100,000 inhabitants resulted significantly higher in males of all age classes (50.8) compared to females (2.8) (RR 18.1; CI95%: 11.5 – 28.4); among males, a higher incidence rate per 100,000 inhabitants was observed in the 25-34 and 35-54 years' age classes compared to other age classes. Regarding georeferencing, a higher HA incidence rate was observed in Municipalities 2 and 3 compared to all other Municipalities, and compared to the city's total (44.0 and 46.1 per 100,000 people, respectively), particularly among males of the 25-34 years' age class (260 and 332.7 per 100,000 people, respectively). Results are shown in tables 1 and 2.

Among the 353 HA cases observed, only 12 (3.4%; 11 males and 1 female) cases reported hepatitis A vaccination. Of these, only one case was vaccinated more than one year prior to symptom onset, whereas the remaining 11 cases underwent vaccination around 10 days prior to symptom onset.

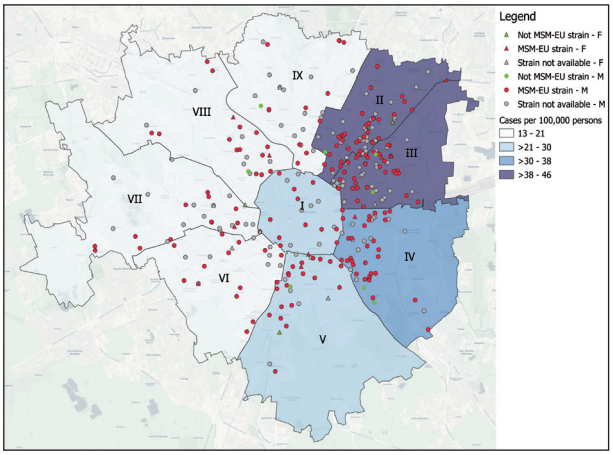

Figure 2. Georeferencing of HA cases and incidence rate in the city of Milan in 2017.
Red color: genotyped cases correlated to one of the European HA epidemic clusters in MSM.
Green color: genotyped cases not correlated to any of the European HA epidemic clusters in MSM.
Gray color: not genotyped cases.
Circle shape: male cases.
Triangle shape: female cases.

Table 1. HA overall incidence by age group in the city of Milan and in its 9 Municipalities in 2017.

Age (y)	City of Milan	M 1	M 2	M 3	M 4	M 5	M 6	M 7	M 8	M 9
Total	25.8	21.7	44.0	46.1	31.6	26.5	16.7	16.8	13.1	18.9
0-14	7.3	0	4.9	11.6	9.6	6.3	5.2	13.0	0	12.2
15-24	18.3	11.4	22.7	35.8	15.6	28.3	0	20.0	0	32.7
25-34	82.6	75.7	144.2	164.8	84.6	50.1	70.3	72.1	50.5	29.1
35-54	38.4	37.0	60.7	67.9	55.2	46.3	19.8	16.8	19.3	28.1
55+	3.8	2.9	4.1	0	3.6	7	5.4	1.6	1.5	4.9

Table 2. HA males incidence by age group in the city of Milan and in its 9 Municipalities in 2017.

Age (y)	City of Milan	M 1	M 2	M 3	M 4	M 5	M 6	M 7	M 8	M 9
Total	50.8	44.5	86.3	93.9	63.8	49.6	32.8	30.7	24.1	37.2
0-14	9.8	0	9.5	22.2	9.2	0	10.1	8.4	0	23.5
15-24	31.6	0	41.4	69.4	29.8	53.2	0	25.8	0	62
25-34	158.5	163.9	260	332.7	165.5	83.8	130.3	144.2	99.5	54.5
35-54	72.8	79.9	111.1	125.7	111.7	86.4	40.7	30.7	31.9	50.8
55+	7.4	6.7	9.4	0	4.4	16.1	4.3	3.7	0	11.4

Genotypic characterization and phylogenetic analysis

Figure 3 represents the phylogenetic tree obtained by analyzing 206 VP1-2A HAV nucleotide sequences from as many HA cases (58.4% of total HA studied cases) along with reference HAV sequences from different genotypes and the three epidemic genotype IA isolates associated with the concomitant European multi-country HA outbreak in MSM. Eleven (5.3%) studied sequences were genotype IB, while the remaining 195 (94.7%) sequences belonged to genotype IA; amongst the latter, 193 (93.7%) were correlated to one of the European HA epidemic clusters in MSM. Particularly, 106 (51.5%) studied sequences showed a mean nucleotide identity of 99.8% (range: 99.3-100%) to the reference sequence VRD-521-2016; 86 (41.7%) sequences revealed a mean nucleotide identity of 100% (range: 99.6-100%) to the reference sequence RIVM-HAV 16-090; and 1 (0.5%) studied sequence was V16-25801-like with a 100% nucleotide identity to the respective reference strain.

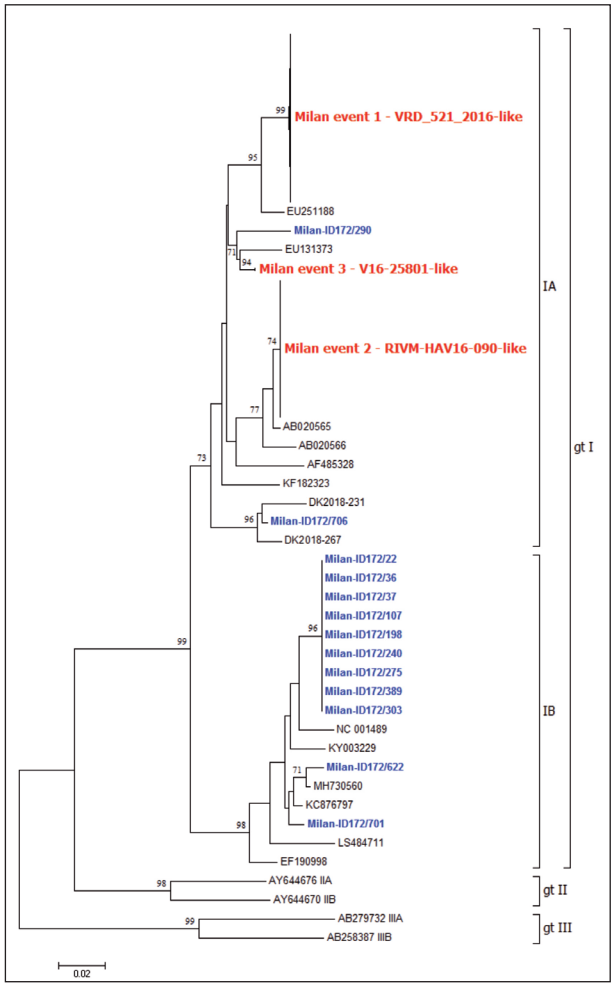

Figure 3. Phylogenetic three of 206 VP1-2A HAV sequences obtained from as many HA cases and reference viral strains.

A HAV sequence was available for 13 out of 20 (65%) female cases: nucleotide sequences correlated to a HA epidemic MSM cluster in 10 cases (76.9%; 6 cases were associated to cluster 2, and 4 cases to cluster 1). Furthermore, 2 additional female cases without a HAV sequence available were found to be epidemiologically linked with a HA male case whose HAV strain belonged to the epidemic cluster 1.

Co-infection with other STDs

In 2017, 16 syphilis and 3 gonorrhea co-infections were reported among HA cases. All subjects were male with a HAV genotype IA infection associated to one of the European MSM clusters. Since STD co-infection diagnoses only involved male subjects, to calculate the RR of STD in HA cases, the incidence of STDs among HA cases was compared to the incidence of STDs in the male population in Milan in 2017. The RR for syphilis infection among HA cases in 2017 was 133.9 (95%CI 81.7 – 219.7) times the risk in the male population in Milan. Similarly, the RR for gonorrhea infection among HA cases in 2017 was 29.7 (95%CI 9.5 – 92.7) times that of the male population in Milan.

Discussion

A multi-country epidemic, mainly affecting MSM, was observed in Europe since the second half of 2016 (3). Similarly, from the first few months of 2017, a significant increase in the number of HA cases was detected even in Italy. Milan was the city with the highest involvement in Lombardy, accounting for around half of the cases observed in the entire region (8). Phylogenetic analysis of approximately 60% of HA Milan cases showed that almost all cases (93.7%) were infected by a HAV strain sharing high nucleotide identity with one of the three viral epidemic strains involved in the European HA outbreak mostly affecting MSM. As further evidence to support the link between the Milan HA epidemic and the European outbreak, it is interesting to note that 70 cases (19.8%) reported international

travels, representing a potential risk factor for importing and spreading HA epidemic throughout the territory of Milan (9). Georeferencing of HA cases in the city of Milan and its nine Municipalities showed a greater incidence in two Municipalities, both characterized by a strong presence of the homosexual community and gay-friendly clubs. This fact is crucial for the organization of specific programs aimed at actively offering HA vaccination to MSM (10), perhaps even in collaboration with Lesbian, Gay, Bisexual and Transgender associations in the area. In fact, only a minority (3.4%) of individuals was previously vaccinated against HA, and nearly all (11 out of 12 subjects) were immunized only few days prior to symptom onset, probably already after exposure. This observation enhances the need to implement HA vaccination programs among MSM.

Epidemiological and molecular analysis of HA cases involving female population allows us to suppose a spillover infection from MSM to females. Consequently, post-exposure vaccination should be promptly offered to all identified contacts (11).

A higher incidence of STD co-infection among male cases with HA infection due to a HAV strain correlated with the European MSM epidemic clusters, confirms an increased sexual promiscuity among MSM (12). However, although sexual promiscuity may have allowed the spread of the HA epidemic, the latter may have allowed to report a greater number of STDs that may have otherwise remained un-diagnosed. The possible spread of STDs during HA outbreaks underlines the need to raise awareness of MSM to adopt safe sexual practices (10).

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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Original article

Emergency treatment in Lombardy: a new methodology for the pre-Hospital Drugs management on Advanced Rescue Vehicles

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Summary. *Background and aim of the work:* The main objectives of our work were the regional harmonization and standardization of pharmaceutical supplies on MSA in Lombardy. *Methods:* The retrospective investigation was articulated in 2 phases: the first was the collection of data in every area of the Region (2012), the second was the analysis and elaboration of the information retrieved. *Results:* Beginning with 24 common drugs used by 8 AATs out of 12 an evaluation of the chemical-therapeutic characteristics was performed. The temporary list, including over 80 drugs classified in more than 25 therapeutic groups, was finally reduced to provide bags that were easier to handle but at the same time complete. Between October and November 2014, the proposed supply, including 71 formulations and approved by the Technical Board of AREU, officially entered into force. At the same time, the working group followed the same procedure to define the standard equipment for the Region's helicopters, with only 58 formulations for relatively reduced weight allowed on board. *Conclusions:* In conclusion, we can state that, thanks to the support of experts, of the literature review, and thanks to the practical experience of the members of the AREU working groups and thanks to the documents coming from AIFA and EMA, the first operative regional project of unified pharmacological supply for MSA was delivered.

Key words: Emergency Medical System, drug supplies, drugs management, datasheet for emergency treatment

Introduction

Emergencies present the most critical issues of medical management and play a crucial role within the evaluation of the quality of the entire national health system. The peculiarity of the pre-Hospital Emergency Medical System (EMS - AREU Lombardy) has led to a deviation from the conventional medical disciplines, highlighting the need of integrating professional experience, promptness of intervention, emotional management and the selection of the best, strictly evidence-based, available and suitable drugs.

The equipment present in Advanced Rescue Vehicles (MSA) has always been variable (until 2012) and based on operative protocols and local regulations (1, 2). Despite the standard minimal compulsory requirements of the drugs , the incomplete specificity of these guidelines led to different choices in the same Region, with each AAT choosing the best drug according to their needs. The lack of standardized regional guidelines and the diversity of the supplies in terms of devices and drugs on MSA (due to the different pharmaceutical registers present in each trust in Lombardy), led to treat patients (with the same needs) by different drugs.

In order to reach the objective a feasible methodology was developed in Lombardy to standardize the drugs and to provide concrete benefits: the answer was the "harmonization and standardization" of rescue management, starting from the standardization of the drug supplies.

The harmonization process was necessary to decrease the differences of drug supplies and protocols in

the Region, and presented several advantages:
- Unified management of the resources
- Draft guidelines and homogenous protocols
- Optimization of the medical services
- Economic benefits (monitoring of costs and consumption) and less bureaucracy for every province

In this paper we have analyzed the situation of the EMS in Lombardy (until 2012). In particular we have focused on MSA, Advanced Ambulances and Medical Rescue helicopters, where the drug supply is available, along with anesthesiologists and experienced critical nurses (ER and Intensive Care Area).

Objectives of The Study

The main objectives of our work were the regional harmonization and standardization of pharmaceutical supplies on MSA in Lombardy.

To reach our goals we proceeded step by step as follows.
- Collection of qualitative and quantitative data on the use of drugs in the AATs in Lombardy (2012)
- Retrospective analysis of the situation in Lombardy
- Evaluation of the drugs already used by the different AATs and analysis of the characteristics of the potentially suitable ones
- Draft of a preliminary list (2013)
- Building a new ad hoc datasheet for emergency treatment
- Final list of medical equipment and drug supplies, common for the whole region
- Approval of the final list of medical supplies by the AREU Committee (2014).

The final results include the implementation of a standard drugs protocol in the pre-Hospital context.

Materials and methods

The retrospective investigation was articulated in 2 phases: the first was the collection of data in every area of the Region (2012), the second was the analysis and elaboration of the information retrieved. The information obtained allowed us to study both the qualitative aspect of the drugs, and the corresponding volumes. To realize this study, AREU set up a Working Group (GdL) made of different professionals, who are involved with territorial emergencies every day. Practical skills developed from experiences of Chiefs of AAT, doctors, nurses, pharmacists, together with the information found in the literature, produced concrete and common solutions.

The data gathered for the first drafting of the list allowed us to highlight the drugs used in more than one AAT. This initial list was then extended to include the drugs potentially suitable to cover all kinds of emergencies. After that, minor and superfluous drugs were excluded.

This methodology produced a number of advantages, although this approach was more time-consuming: the drugs were analyzed several times by all standards; the goal of this project being the harmonization, and not the creation of an ex-novo list. The evaluation of the equipment considered: efficacy, risk-benefit ratio, side effects, route of administration, onset of action, availability, storage, storage conditions and costs. Information was retrieved from the literature, AIFA and EMA official communications (3,4,5,6) and working group members' experience. This particular strategy, which was based on a number of criteria, produced an integrated network of information and concrete results that did not neglect the requirements of the single provinces.

After the common list was drafted, an ad hoc data sheet of the selected drugs was prepared. The role of this sheet was two-fold: first, to provide the medical team with the right choice in a short time, second, to improve the training of the professionals (didactical purpose). The layout of the sheet was simple and clear, and each file was divided in five sections.

The information provided was: general, such as the name of the active ingredient, concentration, commercial name, therapeutic group, indications and contraindications, and instructions for the preparation of the drug. Moreover, the mLs needed for the right dose and the speed of infusion according to the patient's weight was provided for a selection of drugs in order to drastically reduce the risk of dosage mistakes. Table 1 is an example based on the epinephrine data sheet.

It was also considered appropriate to highlight the precautions to be kept in mind before proceeding with the administration and potential side effects, listed

from the most frequent to the least frequent ones. Finally, storage conditions were included in the tables. The terms and sentences reported in the data sheet were the result of discussions aimed at finding standard clear and general sentences.

Concerns regarding drug administration to specific target populations were considered: pediatric, elderly, pregnant or breastfeeding women. Table 2 is the example of a data sheet.

Results

Beginning with 24 common drugs used by 8 AATs out of 12, an evaluation of the chemical-therapeutic characteristics was performed. The aim was to create a temporary list which could be useful and increasingly complete. Substances like infusion solutions and disinfectants were also included, as they are extremely helpful during medical rescue.

The temporary list, including over 80 drugs classified in more than 25 therapeutic groups, was constantly reviewed and finally reduced to provide bags that were easier to handle but at the same time complete. A particularly important role was attributed to the comparison of drugs of the same group in terms of effectiveness, safety, onset of action and costs.

Between October and November 2014, the proposed supply, including 71 formulations and approved by the Technical Board of AREU, officially entered into force (document number 99 – "List of drugs MSA"). The further step of the validation of the equipment was

Table 1. Infusion speed – epinephrine data sheet

Infusion **5 mg** in 50 mL	Dose mcg/kg/min	0,02 - 0,10 mcg/kg/min								
		0,02	0,03	0,04	0,05	0,06	0,07	0,08	0,09	0,10
	Weight kg	InfusionspeednessmL/h								
	30	0,4	0,5	0,7	0,9	1,1	1,3	1,4	1,6	1,8
	40	0,5	0,7	1,0	1,2	1,4	1,7	1,9	2,2	2,4
	50	0,6	0,9	1,2	1,5	1,8	2,1	2,4	2,7	3,0
	60	0,7	1,1	1,4	1,8	2,2	2,5	2,9	3,2	3,6
	70	0,8	1,3	1,7	2,1	2,5	2,9	3,4	3,8	4,2
	80	1,0	1,4	1,9	2,4	2,9	3,4	3,8	4,3	4,8
	90	1,1	1,6	2,2	2,7	3,2	3,8	4,3	4,9	5,4
	100	1,2	1,8	2,4	3,0	3,6	4,2	4,8	5,4	6,0

Table 2. Data sheet of "Lysine acetyl salicylate"

Lysine acetyl salicylate	
Concentration	500 mg/2,5 mL
Commercial Name	Flectadol®
Group	Antiaggregants of platelets. Antithrombotics [Antiinflammatory, anti-pyretics, analgesics]
Indications	Acute coronary syndromes. (in particular STEMI) if administration of ASA per os not possible [hyperthermia, painful syndromes]
Contraindications	Known hypersensitivity. Esophageal varices. 3rd trimester pregnancy. Association with methotrexate. Do not administer when <16 years old.
Preparation	
Dilution	Dilution in SF, RA, RL, G 5%
Administration	
Bolo	**125 mg EV** (80 - 150 mg)
Precautions	Asthma. Peptical ulcer. Esophageal varices. Viral infections in children. Chronic urticaria. Chronic rhinitis. Gout. Kidney and hepatic failure. Thrombocytopenia. Coagulopathies. Crohn Disease. Ulcerative colitis.
Possiblerelevant side effects	Anaphylactoid reaction. Gastralgia. Asthmatic crisis.
Storage	
T ≤ 20°C	

Table 3. New medical equipment supplies for the MSAs of Lombardy

N.	Drug	Formulation	Administr.	Storage	Group
1	Acetilsalicilato di lisina	fl 500 mg / 2,5 ml	ev	2	**Antiaggregant**
2	Acido acetilsalicilico	cp 100 mg / blst	os	1	**Antiaggregant**
3	Acido tranexamico	fl 500 mg / 5 ml	ev	2	**Antifibrinolytic**
4	Adenosina	fl 6 mg / 2 ml	ev	5	**Antiarrhythmic**
5	Adrenalina	fl 1 mg / 1 ml	ev	5	**Circulation**
6	Adrenalina	fl 5 mg / 5 ml	ev	4	**Circulation**
7	Aloperidolo	gtt 10 mg / 1 ml	os	1	**Central Nervous System**
8	Amido idrossietilico 6%	sol 500 ml	ev	2	**ColloidsInfusions**
9	Amiodarone	fl 150 mg / 3 ml	ev	3	**Antiarrhythmic**
10	Atropina	fl 0,5 mg / 1 ml	ev	4	**Circulation**
11	Beclometasonedip	0,8 mg / 2 ml	inal	1	**Respiratory**
12	Betametasone	fl 4 mg / 2 ml	ev	2	**Steroids**
13	$CaCl_2$	fl 1 g / 10 ml	ev	2	**Electrolytes**
14	Carbomix®	sosp 50 g / polv	os	1	**Antidote**
15	Clorfenamina	fl 10 mg / 1ml	ev - im	2	**Antihistamines**
16	Clotiapina	fl 40 mg / 4 ml	ev - im	1	**Central Nervous System**
17	Diazepamos	gtt 5 mg / 1 ml	os	1	**Sedation/hypnotics**
18	Diazepamrett	mcls 5 mg / 2,5 ml	rett	2	**Sedation/hypnotics**
19	Diazepamev - im	fl 10 mg / 2 ml	ev - im	2	**Sedation/hypnotics**
20	Diltiazem	fl 50 mg / 5 ml	ev	2	**Antihypertensive**
21	Dopamina	fl 200 mg / 5 ml	ev	2	**Circulation**
22	Eparina sodica	fl 5000 UI / 1 ml	ev	2	**Anticoagulants**
23	Esmololo	fl 100 mg / 10 ml	ev	2	**Antihypertensive**
24	Fentanyl	fl 100 mcg / 2 ml	ev	4	**NarcoticAnalgesics**
25	Fisiologica	sol 10 ml	ev	5	**CristalloidInfusions**
26	Fisiologica	sol 100 ml	ev	1	**CristalloidInfusions**
27	Fisiologica	sol 250 ml	ev	1	**CristalloidInfusions**
28	Fisiologica	sol 500 ml	ev	2	**CristalloidIinfusions**
29	Flumazenil	fl 0,5 mg / 5 ml	ev	2	**Antido**te
30	Furosemide	fl 20 mg / 2 ml	ev	5	**Diuretics**
31	Glucosio 5%	sol 250 ml	ev	1	**Solution for Infusion**
32	Glucosio 33%	sol 10 ml	ev	5	**Antidote**
33	Ibuprofene	fl 400 mg / 3 ml	im	2	**Minor Analgesics**
34	Idrocortisone	fl 1000 mg / 10 ml	ev	2	**Steroids**
35	Insulina rapida	fl 1000 UI / 10 ml	ev	1	**Antidiabetic**
36	Ketamina	fl 100 mg / 2 ml	ev -im	2	**Sedation/Hypnotics**
37	Labetalolo	fl 100 mg / 20 ml	ev	2	**Antihypertensive**
38	Lidocaina 2%	fl 200 mg / 10 ml	ev	2	**Antiarrhythmic/Local Anesthetic**
39	Lormetazepam	gtt 2,5 mg / 1ml	os	1	**Sedation/Hypnotics**
40	Mannitolo 20%	sol 100 ml	ev	1	**Diuretics**
41	Metoclopramide	fl 10 mg / 2 ml	ev - im	2	**Gastrointestinal**

Table 3. New medical equipment supplies for the MSAs of Lombardy

N.	Drug	Formulation	Administr.	Storage	Group
42	Metilprednisolone	fl 40 mg / 1 ml	ev - im	2	**Steroids**
43	$MgSO_4$	fl 1 g / 10 ml	ev	4	**Electrolytes**
44	Midazolam	fl 15 mg / 3 ml	ev - im	2	**Sedation/Hypnotics**
45	Midazolam	fl 5 mg / 1 ml	ev - im	2	**Sedation/Hypnotics**
46	Morfina	fl 10 mg / 1 ml	ev - sc	2	**NarcoticAnalgesics**
47	$NaHCO_3$ 8,4%	sol 100 ml	ev	1	**Electrolytes**
48	Naloxone	fl 0,4 mg / 1 ml	ev - im - sc	3	**Antidote**
49	Nitroglicerina spray	spray sbl 18 ml	sbl	1	**Antihypertensive**
50	Nitroglicerina	fl 5 mg / 1,5 ml	ev	4	**Antihypertensive**
51	Noradrenalina	fl 2 mg / 1 ml	ev	2	**Circulation**
52	Ondansetrone	fl 4 mg / 2 ml	ev - im	2	**Gastrointestinal**
53	Ossitocina	fl 5 UI / 1 ml	ev - im	4	**Obst-Gyn**
54	Pantoprazolo	fl 40 mg / 10 ml	ev	3	**Gastrointestinal**
55	Paracetamolo	250 mg / supp	rett	2	**Minor Analgesics**
56	Paracetamolo	fl 1000 mg / 100 ml	ev	1	**Minor Analgesics**
57	Propofol	fl 200 mg / 20 ml	ev	3	**Sedation/Hypnotics**
58	Ranitidina	fl 50 mg / 5 ml	ev	2	**Gastrointestinal**
59	Ringer acetato	sol 500 ml	ev	4	**Cristalloidinfusions**
60	Ringer lattato	sol 500 ml	ev	4	**Cristalloidinfusions**
61	Rocuronio	fl 50 mg / 5 ml	ev	4	**Musclerelaxant**
62	Salbutamolo + Ipratropio	gtt 0,375% + 0,75%	inal	1	**Respiratory**
63	Salbutamolo solfato	fl 0,5 mg / 1 ml	ev	2	**Respiratory**
64	Salbutamolo spray	fl 100 mcg / puff	inal	1	**Respiratory**
65	Succinilcolina	fl 100 mg / 2 ml	ev	2	**Musclerelaxants**
66	Sufentanyl	fl 50 mcg / 1 ml	ev	2	**NarcoticAnalgesics**
67	Sugammadex	fl 500 mg / 5 ml	ev	2	**Antidote**
68	Symeticone	gtt 2 g / 30 ml	os	1	**Gastrointestinal**
69	Tenecteplase*	fl 10.000 UI / 10 ml	ev	1	**Tthrombolytics**
70	Urapidil	fl 50 mg / 10 ml	ev	2	**Antihypertensive**
71	Vecuronio**	fl 10 mg / 10 ml	ev	4	**MuscleRelaxants**

* Only for locations far from a Cardiological HUB; ** Until available in stock

the attribution of an ATC code (anatomical, therapeutic and chemical) to every active ingredient selected.

