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Influenza Vaccination Coverage in Patients with Chronic Diseases: A Descriptive Analysis

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SUMMARY

Background: Influenza is a major cause of morbidity and mortality worldwide. Individuals with chronic diseases are at greater risk of severe disease or complications. Annual influenza vaccination is fundamental to reduce the burden of disease. Patients with chronic diseases often remain hard to reach and vaccination coverage data are poorly available. The aim of this study is to evaluate the influenza vaccination coverage in subjects from 6 months to 64 years of age with chronic diseases during the 2023/2024 season in Siracusa Local Health Authority, Italy.
Methods: Records of influenza vaccination during 2023/2024 vaccination campaign were matched with the information on chronic diseases. The dataset included information on sex, age, influenza vaccine, chronic diseases, other vaccines administered.
Results: During 2023/24 influenza season, vaccination coverage among the study population was 16.3% and it significantly differed, depending on the underlying disease. The higher VCs were reached in patients with chronic lung diseases (2627/5596; 46.9%), cardiovascular diseases (3250/7009; 46.4%) and chronic liver diseases (105/250; 42.0%), while the lower values were reached in patients with cancers (652/5630; 11.6%) and in patients with chronic inflammatory diseases and bowel malabsorption syndromes (159/1260; 12.6%).
Conclusions: Although influenza vaccination is a safe, effective, and cost-effective method of preventing influenza infection and its complications, VC rates are not satisfactory, and coverage target indicated by Health Authorities remained very far. Reversing this is likely to require a broad range of interventions on patients, caregivers, parents, healthcare providers and health communication.

Keywords: influenza; influenza seasonal vaccination; vaccination coverage; prevention; chronic diseases; high-risk patients; health communication.

INTRODUCTION

With its annual recurrence, influenza is a major cause of morbidity and mortality worldwide, causing 1 billion cases, 3–5 million cases of severe illness and 290,000–650,000 deaths on average each year due to complications (1,2). Some populations, such as older adults, children younger than 5 years, pregnant people, and people with underlying diseases, are at increased risk of complications (2). The burden from seasonal influenza is two-fold. Firstly, there is the direct health impact caused by severe disease and deaths due to influenza. Secondly, there is the economic impact of the large number of mild-to-moderate cases resulting in time off work, losses to production and pressure and costs on health and social care services (3,4).

All population groups can be affected but people with chronic diseases are at more risk of developing severe influenza and influenza-related complications (1,2), because of their frailty, multimorbidity and immunesenescence (5,6).

Annual influenza vaccination is the most effective measure for preventing both influenza and its complications (1,7). Moreover, administering annual influenza vaccines has been shown to be cost-effective

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and imparts substantial health and economic benefits, including an important reduction in lost days of work (8). Therefore, the World Health Organization (WHO) and National Immunization Technical Advisory Groups (NITAGs) recommend annual seasonal influenza vaccination for these at-risk groups (2,9,10), suggesting a flu vaccination coverage (VC) of at least 75% among older adults and individuals with chronic diseases (11). Although the flu vaccine can be less effective in elderly adults and in people with chronic diseases because of their weaker immune systems, and therefore a weaker immune response to the vaccine (6) , older, vulnerable and high-risk individuals exhibit the greatest benefit from vaccination (12–17).

Despite several high-income countries have included flu vaccination recommendations for subjects with chronic diseases in their national immunization schedules, these population groups remain hard to reach for different reasons and vaccination rates remain below target (18,19). This topic is poor investigated in the literature and vaccination coverage data are poorly available. The Regional Office for Europe of the WHO reported a vaccination coverage of 33.8% in Italian residents with chronic diseases (20). A 2019 Italian study investigated the knowledge and attitudes concerning influenza vaccination in a little sample of adults with chronic diseases, in which less than half (42.1%) received influenza vaccine (21).

There is a large population of chronic disease patients in Italy (22), Chronic diseases affected nearly 40% percent of the Italian population, that is, 24 million Italians of whom 12.5 million have multi-chronicity and risk factors often overlap (23). Chronic diseases are more frequent in the older age groups, reaching 85.4% among people over 75 years old (24), but a significant proportion of those patients are relatively young and active (25–27). In terms of geographic area, the regions of South Italy have a significantly higher prevalence of chronic diseases (28). Specifically, in Sicily there is about one million of people with chronic diseases. Despite the large number of patients with chronic diseases, there are no standardized nor systemic data available on the vaccine coverage of these patients. More information is needed about who gets vaccinated.

Thus, the rationale of this study is to evaluate influenza vaccination coverage in subjects with chronic diseases that increase the risk of complications from influenza. Our study was carried out in Siracusa Local Health Authority (LHA), corresponding to the Province of Siracusa, in Sicily, South Italy, with around 383.604 inhabitants, according to ISTAT data, Italian National Statistics Institute (29), where 59,787 inhabitants were vaccinated during the 2023–2024 influenza season, with a general vaccination coverage of 15.6%; of these, 40,889 were 65 years old or older (VC: 46.5%).

METHODS

This is a descriptive analysis to evaluate flu vaccination coverage in subjects from 6 months to 64 years with higher risk of complications from influenza (study population). The reference study period was the last 2023/2024 influenza vaccination campaign (from October 2023 to February 2024).

Vaccination data were extracted from the provincial immunization database of the local Health Department, that routinely collects data on all administered vaccines. It is a computerized vaccination registry containing information on the vaccination history of every inhabitant of Siracusa Local Health Authority; it can also be used to generate an immunization schedule. Records of influenza vaccination during the reference period were matched with the information on chronic diseases, extracted from a platform of Local Health Authority Health Information System, that allows to know the prevalence of several chronic disease among the population.

In the study period, the following vaccines were recommended and offered in active and free of charge in Sicily (30): live attenuated quadrivalent influenza vaccine (LAIV), indicated for subjects aged from 2 to 17 years old; cell culture based inactivated quadrivalent influenza vaccine (QIV-cc), indicated to subjects aged 2 years and older; inactivated quadrivalent influenza vaccine standard dose (QIV-sd), indicated to subjects aged 6 months and older; high dose inactivated quadrivalent influenza vaccine (QIV-hd), indicated to subjects aged 60 years and older; adjuvanted inactivated quadrivalent influenza vaccine (QIV-a), indicated to subjects aged 65 years and older (Table 1).

In Italy, the vaccination of subjects affected by chronic disease is mainly managed by general practitioners or by family pediatricians for children.

The dataset was decoded in order to identify patients with at least one chronic disease, and according to the Italian Ministry of Health (10) the following major risk categories of diseases were identified: chronic lung diseases, cardiovascular diseases, diabetes mellitus, and other metabolic diseases, chronic renal failure/adrenal insufficiency, hematopathies and hemoglobinopathies, cancer, chronic inflammatory diseases and bowel malabsorption syndromes, chronic liver diseases.

Considering that there was a high overlap between the individuals with chronic diseases and older adults and to avoid duplicate statistics of the sample, we only included the individuals with chronic diseases as one of the study populations in this study. In case of comorbidities, we classified the patient according to the disease uploaded in the computerized vaccination registry by the physician at the time of vaccination.

The final dataset was created, including information on sex, age, influenza vaccine, chronic diseases, other vaccines administered.

Table 1. Influenza vaccines used during the study period

Vaccine's type	Abbreviation	Recommendation of Ministry of Health
Live attenuated quadrivalent influenza vaccine	LAIV	subjects aged from 2 to 17 years old
Cell Culture based inactivated quadrivalent influenza vaccine	QIV-cc	subjects aged 2 years and older
Inactivated quadrivalent influenza vaccine standard dose	QIV-sd	subjects aged 6 months and older
High dose inactivated quadrivalent influenza vaccine	QIV-hd	subjects aged 60 years and older
Adjuvanted with MF59 Inactivated quadrivalent influenza vaccine	QIV-a	subjects aged 65 years and older

RESULTS

From the platform of Local Health Authority Health Information System, 76,331 on 294,371 (25.9%) residents up to 64 years of age reported at least one chronic disease. Of those, 55,439 (72.6%) subjects reported one chronic disease, 12,073 (15.8%) reported two comorbidities, 4,009 (5.3%) three comorbidities and 4,810 (6.3%) more than three comorbidities.