In what follows we report the drugs selected for the medical rescue and particularly for MSAs working in pre-hospital emergencies in the Lombardy Region.

At the same time, the working group followed the same procedure to define the standard equipment for the Region's helicopters.

For reasons related to space and relatively reduced weight allowed on board, a list with fewer drugs was drafted, with only 58 formulations.

Several observations were made after the official lists were defined and the regional AAT acknowledged the work done. The most discussed drugs were: diazepam, single-dose microenemas for the selected dosages and lormetazepam drops, to be substituted with bromazepam drops (substitution denied).

In both cases AREU justified their choices supporting the safety use of the drugs on children, waiting for a specific evidence of literature not yet established

for pediatric population.

Another request was the substitution, which was accepted, of i.v. esomeprazole (40 mg/10 mL), already in use, with i.v. pantoprazole (40 mg/10 mL).

Further issues concerned the availability of some drugs, as they are not included in some hospital registers. In particular, labetalole, that can be obtained from the International Pharmacy since it is not yet manufactured in Italy, and the association of salbutamole + ipratropium, proposed as commercial brand Breva® and Carbomix®, available upon request at the Poison Control Centre. Other reports have been performed) regarding formulation of mannitol (already in use 18% instead of 20% as requested).

Discussion

The evaluation process was not simple: it was difficult to choose the number of drugs because during this selection, an invitation to tender was issued for new emergency backpacks. The prototypes being unavailable, it was hard to imagine how to prepare the equipment.

During the study, concerns regarding administration to specific target populations arose: pediatric and elderly populations, pregnant or breastfeeding women. The pediatric sector was particularly critical because, at the moment, evidence based on the literature does not include the safety profiles and effectiveness of drugs administered to this population. Considering the potential difficulties behind the creation of one supply suitable for both adults and children, with certainly different needs, it was agreed to treat only adults, with the future goal to study a specific list for the pediatric population.

For the elderly we had to take into consideration their fragilities and co-morbidities, thus resulting in polytherapy. In this regard, in the section "precautions" and "contraindications" of the drugs' data sheet all the relevant information has been reported. Concerning pregnant and breastfeeding women, a literature review allowed us to identify which drugs could be safe and which ones, instead, ought to be avoided to prevent damage to the fetus or to the breastfed baby. The research has been carried out evaluating each trimester of pregnancy. Some drugs were forbidden only during the 3rd trimester (e.g. lormetazepam, morphine, midazolam) others only during the 1st trimester (e.g. metoclopramide). Where data were incomplete or conflicting, the standard phrase "NO DATA AVAILABLE" was reported. The same research was performed on breastfeeding women: only 7 drugs out of 71 (beclomethasone, carbomix, insulin, magnesium sulphate, oxytocin, paracetamole and sugammadex) were found to be safe. The others have to be considered carefully. The draft results were retrieved and pooled in an Excel spreadsheet.

Guidelines concerning the storage of drugs were also discussed and provided: particular attention was needed because there are two different locations, the Station and the Car. An accurate evaluation of the literature was performed (5) (6). Storage conditions, chosen at the end of the analysis and discussion within the working group, reported these standard indications:

"No particular precaution"
"2°C < T < 8°C in refrigirator"
"T ≤ 15° C","T < 20° C"
"T < 25°C","T < 30°C".

The essential difference for the storage of the drugs in the locations mentioned was just a matter of organization: in the working Station all the drugs can be found in the medical cabinets or in the fridge, set at around 5 °C to include both formulations requesting T ≤ 15°C (epinephrine 1 mg/1 mL and epinephrine 5 mg/5 mL) and the ones requesting even lower temperatures, 2°C < T < 8°C (insulin, oxytocin, rocuronium and succinylcholine); in MSA we don't have standard containers, but bags (backpacks), bags for infusions and a fridge. The backpack was used for the drugs not requesting any particular care, while all the others are stored somewhere else: six critical formulations must be stored inside the fridge, and the others in cases and thermal bags with temperatures < 25°C and < 30°C. It was then essential to specify the exact location of each drug and to register the results in an Excel file.

At the end of the evaluation, most of the drugs in fact did not need particular arrangements, and could be stored at ambient temperature. Few formulations request lower temperatures (T < 25°C), while only 5

(present in 6 formulations) needed a different storage, in the fridge, (insulin, oxytocin, succinylcholine, rocuronium, adrenaline).

An analysis of narcotics and analgesics was also performed. DPR n. 309 of 9th of October 1990, and further modifications (6)(7), that rule the use, was estimated to be too general for pre-hospital rescue, and did not take into the right consideration the problems deriving from extraordinary emergency situations. The lack of clear indications concerning the Working Stations and MSA made the extra-hospital area uncertain about the governance of these drugs. Major problems were related to tracking the narcotics, not always available and suitable according to the time imposed by the law, and the supply, most of all for the working stations far away from hospitals and not located in hospitals. Being aware of the concrete problems that rescue teams have to face, some solutions were submitted to the Central Narcotics Bureau.

The goal was to guarantee their immediate availability and at the same time their correct management and tracking, according to the law. For this reason, AREU prepared a regional standardized supply to be used as major analgesics that could be stored in the bags inside the MSA. It was proposed to store them in the Working Stations, inside a locked cabinet, with a form indicating the characteristics (type and quantity) of each substance stored both in the station and in the MSA.

Conclusions

The harmonization and standardization of the drugs needed in every MSA allowed us to draft a common supply of 71 drugs, in all the region. However, the process was not straightforward: major issues concerned the choice of some drugs, their safety profiles, the process of procurement and their dosage. The impact on the new equipment led to modifications at different levels, operational, organizational, educational and professional.

In conclusion, we can state that, thanks to the support of experts, of the literature review, and thanks to the practical experience of the members of the AREU working groups and thanks to the documents coming AIFA and EMA, the first operative regional project of unified pharmacological supply for MSA was delivered.

Further development

There are still a few aspects that need to be clarified in future projects:

- Extension of the analysis to the paediatric population to identify safe drugs for this age group. In the list selected by AREU, indeed, few drugs can be guaranteed for children (paracetamol suppositories, diazepam 5 mg/2,5 mL, lormetazepam drops 2,5 mg/mL and ibuprofen vials 400 mg/3 mL); the situation is still uncertain and controversial for all the other drugs
- Optimization of the number of drugs: to simplify the supply and to handle the bags more easily (lighter backpacks), it is necessary to monitor and remove all the drugs that will not be used during the first year of the investigation and those that will be withdrawn from the market according to AIFA and EMA reports.

Proceeding in this direction we will be able to consolidate the EMS network and improve the management and organization of the rescue medical service.

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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. 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.

Glossary

Definitions and abbreviations

AAT = Territorial Agency Articulation (Articolazione Aziendale Territoriale)
AIFA = Italian Medicines Agency (Agenzia Italiana del Farmaco)
AREU = EMS Regional Agency (Azienda Regionale Emergenza Urgenza - Lombardia)
ATC = Anatomical, Therapeutical, Chemical (Anatomico Terapeutico Chimico)
CT = Technical Board (Collegio Tecnico)
DL = Legislative Decree (Decreto Legge)
DM = Ministerial Decree (Decreto Ministeriale)
DPR = Decree of the President of the Republic (Decreto del Presidente della Repubblica)
EMA = EuropeanMedicines Agency
GdL = Working Group (Gruppo di Lavoro)
GU = Official Gazette (Gazzetta Ufficiale)
MSA = Advanced Rescue Vehicles (Mezzi di Soccorso Avanzato)
WHO = World Health Organization (Organizzazione Mondiale della Sanità - OMS)
SOREU = Regional Medical Dispatch Centre (Sala Operativa Regionale Emergenza Urgenza)

Acronyms Used In The Document

blst = blister
dip = dipropionato (dipropionate)
ev = endovena (intra venous)
fl = fiala (ampoule)
flac = flacone (bottle)
g = grammo (gram)
gtt = gocce (drops)
im = intramuscolare (intra muscle)
inal = inalatoria (inhalation)
mcg = microgrammi (micrograms)
mcls = microclisma (micro enema)
mg = milligrammi (milligrams)
mL = millilitri (milliliters)
os = "per via orale" (orally administered)
polv = polvere per preparazioni iniettabili o infusioni (powder for injectable preparations or infusions)
puff = erogazione calibrata per via aerea (calibrated provision for airway administration)
sbl = sublinguale (sublingual)
sc = sottocute (subcutaneously)
sol = soluzioni per preparazioni iniettabili o infusioni (solutions for injectable preparations or infusions)
sosp = sospensione orale (oral suspension)
supp = supposta (suppository)
UI = Unità Internazionale (International unit)
rett = rettale (rectal)
T = temperatura (temperature)
°C = gradi Celsius (Celsius degree)

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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Original article

Prevalence of Huntington Disease in Italy: a systematic review and meta-analysis

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Summary. Worldwide prevalence of Huntington's disease (HD) is quite heterogenous. As Italy is characterized by significant genetic heterogeneity, with presumptive differences between Italian regions, this review was undertaken to define available data of HD prevalence in Italy, to assess geographic heterogeneity, and reconcile possible variation in HD prevalence rates with the availability of genetic testing. *Methods***.** In total, 14 relevant studies were identified from Medline/Embase, and analysis of available Italian regional reports on rare diseases. *Results*. A cumulative prevalence of 3.9/100,000 inhabitants (95% Confidence Interval 3.0 – 5.0) was identified, with apparently higher rates in the last decades (4.1/100,000 vs. 3.0/100,000). The lowest rates were among the resident of the Oristano province in Sardinia, while the highest were reported in three mountainous and rather isolated areas (i.e. Molise, San Marino, Varese; all well over 10 cases/100,000 inhabitants). These differences cannot be not fully explained by varying approaches to case-ascertainment or diagnosis, and a possible "*founder effect*" may therefore be extensively advocated. *Discussion***.** The prevalence of HD in retrieved Italian reports varied up to almost tenfold between different geographical regions. Even though such variation can in part be attributed to differences in case-ascertainment and/or diagnostic criteria, there is consistent evidence of significant founder effects in certain areas such as the provinces of Varese, the Republic of San Marino, and the region od Molise – all of them with estimates > 10/100,000 cases. As our estimates suggest that up to half of Italian HD cases may be still waiting, Public Health approach should improve diagnostic rates in order to guaranteeing palliative and symptomatic interventions (antidepressants, antipsychotics, anti-choreiform medications) to all individuals and their families.

Key words: Huntington's disease, Prevalence, Neurodegenerative disorders, Analyses, genetic linkage, Italy

Introduction

Huntington's disease (HD) is a monogenic, autosomal-dominant, incurable and slowly progressive neurodegenerative disorder characterized by chorea, dystonia, cognitive decline, and psychiatric manifestations, as well as dementia (1,2). The hereditary nature of HD was identified since 19th century, and the discovery of the causal HD gene (i.e. the huntingtin gene, *HTT*; chromosome 4) has established HD as triggered by a CAG triplet repeat expansion (*HTT*), which leads to an expanded polyglutamine stretch in the huntingtin protein, and subsequent protein misfolding (1,3,4). While the average CAG tract length in the general population ranges 16 to 20 repeats, in HD cases it usually exceeds 36 repeats (1,2,5). Interestingly, both severity of clinical features and disease progression are well correlated with the range of CAG tract length: longer the tract (i.e. > 40 repeats), earlier are the manifestations of HD, with a similarly shorter

survival. However, prognosis of HD remains relatively dismal: after the onset of the symptoms, usually between 35 and 55 years of age, life expectancy rarely exceeds 15 to 20 years (2,5–7), following complications such as aspiration pneumonia, myocardial infarction, opportunistic infections (8). As a consequence, people affected by HD can conceive offspring unaware of their status, ultimately maintaining the burden of disease in the general population (2,7–9). Unsurprisingly, HD shows a stable prevalence in population groups of European origin, with rates ranging 5 to 7 cases per 100,000, but clusters of higher prevalence rates have been extensively described, particularly where the population can be traced to a few founders (2). Still, the discovery of the genetic basis of HD has hinted towards a possible underestimate of actual prevalence of this disorder in earlier reports (4,7,9,10). In facts, as before 1993 diagnosis of HD was purely based on the recognition of extrapyramidal clinical features (i.e. chorea, dystonia, bradykinesia, or incoordination) in individuals from a favorable background, whereas people with typical neurological features, but without a family history compatible with the HD diagnosis may have remained largely undiagnosed (7,9,10).

Italy, with its quite heterogenous genetic background, is suspected to be similarly heterogenous in terms of HD prevalence (10,11), but epidemiological reports are substantially lacking, particularly after the introduction of genetic testing (10). Interestingly, while recent estimates from the Italian National Health Institute have reported around 1188 prevalent cases in 2014, prevalence estimates from Squitieri et al. pointed out towards a possible HD burden of around 6500 cases (10,12). Our study will therefore attempt to:

1) Identify the published measurement of HD prevalence in Italy;
2) Ascertain geographic heterogeneity, and reconcile possible variation in HD prevalence rates with the availability of genetic testing.

Materials and Methods

This systematic review has been conducted following the PRISMA (Prepared Items for Systematic Reviews and Meta-Analysis) guidelines (13). We searched into two different settings. On the one hand, we searched conventional scientific databases (i.e. PubMed and EMBASE) for relevant studies until 31/12/2019, without any chronological restriction. The search strategy was a combination of the following keywords (free text and Medical Subject Heading [MeSH] terms): («*Huntington* disease*» OR «*Huntington* chorea*») AND («*Italy*» OR «*Italian*») AND («*epidemiology*» OR «*prevalence*» OR «*frequency*» OR «*occurrence*») (**Figure 1**). On the other hand, we searched Institutional Web Sites of Italian Regional Health Services for reports on rare diseases, identifying prevalence estimates for medical exemptions RF0080 (i.e. diagnosis of HD). Records were handled using a references management software (Mendeley Desktop Version 1.19.5, Mendeley Ltd 2019), and duplicates were removed.

Documents eligible for review were original research publications available online or through interlibrary 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. Only article reporting diagnostic criteria for PD cases, the number of prevalent cases, or crude prevalence rates, were eligible for the full review. Retrieved documents 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 prevalence year); (4) reports lacked definition of the geographical settings, or it was only vaguely defined.

Two independent reviewers reviewed titles, abstracts, and articles. Titles were screened for relevance to the subject. Any articles reporting original studies, 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) Settings of the study: prevalence year, Italian region, level of assessment (i.e. community, province, region);

2) Screening procedures (i.e. clinical assessment vs. clinical assessment assisted by genetic testing)
3) Total number of prevalent PD cases;
4) Number of reference population.

We first performed a descriptive analysis to report the characteristics of the included studies. Crude HD prevalence figures were initially calculated: if a study did not include raw data, either as number of prevalent cases, or referent population (either in general or by age groups), such figures were either reverse-calculated from available data, or obtained from the Italian National Institute of Statistics (ISTAT) site DEMO (http://demo.istat.it/). DEMO includes Italian demographic data for the timeframe 1974 – 2019, at various geographical levels (i.e. national, regional, provincial, local communities).

Pooled prevalence (as prevalent cases/100,000 inhabitants) estimates were then calculated by means of a random effect model (in order to cope with the presumptive heterogeneity in study design). I^2 statistic was then calculated to quantify the amount of inconsistency between included studies; it estimates the percentage of total variation across studies that is due to heterogeneity rather than chance. I^2 values ranging from 0 to 25% were considered to represent low heterogeneity, from 26% to 50% as moderate heterogeneity and above 50% as substantial heterogeneity, being pooled using a fixed-effects model because of the reduced number of samples eventually included. To investigate publication bias, funnel plots were initially generated: publication bias was evaluated by testing the null hypothesis that publication bias does not exist by means of the regression test for funnel plot asymmetry. The null hypothesis was rejected if the p-value is less than 0.10.

All calculations were performed in R (version 3.6.1; R Core Team, 2017. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/) and RStudio (version 1.2.5019) software by means of *meta* package (version 4.9-9), functions *metaprop* for pooling of HD prevalence. The meta package is an open-source add-on for conducting meta-analyses.

Results

Initially, 252 entries were identified, including a total of 230 abstracts from MedLine/EMBASE and 22 Regional reports: as 6 of them were duplicated across the sources, 246 entries were initially screened. After applying the inclusion and exclusion criteria (**Figure 1**), 14 articles were included in the analyses and summarized, including 5 regional reports (14–18) and 9 scientific reports (8,10,11,19–25)(**Table 1**).

The majority of the reports (10 out of 14, 71.4%) were published after 1993. Overall, 8 reports included data retrieved at regional level (57.1%), while 6 studies reported figures at provincial level (42.9%). As two reports included figures both at regional level and provincial level, only discrete provincial figures were included in the final analyses. Eventually, the final sample included a total of 1244 cases (total sample size: 35,105,567 inhabitants), that were retrieved from the region of Lombardy, Friuli Venezia Giulia, Toscana, Lazio, Molise, Apulia, Toscana, with 4 provinces of Emilia Romagna (including San Marino Republic), whose total population includes 47.9% of total Ital-

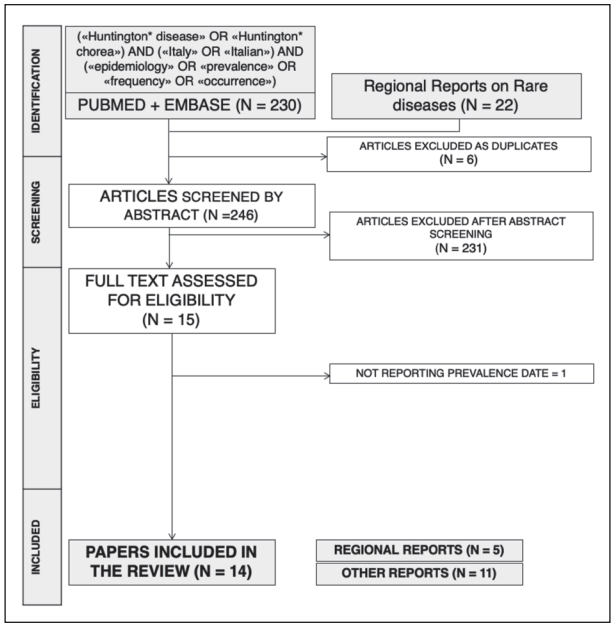

Figure 1. PRISMA flow diagram including keywords employed for the inquiry (i.e «Huntington* disease» OR «Huntington* chorea») AND («Italy» OR «Italian») AND («epidemiology» OR «prevalence» OR «frequency» OR «occurrence»), integrated by analysis of regional reports on rare diseases).

Table 1. Retrieved prevalence studies on Huntington's disease (HD) in Italy. Notes: DRG = diagnosis related groups; * = San Marino Republic, while an independent State, is actually a small enclave in the Emilia Romagna Region.

Study	Prevalence Year	Level of ascertain	Case finding method	Diagnostic criteria	No. of cases	Reference Population	Raw prevalence
Groppi et al. (1)	1979	Provincial, Florence	*Analysis of medical records from medical facilities of the Florence area; interview of 47 neurologists/psychiatrists practicing in the Florence area (years 1970 – 1979)*	Clinical only	37	1,202,013	3.1
Frontali et al. 1990 (2)	1981	Regional, Lazio	*Analysis of medical records from medical facilities of the Lazio region; interview of neurologists/psychiatrists practicing in the Lazio region (years 1975 – 1990); analysis of families with at least one HD case*	Clinical analysis, genetic testing (not specific for HTT), CT study of Central Nervous System	128	5,001,684	2.6
Mainini et al. 1982 (3)	1982	Provincial, Parma & Reggio Emilia	*Records of neurological and psychiatric institutions in the area; interview of neurologists/psychiatrists practicing in the Parma & Reggio Emilia areas; analysis of families with at least one HD case*	Clinical only	39	812,581	4.8
Pavoni et al. 1990 (4)	1987	Provincial, Ferrara	*Analysis of medical records from medical facilities of the Ferrara area; interview of neurologists/psychiatrists practicing in the Ferrara area; analysis of families with at least one HD case;*	Clinical only	7	370,375	1.9
Community of Trieste - Regional Health Service 2013 (5)	2011	Regional, Friuli Venezia Giulia	*Analysis of the institutional database of the Regional Health Service; identification of Medical Exemption code RF0080*	N/A	23	1,229,363	1.9
Reverberi et al. 2014 (6)	2013	Provincial, Reggio Emilia & Modena	*Analysis of medical records (DRG) from the Local Health Units + Hospitals of Reggio Emilia and Modena*	Clinical assessment + Genetic testing	30	1,210,844	2.5
Squitieri et al. 2015 (7)	2013	Regional, Molise	*Report from the Italian Network of Rare disease; analysis of all families (N = 31) with at least one case of HD in the pedigree residing in Molise region*	Clinical assessment + Genetic testing	34	313,341	10.9
Carrassi et al. 2017 (8)	2014	Provincial, Ferrara	*Analysis of medical records (DRG) from the Local Health Units + Hospitals of Ferrara province, identification of Medical Exemption code RF0080*	Clinical assessment + Genetic testing	15	354,673	4.2
Regional Registry of Toscana Region, 2015 (9)	2014	Regional, Toscana	*Analysis of the institutional database of the Regional Health Service; identification of Medical Exemption code RF0080*	N/A	169	3,750,511	4.5
ReLMaR 2015 (10)	2015	Regional, Lombardy; includes provincial estimates	*Analysis of the institutional database of the Regional Health Service; identification of Medical Exemption code RF0080*	N/A	442	10,008,348	4.4

Table 1. Retrieved prevalence studies on Huntington's disease (HD) in Italy. Notes: DRG = diagnosis related groups; * = San Marino Republic, while an independent State, is actually a small enclave in the Emilia Romagna Region.

Study	Prevalence Year	Level of ascertain	Case finding method	Diagnostic criteria	No. of cases	Reference Population	Raw prevalence
Stumpo et al. 2016 (11)	2015	Provincial, San Marino*	*Analysis of medical records (DRG) local General Hospital + analysis of the families with at least a previous diagnosis of HD*	Clinical assessment + Genetic testing	10	31,448	31.8
Regional Registry of Apulia, 2016 (12)	2016	Regional, Apulia	*Analysis of the institutional database of the Regional Health Service; identification of Medical Exemption code RF0080*	N/A	149	4,077,166	3.7
Muroni et al. 2019 (13)	2017	Regional, Sardinia; includes provincial estimates	*Analysis of medical records (DRG) from the Local Health Units + Genetic reference center of Sardinia Region*	Clinical assessment + Genetic testing	51	1,648,176	3.1
Regional Registry of Lazio. 2019 (14)	2017	Regional, Lazio	*Analysis of the institutional database of the Regional Health Service; identification of Medical Exemption code RF0080*	N/A	110	5,898,124	1.9

ian residents (2019 estimates). Interestingly, while all scientific entries published after 1993 included HTT analysis in the case definition, reports published by the Regional Health Services estimated HD prevalence only by means of reported medical exemption code RF0080, without any hints whether the diagnosis was achieved by a clinical assessment or was assisted by genetic testing.

Pooled estimates for HD prevalence are reported in **Figure 2**. Briefly, individual estimates ranged from 0.6/100,000 inhabitants (95%CI 0.0 to 3.5) in Oristano 2019, peaking to 31.8/100,000 in San Marino Republic 2016. More precisely, while half of the estimates reported substantially low prevalence rates (i.e. < 5/100,000 inhabitants), four estimates were included in the usual range for Western Countries (i.e. 5 to 7 cases/100,000 inhabitants), all of them from Lombardy in 2015 (i.e. Brescia: 5.7/100,000, 95%CI 4.5 to 7.2; Milan: 5.2/100,000, 95%CI 4.4 to 6.0; Pavia: 5.3/100,000, 95%CI 3.5 to 7.6; and Sondrio: 5.0/100,000, 95%CI 2.3 to 9.4), with three areas characterized by high or even very high rates, including the regional estimate for Molise (10.9/100,000 inhabitants, 95%CI 7.5 to 15.2), and provincial estimates for Varese 2015 (29.2/100,000 inhabitants, 95%CI 19.1 to 42.8) and San Marino.

Based on the random-effect model, a pooled estimate of 3.9/100,000 inhabitants (95%CI 3.0 to 5.0) was obtained: focusing on the geographical level of ascertain, a significant difference was identified, with an estimate of 3.4/100,000 inhabitants (95%CI 2.1 to 5.4) calculated from regional records, and 4.1/100,000 inhabitants (95%CI 3.0 to 5.5) for studies performed

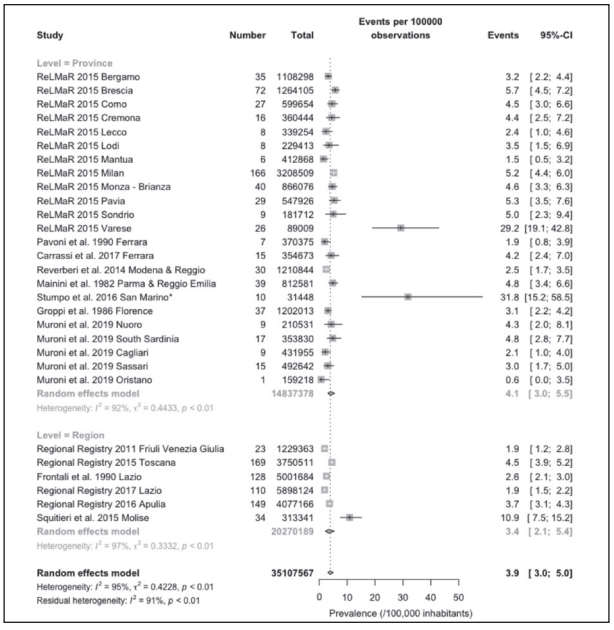

Figure 2. Pooled prevalence of reported studies, with estimates either at regional level or provincial level (Note: ReLMaR = Registro Lombardo Malattie Rare, Regional registry of Lombardy for rare diseases; *San Marino Republic, while an independent State, is actually a small enclave in the Emilia Romagna Region).

at a provincial level (chi squared test p value < 0.001). Heterogeneity was substantial, not only for the summary estimate (I^2 95%, p < 0.001), but also for the subgroup analyses (97% for studies performed at regional level, 92% for studies performed ad provincial level).

Interestingly, also when studies were grouped by publication date (i.e. before vs. after 1993; **Figure 3**), a significant difference was identified, with a pooled prevalence of 3.0/100,000 (95%CI 2.3 to 4.0) vs. 4.1/100,000 (95%CI 3.1 to 5.5) (chi squared test p value < 0.001). Studies performed after 1993 were affected by high heterogeneity values (I^2 = 95%), while in earlier studies a lower but still substantial heterogeneity value (I^2 = 68%). However, in a meta-regression model, the effect of the study year on the residual heterogeneity Q was not statistically significant (Q = 0.4495, p = 0.480).

The presence of publication bias was evaluated using funnel plots and regression test for funnel plot asymmetry, separately for studies performed at regional and provincial level. Each point in funnel plots represents a separate study and asymmetrical distribution indicates the presence of publication bias. First, studies' effect sizes were plotted against their standard errors and the visual evaluation of the funnel plot suggested a significant publication bias only for studies performed at regional level, as the graph appeared slightly asymmetrical (Figure 4b). Still, such subjective evidence from the funnel plot was rejected after the regression test (t = -0.62672, p-value = 0.5539 for regional estimates; t = -1.0009, p-value = 0.3283 for provincial estimates).

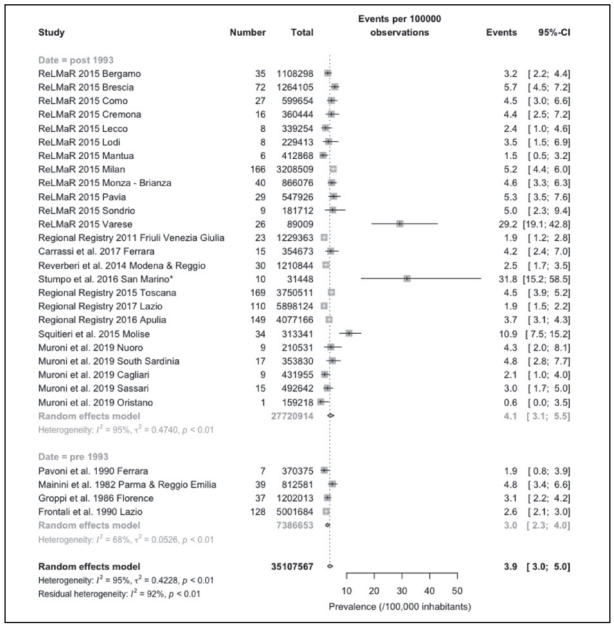

Figure 3. Pooled prevalence of reported studies, with estimates by the year of publication, i.e. pre-1993 vs. post-1993 (Note: ReLMaR = Registro Lombardo Malattie Rare, Regional registry of Lombardy for rare diseases; *San Marino Republic, while an independent State, is actually a small enclave in the Emilia Romagna Region).

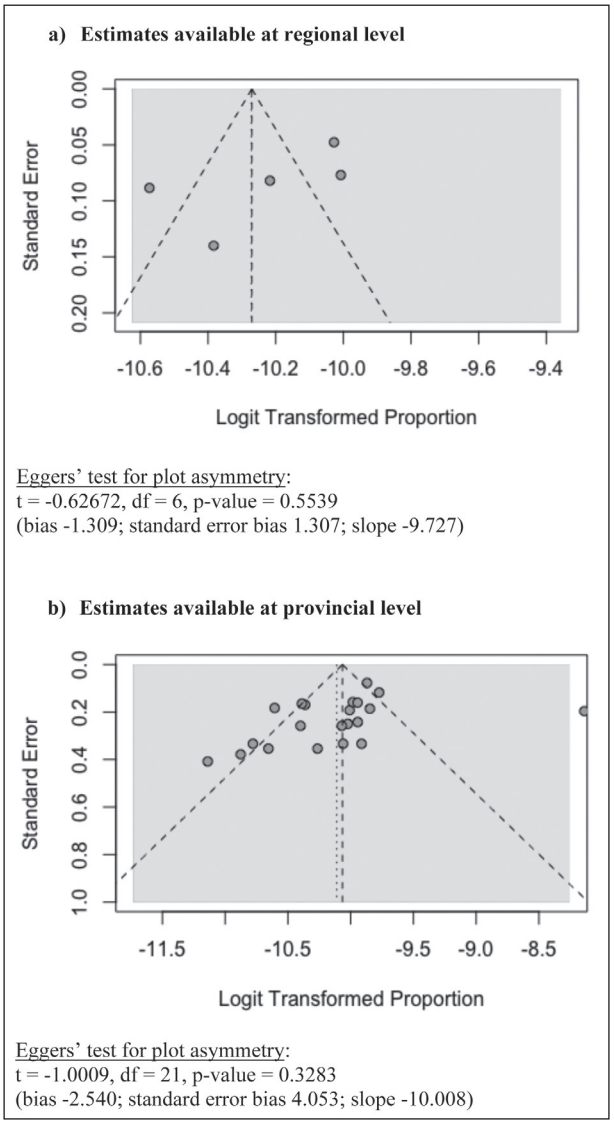

Figure 4. Funnel plots of available studies on the Italian prevalence of Huntington's disease, at regional level (a), and at provincial level (b).

Discussion

HD is a relatively rare disease, whose prevalence rates are, at the same time, stable overtime, strictly population-specific, and possible affected by the "*founder effect*", with possible clusters of higher prevalence even in areas otherwise of normal or low prevalence (2,3,6,7,9,26).

As a consequence, while usual prevalence rates of 5 to 7 /100,000 inhabitants have been diffusely reported (2,9), more recently Rawlins et al. (7) have suggested that such figures may result from a very heterogenous evidence, even focusing on European countries and/or geographical areas inhabited by individuals of European origin. In facts, prevalence rate for continental Western European Countries would be somewhat lower than previously reported, i.e. 3.6/100,000 (95%CI 3.5 – 3.7), with higher figures for United Kingdom (6.7/100,000, 95%CI 6.5 to 7.0), North America (7.3/100,000, 95%CI 6.9 to 7.7), and Oceania (5.6/100,000, 95%CI 5.6 to 6.3), i.e. geographical areas that in the past centuries were involved in significant migratory fluxes from British Islands, with a possible magnification role of the founder effect, particularly in Eastern US (2,7,9).

Available evidence suggests that actual Italian prevalence rates may be somewhat intermediate between those reported in continental Western European Countries and United Kingdom (i.e. 3.9/100,000, 95%CI 3.0 to 5.0), particularly when focusing on more recent studies (i.e. 4.1/100,000, 95%CI 3.1 to 5.5). However, the estimates are quite heterogenous in terms of quality, as derived from studies of strikingly different design (i.e. clinical assessment vs. genetic-based assessment), and databases whose case definition is often unclear. For instance, all regional reports derived their estimates from the total medical exemption for HD (i.e. code RF0080) among regional residents, but it remains unclear how such diagnosis was performed (14–18). In other words, even for reports published after 1993, a possible underestimate remains possible, being of difficult ascertain. Not coincidentally, while the field study of Frontali et al in 1990 suggested a possible prevalence of 2.6/100,000 for the Lazio Region (11), a more recent estimate of 1.9/100,000 was reported by the National Health Agency in 2017 (17).

Despite such preventive caveats, available figures apparently stress the well-known Italian genetic heterogeneity, with areas characterized by prevalence rates well-below estimates for Western European Countries (for example: Oristano, 0.6/100,000; Mantua, 1.5/100,000; Friuli-Venezia-Giulia, 1.9/100,000) (14,18,21), coexisting in the same region in the same timeframe with areas of relatively high prevalence (e.g. South Sardinia, 4.8/100,000; Brescia 5.7/100,000), and even with some significant possible clusters as the province of Varese (29.2./100,000). Possible clusters were also reported in the Molise region (10), as well as in the San Marino Republic (19): all of them are areas characterized by a mountainous and/or somewhat geographically segregated nature, and again – likewise to the Eastern United States, founder effect may have played a prominent role in increasing actual rates. For these reasons, a comparison with other areas from the Alpine Region would be of particular interest, but data are still unavailable.

As a consequence, our estimates suggest that around 2354 HD cases may be prevalent in Italy in 2020 (95%CI 1811 to 3018), or even 2474 (95%CI 1871 to 3320) assuming as a reference only estimates reported after 1993. Such figures are somehow intermediate between the 6500 cases suggested by the report of Squitieri et al. on the Molise region (10), and the 1188 actual cases identified in the National Report on Rare Disease (12), and should be cautiously interpreted, for several reasons. First at all, raw data stratified by sex and age at the prevalence date are scarcely reported in retrieved estimates. Therefore, not only a standardization of HD prevalence rates, but even the actual raw figures are hardly obtainable.

Secondly, our data encompassed only half of Italian population, with the notable exception of Alpine regions: reports on other neurodegenerative diseases extensively suggest that such antiquely quasi-segregated area may largely diverge from national estimates because of the specific genetic composition of original residents (27). Moreover, around half of the total sample included cases from two Italian regions (i.e. Lazio e Lombardy), that have been characterized by large migratory fluxes, from both Southern Italian Regions and Foreign countries. As a consequence, both regions are possibly characterized by a higher number of resi-

dents from areas at low or even very low risk for HD, and that would possibly impair the generalizability of reported estimates (7,9,28).

Despite its potential interest, our study is affected by several limitations.

In first place, we addressed a topic (i.e. prevalence of HD), that rarely achieved a full publication on peer-review journals. Therefore, the majority of the possible evidence included in this report is drawn either from other scientific publications (i.e. abstracts and scientific reports), or from regional record, whose reliability has been often discussed.

Second, we explored a relatively large timeframe, starting with 1982: between the earlier reports of Reverberi et al. (24) and the more recent report of Muroni et al. (21), not only genetic counseling was introduced, but also clinical diagnostic criteria have progressively evolved, being progressively refined. However, the meta-regression model hinted towards a non-significant effect of the study year on the residual heterogeneity Q. Therefore, the differences we identified in the estimates between pre- and post-1993 studies may rather found their roots in other factors, such as the different geographical settings, or the heterogenous sampling strategy.

In summary, notwithstanding potential bias and aforementioned limitations, it should be stressed that our crude prevalence estimates hint towards a HD burden of disease that is nearly the double of that more recently acknowledged by the National Report on Rare Diseases (i.e. 1188 cases for 2014) (12,29). In other words, despite all its limitation, our study suggests that up to half of all Italian cases of HD may have failed to receive an appropriate diagnosis, possibly because of a mixture of low suspicion in subjects from non-symptomatic families (1,2,6,9), and unfamiliarity with rare diseases and their diagnosis in the main Healthcare providers (e.g. Pediatrician for early onset cases, General Practitioners, Internists, but also figures potentially able to identify early signs/symptoms likewise the occupational physician) (30–32), the latter being a shared problem for several less common clinical conditions and infectious diseases (33–36).

In other words, available estimates suggest that Italian Health Service would actually fail in guaranteeing appropriate services for all HD cases. Even though a curative therapy for HD still does not exist, palliative and symptomatic interventions (antidepressants, antipsychotics, anti-choreiform medications) should be ensured to all individuals and their families.

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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Original article

Suicide prevention from a public health perspective. What makes life meaningful? The opinion of some suicidal patients

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Summary. *Background and aim of the work:* Suicide is a worldwide phenomenon, with a relevant number of victims. Moreover, repercussions of suicidality-across its entire spectrum-involve not only the individual but also survivors and communities, in a profound and lasting way. As such, suicidality represents a crucial public mental health concern, in which risk/protection factors' study represent a key issue. However, research primarily focused on suicidality risk factors. This study, moving from Frankl's first observations on "Meaning in Life" (MiL) as protective against suicidality, aimed to identify the main themes that suicidal patients identified as MiL carriers, or potential carriers, in their existences. *Methods:* Qualitative study on 144 patients admitted to the Geneva University Hospital's emergency department for suicidal ideation (SI) and suicide attempt (SA). *Results:* Interpersonal/affective relationships constituted the main theme (71.53%), with emphasis on family (39.80%), children/grandchildren (36.89%). Profession/education, intellectual/non-intellectual pleasures, and transcendental dimension also emerged. *Conclusions:* These aspects could be considered among a public health agenda's points for suicide prevention programs taking into account also protective factors promotion/support, including community's mental health resources. Reconnecting to introduction's historical part, our findings are consistent with Frankl's observations. Even if exposed to "absurd" and reluctant to deliberate on this, he seems approach Camus conceptualization who, confronted to the necessity of predictable and conform to recognizable personal patterns transcending chaos for a sense-giving perspective, invited to imagine that a meaning, even a "non-absolute meaning", may lie in apparent smallest things and that Sisyphus can have "the possibility to revolt by trying to be happy".

Key words: suicide, suicidality, prevention, public health, meaning in life, protective factors

"I consider suicide to be the result of fractures – with oneself, with other people, with nature, with the opportunity to experience feelings of well-being and to appreciate that what which surrounds us".

M. Pompili, 2010, "Exploring the phenomenology of suicide". Suicide and Life-Threatening behavior, 40, 234-244

Introduction

Suicide is a worldwide phenomenon, with an annual number of deaths estimated by the United Nations to be on average higher than those caused by murders and all wars combined (1). For this reason, the World Health Organization (WHO) has dedicated special and continuous attention to it since 1950, i.e. two years after its foundation (2,3). According to the latest WHO report (4), the global annual mortality rate is about 10.7 per 100,000 and suicide attempts (SA) are up to 30 times more common. In addition, the repercussions of suicidality–across its entire spectrum–involve not only the individual but also survivors, including family members, friends and communities as a whole, in a profound and lasting way (2, 3b). Consistent with this, suicidality is a crucial public mental health concern. Within the latter, the study of risk and protection factors is a key issue (5). However, research has focused primarily on suicidality risk factors, paying little attention to protective factors that can mitigate the deleterious effect of stressors (6).

Following Viktor Frankl's chronicles of his observations among Nazi concentration camp prisoners, "Meaning in Life" (MiL) has been considered among the most relevant protective factors against suicide (7,8). In his first book, *"Man's Search For Meaning. From Death Camp to Existentialism"*, Viktor Frankl identified a crucial resource in individuals finally presenting the best chance to survive through the "will to meaning" *(Der Wille zum Sinn)* (7). As opposed to the "existential vacuum", Frankl subsequently proposed that MiL can arise from three factors related to human possibilities. These are creativity, i.e., addressing personal realization, perception and search for beauty with an emphasis on a sense of authenticity towards some encounters or situations, and an individual's effort to self-determine their inner attitude (9).

On a somewhat paradoxical note, debates on MiL appear to have deviated from Frankl's initial interrogation of the attempt of individuals to continue living, despite being overwhelmed by miserable, incomprehensible, yet inescapable conditions of suffering. Therefore, although conceptually challenging, the specific association between MiL and suicidality remains poorly explored (for a systematic review, see 10).

Finally, even fewer studies addressed the content that suicidal individuals attributed to their subjective MiL, i.e., what makes or could have made their existence someway meaningful.

The aim of this qualitative study was to identify and report the main contents that a cohort of suicidal patients, attending a psychiatric emergency department (ED) for suicidal ideation (SI) and suicid attempt (SA), attributed to their subjective MiL.

Material and methods

Sample

The study included patients (n = 144) aged ≥ 18 years admitted to the psychiatric ED of the University Hospital of Geneva because of SI or SA (for recruitment details, see 11-13). This paper presents qualitative data not previously published.

Ethical considerations

This study was approved by the research ethics committee of Geneva (Switzerland) under the registration number 14-168.

Thematic analysis

Participants took part in semi-structured interviews, which were transcribed verbatim. Example questions were *"Outline any areas that currently give or could give meaning to your life"; "If these were to be placed in order of importance, what is the most important? Also, what are the accessory reasons?"*. Thematic analysis was applied according to the framework proposed by Braun and Clarke (14), which aims to identify and report patterns (themes) within data. The analysis steps, which were not intended as a linear process but rather a recursive process reciprocally moving as required throughout the different phases, were: 1) data familiarization (reading and re-reading transcripts and recording initial ideas); 2) generating initial codes by systematically coding emerging features of the data across the entire data set and collating data relevant to each code; 3) searching for themes capturing the essential qualities of the account through collating codes into potential themes and gathering all data relevant to each theme; 4) reviewing themes by checking if they map onto the originally coded extracts; 5) defining and naming

themes by generating clear descriptions and names for each theme; and 6) producing the report including selecting vivid, compelling extract examples (14).

According to this methodology, themes were inductively derived from the data rather than identified in advance or fitted into a pre-existing theme/codes frame or theory. Using a semantic approach, themes were identified within the explicit contents of the data. An analysis of their latent content, beyond those was reported by the participant, aimed to shape data as well as assumptions and conceptualizations, was not performed. Finally, themes were organized and presented using clusters, and super- and subordinate levels (14-16). This methodology is similar to the Interpretative Phenomenological Analysis (IPA) by Smith (17,18). However, the thematic analysis did not originate from a particular epistemological position, element that provides it with greater flexibility, including the possibility of assigning percentage values, while maintaining internal consistency and coherence (19).

Three independent raters examined all transcripts for the identification of codes and themes. Findings were compared and, following discussion with senior researchers, codes and themes were defined by consensus. In consideration of this large sample size, percentage values representing the prevalence of the main themes were also provided.

Results

Sociodemographic and psychiatric characteristics of the participants

The sociodemographic characteristics of the participants are summarized in Table 1. The main reason for inclusion in the study was SI in 64.58% (n = 93) of patients, compared to 35.42% (n = 51) of patients with SA. The majority of patients presented with a psychiatric diagnosis according to the Mini-International Neuropsychiatric Interview (20). The most prevalent diagnoses were major depressive episodes (75%, n = 108) and alcohol dependence (74,31%, n = 107).

Theme: Interpersonal and affective relationships

Interpersonal and affective relationships were the main themes that give or could give MiL to suicidal patients (71.53%, *n* = 103). Particular emphasis was placed on family (39.80%, *n* = 41) and children and grandchildren (36.89%, *n* = 38), both current or expected: *"My family, the most important thing"* [ID 157]; *"Making my family happy"* [ID 32]; *"The idea of having a family one day* " [ID 45]; *"My better future: a family and some children"* [ID 234]; *"My future life = child"* [ID 25]; *"My pregnancy"* [ID 22]"; *"Loving my children greatly"* [ID 139]; *"What remains to be taught to my grandson"* [ID 57]; *"My children and grandchildren: They are my whole life; it is for them that I am still there"* [ID 21]; *"My children. That's all"* [ID 70]; and *"My children give meaning to my life"* [ID 215].

Concerning accessory thematic areas that give or could give a meaning to suicidal patients, interpersonal and affective relationships still represented the majority of answers (45.43%, *n* = 159). However, family (17.61%, *n* = 28) and the presence of children and grandchildren (6.92%, *n* = 11) were less prominent compared to other relationships, such as a partner, friends, "others" considered from an altruistic perspective, and animals. These latter were expressed generally or addressed to a specific relationship, as follows: *"The sentimental life"* [ID 1]; *"Being in a relationship with a partner"* [ID 69]; *"Sharing my life with friends"* [ID 41]; *"[...] reconnecting with others"* [ID 146]; *"[...] using my abilities to help others"* [ID 36]; *"The desire to help people in need, orphans, the poor"* [ID 139]; *"Relationship with animals"* [ID 54]*; "He, only him*" [ID 169]; *"An unfor-*

Table 1. Sociodemographic characteristics of the participants (*n* = 144).

		n	%
Sex	Female	90	37.5
	Male	54	62.5
Age group	< 20 years	14	9.72
	20-29 years	44	30.55
	30-39 years	30	20.83
	40-49 years	26	18.05
	50-60 years	22	15.28
	> 60 years	8	5.57
Citizenship	Swiss	85	59.03
	Non-Swiss	59	40.97
Marital Status	In a relationship	57	39.58
	Single	87	60.42
Children	Yes	61	42.36
	No	83	57.64
Professional status	Employed/student	88	61.12
	No activity	56	38.88

tunately impossible love for a partner" [ID 130]; *"The friendship of a very old friend"* [ID 130]*; "Helping my wife to recover"* [ID 5]; and *"My mare"* [ID 206].

Theme: Profession and education

The second main thematic area that gives or could give MiL to suicidal patients was a profession and education (9.03%, *n* = 13). Concerning the accessories thematic areas, the second most important area was profession and education represented (18.29%, *n* = 64).

Answers concerned several facets of the profession and education, including having a profit/providing solvability, dignity/consistent employment, self-realization, and social image. The main area of MiL indicated by one patient [ID 68] was: *"My work in the office"* and as an accessory: *"Closing sales, keeping customers, satisfying the boss, getting the desired salary, paying everything I need, building wealth"* [ID 68]. Patients often privileged some of these facets: *"My routine and my dignity: working as I have always done"*[ID 139]; "*Finding professional stability"* [ID 85]; *"My studies in art"* [ID 83]; *"Doing a work that brings elements of knowledge"*[ID 184]; *"My professional ambitions"* [ID 160]; and *"My academic career"* [ID 133].

Theme: Intellectual and non-intellectual pleasures

The third main thematic area associated with MiL was related to intellectual pleasures, i.e., the search for harmony and beauty, expressions of creativity and art forms, including music, painting, literature, theatre and dance, cinematography, and science-related activities (9.02%, *n* = 13). Non-intellectual pleasures, including sports, recreational activities, convivial occasions and travels, were present in a limited number of cases (4.17%, *n* = 6).

As an accessory theme, intellectual pleasures were always represented (10.57%, *n* = 37); however, to a lesser degree than for non-intellectual pleasures (13.14%, *n* = 46).

Some examples of intellectual pleasures giving MiL were exemplified as: *"Contemplation of the beauty of nature"* [ID 155]; *"The possibility of imagining"* [ID 161]; *"Discussion, exchange of ideas"* [ID 150]; *"Thinking, literature, philosophy... thinking intellectual joys with my loved ones"* [ID 130]; *"Music. I play the piano"* [ID 95]. Some non-intellectual pleasures giving MiL were represented by: *"[...] the sewing I do"* [ID 17]; *"A coffee and a cigarette in a bistro"* [ID 17]; *"Weekend evenings"* [ID 213]; and *"A beautiful evening to walk on a beach in Corse"* [ID 238].

Theme: The transcendental dimension

The transcendental dimension (spirituality and religion) was found as the main theme in 2.08% of patients (*n* = 3) and as an accessory theme in 7% of answers (*n* = 7). Answers included: *"The complexity of the world we live in"* [ID 161]; *"The creation"* [ID 65]; *"My faith"* [ID 72]; *"My faith in God"* [ID 57]; and *"God knows why he sent me to Earth and I am very happy to be the servant of the living God [...]"* [ID 17].