During 2023/24 influenza season, 12,428 (16.3%, the study population) of 76,331 subjects from 6 months to 64 years old with at least one chronic disease received the influenza vaccine. Socio-demographic characteristics, comorbidities, types of influenza vaccine administered, and co-administration of other vaccines are shown in Table 2.

Female were 6,506 (52.2%) and the mean age was 50.6 years. The most frequent diseases identified were cardiovascular diseases (n.3,250; 26,2%); chronic lung diseases (2,627; 21.1%); diabetes mellitus and other metabolic diseases (1,968; 15.8%). Overall, these three categories of diseases affect 63.1% of the study population.

Chronic lung diseases, cancer, chronic inflammatory diseases and bowel malabsorption syndromes, hematopathies and hemoglobinopathies are more frequent among females, while cardiovascular diseases, diabetes mellitus/other metabolic diseases, chronic liver diseases and chronic renal failure/adrenal insufficiency are more frequent among males in the study population.

Regarding the distribution of the different vaccines in the study population, about 95% received the

Table 2. Demographic characteristics, chronic diseases (stratify by sex), and co-administration of other vaccines of the study population (12,428 subjects)

	n	%
Gender		
Female	6,488	52,2%
Male	5,940	47,8%
Chronic diseases		
Cardiovascular diseases	3,250	26,2%
female	*1589*	*48,9%*
male	*1661*	*51,1%*
Chronic lung diseases	2,627	21,1%
female	*1437*	*54,7%*
male	*1190*	*45,3%*
Diabetes mellitus and other metabolic diseases	1,968	15,8%
female	*973*	*49,4%*
male	*995*	*50,6%*
Cancer	652	5,2%
female	*453*	*69,5%*
male	*199*	*30,5%*

Chronic inflammatory diseases and bowel malabsorption syndromes	159	1,3%
female	*98*	*61,6%*
male	*61*	*38,4%*
Hematopathies and hemoglobinopathies	119	1,0%
female	*72*	*60,5%*
male	*47*	*39,5%*
Chronic liver diseases	105	0,8%
female	*42*	*40,0%*
male	*63*	*60,0%*
Chronic renal failure/adrenal insufficiency	84	0,7%
female	*35*	*41,7%*
male	*49*	*58,3%*
Other diseases	2,034	16,4%
Other vaccines in addition to the flu vaccine		
COVID-19 vaccines	324	2,6%
Pneumococcal vaccines	523	4,2%
Shingles (herpes zoster) vaccines	126	1,0%

inactivated quadrivalent influenza vaccine standard dose (QIV-sd) (not reported in the table).

During the vaccination campaign 2023/2024, 973 (7.8%) subjects received other vaccines in addition to the flu vaccine: 523 (4.2%) received pneumococcal vaccines, 324 (2.6%) COVID-19 vaccine and 126 (1.0%) shingles (herpes zoster) vaccine (Table 2).

Regarding the vaccination setting, more than 99% of study population were vaccinated by the general practitioner or family doctor (data non reported).

Overall, VC among the study was 16.3% and it differed depending on the underlying disease. The higher VCs were reached in patients with chronic lung diseases (2627/5596; 46.9%), cardiovascular diseases (3250/7009; 46.4%) and chronic liver diseases (105/250; 42.0%). The lower VCs were reached in patients with cancers (652/5630; 11.6%) and in patients with chronic inflammatory diseases and bowel malabsorption syndromes (159/1260; 12.6%). The VCs reached per chronic disease are described in Table 3.

Table 3 - Frequency of chronic disease, number of vaccinated and influenza vaccination coverage (%) of subjects aged between 6 months and 64 years and suffering from at least one chronic disease, per comorbidity.