Partial or no themes for MiL

Only a partial or uncertain MiL was described in 1.39% patients (*n* = 2). Responses included: *"My daughter and my husband, but it's not enough. I need something for myself."* [ID 37]; and *"I can't find anything... except work?"* [ID 80]. No themes related to MiL were identified in 3.47% of patients (*n* = 5), with responses such as *"Nothing"* [ID 74]; and *"Nothing at this time"* [ID 99].

Discussion

In agreement with the limited research in this field (21), our results confirm that family, social support, and interpersonal connectedness are strong parameters favouring MiL in suicidal patients. Within the aspect family, particular emphasis was placed on the protective role of children and grandchildren. Beyond the post-partum period, pregnancy and parenthood have been shown to reduce the risk of suicide, particularly in mothers (22). After controlling for several potential confounding factors, a recent meta-analysis of 36 studies of more than 100 000 000 individuals, showed that the suicide risk was almost two times greater in non-married than married individuals (odds ratio (OR) 1.9; 95% CI 1.8-2.1) (23). Compared to married individuals, sub-analyses revealed that the elevated risk was roughly comparable for those who were single (OR 2), divorced (OR 3), or widowed (OR 2) (23). The authors hypothesized that although marriage increases MiL, it also facilitates social integration

within a community (23). The impact of family and progeny support was emphasized particularly in older individuals, who face the highest suicide risk when living alone without filial support, and are widowed, especially among men (24).

Interestingly, our results on social support are substantiated by a study of nationally representative samples, in which social support was associated with a decreased risk of suicide in the United States (OR 0.7) and in England (OR 0.9) (25). Although variously defined, interpersonal connectedness generally refers to a sense of integration into a network that leads to a sense of belonging: the perception of being part of something meaningful outside ourselves, and that people care about our situation and have positive feelings about us (26). The role of the lack of connectedness as a relevant risk factor for SB has been widely described in recent years throughout the entire life span (26). Intriguing correlations have been made between two constructs of the "Interpersonal Psychological Theory", such as "perceived belongingness" and "thwarted burdensomeness", and MiL in the older suicidal population. In the paper "Does perceived burdensomeness erode meaning in life among older adults?" (27), it was elucidated that "perceived belongingness" could contribute to suicide morbidity by undermining MiL (27), whereas "thwarted burdensomeness" was associated with increased SA and more lethal methods, resulting in a poorer prognosis (28). As poignantly synthesized in two works titled and sub-titled "Alone without purpose: Life loses meaning following social exclusion" (29) and "Being alone without MiL and struggling to achieve reconciliation" (30), these feelings in the older population may be associated with a lack of attribution of MiL for the whole past existence and an effort to find it tensioned to rapprochement with others, including with one's family (27,29,30).

Unemployment and economic strain may lead to a higher risk of suicide (31). The relationship between economic conditions and suicide is complex and has been associated with several factors, illustrating the interplay of societal effects, including loss of social status and connectedness, lower per capita and dedicated to family income, and degradation of the quality and quantity of health care that a community can offer its citizens, with the individual's personal risk profile and vulnerability (32). We can postulate that in a culture with Calvinist roots such as Switzerland, the reduction of MiL toward the personal inadequacy of feeling associated with a lack of a work or study activity, under all aspects listed by the patients including having a profit/providing solvability, dignity/habit of having a job, self-realization, and social image, is particularly emphasized.

The protective effect of religiosity, spirituality, and suicidality is controversial. Since initial studies on the benefits of religiosity and participation in religious activities on suicidality(33), research moved to a more specific analysis of the relationships between dimensions of religion/spirituality (i.e., affiliation, participation, and doctrine), SI and type of SB (including SA, suicide completion), and the concerned population (with or without mental illness). Particular emphasis was placed on related social support influence. Among both the general population and individuals with a mental illness, religious attendance at least once annually was associated with decreased SA and this relationship persisted even after the removal of the influence of social support (34). In contrast, individuals belonging to both populations that considered themselves spiritual were also less likely to attempt suicide; however, this relationship was not maintained after adjusting for social support (34). A recent systematic review on religion and suicidality found that religious affiliation does not necessarily protect against SI but against SA (35). Whether a religious affiliation protects against SA may depend on the culture-specific implications of affiliating with a particular religion, since minority religious groups can feel socially isolated. After adjusting for social support measures, religious service attendance is not especially protective against SI but against SA, potentially protecting against suicide completion. In our sample, this transcendental dimension, including religion and spirituality, accounts for a minority of the patients. However, we did not explore their different facets as well as the impact of social support.

All of these aspects that suicidal patients have identified as carriers of MiL in their existences and, consequently, possible elements that favor a distancing from suicidality, could be considered among the points of a mental public health agenda. The promotion and support of protective factors, rather than the only in-

tervention addressed to risk factors, could be part of those suicide prevention programs that–as Potter and colleagues already pointed out in 1995–"should include more than one strategy and, where appropriate, should be strongly linked with the community's mental health resources" (36). This seems especially valuable to deal with aspects of suicidality that are unrelated, or not necessary related, to the effects of psychiatric disorders, which nevertheless play an extremely relevant role in this context. But, at least for the time being, it seems that outside a pathologic perspective there are fewer means to try to understand and manage suicidality.

In conclusion, reconnecting to the historical part of the introduction, the findings in our sample appear to be consistent with Viktor Frankl's conceptualization of MiL and the three previously outlined aspects proposed as protective factors against suicidality (9). Our findings confirm authentic relationships, creativity and every day human activities, intellectual or non-intellectual as relevant resources. Even if personally exposed to the "absurd", Viktor Frankl was reluctant to deliberate on this aspect. He appeared to preferably address even the humblest aspect or activity that could permit face to situations where MiL is disrupted, to construct or reconstruct a framework in an attempt to continue to live. Paradoxically, by adopting this attitude, he closely approached an eminent theorist of the "absurd", Albert Camus. The latter confronted to the necessity of predictable and conform to recognizable personal patterns transcending chaos for a sense-giving perspective, invited to imagine that a meaning, even a "non-absolute meaning", may lie in the apparent smallest of things and that Sisyphus can have "the possibility to revolt by trying to be happy" (37).

Limitations

This work has several limitations. First, the cross-sectional design (without a longitudinal perspective) precludes the evaluation of prediction. In this sense, the discussion-addressing the predictive factors of SB protection-is merely speculative. Second, we lacked a control group, fact that limited the validity of our results. Third, associations with the eventual presence and type of a psychiatric diagnosis were not investigated. Thus, a more informative picture of subjective MiL in suicidal patients including possible inferred observations from this latter aspect could not been performed.

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Original article

Nuovi indirizzi nelle politiche vaccinali: il ruolo della medicina di famiglia

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New challenges in vaccination policies: the role of General Practitioners. Summary: The phenomenon of "Vaccine Hesintacy" and the consequent decrease in vaccination coverage with the re-ignition of some epidemic outbreaks has led Italian national and regional authorities to set a new vaccination plan (PNPV 2017-19) and even coercive measures such as the the Law n.119/2017. In addition, there have been initiatives by scientific societies also in order to increase involvement of professionals in information and education campaigns. Among the professional figures involved, the general practitioners represents the starting point from which to regain the citizen's trust. This article assesses their important role in the implementation of vaccination policies in Italy by identifying the essential points of the campaigns carried out on their patients.

Key words: National vaccination plan, vaccination coverage, Law 119/2017, family doctors

Riassunto: Il fenomeno della "Vaccine Hesintacy" ed i conseguenti cali delle coperture vaccinali, con riaccensione di alcuni focolai epidemici, ha indotto le autorità nazionali e regionali a provvedimenti programmatici e coercitivi: il PNPV 2017-19 e la Legge 119/2017. In aggiunta sono state promosse iniziative delle società scientifiche al fine di coinvolgere in modo maggiore i professionisti in campagne informative ed educative. Tra le figure professionali interessate il medico di medicina generale rappresenta il punto di partenza dal quale riconquistare la fiducia del cittadino. La presente nota ne valuta l'importante ruolo nell'implementazione delle politiche vaccinali in Italia, individuando i punti essenziali delle campagne svolte sui propri assistiti.

Key words: piano nazionale vaccini, coperture vaccinali. Legge 119/2017. medicina generale

Introduzione

In Italia, negli ultimi anni, si è verificato un consistente calo delle coperture vaccinali e i dati dell'anno 2016 mostravano come, per nessuna vaccinazione, si raggiungeva su base nazionale i target previsti dai piani vaccinali. Il fenomeno, ha coinvolto in modo particolare le vaccinazioni dell'infanzia sia obbligatorie che raccomandate (1, 2).

Questo trend negativo ha indebolito l'*Herd Immunity,* consentendo una maggiore circolazione di patogeni come la nota recrudescenza del morbillo del 2017 (3). Le principali cause della *Vaccine Hesitancy* sono rappresentate da:

- Malattia *virtualmente* sconosciuta alla popolazione (4);
- Mancanza di informazioni corrette con la complicità della diffusione dei *"new-media"* (4, 5);
- Cambiamento del rapporto medico-paziente e/o scarsa fiducia nelle istituzioni sanitarie (4).

Le nuove politiche vaccinali italiane

Il 2014 è stato l'anno più critico per l'Italia; infatti si sono verificati il c.d. *"Caso Fluad"* (6) e la pubblicazione di diverse sentenze che associavano ai vaccini effetti non confermati da studi scientifici. Nel 2007 la Regione del Veneto aveva tentato di individuare nella sospensione della obbligatorietà vaccinale un metodo per contenere la *Vaccine Hesitancy* e la diffusione di movimenti anti-vaccinazioni, tuttavia la manovra non ha ottenuto l'effetto sperato (7). Le autorità sanitarie nazionali hanno così iniziato, dal secondo semestre del 2014, ad intraprendere iniziative politiche, scientifiche e propagandistiche volte al rilancio delle vaccinazioni. L'elemento essenziale è stata la predisposizione del nuovo e innovativo Piano Nazionale Prevenzione Vaccinale (PNPV 2017-2019) che, oltre a una estesa offerta attiva e gratuita di vaccini efficaci, ha anche previsto azioni di supporto e di contrasto all'esitazione vaccinale (8).

Sulla base del provvedimento californiano, Senate Bill 277 (2015) (9) che ha riportato nell'arco di due anni le coperture MPR oltre il 95%, in Italia nel luglio 2017, è stata emanata la legge n. 119 che ha previsto l'estensione dell'obbligo da 4 a 10 vaccini con esclusione dagli asili dei bambini non vaccinati e multe per i non vaccinanti (10).

La Vaccine Recovery

I primi dati sulle coperture vaccinali, dopo l'entrata in vigore della legge 119/2017, hanno mostrato un incremento dell'1% per la vaccinazione esavalente dell'infanzia e del 4% per la vaccinazione MPR (11-13). Anche i dati sulla vaccinazione antinfluenzale negli anziani hanno mostrato incrementi lievi, ma costanti a partire dalla stagione invernale 2015-16, che fa ritenere come sia in corso una fase di migliorata confidenza di tutta la popolazione nei confronti delle pratiche vaccinali (14-16). È difficile poter confermare che si tratti di una fase duratura di *"Vaccine Recovery"*, ma certamente il tema delle vaccinazioni viene oggi sviscerato dalla stampa e dai media con una maggiore valenza scientifica (17-19). In questo contesto ogni iniziativa di *"spinta gentile"* o *nudging*, unica possibile oggi per i vaccini di adulti e anziani, rappresenta il terreno di confronto e sfida dei professionisti in campo tra cui il MMG riveste un ruolo chiave (20-22).

Il ruolo del MMG e il management vaccinale

Per decenni il medico di medicina generale è stato considerato solo come mero esecutore delle vaccinazioni dell'adulto, come nel caso delle campagne antinfluenzali, risultando in tal modo escluso in molte regioni dalla definizione delle politiche vaccinali. Tuttavia, a dispetto di questa visione, il MMG ha potenzialità più ampie per una serie di ragioni:

- Rapporto fiduciario, basato sulla libera scelta, con il proprio assistito;
- Formazione scientifica e culturale che gli conferisce anche competenze manageriali;
- Posizione all'interno del tessuto del SSN come primo approccio e garante dei bisogni di cure primarie (23).

La conoscenza del paziente, della sua storia clinica, dello stato vaccinale, della stratificazione del rischio, unitamente al suo contesto sociale ed assistenziale (l'inserimento - o meno - in un nucleo familiare o in una struttura residenziale, l'eventuale stato di abbandono), consolidano la capacità del MMG di individuare, per ciascun paziente, un piano di prevenzione personalizzato che porti alla proposta delle vaccinazioni più appropriate.

La legge 119/2017 mette in risalto il ruolo del MMG nella prevenzione vaccinale, prevedendo in modo diretto il coinvolgimento dei medici di famiglia e pediatri di libera scelta (PLS), con funzioni certificative (10). Tuttavia già precedenti atti normativi citavano l'importanza del MMG nell'attività di prevenzione vaccinale. Testimonianza di ciò è l'art.45 dell'A.C.N. dove la pratica vaccinale nei confronti dei propri assistiti rientra, non solo nei doveri generici, ma anche degli obblighi del MMG. (24)

Inoltre bisogna ricordare che il MMG nello svolgere la sua attività a livello territoriale collabora con il Dipartimento di Prevenzione, come previsto fin dalla istituzione del SSN con la L. 833/78 (25) e il D.lgs 502/92 s.m.i. (26).

Organizzazione di una campagna vaccinale: strumenti e modalità operative

Compito del medico non è convincere ma accompagnare nel cammino il paziente verso scelte efficaci e consapevoli; si tratta quindi di aiutare la persona che ha incertezze o difficoltà ad accettare la vaccinazione, a superare dubbi e paure, determinando un aumento del livello di conoscenza e consapevolezza, per prendere decisioni a favore della propria salute. Mai come in quest'ambito è da considerarsi superato l'approccio paternalistico–coattivo a favore di un approccio proattivo e consapevole.
Un'ipotetica campagna vaccinale dovrebbe prevedere pertanto i seguenti momenti (27).

Selezione dei pazienti target: numeri e nominativi

Il primo impegno consiste nell'identificare, nell'archivio dei propri pazienti, la coorte candidabile alla vaccinazione, sulla base dei criteri fissati dal programma vaccinale della regione o della ASL di appartenenza. In questo si ribadisce il valore aggiunto della medicina generale: la conoscenza della persona e del territorio.

Nel selezionare i pazienti idonei, il medico attinge ai dati anamnestici raccolti grazie al proprio software gestionale, che consente di creare schede sanitarie individuali, quindi vere e proprie cartelle cliniche elettroniche complete di dati anagrafici, socio-assistenziali (esenzioni e ricoveri ecc.) e soprattutto informazioni relative a condizioni di rischio e malattie croniche. Informazioni particolarmente importanti, oltre ad età e patologie, sono rappresentate dalle eventuali controindicazioni al vaccino.

Una volta raccolti i nominativi e quindi quantificato il numero dei soggetti, il MMG provvede a richiedere all'azienda sanitaria di competenza l'approvvigionamento delle dosi di vaccino necessarie. In alcune aziende, relativamente a progetti specifici, vengono previsti elenchi stilati dalle stesse ASL o individuate caratteristiche specifiche per la creazione di elenchi (coorti per età, patologie, pazienti istituzionalizzati etc.) che raccolgono le indicazioni di eleggibilità del paziente (27- 29).

Counseling vaccinale

Stabiliti gli idonei alla vaccinazione, il passo successivo è rappresentato dall'informazione del paziente, per motivarlo a superare la sempre più frequente esitazione vaccinale. Tutto questo richiede ai medici conoscenze aggiornate, capacità di *counseling* e individuazione dei tempi. In tal senso, l'impegno educativo per il medico è aumentato rispetto al passato, poiché deve confrontarsi con una moltitudine di notizie divulgate in modo massiccio, offerte da fonti spesso condizionate da interessi che esulano dalla salvaguardia della salute, e quindi non equilibrate, fuorvianti e palesemente discutibili dal punto di vista scientifico, tra cui annoveriamo le *fake news*.

Decisivo è il ruolo che i medici di famiglia possono svolgere attraverso informazioni approfondite, corrette, rese in un linguaggio semplice che aiuti il paziente (o il *care-giver*, come spesso accade nel caso degli anziani) a valutare le informazioni ricevute e compiere le proprie scelte.

Assume particolare rilievo informare gli assistiti dei rischi connessi alle malattie infettive e delle complicanze invalidanti, potenzialmente legate all'infezione, oltre che delle caratteristiche del vaccino, dei possibili rischi e della modalità di somministrazione.

Esitare nella descrizione dei potenziali effetti collaterali o avversi, o essere superficiali nell'esposizione, può generare diffidenza. Pertanto l'adozione di una corretta strategia di comunicazione permette di vincere resistenze date da barriere socio-culturali e convincimenti personali (30).

Un valido supporto a questo compito, può essere offerto dall'affissione di poster educazionali e dalla divulgazione di materiale informativo nelle sale di aspetto. Nel caso in cui si determini la scelta di rinviare temporaneamente, o il paziente rifiuti la vaccinazione, occorre informare sulle possibili precauzioni da mettere in atto per prevenire la malattia, monitorare le condizioni cliniche, valutando nel tempo la possibilità di riproporre l'intervento vaccinale. Obiettivi di un *counseling* efficace sono quindi:

- Impostare un colloquio nel quale sia previsto un adeguato tempo di ascolto, per far emergere i dubbi e creare reciproca fiducia;
- Acquisire la consapevolezza che la scelta della vaccinazione è una decisione dell'assistito da condividere con il medico di famiglia (27-29).

Approvvigionamenti e conservazione dei vaccini

Questa fase appare rilevante al fine di non vanificare l'offerta per la mancanza di scorte o una loro conservazione non adeguata, compromettendone l'efficacia.

Pertanto da un lato deve essere attivata una efficace connessione con le farmacie delle ASL e dall'altro deve essere prevista la presenza negli ambulatori di frigoriferi efficienti, che prevedano eventualmente sistemi di allarme o di emergenza in caso di interruzione delle forniture elettriche.

Seduta Vaccinale

Si tratta del percorso temporale e operativo che inizia con l'apertura dell'ambulatorio dedicato per la campagna di vaccinazione e termina con la chiusura dello stesso. Nell'ambito organizzativo il MMG può, soprattutto se opera in uno studio singolo, somministrare le vaccinazioni negli stessi orari di apertura convenzionali dell'ambulatorio, per offrirli ai propri assistiti in occasione della visita. Ciò facilita l'adesione soprattutto dei soggetti in età lavorativa, che possono concordare una vaccinazione su prenotazione, evitando quindi l'astensione dal lavoro. In medicina generale si può prevedere che la seduta vaccinale sia condotta e rivolta:

- Agli assistiti di un medico che lavora in singolo;
- A tutti gli assistiti afferenti a una medicina di gruppo indipendentemente dalla presenza in studio del curante, potendo egli esser vicariato dagli medici componenti il gruppo;
- Solo agli assistiti di ogni singolo medico della medicina di gruppo (o eventualmente delle case della salute), che si fa carico della prevenzione dei propri pazienti.

La seduta, si può condurre in giorni e orari dedicati oppure negli orari abituali di apertura dello studio.

Tenendo pur conto degli aspetti e abitudini individuali di ogni professionista, che opera all'interno della medicina di gruppo e delle necessità assistenziali dei pazienti afferenti ad ogni professionista, l'organizzazione della seduta vaccinale più consona e funzionale al suo scopo, si ritiene sia quella di prevedere spazi e tempi dedicati e che comprenda l'esecuzione della vaccinazione di tutti gli assistiti della medicina di gruppo, con i medici afferenti ad essa che, a rotazione, si alternano nella stessa seduta o in altre. Infatti, organizzare giorni e un ampio arco temporale dedicato alla seduta vaccinale, permette di ottimizzare i tempi e raggiungere la maggior parte degli assistiti eleggibili.

La seduta vaccinale prevede i seguenti momenti:

- Preparazione della seduta e accoglienza del paziente con compilazione e/o aggiornamento della scheda anamnestica e verifica dell'idoneità alla vaccinazione;
- Informazioni all'assistito, chiarimenti a domande, dubbi o necessità particolari;
- Raccolta del consenso informato;
- Esecuzione della vaccinazione seguito da periodo di osservazione e segnalazione di reazioni avverse.

Un aspetto importante in medicina generale riguarda la vaccinazione in soggetti "difficili da raggiungere" per situazioni sociali e/o culturali, i soggetti allettati, con limitazione della deambulazione e privi di rete familiare ovvero soggetti che solitamente sfuggono all'igiene pubblica. In molti casi infatti, la vaccinazione è effettuata a domicilio, all'incirca nel 10% dei soggetti da vaccinare (percentuale che cresce progressivamente nel tempo con l'invecchiamento degli utenti) e prevede l'estensione dell'offerta vaccinale a soggetti terzi come genitori, familiari o *care-givers* (27-29).

Supporti informatici e anagrafi vaccinali

La somministrazione di un vaccino è un'informazione sanitaria importante che deve essere rintracciabile da qualsiasi struttura in qualsiasi istante. Ad oggi in Italia non esiste un'anagrafe vaccinale nazionale e ciò determina la perdita dei dati, sia nell'arco temporale della vita del paziente, sia nel caso di spostamenti abitativi. Il sistematico utilizzo da parte del MMG di cartelle cliniche elettroniche rappresenta un innegabile vantaggio nella conservazione dei dati e nella tracciabilità delle vaccinazioni somministrate. I sistemi informatizzati utilizzati oggi dal MMG, necessari all'archiviazione dei dati e alla realizzazione dell'integrazione interna al sistema della medicina generale, presentano caratteristiche che consentono di:

- Semplificare le procedure richieste dalle norme contrattuali e legislative permettendo di operare, anche in mobilità, attraverso un *cloud* utile nelle attività domiciliari;
- Offrire al medico la libertà di scegliere gli strumenti software;

- Presentare capacità di analisi e controllo dei dati in uscita e in entrata, garantendo la protezione dei della Privacy del paziente e del medico (27).

Recentemente l'ECDC ha pubblicato linee guida finalizzate all'implementazione degli *Informatic Immunization Systems* (IISs). Tali *databases* erano già stati incentivati nel 2011 dal Consiglio dell'UE e sono menzionati anche nel piano vaccinale europeo 2015-2020 (31).

Possibili criticità

Dalla descrizione dell'attività preventiva vaccinale del medico di famiglia, emerge una notevole flessibilità organizzativa e strategica nel raggiungimento degli obiettivi di copertura; tuttavia esiste la possibilità di ampi margini di miglioramento, a partire del disomogeneo e spesso limitato coinvolgimento del MMG nelle campagne vaccinali da parte delle aziende sanitarie e dei loro vertici (32, 33): infatti in alcuni contesti, il medico è solo un facilitatore o seleziona la quantità di vaccini e non la tipologia. Inoltre, la mancanza di un feedback degli obiettivi raggiunti dalla campagna potrebbe non incoraggiare l'attività preventiva svolta dal MMG (33).

Conclusioni

L'approvazione del PNPV 2017-19, che ha esteso le vaccinazioni anche nell'adulto, nell'anziano e nei soggetti a rischio con ambiziosi obiettivi vaccinali in un contesto di *vaccine hesitancy*, ha reso rilevante l'apporto della medicina di famiglia per le nuove sfide. Tale contributo che, nel recente passato, ha permesso il raggiungimento di coperture rilevanti per la vaccinazione antinfluenzale negli over-65enni, potrebbe oggi essere esteso ad esempio agli altri due vaccini tipici dell'età avanzata e delle categorie a rischio, ossia l'antipneumococcica e l'anti herpes zoster. In quest'ottica appare pertanto fondamentale che i medici di famiglia e le loro associazioni si attivino, non solo per un opportuno aggiornamento professionale sulle potenzialità delle nuove strategie immunitarie, ma anche per l'organizzazione di campagne vaccinali. Quest'ultima è finalizzata ad ottimizzare l'uso delle tecnologie informatiche in dotazione, a facilitare i dialoghi con i pazienti sugli aspetti meno conosciuti o controversi, a favorire i lavori d'equipe in stretta connessione con i servizi delle ASL e a snellire i tempi e le modalità di somministrazione dei vaccini. Un discorso a parte, meriterebbe la problematica degli incentivi per il raggiungimento dei targets di copertura vaccinale, previsti dai piani e dagli obiettivi specifici stabiliti, sempre più frequentemente, dalle Regioni. A tale riguardo, sarebbe forse auspicabile che gli incentivi economici passino, dalle quote per vaccinazione somministrata, a premialità sulla base delle coperture ottimali raggiunte tra i propri assistiti.

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Coperture vaccinali anti-influenzali in Regione Lombardia: un'analisi ventennale di trend (1999-2019)

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Influenza vaccination coverage in Lombardy Region: a twenty-year trend analysis (1999-2019). Abstract: Recent events and phenomena, such as A(H1N1) pandemic in 2009, "Fluad case" (2014-2015) and the spread of vaccine hesitancy, affected influenza vaccination coverage rates in Italy. In this study, the annual coverage rates in Lombardy Region and in Italy (from 1999-2000 season) have been critically described and compared. Regarding both the general population and the elderly over-65s, Lombardy's coverages always remained consistently below the national average. However, declines and peaks occurred simultaneously. The current slight recovery, both at national and regional level, is not sufficient. Coverages are still widely below the recommended thresholds.

Key words: vaccines, immunization, vaccination coverage rate, influenza, Lombardy, Italy

Riassunto. Eventi e fenomeni degli ultimi anni, quali la pandemia A(H1N1) del 2009, il "caso Fluad" (2014-2015) e la diffusione dell'esitazione vaccinale, hanno influito sui livelli di coperture per vaccinazione antinfluenzale in Italia. In questo studio, sono stati descritti criticamente e raffrontati i livelli annui e il trend di copertura media per vaccinazione antinfluenzale in Regione Lombardia a confronto con il dato nazionale a partire dalla stagione 1999-2000. Sia considerando la popolazione generale, sia gli over 65, i dati della Lombardia si sono sempre mantenuti stabilmente inferiori alla media nazionale. Cali e picchi si sono comunque verificati in contemporanea con quelli nazionali. L'attuale lieve recupero è tuttavia insufficiente. Le coperture sono ancora ampiamente al di sotto delle soglie raccomandate.

Parole chiave: vaccini, immunizzazione, copertura vaccinale, influenza, Lombardia, Italia

Introduzione

L'influenza è un rilevante problema di Sanità pubblica per l'impatto epidemiologico, clinico ed economico (1). Nella maggior parte dei casi, l'infezione è autolimitante. Tuttavia, in soggetti a rischio, possono verificarsi complicanze gravi o mortali (2).

La vaccinazione, efficace intervento di prevenzione primaria (3-5), rappresenta la miglior strategia per combattere la malattia. Essa è fortemente raccomandata a: anziani di età ≥ 65 anni, bambini ≥ 6 mesi e adulti ≤ 65 anni a rischio, gravide, pazienti cronici o immunodepressi, personale sanitario, familiari e contatti di soggetti ad alto rischio, soggetti addetti a servizi pubblici, lavoratori a contatto con animali potenzialmente fonti di infezione, donatori di sangue (2).

Per ridurre morbosità, complicanze e mortalità per influenza, il Piano Nazionale Prevenzione Vaccinale (PNPV) 2017-2019, sulla scia delle raccomandazioni dell'Organizzazione Mondiale della Sanità

(OMS), ha fissato obiettivi di copertura del 75% (minimo perseguibile) e del 95% (ottimale)(6).

Negli ultimi anni si è diffuso in Italia il fenomeno dell'esitazione vaccinale, definito come *"ritardo nell'accettazione o rifiuto della vaccinazione, nonostante la disponibilità di servizi vaccinali"* (7). In concomitanza del clamore mediatico, si è verificato un calo delle coperture, con abbassamento della soglia critica di sicurezza e conseguente esposizione della popolazione a maggior rischio infettivo (8, 9).

In questo studio si analizzano i dati nazionali italiani e di Regione Lombardia delle coperture per vaccinazione antinfluenzale negli ultimi 20 anni, esplorando possibili associazioni tra cali ed eventi e fenomeni nazionali.

Metodi

Dall'archivio del Ministero della Salute Italiano (elaborazione dall'Istituto Superiore della Sanità, ISS, e piattaforma EpiCentro) (10) sono state estrapolate le coperture medie per vaccinazione antinfluenzale per 100 abitanti in Italia e Regione Lombardia dalla stagione 1999-2000 al 2018-2019 (Tabella 1).

Sono stati considerati i dati relativi alla popolazione generale e di età ≥ 65 anni.

Sono state calcolate le "*differenze percentuali in calo*" dal picco di maggiore copertura alla flessione del 2014-2015 e le "*differenze percentuali in recupero*" dalla stagione 2014-2015 all'ultima stagione 2018-2019 (Tabella 2).

Tabella 1. Coperture vaccinali medie (vaccinazione antinfluenzale) in Italia ed in Lombardia nella popolazione generale e negli over 65 (stagioni dal 1999-2000 al 2018-2019), aggiornamento al 15 luglio 2019. Ministero della Salute, Istituto Superiore della Sanità, EpiCentro (10).

Stagioni	Popolazione generale (%)		Popolazione > 65 anni (%)	
	Lombardia	Italia	Lombardia	Italia
1999-2000	9,1	10,5	39,6	40,7
2000-2001	10,4	12,6	46,7	50,7
2001-2002	12,2	14,1	53,8	55,2
2002-2003	13,5	15,6	58,7	60,3
2003-2004	14,7	17,5	60,9	63,4
2004-2005	15,7	17,7	65,3	66,6
2005-2006	16,2	19,4	64,0	68,3
2006-2007	15,3	18,6	63,1	66,6
2007-2008	14,7	18,4	58,6	64,9
2008-2009	15,5	19,1	61,7	66,3
2009-2010	13,2	19,6	63,1	65,6
2010-2011	12,6	17,9	54,2	62,4
2011-2012	13,4	17,8	57,9	62,7
2012-2013	11,4	14,9	48,2	54,2
2013-2014	11,7	15,6	48,6	55,4
2014-2015	11,4	13,6	46,3	48,6
2015-2016	11,6	13,9	47,7	49,9
2016-2017	12,1	15,1	47,5	52,0
2017-2018	12,1	15,3	47,7	52,7
2018-2019	12,9	15,8	48,2	53,1

Legenda: celle verdi = picco massimo di coperture vaccinali in Lombardia e Italia; celle arancioni = copertura vaccinale nella stagione 2014-2015.

Tabella 2. Differenze % delle coperture vaccinali (vaccinazione antinfluenzale) in Italia ed in Lombardia, nella popolazione generale e negli over 65, dalla stagione 2014-2015 (caso Fluad) alle stagioni con massima copertura e all'ultima stagione 2018-2019. Aggiornamento al 15 luglio 2019. Ministero della Salute, Istituto Superiore della Sanità, EpiCentro (10).

		CV max (%) (stagione)	2014-2015 (%)	2018-2019 (%)	Differenza % in calo	Differenza % in recupero
Popolazione generale	L	16,2 (2005-2006)	11,4	12,9	- 4,8 %	+ 1,5 %
	I	19,6 (2009-2010)	13,6	15,8	- 6,0 %	+ 2,2 %
Popolazione over 65	L	65,3 (2004-2005)	46,3	48,2	- 19,0 %	+ 1,9 %
	I	68,3 (2005-2006)	48,6	53,1	- 19,7 %	+ 4,5 %

Legenda: L = Lombardia; I = Italia; CV max = copertura vaccinale massima; Differenza % in calo = differenza fra le coperture vaccinali nella stagione 2014-2015 e quelle della stagione con massima copertura; Differenza % in recupero = differenza fra le coperture vaccinali nella stagione 2018-2019 e quelle nella stagione 2014-2015.

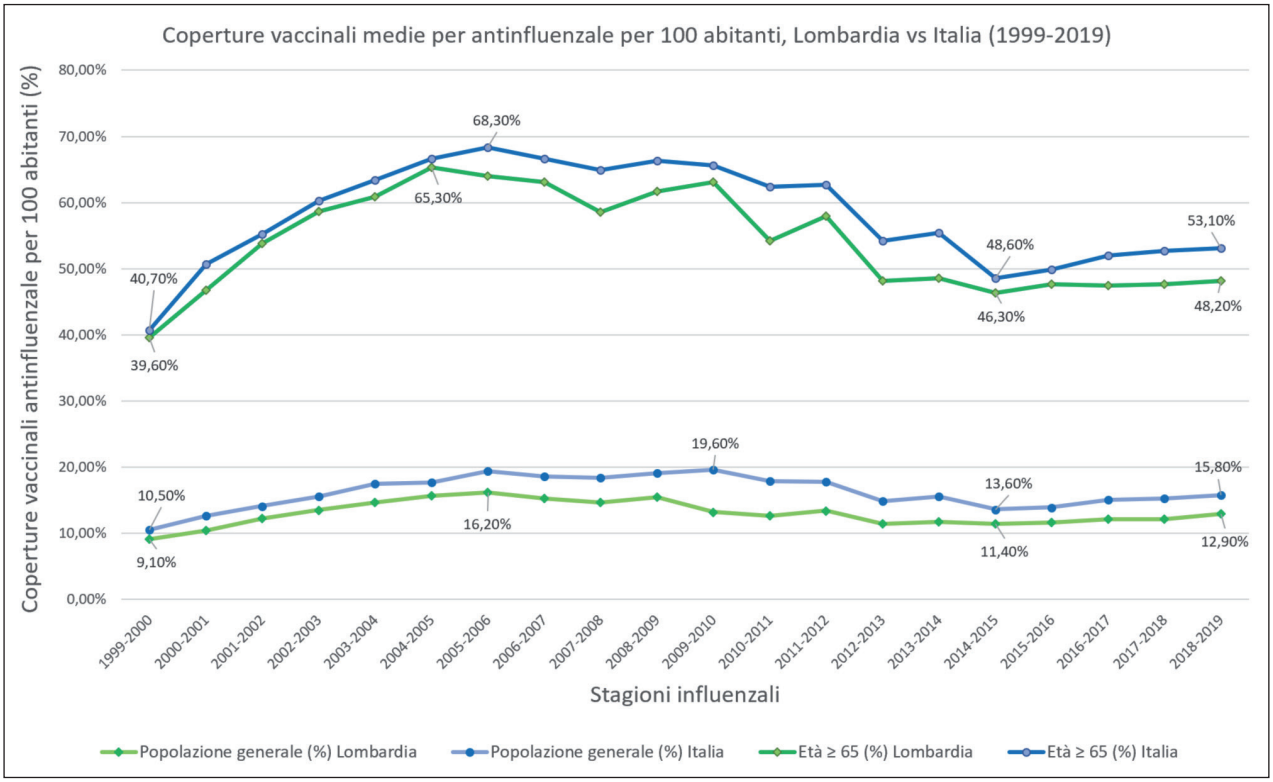

Figure 1. Coperture vaccinali medie (vaccinazione antinfluenzale) in Italia ed in Lombardia nella popolazione generale e negli over 65 (stagioni dal 1999-2000 al 2018-2019), aggiornamento al 15 luglio 2019. Ministero della Salute, Istituto Superiore della Sanità, EpiCentro (10).

Risultati

Sia considerando la popolazione generale, sia gli over 65, i dati della Lombardia si sono sempre mantenuti stabilmente inferiori alla media nazionale, con andamenti eterogenei nel corso delle stagioni considerate (Tabella 1, Figura 1).

Popolazione generale

In Italia la massima copertura vaccinale media è stata registrata nella stagione 2009-2010 (19,6%), in prima ipotesi come effetto di trascinamento della maggior sensibilità della popolazione in seguito alla pandemia di virus influenzale "suino" A(H1N1)pdm09 (primavera 2009) (11); mentre in Lombardia il picco di copertura è anticipato alla stagione 2005-2006 (16,2%).

Sia in Lombardia sia in Italia le coperture sono state stabilmente basse negli ultimi 20 anni, con lievi oscillazioni (Tabella 2: Italia -6%, Lombardia -4,8%), che non fanno pensare ad una chiara associazione al fenomeno dell'esitazione vaccinale (7-9), né tantomeno che le coperture abbiano risentito del "caso Fluad" (12).

Popolazione di età ≥ 65 anni

Seppure ben più elevata che nella popolazione generale, i livelli di copertura sono sempre stati insufficienti, con un andamento in crescita soltanto nei primi anni 2000. Picchi di massima copertura si sono verificati nella stagione 2005-2006 in Italia (68,3%) e nel 2004-2005 in Lombardia (65,3%).

Negli anni a seguire, si sono avute oscillazioni di qualche punto percentuale in più per la Lombardia rispetto alla media italiana, che sono culminate in un progressivo declino delle coperture vaccinali fino alla massima flessione nella stagione 2014-2015 (Tabella 2: Italia -19,7%, Lombardia -19%), complice forse la confusione mediatica, la mala-informazione e la sfiducia generale che ha pervaso la popolazione negli anni di massima diffusione del fenomeno dell'esitazione vaccinale (7-9) e del "caso Fluad" (12).

Negli ultimi 4-5 anni, si registra un lieve recupero, più pronunciato in Italia che in Lombardia (Tabella 2: Italia +4,5%, Lombardia +1,9%).

Tuttavia, le coperture sono ancora lontane dai livelli precedenti, e quindi ancor più distanti dai livelli raccomandati (6).

Conclusione

In generale, le coperture vaccinali per antinfluenzale in Lombardia si sono sempre mantenute stabilmente inferiori alla media Italiana (10), con andamento eterogeneo. Nella popolazione generale le coperture sono basse e stazionarie negli ultimi 20 anni, mentre negli over 65 sono rapidamente diminuite da metà anni 2000 ad oggi. Nonostante un attuale lento recupero all'incirca ai valori dell'anno pre-Fluad, permangono abbondantemente sotto le soglie raccomandate da OMS e PNPV (6).

La scarsa informazione e la sfiducia generale conseguenti alla pandemia 2009 (11), al caso Fluad (12) e al fenomeno dell'esitazione vaccinale (7-9), hanno contribuito a creare un'alterata percezione del rischio di morte e complicanze dell'influenza.

La vaccinazione antinfluenzale non rientra fra quelle rese obbligatorie dalla Legge n.119/2017 (13, 14), e pare che le coperture non ne abbiano risentito in maniera importante.

Le coperture sotto media della Lombardia devono essere oggetto di successive elaborazioni e raccolta dati, cercando spiegazioni, che potrebbero essere: elevato numero di stranieri, azioni informative ed educative non completamente adeguate, bias nella notifica dei vaccinati, diverso atteggiamento degli operatori sanitari.

Per il futuro si auspica che il potenziamento della rete di sorveglianza Ministeriale (15), degli interventi di educazione sanitaria e degli obiettivi delle aziende sanitarie (16) conducano ad un aumento delle coperture vaccinali per antinfluenzale nella popolazione generale, ma soprattutto negli anziani, con la speranza di raggiungere, superare e mantenere durevolmente la soglia minima di sicurezza (6).

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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"Attiva l'Attesa": studio pilota presso uno stabilimento termale

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"Activate your Wait" project : pilot study carried out at a thermal centre. Abstract: Physical activity is recognised as a major health determinant, with positive effects on health, environmental sustainability and economy. National surveillance data show that one out of three Italians - adult and elderly alike - declares to be sedentary, with a progressively increasing trend. From the urgent need to implement strategies to promote physical activity the "Activate your Wait" ("Attiva l'Attesa") project was born, aimed at transforming the waiting pauses during day to day life into opportunities to perform simple stretching and active mobilization exercises. The pilot study was carried out at the Terme S. Egidio, Suio Terme Castelforte (Latina). The results of the questionnaire distributed in the pre-intervention phase, aimed at assessing the users' interest in the project and physical activity in general, are reported. The questionnaire was administrated in the waiting rooms in September 2018 and September 2019. A total of 129 subjects responded to the questionnaire: 43% declared themselves sedentary, 73% reported willingness to perform simple physical exercises while waiting, and 76% believed that physical activity during waiting moments could have a positive impact on health. The project's subsequent goal is to identify suitable exercises to be proposed during the intervention period, which can be easily reproduced independently by users in their everyday life.

Key words: physical activity, waiting pauses, health, prevention, health promotion

Riassunto. L'attività fisica è riconosciuta quale uno dei principali determinanti di salute, con effetti positivi sulla salute, sullo sviluppo sostenibile e sull'economia. Dai dati di sorveglianza nazionali dell'Istituto Superiore di Sanità emerge che oltre un terzo della popolazione italiana (adulta e anziana) si dichiara sedentario, con un trend in progressivo aumento. Dall'urgenza di implementare strategie di promozione dell'attività fisica nasce il progetto "Attiva l'attesa", il cui obiettivo è trasformare le pause d'attesa della vita quotidiana in opportunità per svolgere semplici esercizi di stretching e mobilizzazione attiva. Lo studio pilota è stato effettuato presso le Terme S. Egidio, Suio Terme Castelforte (Latina). Vengono riportati i risultati del questionario, somministrato nella fase pre-intervento, volto a valutare l'interesse degli utenti verso il progetto e l'attività fisica in generale. Il questionario è stato distribuito nelle sale d'attesa dello stabilimento termale nel settembre 2018 e nel settembre 2019. Al questionario hanno risposto 129 soggetti: il 43% si dichiarava sedentario, il 73% disponibile ad eseguire semplici esercizi durante le attese e il 76% sosteneva che l'attività fisica durante le attese avesse un impatto positivo sulla salute. Obiettivo futuro è proseguire il progetto individuando e proponendo esercizi adeguati che possano essere ripetuti autonomamente dagli utenti nella quotidianità.

Parole chiave: attività fisica, pause di attesa, salute, prevenzione, promozione della salute

Introduzione

L'attività fisica è riconosciuta come uno dei principali determinanti di salute, con effetti positivi sulla salute, sullo sviluppo sostenibile e sull'economia (1, 2, 3).

Nonostante tali evidenze, nel mondo, 1 adulto su 4 e 3 adolescenti su 4 non svolgono attività fisica secondo le raccomandazioni dell'Organizzazione Mondiale della Sanità (OMS) (1). In alcuni Paesi i livelli di inattività raggiungono il 70% a causa del cambiamento dei trasporti, dell'uso della tecnologia e dell'urbanizzazione (1,4).

Dalla sorveglianza PASSI (5) è emerso che nel periodo 2015-2018 il 34,5% della popolazione italiana tra 18 e 69 anni si dichiarava sedentario con un trend in aumento, tale percentuale risultava ancora più elevata negli anziani (over 65 anni) raggiungendo il 39,8% (Sorveglianza PASSI d'Argento 2016-2018) (6).

Diventa pertanto urgente implementare strategie di promozione dell'attività fisica, come ribadito dall'OMS nel *"Global Action Plan in Physical Activity 2018-2030"* che ha definito quattro obiettivi strategici: *active society, active environment, active people and active system*, da realizzare attraverso azioni politiche applicabili in tutti i Paesi, con l'obiettivo di ridurre del 15% la prevalenza globale di inattività entro il 2030 (1). Il Piano rimarca la necessità di un approccio *life-course* integrato che agisca a più livelli e su diversi aspetti, come sostenuto anche dal programma "Guadagnare Salute" (7) e dal Piano Nazionale della Prevenzione (8) sul modello della promozione della salute (9).

L'OMS definisce attività fisica qualunque movimento determinato dal sistema muscoloscheletrico che si traduce in un dispendio energetico che supera quello delle condizioni di riposo (1); in questa definizione quindi rientrano non solo le attività sportive ma anche i semplici movimenti quotidiani.

Da queste considerazioni e dalla collaborazione tra le Scuole di Specializzazione in "Igiene e Medicina Preventiva" e "Medicina Fisica e Riabilitativa" dell'Università di Parma è nato il progetto "Attiva l'Attesa", il cui obiettivo è trasformare le pause d'attesa della vita quotidiana (es. sale d'attesa dei medici, uffici, fermate dei mezzi pubblici) in opportunità per svolgere semplici esercizi di stretching e di mobilizzazione attiva.

Lo studio pilota del progetto, articolato in diverse fasi (pre-intervento, intervento, post-intervento), è stato effettuato presso le Terme S. Egidio, Suio Terme Castelforte, in provincia di Latina. Vengono riportati i risultati del questionario, somministrato nella fase pre-intervento, volto a valutare l'interesse degli utenti verso il progetto e l'attività fisica in generale.

Materiali e Metodi

Il questionario semi-strutturato era costituito da 11 domande relative a: livello di attività attuale, attività fisica svolta in passato, modalità di occupazione delle attese e disponibilità a svolgere esercizi. In due giornate, una nel settembre 2018 e una nel settembre 2019, il questionario è stato distribuito agli utenti delle Terme nelle sale d'attesa durante le pause tra i trattamenti terapeutici. È stata effettuata un'analisi descrittiva dei risultati e per ciascuna domanda sono state calcolate le percentuali sui rispondenti.

Risultati

Al questionario hanno risposto 129 utenti (rispondenza 100%), di cui 63% donne, di età compresa tra 18 e 90 anni (mediana 71); nel 50% dei casi i soggetti possedevano la licenza elementare e il 68% era pensionato. Per quanto concerne l'attività fisica svolta abitualmente (rispondenti n.121), il 43% si dichiarava sedentario, il 44% parzialmente attivo e solo il 13% attivo. Tra i sedentari (rispondenti n.52), le motivazioni della sedentarietà erano principalmente la mancanza di volontà 32%, le difficoltà fisiche 29% e la mancanza di tempo 22%. Riguardo all'attività fisica svolta in passato (rispondenti n.123), il 6% dichiarava di aver svolto attività agonistica, il 54% attività non agonistica e il 40% nessuna attività. Il 60% affermava di preferire sempre le scale all'ascensore per recarsi ad un piano superiore (rispondenti n.127). Le attese venivano occupate (rispondenti n.126) principalmente conversando per il 63% degli utenti, utilizzando il cellulare per il 16% e leggendo giornali per il 9%. Alla domanda relativa alla disponibilità a eseguire semplici esercizi durante le attese (rispondenti n.128), il 62% ha risposto "sì", l'11% "più sì che no", l'1% "più no che sì", il 19% "no", il 7% ha mostrato indecisione. Tra coloro che hanno risposto in maniera positiva (rispon-

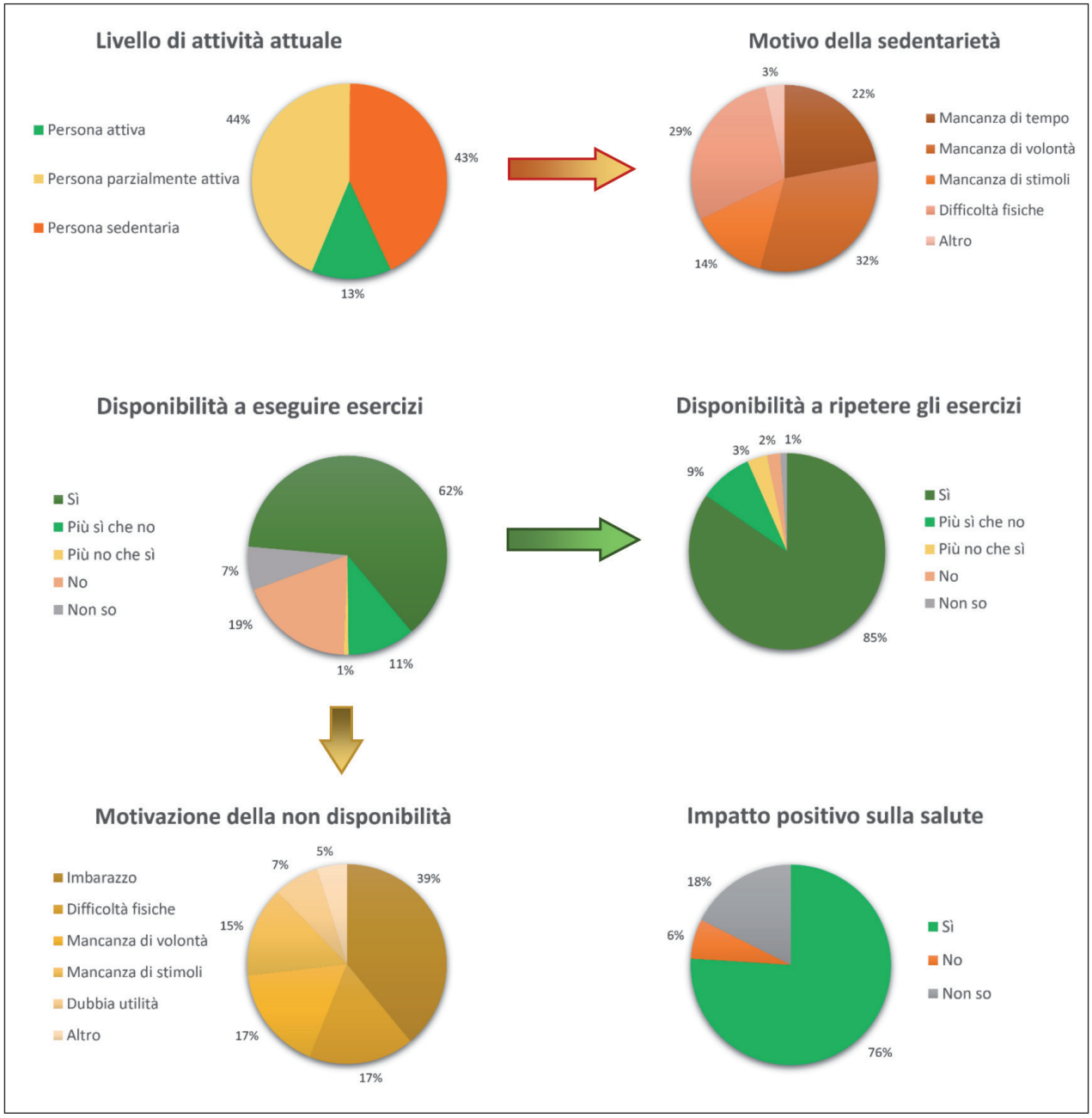

Figure 1. Livello di attività fisica attuale e disponibilità degli utenti (%) a svolgere semplici esercizi di stretching e di mobilizzazione attiva durante le pause di attesa.

denti n.91), l'85% si dichiarava disposto a ripetere gli esercizi in caso di un'attesa maggiore di 5 minuti, mentre la ragione della risposta negativa (rispondenti n.37) era per il 39% l'imbarazzo. Il 76% (rispondenti n.125) sosteneva che l'attività fisica durante le attese avesse un impatto positivo sulla salute.