Chronic disease	n. of people from 6 months to 64 years with chronic disease	n. of vaccinated	Vaccination coverage (%)
Chronic lung diseases	5596	2627	46,9
Cardiovascualar diseases	7009	3250	46,4
Chronic liver diseases	250	105	42,0
Diabetes mellitus and other metabolic diseases	5620	1968	35,0
Chronic renal failure/adrenal insufficiency	332	84	25,3
Hematopathies and hemoglobinopathies	517	119	23,0
Chronic inflammatory diseases and bowel malabsorption syndromes	1260	159	12,6
Cancers	5630	652	11,6

DISCUSSION

The present study described influenza vaccination coverage in subjects from 6 months to 64 years of age with at least one chronic disease during the 2023/2024 season in Siracusa LHA.

Our study showed a VC value of 16.3% in the study population, ranging from 46.9% to 11.6% depending on the underlying disease. These values are very far from the minimum achievable goal [15]. Higher coverage was reached in patients with cardiovascular diseases, chronic respiratory diseases, metabolic disorders (including diabetes mellitus) and chronic liver diseases, while lower VC have been achieved in patients with cancer, chronic inflammatory diseases and bowel malabsorption syndromes and kidney disease. Primary care physicians play a key role in the vaccination of their patients and their presence in the management of those patients could be associated with a higher frequency of vaccination advice in comparison with other chronic medical diseases that are more likely to be followed by different specialist physician rather than a primary care provider (31–34).

In Italy, influenza VC is far from the goal, although it increased in the last years, peaking the highest recorded in the 2020-2021 season with the outbreak of COVID-19 (35). According to the PASSI survey, flu VC in the season 2021/2022 was 28.7% among subjects 18-64 years old with at least one chronic disease, ranging from 20.1% in subjects with chronic liver diseases to 37.5% in subjects with diabetes (36).

In Europe, although all countries recommend flu vaccination in people with chronic diseases, VCR still far from desirable rate (37), despite the trend increased compared to the past. Moreover, VCR data in those subjects are very scarce, with only four countries reported and the coverage level was greater than or equal to 75% in only three countries (37).

During the study period, 30 subjects reporting a history of drugs or alcohol abuse were vaccinated (data not reported in the Table 2). Addicted people experience high rates of communicable disease and a high prevalence of chronic health diseases (38). The European Monitoring Centre for Drugs and Drug Addiction additionally recommends influenza vaccination for those patients (39). Despite these recommendations, addicted people experience barriers to vaccination and there is evidence that flu vaccine uptake among those people is suboptimal (40). There are very few and often self-reported data on VC among addicted people, precluding synthesis of coverage estimates and comparison to general population (41).

Coverage data are critical to understand vaccine uptake and population immunity, enabling Public Health Authorities to assess coverage gaps and to measure trends over time, both of which are key components of every surveillance program. The number of people with chronic diseases has increased (42,43), it is therefore not surprising that the need has also grown for better data on when, where and who received which vaccine. Despite this and the efforts to promote immunization of high-risk subjects are specific objectives of most national immunization plans, many countries report difficulties in estimating VC data regarding the individuals with chronic medical diseases (44). The limited available evidence suggest that those patients are often under-vaccinated, in general less than the elderly, even in countries with well-functioning healthcare systems (20,31). Those impediments may reflect a lack of information systems or other standardized methodologies for making these data available (45). Even if it is more complex to implement a targeted risk-group strategy than an age-based approach, we think it could be very useful to establish homogeneous and standardized methods to quantify VC in other categories in addition to the older ones, such as chronic patients, pregnant women, HCWs, prisoners, drug addicts and others.

Influenza VCR is sometimes characterized by changes triggered by unpredictable events (46). For example, the COVID-19 pandemic has influenced increased acceptance of influenza vaccination in 2020-2021 in people who were previously eligible for the vaccine but routinely unvaccinated, determining the highest VC recorded in the past 15 years (36,47). Conversely, the report of four deaths allegedly caused by administration of an influenza vaccine (the so-called "Fluad case"), dramatically reduced the influenza vaccine uptake, contributing to the failure of the 2014/2015 vaccination campaign (48,49).