Conclusioni

Nonostante oltre un terzo del campione sia risultato sedentario, la grande maggioranza si dichiarava disponibile ad eseguire esercizi durante le pause d'attesa; fra i meno propensi l'imbarazzo rappresentava il

maggiore ostacolo nello svolgere attività fisica in luoghi pubblici e ciò potrebbe rappresentare un fattore limitante da considerare. Obiettivo futuro è proseguire il progetto con l'individuazione di esercizi da proporre agli utenti durante l'intervento, adatti ad ogni età e riproducibili autonomamente nel quotidiano. In un contesto in cui le opportunità per svolgere attività fisica vanno diminuendo e la sedentarietà ha raggiunto valori elevati, questo progetto rappresenta un importante contributo per promuovere la cultura del movimento nell'intera popolazione.

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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Contaminazione fungina dell'aria in un edificio universitario

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Fungal contamination in a University building . Abstract: *Background.* It is recognized that airborne fungi can cause illnesses in humans but data on environmental exposure are still poor. The aim of this study was to evaluate the fungal airborne contamination in a university building. *Methods.* The study was performed in February and May 2018; air samples were collected, before activity (on Monday) and during activity, (on Friday), both through active (CFU/m^3) and passive (Index of microbial air contamination, IMA) method. Fungi were identified by using the scotch test. *Results.* In February the median fungal contamination value decreased from 14 CFU/m^3 before activity to 7 CFU/m^3 during activity, while IMA median remains 0. Instead in May both increased during activity (from 87 to 140 CFU/m^3; from 5.5 to 7.5 IMA). Overall values increased in May compared to February. *Aspergillus* spp., *Penicillium s*pp., *Cladosporium* spp. *Absidia* spp. were the genera most frequently isolated in both months, while in May *Chaetomium* spp. e *Ulocladium* spp. were recovered too. *Conclusions.* Seasonal trend in the levels of fungal contamination of the air was observed, with a statistically significant increase in May. This study represents the first step of a wider study aimed at enhancing knowledge about air fungal contamination.

Key words: air, indoor environment, fungal contamination, air sampling

Riassunto. *Introduzione.* La contaminazione fungina dell'aria è associata a diverse patologie nell'uomo ma i dati relativi all'esposizione sono scarsi. Scopo dello studio è la valutazione della contaminazione fungina dell'aria in un edificio universitario. *Metodi.* Lo studio è stato condotto nei mesi di febbraio e maggio 2018; i campioni sono stati raccolti prima dell'attività (lunedì) e durante l'attività (venerdì), sia con metodo di campionamento attivo (UFC/m^3) che passivo (Indice Microbico Aria, IMA). Gli isolati sono stati identificati mediante scotch tape. *Risultati.* In febbraio la mediana della carica fungina è diminuita da 14 UFC/m^3 prima dell'attività a 7 UFC/m^3 durante la stessa, mentre per IMA è rimasta 0. Al contrario, in maggio, entrambi i parametri sono aumentati durante l'attività (da 87 a 140 UFC/m^3; da 5,5 a 7,5 IMA). Nel complesso, tutti i valori sono aumentati in maggio rispetto a febbraio. I generi più frequentemente isolati nei due mesi sono stati *Aspergillus* spp., *Penicillium* spp., *Cladosporium* spp. e *Absidia* spp., mentre in maggio anche *Chaetomium* spp. e *Ulocladium* spp. *Conclusioni.* È emerso un andamento stagionale dei livelli di contaminazione fungina dell'aria con un aumento statisticamente significativo in maggio. Questo studio rappresenta la prima fase di una più ampia indagine.

Parole chiave: aria, ambienti confinati, contaminazione fungina, campionamento dell'aria.

Introduzione

L'esposizione ad aria contaminata da specie fungine in ambienti di vita e di lavoro rappresenta un rischio per patologie infettive, allergiche e tossiche (1,2).

Tuttavia, manca una quantificazione dell'impatto sulla salute ad essa associato, anche per una carenza di studi relativi alla contaminazione fungina valutata con un approccio standardizzato. In questo studio è stato valutato il livello di contaminazione fungina in un ambiente di lavoro universitario.

Metodi

Lo studio è stato condotto in un plesso del Dipartimento di Medicina e Chirurgia dell'Università di Parma. I campionamenti dell'aria sono stati effettuati con metodo attivo e con metodo passivo, nei mesi di febbraio e maggio 2018, sui 3 diversi piani della struttura che ospita uffici, aule didattiche e laboratori. Per ogni piano sono stati individuati 5 siti di campionamento (Tabella 1).

Il campionamento dell'aria è stato effettuato a inizio settimana (lunedì), prima della ripresa dell'attività lavorativa, e a fine settimana (venerdì), durante il suo svolgimento, mediante metodo attivo per la valutazione della concentrazione fungina (unità formanti colonia per m^3, UFC/m^3) e metodo passivo per la misura del tasso di sedimentazione (Indice Microbico Aria, IMA) (3-5).

Per il campionamento attivo sono stati aspirati, 500 litri di aria con il campionatore DUOSAS 360 utilizzando piastre RODAC di 55mm; per la determinazione

Tabella 1. Contaminazione fungina (UFC/m^3) e IMA prima e durante l'attività

Piano	Sito	UFC/m^3*				IMA**			
		Prima dell'attività		Durante l'attività		Prima dell'attività		Durante l'attività	
		Febbraio	Maggio	Febbraio	Maggio	Febbraio	Maggio	Febbraio	Maggio
Piano Terra	**Corridoio**	16	40	4	134	0	0	0	11
	Ballatoio	16	78	4	146	2	6	0	11
	Laboratorio	12	86	8	786	0	4	1	29
	Studio	10	62	12	146	0	5	0	3
	Fan coil	18	76	6	162	5	0	1	2
	Mediana	**16**	**76**	**6**	**146**	**0**	**4**	**0**	**11**
	Media (DS)* **	**14,4 (3,3)**	**68,4 (18,1)**	**6,8 (3,3)**	**274,8 (285,9)**	**1,4 (2,2)**	**3,0 (2,8)**	**0,4 (0,5)**	**11,2 (10,8)**
Primo Piano	**Corridoio**	16	102	12	174	0	8	44	9
	Ballatoio	4	100	12	168	0	12	0	5
	Laboratorio	16	76	16	92	0	12	0	3
	Studio	12	88	16	244	1	13	0	17
	Fan coil	18	84	10	680	0	0	2	31
	Mediana	**16**	**88**	**12**	**174**	**0**	**12**	**0**	**9**
	Media (DS)	**13,2 (5,6)**	**90,0 (11,0)**	**13,2 (2,7)**	**271,6 (234,6)**	**0,2 (0,4)**	**9,0 (5,4)**	**9,2 (19,5)**	**13,0 (11,4)**
Secondo Piano	**Corridoio**	8	166	0	92	0	15	0	6
	Ballatoio	14	90	2	118	0	3	0	6
	Laboratorio 1	4	176	6	68	0	34	0	20
	Studio	14	86	8	72	0	8	0	6
	Fan coil	10	148	0	60	1	2	0	9
	Laboratorio 2	14	90	2	68	0	4	1	3
	Mediana	**12**	**119**	**2**	**70**	**0**	**6**	**0**	**6**
	Media (DS)	**10,7 (4,1)**	**126 (41,9)**	**3,0 (3,3)**	**79,7 (21,6)**	**0,2 (0,4)**	**11,0 (12,2)**	**0,2 (0,4)**	**8,3 (6,0)**
Totale	**Mediana**	**14**	**87**	**7**	**140**	**0**	**5,5**	**0**	**7,5**
	Media (DS)	**12,6 (4,4)**	**96,7 (36,5)**	**7,4 (5,2)**	**200,6 (214,5)**	**0,6 (1,3)**	**7,9 (8,5)**	**3,1 (10,9)**	**10,7 (9,1)**

* Unità formanti colonia/m^3; ** Indice Microbico Aria; *** Deviazione standard

dell'IMA, piastre Petri di 9 cm di diametro sono state posizionate nei punti prescelti e lasciate aperte per un'ora. È stato utilizzato il terreno colturale Sabourad Dextrose Agar e le piastre sono state incubate a 24°C per 5 giorni. L'identificazione dei miceti è stata effettuata al microscopio ottico dopo scotch test e successiva colorazione con blu di lattofenolo delle colonie isolate.

I dati sono stati analizzati utilizzando SPSS 25.0 (IBM SPSS Inc., Chicago-IL). Analisi della varianza e test della mediana sono stati utilizzati per il confronto dei risultati. Un valore p ≤0,05 è stato considerato statisticamente significativo.

Risultati

Nella Tabella 1 sono riportati in dettaglio i valori di contaminazione fungina ottenuti, suddivisi per piano, momento e sito di campionamento.

Considerando i dati nel loro complesso, in febbraio, prima dell'attività, sono state rilevate da 4 a 18 UFC/m^3 (mediana 14) e da 0 a 5 IMA (mediana 0). Durante l'attività il range di valori è risultato 0-16 UFC/m^3 con una riduzione del valore della mediana a 7 UFC/m^3 e di 0-44 IMA con mediana pari a 0.

Nel mese di maggio, prima dell'attività, le UFC/m^3 erano comprese tra 40 e 176 (mediana 87) e tra 0 e 34 IMA (mediana 5,5). Durante l'attività i valori hanno oscillato tra 60 e 786 UFC/m^3 (mediana 140) e tra 2 e 31 IMA (mediana 7,5).

Valutando l'andamento dei risultati ottenuti nei due mesi, sia in generale che nei singoli piani (Tabella 1), si osserva un aumento dei valori nel mese di maggio rispetto a febbraio, con differenze che sono risultate statisticamente significative sia per UFC/m^3 che per IMA.

Relativamente al mese di febbraio, prima dell'attività, i valori medi più elevati sono stati osservati al piano terra mentre, durante l'attività, al primo piano. Nel mese di maggio, prima dell'attività, i valori più elevati sono stati registrati al secondo piano che, invece, durante l'attività è risultato quello con valori inferiori.

In entrambi i mesi di campionamento sono stati isolati con maggiore frequenza A*spergillus* spp., *Penicillium* spp., *Cladosporium* spp., *Absidia* spp., mentre nel solo mese di maggio anche *Chaetomium* spp. e *Ulocladium* spp.

Conclusioni

Dallo studio emerge un andamento stagionale dei livelli di contaminazione fungina dell'aria con un aumento statisticamente significativo in maggio, mese in cui è stata isolata anche una maggiore varietà di generi fungini rispetto a febbraio. Tali risultati sono in linea con altri studi (6-8).

Confrontando i valori ottenuti in assenza e in presenza di attività, al contrario di quanto atteso, in febbraio complessivamente sono risultati più elevati i valori in assenza di attività, mentre nel mese di maggio quelli ottenuti durante l'attività lavorativa, con la sola eccezione del secondo piano. In alcuni casi, in singoli ambienti, sono stati rilevati valori di picco che, unitamente alla precedente osservazione, meritano un ulteriore approfondimento.

Facendo riferimento ai valori proposti dall'European Collaborative Action nel 1993 (9) e riportati successivamente dall'INAIL (10), lo studio ha evidenziato un livello di inquinamento "basso" (limite <100 UFC/m^3) nel mese di febbraio e "intermedio" (<500 UFC/m^3) in maggio, pur con alcuni sforamenti. È evidente che i limiti proposti per la concentrazione fungina circa trent'anni fa debbano essere riconsiderati, così come debbano essere definiti valori limite relativamente al tasso di sedimentazione per la sola componente microbica fungina, attualmente mancanti.

Il lavoro costituisce la prima fase di un più ampio studio mirato ad approfondire la conoscenza sulla contaminazione fungina dell'aria in ambienti lavorativi confinati, e intende contribuire anche alla definizione di valori di riferimento per la prevenzione del rischio in ambienti confinati derivante da spore fungine aerotrasportate.

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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Ricordo di un direttore sanitario illuminato: Enrico Ronzani

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Life and achievements of an hospital director: Enrico Ronzani . Abstract: The paper illustrates the life and the achievements of Enrico Ronzani, born in Padua and graduated in Medicine at the Bologna University. He directed the hospitals of Florence and the Ospedale Maggiore of Milan, promoting its growth until it became the seat of the Medical School promoted by Prof Mangiagalli, and he himself became Full Professor of Hygiene. In such a position he taught Hygiene also to Architets and Engineers, built the new Institute of Hygiene and helped to design and build the new great Hospital of Niguarda. But, most of all, he was successful in designing, promoting and officializing the job of the Hospital Directors, which was subsequently recognized by the law; and, publishing a series of books on the role of the modern hospitals, he prefigured their position in a web of medical institutions to include also those devoted to pre- and post-hospital assistance to the population. Practically he foresaw what was realized many years later through the creation of the Italian National Health Service (Law 833 of 1978).

Key words: Ronzani Enrico, hospital director, hospital, hygiene

Riassunto. Gli Autori illustrano le tappe salienti della vita e delle opere del Prof Enrico Ronzani, padovano laureato a Bologna e Direttore sanitario a Firenze e poi all'Ospedale Maggiore di Milano. La sua carriera di Direttore Sanitario e di protagonista dello sviluppo dell'Ospedale, fino a partecipare alla progettazione ed alla costruzione del nuovo Niguarda, si è incrociata con la nascita dell'Università di Milano, dove egli è stato il primo ad insegnare Igiene agli studenti dei Medicina, di Ingegneria e di Architettura, attivando l'Istituto di Igiene e svolgendovi una nutrita attività scientifica fino a raggiungere la posizione di professore ordinario. È stato il teorizzatore della figura del Direttore Sanitario d'Ospedale, del quale ha messo a punto i ruoli scientifici, tecnici, organizzativi e gestionali, aprendo un'apposita Scuola e portandone a compimento il riconoscimento giuridico. Anticipatore della modernità, si è battuto per il collegamento degli ospedali in rete tra loro e con la sanità di territorio, prefigurando quanto sarà poi realizzato ben più tardi dalla legge 833 del 1978 che ha istituito in Italia il Servizio Sanitario Nazionale. (www.actabiomedica.it)

Parole chiave: Ronzani Enrico, hospital director, hospital, hygiene

Introduction

Se parlare di Enrico Ronzani, per uno di noi (ERj), richiama alla mente un nonno che ha onorato la famiglia come grande medico e personaggio pubblico, per l'altro (GMF) rievoca un antenato simbolico, dalla duplice valenza: Direttore Sanitario dello stesso Ospedale Maggiore di Milano dove egli ha trascorso gli anni della sua formazione professionale; ma anche Professore Ordinario di Igiene nell'allora neonata Facoltà medica di Milano, e quindi predecessore del Maestro, Augusto Giovanardi, che l'ha formato nella disciplina

Relazione tenuta il 9 Dicembre 2019 al Convegno "Le Direzioni sanitarie, una componente essenziale del Sistema Sanitario Nazionale", organizzato dall'Accademia Lombarda di Sanità Pubblica, dall'Associazione Nazionale dei Medici di Direzione Sanitaria (Sezione Lombardia), dalla Società Italiana di Igiene, Medicina Preventiva e Sanità Pubblica (Sezione Lombardia), dall'Ordine Provinciale di Milano dei Medici Chirurghi e degli Odontoiatri e dall'Associazione Italiana dell'Ospedalità Privata (Regione Lombardia)

dell'Igiene, e l'ha poi avviato alla cattedra nella stessa Università, e successivamente alla Sapienza di Roma.

Figura di grande spessore quella di Ronzani, con l'anima ospedaliera mescolata a quella universitaria; un igienista che sentiva in sè una missione pedagogica che l'ha portato anche fuori dai confini tradizionali dell'igiene medica, a condividere ricerche e ad insegnare ad ingegneri e ad architetti, che poi son quelli che costruiscono gli ospedali (1, 2). Ma la sua missione principale è stata quella di definire, preparare ed istituzionalizzare la figura del Direttore Sanitario (3).

Enrico Ronzani (4) nasce nel 1877 a Padova, dove studia Medicina, laureandosi poi a Bologna nel 1903.

Allievo di Serafini, igienista a Padova, nel 1904 è Assistente, nel 1906 Aiuto e professore incaricato di Igiene, nel 1909 (a 32 anni) Libero Docente. Nel 1911 vince il posto di Vice Direttore dell'Arcispedale di S Maria Nuova di Firenze, ma si divide tra Firenze e Padova, dove insegna Igiene nella Facoltà di Ingegneria, ed è per qualche tempo coadiutore della Direzione Sanitaria dell'ospedale.

Due anni dopo, nel 1913, vince il posto di Vice Direttore degli Istituti Ospitalieri di Milano, e nel 1914 ne è già Direttore Sanitario, a soli 37 anni.

La prima guerra mondiale lo coinvolge nel 1915, e lo vede all'opera nella Direzione sanitaria militare di Padova, dove scala i gradi da sottotenente a maggiore. Dal 1917 al 1919 è in zona di guerra, per concludere l'esperienza bellica con i gradi di Colonnello della Sanità militare.

Mentre è ancora sotto le armi è nominato nella Commissione che dovrà scegliere il luogo dove sorgerà il nuovissimo ospedale di Milano che lui stesso da tempo andava proponendo; e nel 1918 il Ministro dell'Interno lo nomina nella Commissione d'inchiesta sull'assistenza ospedaliera in Italia.

Nel 1919 riassume la Direzione Sanitaria a Milano e ricolloca la sua Libera Docenza da Padova a Pavia, allora unica sede Medicina in Lombardia (c'erano già due università a Milano, ma erano il Politecnico e la Bocconi). A Pavia conosce Luigi Mangiagalli, che lo coinvolge nella creazione, a partire dal 1924, della Facoltà medica della nascente università di Milano e del relativo Istituto di Igiene. Ottenuti gli spazi nel vecchio ospedale del Filarete, Ronzani li arreda e li attrezza con pochi soldi (in parte anche suoi) e vi insegna come docente incaricato;

Ma come Direttore Sanitario si occupa anche degli spazi per il resto della nascente Facoltà di Medicina: partecipa tra il 1914 ed il 1934 alla progettazione, costruzione ed organizzazione interna dei Padiglioni che vanno sorgendo al di là di Via Sforza, in un'area adiacente ai preesistenti Istituti Clinici di Perfezionamento: Guardia e Accettazione, Anatomia Patologica, Pasini, Bosisio, Borghi, Monteggia, Sacco, Bertarelli, Granelli, Zonda, Convitto (5), mentre si occupa anche di realizzare il grande Sanatorio di Garbagnate ed i nuovi ospedali di Udine, di Gorizia e di Como (6). In quegli anni conclude i lavori la Commissione deputata alla scelta del terreno su cui dovrà sorgere il nuovo, grande Ospedale Maggiore, battezzato "Ospedale del Perdono" (7).

Una parentesi turbolenta la vive nel 1929, quando il Commissario prefettizio dell'Ospedale Maggiore, il Cav. Atto Marolla, lo solleva dalla Direzione Sanitaria (8). Il suo ricorso ha un immediato successo, ed il Consiglio di Stato lo reintegra nel 1930, con il recupero dell'anzianità, tra gli applausi del Consiglio della Facoltà di Medicina, i complimenti del Senatore Sanarelli, igienista della Sapienza, e addirittura la soddisfazione del Ministro dell'Interno Urbinati (9).

Rammentiamo in proposito che il Ministero della Sanità era di là da venire (fu istituito nel 1958), e la Sanità, dall'Unità fino a quella data, aveva fatto capo, prima come Direzione generale di Sanità, poi come Alto Commissariato per l'Igiene e la Sanità, al Ministero dell'Interno, il "Ministero di Polizia". Ed in effetti la futura Sanità pubblica era stata definita fin dall'origine dal grande Giovanni Pietro Frank (1745-1821), professore di Medicina a Gottinga, poi a Pavia e pure Direttore di Sanità per il governo austro-ungarico del Lombardo-Veneto, come *Medizinische Polizei* (10).

Da quel momento si susseguono per lui le più grandi soddisfazioni:

- nel 1931, diventa Presidente della Reale Società Italiana di Igiene;
- nel 1931 diventa direttore della rivista "L'Ospedale Maggiore";
- nel 1931 il Consiglio dell'Ospedale Maggiore bandisce il concorso nazionale per il nuovo ospedale (11) ed i vincitori gli affidano la consulenza sanitaria

del progetto, da lui auspicato fin dal 1914; progetto che l'Ing Giulio Marcovigi e l'Architetto Giulio Arata consegneranno nel Gennaio 1932. In pochi anni il progetto è realizzato, e nel 1939 nasce così il grande Ospedale di Niguarda (12) (Fig. 1), che ha festeggiato nel 2019 l'ottantesimo compleanno;

- a far tempo dal 1932, nel Politecnico di Milano, riceve l'incarico di insegnamento di "Igiene applicata all'Ingegneria" e dal 1933 quello di "Igiene applicata all'Edilizia" per la Facoltà di Architettura (1, 2). Insegnamenti che gli igienisti universitari milanesi dopo di lui (A Giovanardi, GM Fara, F Bergamini, C Signorelli) non abbandoneranno mai, fino a consegnare il testimone, nel 2019, al Prof Stefano Capolongo, da loro formato, primo architetto in Italia a divenire docente ordinario di Igiene;
- nel 1934 anche Ronzani diventa finalmente professore straordinario di Igiene, confermato ad ordinario (Fig 2) nel 1938; è così uno dei primi operatori sanitari che raggiunge la cattedra di Igiene, come faranno pochi altri dopo di lui;
- è nominato per il triennio 1938-40 nel Consiglio Superiore di Sanità, e riconfermato per il triennio successivo;
- nel 1938 il Ministero dell'Educazione Nazionale autorizza l'Università di Milano ad aprire la prima Scuola di Perfezionamento in Italia per aspiranti Direttori Sanitari d'Ospedale.

Enrico Ronzani è giunto al culmine della sua parabola, ma avrebbe ancora molti anni davanti a sé per realizzare quanto ancora ha in mente. Purtroppo, nello stesso anno dell'inaugurazione di Niguarda, scoppia la Seconda Guerra Mondiale, nella quale l'Italia è coinvolta dall'anno successivo. Gli tocca assistere ai terribili bombardamenti dell'Agosto 1943 su Milano, che scempiano l'edificio della Ca' Granda (Fig 3), l'Istituto di Igiene lì dentro collocato e molti dei nuovi edifici che lui stesso aveva costruito. Non sopravvive a quegli eventi: pochi mesi dopo, un infarto lo stronca a soli 66

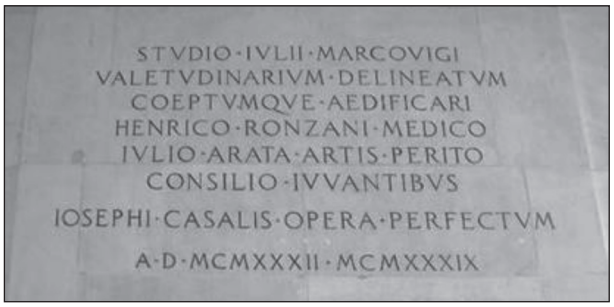

Figure 1. Lapide che ricorda l'inaugurazione del nuovo ospedale di Niguarda.

Figure 2. Enrico Ronzani professore ordinario di igiene a Milano, 1938.

Figure 2. L'ospedale Maggiore di Milano (la Ca' Granda) dopo le bombe del 1943.

anni, mettendo prematuramente fine ad una carriera di grande impegno e di indiscutibile successo.

Ma le sue realizzazioni sono ancora lì a testimoniare la sua vita intensa e proficua, così come hanno fruttificato le novità che ha portato nel mondo dell'Igiene e della Tecnica Ospedaliera.

Il **pensiero**, la **ricerca e l'azione** in Ronzani appaiono momenti indissolubilmente legati tra loro. Igienista concreto, pratico, fa ricerca nei campi nei quali vuole offrire soluzioni concrete.

Possiamo così riassumere i temi principali di Ronzani: fin da subito, **aspetti specifici dell'Igiene**, come ad esempio le conseguenze sulla salute dei *contaminanti gassosi dell'aria*, così comuni nelle aziende chimiche (13-15), con risultati che saranno utilizzati nelle normative italiane di quegli anni per la tutela della salute dei lavoratori; o il tema degli *alimenti*: ne studia la composizione, il bilanciamento, il valore nutrizionale, ma va subito agli aspetti applicativi, come l'alimentazione dei pazienti in ospedale, un problema tanto antico quanto attualissimo, e spesso non ben risolto nemmeno oggi (16): egli giustamente attribuisce al cibo sicuro, bilanciato e appetitoso un ruolo fondamentale sia nella guarigione che nel mantenimento della salute: sembra di ascoltare oggi Carlin Petrini, il fondatore di *Slow Food*, di *Terra Madre* e dell'Università di Pollenzo, con il suo cibo *buono*, *pulito* e *giusto* (17). Altro tema è la **medicina sociale**, con particolare attenzione a due aspetti:

- l'***educazione igienica*** della popolazione, realizzata approfittando dei periodi di degenza e di convalescenza, perché impari a tenersi lontana da fattori di rischio infettivi, comportamentali ed ambientali (18); e
- ***l'edilizia popolare***, approfondendo, con visione di grande modernità, le caratteristiche di casa, quartiere e città, sotto due possibili aspetti: di agenti morbigeni quando inadeguati, ma di luoghi che possono favorire una vita sana ed attiva quando realizzati in modo igienicamente corretto (19, 20) – e parla come un precursore del progetto Healthy Cities dell'OMS, mentre traspare moltissimo la sua frequentazione assidua del Politecnico di Milano.

  E infine la sua divorante passione: l'**igiene e la tecnica ospedaliera,** iniziata fin dal 1910, quando pubblicò a Padova, per i tipi degli Editori Fratelli Druker, la sua prima opera intitolata "Del Governo tecnico sanitario degli ospedali" (16), ove tratta, oltre che degli aspetti tecnici cui deve rispondere la realizzazione di un ospedale *moderno*, della funzione principe e più ampia di "*governo*" della struttura sanitaria, come esplicitato nella sua presentazione: "*…poiché gran parte di questo libro si riferisce specialmente all'esplicazione dell'opera del direttore sanitario, ho creduto innanzitutto esporre le mansioni e gli incarichi inerenti a tale ufficio…*", affermando che tale funzione richiede la presenza di un medico appositamente preparato, il "Direttore sanitario".
- La maturità, nel 1938, vede invece la comparsa del "Trattato di Igiene e Tecnica Ospedaliera" (21), alcuni capitoli del quale sono affidati alla collaborazione delle più brillanti figure mediche e tecniche dell'epoca. In questa monumentale opera, che ancor oggi viene per certe parti consultata, importanti capitoli sono dedicati alla progettazione, e quindi a studi accurati sulle aree candidate ad ospitare l'ospedale, sui materiali edilizi e di arredo, sulle modalità costruttive, sulle attrezzature diagnostiche e curative che devono offrire qualità, quantità e gamma di prestazioni adatte al territorio da servire. Nel pensiero di Ronzani, pur legato a tipologie edilizie e procedure terapeutiche che oggi han fatto il loro tempo, appare sempre presente, però, un concetto allora poco condiviso, quello di **rete ospedaliera integrata**, e soprattutto quello di **rete tra ospedale e sanità di territorio**. Questo sì un concetto rivoluzionario per allora: oggi parliamo serenamente di piano sanitario integrato, ma all'epoca di Ronzani solo l'ospedale era considerato la sede della vera cultura medica.

E, come ultimo aspetto, ricordiamo il Ronzani **docente**: didatticamente, è un insegnante appassionato della sua disciplina, che si offre anzitutto agli studenti di medicina, ma è anche un disseminatore del pensiero igienistico al di fuori dal mondo medico: di questa necessità convinto precocemente, già a Padova offriva un insegnamento di Igiene applicata agli studenti ed ai laureati di Ingegneria, dimostrando un'interdisciplinarietà ante-litteram, che proseguirà poi nel Politecnico di Milano, insegnando sia agli ingegneri che agli architetti (1, 2).

Ma il suo impegno più grande è la **formazione del Direttore Sanitario d'Ospedale**. Già nel suo rivo-

luzionario libro giovanile sul governo tecnico sanitario degli ospedali (16) affermava che "tale funzione richiede la presenza di un medico appositamente preparato, il *Direttore sanitario*", del quale effettua *ante litteram* una vera e propria *job description*. E per tutta la vita si batte per l'istituzionalizzazione di questa figura che, ricordiamo – pur essendo già diffusa - non era prevista in via esclusiva e non ne erano definiti i requisiti. È solo nel 1938, con il RD 1631 ("legge Petragnani"), notoriamente da lui ispirato, che il Direttore sanitario viene istituzionalizzato, ed immediatamente Ronzani propone al Ministero dell'Educazione Nazionale – che la autorizza - la creazione della prima Scuola di Perfezionamento per aspiranti Direttori Sanitari, e dà alle stampe da Garzanti la sua opera più nota, il già citato Trattato di Igiene e Tecnica Ospedaliera (21). Qui vediamo nuovamente il tratto scientifico e insieme pratico che lo contraddistingue:

- individua e definisce con la sua ricerca i requisiti del Direttore Sanitario;
- interloquisce con Petragnani, Direttore Generale per la Sanità del Ministero dell'Interno, anche lui un Ordinario di Igiene, per la definizione legislativa di quella figura;
- non appena creata, ne programma i corsi di formazione, il primo dei quali apre tempestivamente a Milano, la sua sede universitaria;
- e, infine, realizza anche il libro di testo per quei corsi.

E così il ciclo è completo!

In conclusione

Quella di Ronzani è una figura con due distinte anime, che fin da subito fruttuosamente convivono: l'ospedaliera e l'universitaria.

È una figura innovativa anche nel campo dell'igiene scientifica: uomo di punta nelle proprie competenze, ma sensibile alle esigenze d'interdisciplinarietà, comportamento non comune nella sua epoca di diffusa auto-referenzialità; aperto alla modernità: l'igiene del lavoro, l'alimentazione, la casa, la città, l'ospedale stesso ripensati non solo in funzione di lotta contro le le malattie, ma come strumenti in grado di incrementare la salute attraverso la conoscenza; e infine l'aperta al futuro: l'ospedale inteso non come entità a sé, ma all'interno di una rete insieme con gli altri ospedali, e addirittura insieme con tutte le altre strutture sanitarie.

Ronzani è quindi a buon diritto considerato il padre del direttore sanitario di oggi; ed, aggiungiamo senza ombra di dubbio, anche di quello di domani!

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Conoscenze alimentari in pazienti afferenti ad un centro di diabetologia

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Food knowledge of patients at the first access to a Diabetology center . Abstract: Diabetes represents a constantly increasing disease: family history, age and lifestyles represent the main risk factors for this pathology and for the complications related to it. Considering the importance of the diet for the prevention and treatment of diabetes, the purpose of this study was to evaluate the food knowledge of patients at the first access to a Diabetology center, and to investigate their possible influence on some blood parameters. Moynihan's questionnaire was administered. The relationship between the scores obtained and the variables glycated hemoglobin, BMI, fasting glucose was analyzed by multiple regression based on the ordinary least squares method (OLS model). The response rate was 73.3%. The average total score obtained from the questionnaire was 23.61 and a statistically significant correlation (p<0,0473) was observed between the best scores in the questionnaire and the Hb1Ac values. This study represents the first step of a wider investigation with the aim to promoting patient training to verify over time the positive effects on food choices and clinical parameters.

Key words: food knowledge, type 2 diabetes, Moynihan questionnaire, primary prevention, public health

Riassunto. Il diabete rappresenta una patologia in costante aumento: familiarità, età e stili di vita rappresentano i principali fattori di rischio per questa malattia e per le complicanze ad essa correlate. Considerando l'importanza del regime alimentare per la prevenzione e il trattamento di questa patologia, scopo del presente studio è stato quello di valutare le conoscenze alimentari di pazienti al primo accesso presso un centro di Diabetologia e di indagare sulla loro eventuale influenza su alcuni parametri ematici. È stato somministrato il questionario di Moynihan. La relazione tra i punteggi ottenuti e le variabili emoglobina glicata, BMI, glicemia a digiuno, è stata analizzata attraverso regressione multipla basata sul metodo dei minimi quadrati ordinari (modello OLS). Il response rate è stato del 73,3%. Il punteggio medio totale ottenuto dal questionario è stato di 23,61 ed è stata osservata una correlazione statisticamente significativa (p<0,0473) tra i migliori punteggi del questionario e i valori di Hb1Ac. Questo studio è il primo passo di un'indagine più ampia che verrà condotta nell'ottica di promuovere una formazione del paziente volta a verificare nel tempo le ricadute positive sulle scelte alimentari e sui parametri clinici.

Parole chiave: conoscenze alimentari, diabete di secondo tipo, questionario di Moynihan, prevenzione primaria, sanità pubblica

Introduzione

Nel mondo 1 adulto su 11 è malato di diabete; tale numero è destinato ad aumentare e si stima che da 415 milioni di malati del 2017 si passerà a 642 milioni nel 2040. In Italia il 5,3% della popolazione è affetta da diabete, con una prevalenza maggiore al crescere dell'età e una diffusione maggiore al sud (1-3). Familiarità, età e stili di vita (dieta non equilibrata, incremento quotidiano dell'introito calorico, maggior consumo di cereali raffinati, sedentarietà, …) rappresentano i principali fattori di rischio per questa patologia e per le complicanze ad essa correlate (4-9). E' stato osservato, ad esempio, che quasi il 30% degli obesi soffre di diabete (età 45-60 anni) e molti di essi non praticano attività fisica (2). A tal proposito, il Ministero della Salute ha lanciato una campagna di prevenzione suggerendo linee di indirizzo sull'attività fisica per diverse fasce di età (10) e annualmente propone la Giornata Mondiale del Diabete seguendo le indicazioni dell'International Diabetes Federation (IDF) e dall'Organizzazione Mondiale della Sanità (OMS) allo scopo di sensibilizzare e informare l'opinione pubblica sul diabete, sulla sua prevenzione e gestione (11, 12).

Considerando che anche il regime alimentare è importante per la prevenzione e il trattamento di questa patologia, scopo del presente studio è stato quello di valutare le conoscenze alimentari della popolazione al primo accesso presso il centro di Diabetologia di Fermo (Rete Diabete della Regione Marche) e la loro eventuale influenza su emoglobina glicata (HbA1c%), Indice di Massa Corporea (BMI) e glicemia a digiuno.

Materiali e Metodi

Lo studio osservazionale svoltosi fra Marzo e Settembre 2019, ha previsto la somministrazione in forma anonima del questionario di Moynihan, validato nella sua versione italiana (13, 14). La popolazione in studio doveva rispettare i seguenti criteri di inclusione: a) primo accesso alla U.O.S.D. Diabetologia dell'Area Vasta 4 di Fermo – ASUR Marche; b) essere maggiorenni; c) diagnosi di diabete di secondo tipo o di ridotta tolleranza glucidica; d) possibilità di partecipare autonomamente allo studio. I pazienti dopo aver aderito volontariamente venivano informati sulle motivazioni dello studio e esprimevano consenso scritto.

Il questionario di Moynihan, composto da 15 domande a risposta multipla o a risposta aperta, esplora le conoscenze dei vari tipi di alimenti e della loro composizione in macro/micronutrienti e di fibre. Il punteggio 1 viene assegnato alle risposte esatte, 2 a quelle errate. Di conseguenza, la valutazione finale prevede i seguenti punteggi: ottimo (punteggio 15-17,9), buono (18-21,8), sufficiente (22-25,9), insufficiente (≥26).

Dalle cartelle cliniche venivano, inoltre, estratti i dati di glicemia, BMI e HbA1c%.

L'esistenza e l'andamento del legame funzionale tra i punteggi ottenuti dal test (convertiti in una specifica scala proporzionale: ottimo 4, buono 3, sufficiente 2, insufficiente 1) e Hb1Ac%, BMI, glicemia a digiuno, sesso ed età sono stati definiti utilizzando una regressione multipla basata sul metodo dei minimi quadrati ordinari (modello OLS), utilizzando il software open-source Gretl.

Risultati

Dei 390 pazienti al primo accesso presso il Centro di Diabetologia, 105 rispettavano tutti i criteri di inclusione. Di questi, 77 hanno completato correttamente la compilazione del questionario (response rate 73,3%).

Le caratteristiche del campione e i principali dati analitici sono sintetizzati in tabella 1. Il punteggio medio totale ottenuto dal questionario è di 23,61 (DS 3,22 - min 16, max 29), interpretabile come "sufficiente".

Mentre per la maggior parte dei parametri analizzati non è stata evidenziata una differenza sostanziale in relazione ai risultati del questionario, l'HbA1c% media ha evidenziato un trend di decremento all'aumentare del livello di conoscenza: "insufficiente" 7,94±1,58, "sufficiente" 8,24±2,32, "buono" 8,13±2,23, "ottimo" 6,32±0,36. Questo risultato è stato confermato anche dall'analisi statistica (tab. 2).

Per tutti gli altri parametri analizzati non è stata riscontrata una correlazione inversa con la variabile

Tabella 1. Caratteristiche popolazione e risultati complessivi

Caratteristiche generali popolazione	**Valori**
Uomini	N 47 (61,1%)
Donne	N 30 (38,9%)
Età	64,73±11,28
BMI	30,83±5,61
Emoglobina Glicata (Hb1Ac %)	8±2,03
Glicemia a digiuno (mg/dl)	160,74±63,83
Valutazione Questionario	**Punteggio**
"ottimo" 5 pazienti	16,60±0,62
"buono" 15 pazienti	20,33±1,09
"sufficiente" 31 pazienti	23,57±1,28
"insufficiente" 25 pazienti	27,03±1,04

dipendente, anche se nei pazienti con i risultati più performanti del test sono stati osservati valori medi di BMI (29,02) inferiori alla media riscontrata nella popolazione osservata (30,83).

Conclusioni

Il presente studio, pur con alcune limitazioni, quali ad esempio la numerosità campionaria dovuta ai criteri di inclusione (es. incapacità di rispondere autonomamente al questionario), evidenzia come l'educazione in campo alimentare possa influenzare positivamente alcuni parametri ematici correlati al diabete.

Per quanto riguarda il BMI, sebbene non sia stata riscontrata una correlazione statisticamente significativa, si osservano valori di BMI inferiori alla media nei soggetti con migliori conoscenze alimentari.

Relativamente ai valori glicemici a digiuno, la mancata correlazione statistica potrebbe essere imputata all'eterogenità del dato legata a possibili bias di esecuzione del test e a comportamenti non corretti a breve termine da parte del paziente.

Questa indagine preliminare ha evidenziato l'importanza di educare il paziente a corretti stili di vita che comprendano anche una scelta consapevole in campo alimentare. Pertanto, questo studio è soltanto il primo passo di un'indagine più ampia che verrà condotta nell'ottica di promuovere una formazione del paziente volta a verificare nel tempo le ricadute positive sulle scelte alimentari e sui parametri clinici.

In questo contesto, interventi che mirano all'educazione su abitudini alimentari salutari sono da considerarsi parte integrante della prevenzione e/o terapia di varie malattie croniche quali il diabete ma anche obesità, ipertensione, ecc. (15-22). È stato anche osservato che gli interventi sul semplice aspetto conoscitivo dell'alimento non sono da considerarsi risolutivi per il miglioramento del quadro clinico nel suo complesso, ma potrebbero rappresentare un prerequisito indispensabile per avviare qualsiasi specifico provvedimento educativo alimentare (23, 24). L'approccio esclusivamente prescrittivo della dieta ha rilevato nel tempo numerose difficoltà, risultando a volte controproducente e implicando in molti casi l'abbandono della dieta medesima (25-27).

La gestione integrata della patologia da parte di una équipe multidisciplinare (medico, infermiere, dietista, educatore e tutte le altre figure professionali coinvolte nell'assistenza) potrebbe risultare utile al fine di fornire una educazione appropriata all'autogestione della patologia e alla presa in carico del paziente tramite regolari follow-up. Tale gestione integrata sarà rivolta principalmente al mantenimento delle competenze acquisite e alla prevenzione delle complicanze (28, 29). Ogni nuovo elemento in grado di influenzare

Tabella 2. Livelli di relazione e dipendenza tra variabili (Variabile dipendente: Punteggio Convertito)

	Coefficiente	*Errore Std.*	*rapporto t*	*p-value*	
const	0,774573	0,998307	0,7759	0,4404	
BMI	0,0238480	0,0181097	1,317	0,1921	
Glicemia	0,00443476	0,00207366	2,139	0,0359	**
Età	0,0115478	0,00897047	1,287	0,2022	
Sesso	0,190175	0,212321	0,8957	0,3734	
HbA1c%	−0,134168	0,0664634	−2,019	0,0473	**

l'autogestione della malattia, dovrà prevedere da parte dell'équipe sanitaria uno specifico intervento educativo pianificato e strutturato.

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Air microbial contamination in dental clinics: comparison between active and passive methods

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Summary. The aim of this study was to evaluate the correlation between the microbial air contamination values obtained by active sampling (colony-forming units per cubic metre, CFU/m^3) and by passive sampling (Index of microbial air contamination, IMA) and to calculate the corresponding equations. Air sampling was performed in ten dental clinics (DC), before (T0), during (T1) and after (T2) the clinical activity, for five consecutive days, once a month for a period of three months, for a total of 450 air samplings. The correlation was evaluated using the Spearman test, and a p value below 0.05 was considered statistically significant. A statistically significant correlation was found considering both the results obtained from the total observations and from the single sampling times, T0, T1 and T2. Different correlation patterns were observed stratifying by DC. Both methods were able to evaluate the microbial air quality and highlight critical situations; therefore, both can be used with this aim. However, in particular during the activity, passive sampling resulted more sensitive, and for its simplicity, economy and standardization by IMA, as suggested by several authors, can be suggested for routine monitoring.

Key words: dental clinic, microbial contamination, air, active sampling, passive sampling, correlation

Introduction

Dental clinics (DC) are care settings where the risk of airborne infections is particularly relevant (1-5). The main factor increasing the criticality of the dental environment for airborne infections is the type of instruments used which produce aerosols containing microorganisms from the oral cavity, upper airways and possibly blood. The smaller particles can float in the air over a long period before they settle on surfaces or enter the respiratory tract and penetrate the small passages of the lungs, while larger particles settle easily onto environmental surfaces (5). From the surfaces, microorganisms can be resuspended in the air or can be transferred to healthcare workers' and patients' hands or any other objects or environmental surfaces. Microbiological air sampling represents a useful tool to identify the presence of risk situations and evaluate the effectiveness of the preventive measures undertaken; in this field the Italian Society of Hygiene, Preventive Medicine and Public Health, has given an important contribution (6-8). Active and passive sampling can be used; the active method measures the concentration of viable microorganisms in the air, expressed as colony forming units per cubic metre (CFU/m^3), while passive method measures the rate at which viable micro-

organisms settle on surfaces (9). Passive method has been standardized by the Index of microbial air contamination, IMA (10,11).

The aim of this study was to evaluate the correlation between the CFU/m^3 and IMA values from a multicentre study by Pasquarella et al, 2012 (8).

Materials and methods

Microbial air samplings were performed in ten dental clinics (DC) before (T0), during (T1) and after (T2) the clinical activity, for five consecutive days, once a month for a period of three months. A total of 450 samplings were collected by active sampling and passive sampling, as previously described (8). The analysis of the results was performed by using SPSS 25.0 (IBM SPSS Inc., Chicago-IL). Correlation between CFU/m^3 and IMA was evaluated using the Spearman test, considering the data both in their totality and subdivided by sampling time (T0, T1 and T2) and by clinic. In order to estimate linear regression, n. 5 extreme outliers were removed.

Results

A significant correlation between the results of the two methods was found considering both the results obtained from the total observations and from the single sampling times, T0, T1 and T2 (Table 1). By stratifying the results by DC, the correlation was significant at time T0 for three dental clinics (No 4, 6, 8), at time T1 for 4 DC (No 6, 7, 8, 10), and at time T2 for two DC (No 3, 8). One DC (No 8) presented a significant correlation both considering the single sampling times and the total samplings performed, with a rho of Spearman ranging from 0.785 to 0.811, while for three DC (No 1, 2 5) in any of the sampling times a correlation was found. DC 9 showed a statistically significant correlation for total values, but not for the single sampling times. Although non normal distribution was found, by eliminating the CFU/m^3 outliers, the bivariate pattern was approximately linear and the following equations were found where "x" = CFU/m^3 value and "y" = IMA value: T0: y = 9.46+0.07x; T1: y = 18.71+0.07x; T2: y = 12.39+0.04x. Total: y = 12.23+0.07x.

Conclusions

The results obtained showed different correlation patterns. The strongest correlation between CFU/m^3 and IMA values was found when highest air microbial contamination values were recorded. This finding is consistent with the results reported by Petti et al. in local study, showing a significant correlation for high air microbial contamination levels, but no correlation for low contamination levels (12). Comparing the values of the obtained equations with the relationships from the recommended limits defined by the EU Guidelines

Table 1. Correlation between the CFU/m^3 and IMA values, for sampling time and dental clinic, rho di Spearman (p value)

Dental clinic	Sampling time			
	T0	**T1**	**T2**	**T0, T1, T2**
Dental clinic 1	n.s.	n.s.	n.s.	n.s.
Dental clinic 2	n.s.	n.s.	n.s.	n.s.
Dental clinic 3	n.s.	n.s.	0.719 (0.004)	0.643 (<0.001)
Dental clinic 4	0.676 (0.011)	n.s.	n.s.	0.533 (<0.001)
Dental clinic 5	n.s.	n.s.	n.s.	n.s.
Dental clinic 6	0.598 (0.018)	0.571 (0.026)	n.s.	0.588 (<0.001)
Dental clinic 7	n.s.	0.662 (0.007)	n.s.	0.430 (0.003)
Dental clinic 8	0.555 (<0.032)	0.727 (0.002)	0.811 (<0.001)	0.785 (<0.001)
Dental clinic 9	n.s.	n.s.	n.s.	0.644 (<0.001)
Dental clinic 10	n.s.	0.524 (0.045)	0.530 (0.042)	0.684 (<0.001)
Total	0.497 (<0.001)	0.473 (<0.001)	0.399 (<0.001)	0.606 (<0.001)

T0, T1, T2: before, during, after clinical practice; n. s. not significant

to Good Manufacturing Practice (13), it could be seen that at Grade D, which was proposed as target value in dental clinics, corresponding to 200 CFU/m^3 and 100 CFU/4h (25 CFU/h), the relationship obtained in our study, considering the T1 sampling time, the IMA values corresponding to 200 CFU/m^3 were 32.71 showing, during the activity, a higher sensitivity of the passive sampling. This could be explained considering the high fluctuation of microbial contamination in dental clinics due to the frequent aerosol product (3) and the cumulative measurement of contamination provided by the use of settle plates exposed for one hour (12). Both methods, active and passive, were able to evaluate the microbial air quality and highlight critical situations, so that both can be used with this aim. However, in particular during the activity, passive sampling showed to be more sensitive, and for its simplicity, economy and standardization by IMA, as suggested by several authors (3,10,12), can be suggested for routine air microbial monitoring.

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One-shoulder carrying school backpack strongly affects gait swing phase and pelvic tilt: a case study

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Abstract: The use of backpacks is common to both adults and children and often leads to the onset of musculoskeletal discomforts. Although a large number of studies have focused on the optimal load for children schoolbags, there is no general consensus. Here we report a 13-yr old girl case study, showing the impact of weight and wearing the school backpack on gait parameters. The variation of gait parameters and pelvis angles in different conditions were studied: without backpack (CTRL), or with backpack at 10% Body Weight (10BW), 15% BW (15BW) and 20% BW (20BW), carried "on both shoulders" (2S), "on one shoulder" (1S), or "with one hand" (1H). Swing phase was comparably modified by 2S/20BW and 1S/10BW conditions, suggesting that a lower backpack weight was sufficient to induce gait alterations when carried in asymmetrical conditions. Pelvic tilt, which was preserved by a two-shoulders distributed 10% BW load (2S/10BW), was strongly reduced in asymmetrical condition (1S/10BW), suggesting that a low weight carried on a single shoulder generates postural modifications including reduction of pelvic tilting, which is known to be associated to low back pain.

Key words: backpack load, schoolbag carrying, pelvic angles, back pain

Introduction

The use of backpacks is common to both adults and children and often leads to the onset of musculoskeletal discomforts; therefore, recently a large number of studies have focused on the optimal load for children schoolbags, suggesting a safer schoolbag load of about the 10-15 percentage of body weight (PBW) (1,2). In the landscape of evidences, scientific literature mostly shows cross-sectional study designs in primary school children (1-3). In parallel with the safer weight of backpacks, also the time spent in carrying has been investigated (4), in order to draft guidelines for teachers, parents and children too. However, results are still confusing (5), suggesting that the back pain in children carrying schoolbags might be a multifactorial problem (1,6), associated to gender (3), body mass index (BMI) and/or different biomechanical and physiological response to load (7).