Suboptimal coverage is a complex issue influenced by socio-demographic, programmatic and psychological factors (46,50,51). The fact that vaccination rates among at-risk populations remain low despite recommendations indicates a continuing failure to provide appropriate standards of care (52,53). Reversing this is likely to require a broad range of interventions and a multifactorial approach. A review from countries with high influenza VCRs, identified different key factors for a successful influenza vaccination programme and clustered them into five main pillars: health authority accountability and strengths of the influenza programme, facilitated access to vaccination, healthcare professional accountability and engagement, awareness of the burden and severity of disease and belief in influenza vaccination benefit (46).

In our opinion, the most important encouraging factors for reaching higher coverage rates are a proactive behaviour of healthcare workers. High coverage reached in different countries may have been due to the fact that general practitioners were encouraged to proactively recommend the vaccine to their at-risk patients (34). Patients in high-risk clinical groups are more likely to receive an influenza vaccine after they receive information on the benefits of vaccination to their own health compared with social

benefits to others. This correlation is even stronger when the patient perceives themselves as personally at higher risk (32). The role of health communication in delivering correct information exclusively based on facts and scientific evidence (48,49,54), is also crucial.

Our study had several strengths. The first was represented by the large sample and wide range of diseases included in our analysis. Another strength was the use of comprehensive information systems as data sources, and the large number of individuals in the chronic disease management system. This system was opt-in for individuals with certain chronic diseases and an estimated at least 80% of individuals with chronic disease participate in it. Even with poorly available, we reported data on VC among persons with drug or alcohol abuse, a topic little investigated in the literature, although this is a population at elevated risk.

Our study also had some potential limitations, that include the use of only one data source to identify chronic subjects and the lack of data on multiple comorbidities as drivers of flu vaccination. Furthermore, while the dataset offered comprehensive health-related information about the patients' health diseases, certain variables relevant to influenza vaccination behaviour, such as attitudes and beliefs, were not measured, limiting the depth of this study's analysis. However, in our opinion, our study provided useful information about VC among patients at a high-risk of severe influenza.

In conclusion, we think that patients with chronic diseases should be targeted for attaining high VC compared to the remaining population, for whom, annual flu vaccination (and in general every vaccination) should be considered as a critical part of medical care and may be a life-saving act (31,55,56). To effectively address vaccination gaps, it is necessary to understand the key barriers to vaccination in individual with chronic diseases at different levels of the health care delivery systems including the individual, health care provider, and policy level (57).

Any intervention to increase vaccine uptake among patients with chronic diseases should be monitored and evaluated systematically, starting from the quantification and evaluation of VC, to guide development and wider implementation. Coverage data are essential for any surveillance programmes, to understand whether it is sufficient to prevent transmission of disease, to identify gaps in coverage, and to efficiently direct interventions where gaps exist.

AUTHORS' CONTRIBUTIONS

Conceptualization, FC; methodology, FC; acquisition of data, FC, CR; formal analysis and interpretation of data, FC, FB; writing - original draft preparation, FC; writing - review and editing, FC, FB, CF; statistical analysis, FC; supervision and project administration, FC, MLC.

All authors have read and agreed to the submitted version of the manuscript.

INFORMED CONSENT STATEMENT

As this study constituted public health surveillance, ethical approval from the institutional review board was not required. All data were provided and analyzed anonymously.

ABBREVIATIONS

VC: vaccination coverage; VCR: vaccination coverage rates; LHA: Local Health Authority; HCW: health care worker

LAIV: live attenuated quadrivalent influenza vaccine; QIV-cc: cell culture based inactivated quadrivalent influenza vaccine; QIV-sd: inactivated quadrivalent influenza vaccine standard dose; QIV-hd: high dose inactivated quadrivalent influenza vaccine; QIV-a: adjuvanted inactivated quadrivalent influenza vaccine.

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