We also hypothesize that backpack wearing habits may as well impact on musculoskeletal system and, in particular, on gait parameters (8). Therefore, here we report a 13-years-old girl case study, showing the impact of weight and wearing the school backpack on gait parameters.

Materials and Methods

Stabilometric and gait analyses were performed on a 13-yr old girl, after parents' consent. Anthropometric data (height, weight, body mass index and percentage of fat mass) were collected. Fat mass (%FM) was tested using bioelectrical impedance analyser

(BIA) (InBody 230; Biospace, Seoul, South Korea). Stabilometric analysis was done through PoData system (Chinesport, Udine, Italy) to achieve plantar pressure body weight distribution, during orthostatic position. Gait analysis was performed using a wearable inertial sensor (G-sensor, BTS Engineer), placed at the level of S1, on a 10-mt walking distance. We studied the variation of gait parameters (speed, percentage of stride length and swing phase) and pelvis angles (tilt, pelvic obliquity and rotation).

The test was performed without backpack, as control (CTRL), or with backpack at 10% BW (10BW), 15% BW (15BW) and 20% BW (20W), carried "*on both shoulders*" (2S), "*on one shoulder*" (1S), or "*with one hand*" (1H). We waited ten minutes between tests.

Results

Anthropometric data were: 52.8 kg weight, 155 cm height, BMI 22 (normal range 17.3-23.3) and 22 %FM (normal range 17-27).

Stabilometric analysis showed asymmetrical body weight distribution on plantar pressure (46% left vs 54% right) at CTRL condition.

Gait analysis showed no differences in gait speed comparing all the different conditions of backpack weight on two-shoulders carrying (2S). However, both gait speed and percentage of stride length (%SL) were reduced in the asymmetrical schoolbag wearing (1S and 1H), independently from PBW backpack weights (10-20BW). Of note, swing phase, which increased accordingly with backpack weight (from 10BW to 20BW conditions), was comparable between the 2S/20BW and 1S/10BW conditions (39.00 ± 4.43 % cycle), suggesting that a lower backpack weight (10BW) was sufficient to induce gait alterations when carried in asymmetrical conditions (1S and 1H). Pelvic angles were modified (CTRL: tilt range 6.7-7.4; obliquity range 10.3-10.6; rotation range 14.3-14.3) according with backpack weights and wearing, showing a progressive reduction of all the parameters (Table 1). Of note, in 2S condition, obliquity and rotation progressively reduced starting from 10BW to 20BW, whereas tilt started to decrease from 15BW. On the contrary, in 1S condition, both tilt and rotation progressively reduced starting from 10BW, whereas obliquity dramatically reduced in 20BW. In 1H, all parameters strongly decreased starting from 10BW and their ranges appeared about 3 degrees in 20BW.

The comparison between CTRL and 2S/10BW conditions – commonly considered the best condition to carry a backpack[2] – showed that a 10% BW backpack load induced the reduction of both pelvic rotation and obliquity, however preserving pelvic tilting angle (Figure 1A).

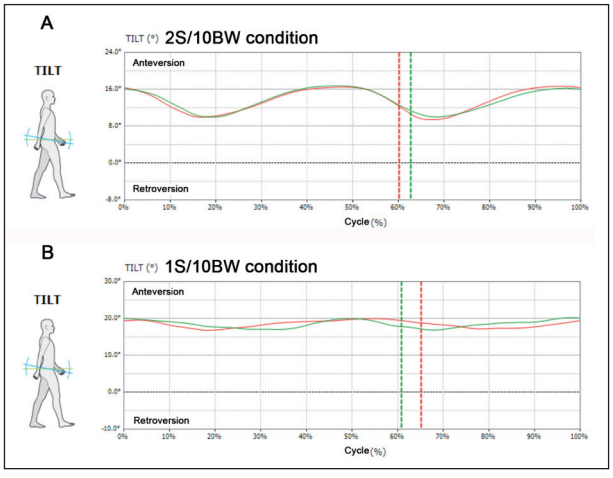

Figure 1. Pelvis tilting range in 2S/10BW (A) and 1S/10BW (B) conditions during left (red lines) and right (green lines) limbs gait cycle.

Table 1. Pelvic angle ranges according with backpack weights and wearing

	2S			1S			1H		
	Tilt (°)	**Obliquity (°)**	**Rotation (°)**	**Tilt (°)**	**Obliquity (°)**	**Rotation (°)**	**Tilt (°)**	**Obliquity (°)**	**Rotation (°)**
10BW	7.2-6.8	5.1-4.7	6.0-5.8	3.1-3.3	9.5-9.9	10.6-10.7	5.6-4.2	8.4-7.8	6.6-6.3
15BW	3.8-4.5	5.0-5.7	7.3-8.0	3.6-3.3	8.7-8.7	6.7-6.8	6.9-4.9	5.0-4.4	6.6-6.5
20BW	3.2-3.2	2.4-2.2	5.5-5.7	5.5-5.5	2.9-2.9	7.2-7.1	2.9-3.8	2.8-2.3	3.9-2.5

Legend. 10BW: backpack at 10% BW; 15BW: backpack at 15% BW; 20BW: backpack at 20% BW;
2S: backpack carried on both shoulders; 1S: backpack carried on one shoulder; 1H: backpack carried on one hand

Conclusions

Our data show that swing phase was comparably modified by 2S/20BW and 1S/10BW conditions, suggesting that a lower backpack weight is sufficient to induce gait alterations when carried in asymmetrical conditions. In this case, moving the load on a single shoulder (1S/10BW), the control of both pelvic rotation and obliquity became less efficient, increasing both these angle ranges. Consequently, pelvis stabilization is obtained minimizing pelvic tilting (Figure 1B), which is known to be associated to low back pain (9). Therefore, prolonged periods of asymmetrical carriage of even light weights (10%BW) generate postural alterations that might predispose to low back pain.

Further research is needed to evaluate the impact of school backpack load and its incorrect carrying on children's health bodies in order to develop evidence-based guidelines and targeted prevention measures.

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The campaign "This Is Public Health" in Italy, set up by a team of Public Health Schools in Northern Italy

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Abstract: Despite the great effort to raise awareness among health promotion, nowadays Public Health policies are not often recognized as important tools. For this reason, the Health in All Policies (HiAP) approach is instrumental in tackling this information gap. In 2018, the US Association of Schools & Programs of Public Health (ASPPH) launched an international campaign called "This is Public Health" (TIPH), whose aim was "to brand public health and raise awareness of how it affects individuals, communities and populations". The Association of Schools of Public Health in the European Region (ASPHER), in coordination with ASPPH, decided to create a European campaign to support and to reproduce the American one, by opening a challenge among the European Public Health Schools. The Schools and Programs of PH of Vita-Salute "San Raffaele" University, Milan, University of Parma, University of Pavia and Politecnico of Milan won this bid. In this "briefing on" we present a report on the Italian project for raising awareness of Public Health among general population and health care personell.

Key words: This is Public Health (TIPH), Health in All Policies (HiAP)

Introduction

It is well known among experts that Public Health (PH) activities are not always well perceived as strategic tools among the Governement policies not only for health protection of populations but also in view of socio-economic development. The general population, especially those working in non-healthcare related fields, underestimates the crucial role of Public Health policies as vaccinations, food & veterinary controls, energy saving, transport regulation, healthcare design and city planning (1-9): these activities are of increasing importance and need more attention from institutions, health care personell and other professionals (10-17). The Health in All Policies (HiAP) approach is instrumental in tackling this information gap (18, 19). Originally conceived in the EU, HiAP is now included in WHO's Sustainable Development Goals.

In the United States, in 2018, the Association of Schools & Programs of Public Health (ASPPH) launched a campaign called "This is Public Health" (TIPH), whose aim was "to brand public health and raise awareness of how PH affects individuals, families, communities, and populations"(20). The Association of Schools of Public Health in the European Region (ASPHER), cooperating with ASPPH, determined to create a European campaign to reproduce the American one. An open bid was set, in which PH Schools affiliated to ASPHER were requested to formulate country-specific proposals. The winners were: Braun

School of Public Health and Community Medicine, from Hebrew University-Hadassah, Department of International Health, CAPHRI, from University of Maastricht, Faculty of Public Health of Sofia Medical University, School of Health and Related Research (ScHARR), from University of Sheffield, Schools of Public Health of Vita-Salute "San Raffaele" University, Milan, University of Parma, University of Pavia and Politecnico of Milan (co-ordinated by the *Accademia Lombarda di Sanità Pubblica*). In addition, ASPHER was secured partial awards to Krakow Institute of Public Health, Jagiellonian University, University of Bologna, and the Faculty of Public Health of Lithuanian University of Health Sciences.(21)

The *Accademia Lombarda di Sanità Pubblica* (22) set up a proposal to increase PH awareness both in the general population and in healthcare workers.

Methods

The preliminary phase was dedicated to the Project setup and was conducted by the ten new Public Health Residents of the Vita-Salute "San Raffaele" University, with the coordination and supervision of the PI and the Schools' Directors. The working group extensively discussed the need for an appropriate translation of the catchphrase and a new graphic rendering of the TIPH logo in Italian language. An agreement was finally reached to adapt all the elements of the campaign, re-elaborating them according to the Italian context. The word "health" has a double meaning in Italian ("*salute*" and "*sanità*"); furthermore, people with limited English proficiency are a large part of the target population. Finally the team eventually has decided for a non-literal translation ("*Per la salute di tutti*").

To further boost the campaign online, the group created "This is Public Health Italy: Per la Salute di Tutti" accounts and pages on the main social media (i.e. Facebook, Twitter, Instagram), determining to set a weekly topic for the posts: they decided for the UN Sustainable Development Goals (SDGs), by examination of them in the scene of Italian situation nowadays.

Subsequently, the PI assigned tasks to each of the team's members from the various PH Schools involved. The operational phase is currently underway, and a series of activities are already in schedule. As an instance, an achievement in progress is to contribute to the health environment of a series of hospitals, starting from San Raffaele Hospital in Milan (affiliated to Vita-Salute University), and Piccole Figlie Hospital, hospital affiliated to the Public health School at the University of Parma. The TIPH team propose is to adopt a number of healthy behaviors from the teaching hospitals connected to the Schools (i.e. healthy eating, not smoking, recycling): posters with specific slogans are being created, hospital attenders as target (healthcare providers, patients and patients' relatives): this contribution has as a purpose to connect the aforementioned healthy gestures to the "This is Public Health – Per la Salute di Tutti" campaign logos (Figure 1).

In addition all laws and resolutions enacted by local governments (Lombardy Region and Emilia Romagna Region) are being thoroughly analysed, to assess their direct or indirect PH impact; this project will be accomplished in collaboration with the Public Health School of University of Bologna, which was awarded with a partial grant in the same APPH-ASPHER campaign.

Spreading the project will be a key for its success. In the next months, multiple promotional events will be organized, addressing both operators and the public at large.

Figure 1. Official logos of the "This is Public Health" campaign from USA, Europe and Italy

Surveys will be administered before and after the events, both to assess baseline knowledge and attitudes towards PH initiatives, and to verify the interventions' effectiveness in raising awareness.

Running a social media photo contest will be a useful option for targeting younger age groups, following in the steps of the US campaign.

Side events will be organized, such as congress, meeting, press conferences, with the purpose of giving the latest updates about the campaign and its importance, in line with the spirit of the project and the previous experiences (Figure 2).

Conclusion

Italy is a challenging country with a struggling economy but a public National Health Service (NHS) able to guarantee to all the population the most important health care with positive health indicators. Despite the current concerns regarding the sustainability of the NHS and a persistent geographic gap (North-South) for budgets and health care outcomes (23, 24) Italy Health System is considered as one of the best performing in the world according to recent international reports.

In light of this scenario, stronger recognition of the role and the importance of PH is essential. PH awareness is ultimately directed at informing policy makers and improving community health (25). While the potential impact of TIPH in Italy is still to be evaluated, the basis for its potential success can only lie in the delivery of a culturally appropriate message. TIPH-Italy is therfore a wonderful opportunity of making PH accessible and comprehensive to health care workers and the general population in an effective and entertaining way.

Figure 2. Pictures of the "This is Public Health" campaign: a) launch day in Milan; b) TIPH event in the USA; c) proposal for an hospital-based campaign in Milan (San Raffaele Hospital).

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COVID-19 in Italy: impact of containment measures and prevalence estimates of infection in the general population

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Abstract: Since the beginning of the COVID-19 epidemic in Italy, the Italian Government implemented several restrictive measures to contain the spread of the infection. Data shows that, among these measures, the lockdown implemented as of 9 March had a positive impact, in particular the central and southern regions of Italy, while other actions appeared to be less effective. When the true prevalence of a disease is unknown, it is possible estimate it, based on mortality data and the assumptive case-fatality rate of the disease. Given these assumptions, the estimated period-prevalence of COVID-19 in Italy varies from 0.35% in Sicily to 13.3% in Lombardy.

Key words: COVID-19, containment, prevalence, mortality

On April 7th, 2020, the number of notified COVID-19 cases in Italy is above 135,000, with almost 17,000 deaths (1). Italy, second only to the US for the number of COVID-19 notified cases, but first for of deaths, is facing an unedited challenge (2). The epidemic is disproportionately hitting some northern areas, pushing the Italian National Health Service capacity of some areas to their limits (3-5).

Lessons from China's successful battle against COVID-19 show how containing measures including cases isolation, contact tracing, and quarantine and mitigation measures, including general lockdown and social (or personal) distancing, seem to have worked (6-8).

As COVID-19 was first reported in Italy (23rd January 2020), the Government has progressively introduced restrictive measures (1,9). The most relevant actions taken by the Government from 25 January to 21 March 2020, are described in Table 1. Prevention measures, taken in late January, such as health-checkpoints in airports and a flight ban from China, rapidly escalated when the first autochthonous cases were detected in the area of Casalpusterlengo, Castelnuovo d'Adda and Codogno in the Lombardy Region (21 February) (Figure 1).

Containment measures at first had been the self-isolation of infected patients and the creation of a "red-zone" in a limited area. Afterward, the Government strategy changed into a severe mitigation response, up to the lockdown to all the country. Other mass-measures were introduced, such as a strong recommendation to avoid at-risk behaviors and the suspension of all non-essential businesses in the entire nation.

The proportion of the infected population in Italy was estimated based on available published Italian data. This preliminary analysis did not consider infections notified within the national surveillance system to avoid biases due to the heterogenous proportion of population tested in different regions (1). The number of official deaths was considered to be less biased; therefore, we included an adjustment in our model due to the undiagnosed deaths, especially in the first phase of the epidemic (10). The average increase of 20% in the number of deaths was introduced accordingly to a recent Italian specific report (11). The adjusted case-

Table 1. Health protection measures against COVID-19 in Italy, 25 January- 23 March 2020

Date	*Public health measure implemented*	*Place*	*Authority*
25/01	**Health checkpoints for passengers** coming from China or from areas where one sustained autochthonous transmission of the new Coronavirus has occurred.	Airports, Italy	Ministry of Health
30/01	**Air traffic from China is banned**	Airports, Italy	Government
21/02	**Mandatory supervised quarantine for 14 days** for all individuals who have come into close contact with confirmed cases of disease; **Mandatory communication** to the Health Department from anyone who has entered Italy from high-risk of COVID-19 areas, followed by **quarantine and active surveillance**.	Public Health department in identified areas	Ministry of Health
23/02	**Red zones**: adoption of an adequate and proportionate containment and management measures in areas with >1 person positive to COVID-19 with unknown source of transmission.	11 municipalities in Lombardy Region	Government
23/02	**Suspension of all public events** or open to the public, of any nature; Schools (all levels), public places, gyms, and other places of aggregation	5 Regions in Northern Italy	Ministry of Health
02/03	**Proposal to extend the "red zone"** to three additional municipalities in the provinces of Bergamo and Brescia from local authorities	Three municipalities in Lombardy Region	(not adopted)
08/03	**The "national" Red Zone**: avoid any movement of people except for motivated by proven work needs or situations of necessity (health, food and assistance); public and private employers should encourage to use days of ordinary leave and holidays and smart working; closing of ski facilities; limit travel and activities and sanitization measures and reduce close contacts	Lombardy Region (and other affected areas in 5 additional regions)	Government
11/03	Suspension of all business activities; **Suspension of all commercial activities non-indispensable for production**. Maximum use by companies of smart-working methods for activities that can be performed at home or remotely. Sanitation of workplace areas.	Italy	Government
23/03	**Extension of the ban on non-indispensable activities.** A list of 80 authorized activities is published. The ban extends limitations on individual freedom and on other business activities that were not explicitly closed by the previous measures.	Italy	Government

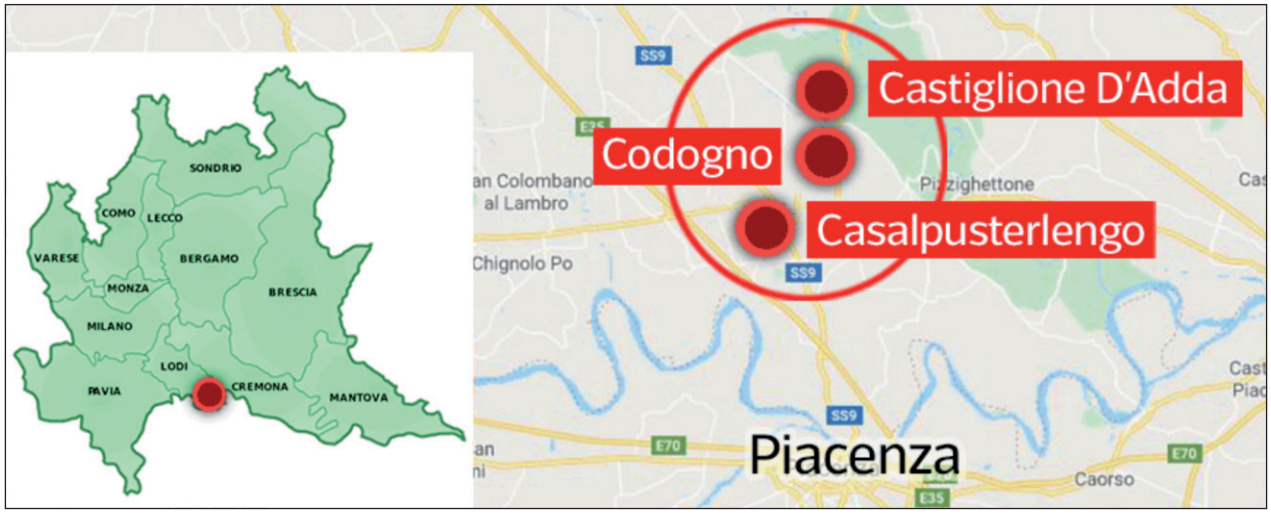

Figure 1. First "Red Zone" Area (February 23rd)

fatality rate for Europe (0.85%) was derived considering the averaged estimates of three reports, two carried out in UK and the other in Italy (12-14). From these parameters, we obtained a model to estimate the current period prevalence in the general population of the 19 Italian regions and the 2 autonomous provinces (Table 2). These data vary among Italian regions from 0.35% infection proportion in Sicily and Basilicata to 11.2% in the Lombardy region and are a useful tool to inform the planning of further containment measures in different geographical areas.

Conclusions

The epidemic showed an evident spread. If we analyze these trends, we can outline the following, preliminary considerations:

a) The measures to suspend flights from China (which were not adopted by other EU countries) and airports' checkpoints with *thermoscan* did not have a significant effect in containing the epidemic.
b) The implementation of a "red zone" in Lombardy effectively contained the spread of the infection within that area. On the other hand, the "red zone" measure did not have the same effect outside that area. In fact, three of the neighboring provinces (Bergamo, Brescia, and Piacenza) recorded the highest incidence rates in the weeks following the establishment of the red zones (1,5). Perhaps these actions were adopted too late (or considering a too small area) when the virus had already spread for several days without notice of it.
c) The failure to establish a second "red zone" near Bergamo in the Municipalities of Alzano and Nembro (Figure 2), despite the proposal of local authorities (on March 3rd), led to a dramatic outbreak with about 10,000 cases in Bergamo with over 1,000 death toll and similar figures in the

Table 2. Population, Number of deaths and estimates of infection period prevalence in the Italian Regions and Autonomous Provinces

Regions and Autonomous Provinces	*Population M (mil)*	*N. of deaths*	*Period Prevalence*
Piemonte (Piedmont)	4.4	1.319	4.3%
V.d'Aosta (Aosta Valley)	0.13	100	11.2%
Lombardia (Lombardy)	10.1	9.484	13.3%
Prov. Aut. Bolzano	0.52	174	4.7%
Prov. Aut. Trento	0.54	244	6.4%
Veneto	4.9	695	2.0%
Friuli-Venezia Giulia	1.3	164	1.8%
Liguria	1.6	620	5.6%
Emilia-Romagna	4.5	2.180	6.9%
Toscana (Tuscany)	3.7	369	1.4%
Umbria	0.88	49	0.78%
Marche	1.5	630	5.8%
Lazio	5.9	238	0.57%
Abruzzo	1.3	172	1.9%
Molise	0.31	13	0.60%
Campania	5.8	216	0.53%
Puglia (Apulia)	4.0	209	0.73%
Basilicata	0.56	14	0.35%
Calabria	1.9	60	0.43%
Sicilia (Sicily)	5.0	125	0.35%
Sardegna (Sardinia)	1.6	52	0.45%
Total Italy	60.4	17.127	4.0%

Figure 2. Missed "Red Zone" Area (March 3rd), from Regione Lombardia & Corriere della Sera

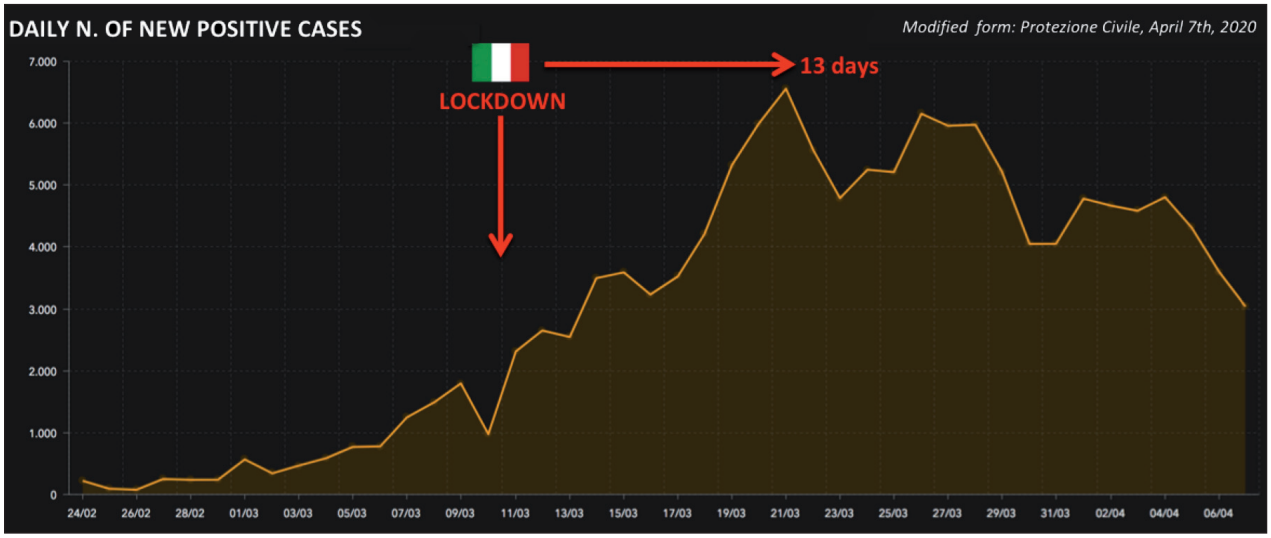

Figure 3. Trend of overall new notified cases in Italy (Protezione civile, 7,4,2020)[1]

neighboring areas (Brescia and Piacenza) (5).

d) General mitigation measures seem to be effective to flatten the epidemic curve of new notified infections (Figure 3) with more effect in controlling the epidemic in the central-southern than in the Northern regions (1).

The difference was in the time when the mass-measures were adopted. At the time of the national lock-down, the central-southern regions only had few circulating cases. Timing appeared to be a crucial factor in determining the effect of mitigation measures (Figure 4).

Overall, containment measures (red zones) and mitigation (general lockdown) can be effective if taken at an early stage of the epidemic ad on large areas. Also, the community management of suspects, contacts, and cases could alleviate hospital burden and perhaps even improve disease prognosis.

The post-epidemic phase might benefit from the availability of forthcoming antibody serological tests. The benefit could be substantial for a large part of the country population, but especially central and southern Italy, that would not yet be infected, as shown by our estimates.

Figure 4. Estimate of Period Prevalence of infected people in the Italian regions as at 7 April, 2020

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