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Systematic Review and Meta-Analyses

Identifying people at risk for influenza with low vaccine uptake based on deprivation status: a systematic review

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Background: Influenza vaccination is an important public health intervention for controlling disease burden, but coverage rates are still low also in risk groups. In order to identify non-vaccinating subgroups, deprivation and socio-economic indices, i.e. measures used to synthetically describe people's socio-economic status while taking into account several dimensions, may be used. We aimed to synthetize evidence from studies investigating association between deprivation/socio-economic indices and influenza vaccination coverage in population at risk—persons ≥65 years of age, individuals with comorbidities, pregnant women and health-care workers. **Methods:** We searched PubMed, ISI WoS, CINAHL and Scopus to identify observational studies published up to October 10th 2017 in English or Italian. Studies reporting quantitative estimates of the association between deprivation/socio-economic indices and influenza vaccination coverage in populations at risk were included. **Results:** A total of 1474 articles were identified and 12 were eventually included in the final review. Studies were mostly cross-sectional, performed in European countries, from 2004 to 2017. Seven studies focussed on deprivation and five on socio-economic indices. Studies on deprivation indices and vaccination coverage showed that people from the most deprived areas had lower coverage. Regarding socio-economic condition, results were contrasting, even though it may also be concluded that people from lower groups have lower vaccination coverage. **Conclusions:** Our work supports the possibility to identify people likely to have lower influenza vaccination coverage based on deprivation/socio-economic indices. Efforts should be performed in order to further strengthen robustness, transferability and suitability of these indices in addressing public health problems.

Introduction

Seasonal influenza virus circulates worldwide and can affect people in any age group. Depending of the local climate, seasonal influenza epidemics occur mostly during the wintertime while in the tropical regions seasonality is less obvious and can occur at any time of the year. Even though most people will recover completely without any sequelae, the influenza can cause some serious complications, invalidity and even death.[1] Severe infection and influenza-related complications typically occur in pregnant women, children <59 months of life, individuals with chronic medical conditions (such as chronic cardiac, pulmonary, renal, metabolic, neuro-developmental, liver or haematologic diseases), immunocompromised persons and older adults (aged ≥65 years).[2] According to the current statistics, from 291 000 to 646 000 people worldwide die from seasonal influenza-related respiratory illnesses each year. The highest mortality rates were estimated among people aged 75 years or older (51.3–99.4 per 100 000 individuals).[3] In the European region, the European Center for Disease Prevention and Control (ECDC) estimates 44 000 people die every year because of respiratory diseases associated with seasonal influenza.[4] According to annual surveys funded by the ECDC and World Health Organization (WHO), even though 34 000 (over 75%) of these deaths in Europe are among people aged 65 years or over, the vaccine uptake remains low in this group.[4]

Immunization against influenza is an important tool for reducing morbidity and mortality among high-risk patients, including the elderly. Influenza vaccination in population ≥65 years decreases the incidence of disease and hospitalization as well as the risk of influenza-related complications and death.[5,6] The WHO recommends annual influenza vaccinations for specific risk groups, i.e. elderly individuals (≥65 years old), population with chronic diseases, pregnant women, children from 6 months to 5 years old and health-care workers (HCWs).[7] In fact, the HCWs are at risk for acquiring influenza virus infection due to the increased exposure to patients and, at the same time, they are even considered a potential source of transmission.[8] Still, recommendations vary from country to country, even from one region to another and go from universal recommendations across the recommendations for specific risk groups to no recommendation at all.[8] Although, during the eight seasons covered in the VENICE report (2007–08 to 2014–15), an increasing number of Member States recommended the vaccine to high-risk groups as identified by WHO and ECDC.[9] Nevertheless, despite these efforts, the influenza vaccination coverage is unsatisfactory in many countries as reported in the VENICE surveys: vaccination coverage ranged from 1.0 to 76.3% (median 47.6%) for older adults, from 28.7 to 78.7% (median 44.4%) for those with chronic medical conditions, from 0.3 to 58.2% (median 22.6%) for pregnant women and from 5.7 to 54.4% (median 26.9%) for HCWs.[9]

Inequalities in vaccine uptake amongst individuals belonging to different risk groups could be related to several socio-economic factors and determining their role could enable planning targeted interventions and adjustment of vaccination programmes in order to improve the vaccine uptake.[10,11] Socio-economic factors affecting influenza vaccine uptake may vary across different risk groups and also with the type of vaccine (seasonal or pandemic).[11–13] A recent systematic review and meta-analysis[14] on the effect of several single factors on vaccine uptake amongst individuals aged ≥60 years of age in Europe concluded that living alone, being unmarried or an immigrant and residing in a deprived area were associated with lower vaccine intake. On the contrary, no consistent effect was observed for education, social class and urban residence.

The use of socio-economic deprivation indices has been proposed to identify and evaluate the relationship between socio-economic conditions and health.[15,16] In fact, deprivation indices in respect to single factors have the advantage of describing socio-economic status (SES) taking into account several dimensions, while remaining synthetic and easily interpretable.[17] These indices, producing a geographical description of the population's health conditions and approximating the individual's SES according to the area of residence, could be useful to identify populations at higher risk.[15,16] In fact, SES is considered one of the main social determinants of the health status and also of individuals' ability to follow preventive and treatment indications[11] but few studies have specifically focussed on the role played by deprivation indices in determining vaccine uptake.[18–22]

Nonetheless, since the role of deprivation indices is becoming increasingly relevant to develop targeted interventions, we aimed to systematically assess and quantify the association between these indices and influenza vaccination uptake amongst individuals considered at high-risk, through a systematic review of available literature on the topic.

Methods

Literature search

Identification of the potentially eligible studies was carried out in line with the recommendations from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement[23] and through a multi-engine literature search of PubMed, ISI Web of Science (WoS), CINAHL and Scopus databases. Each database was systematically screened using a specific search query as a combination of subject headings and text words, to search for studies published up to October 10th 2017, in English or Italian. The following search query was used to retrieve the potentially eligible studies from PubMed: *((vaccin* OR immuni* OR prevent*) AND (coverage OR campaign OR adherence OR program) AND influenza AND (Index of deprivation OR deprivation index OR socio-economic status OR socio-economic status OR SES OR deprivation status OR ((socio-economic OR socio-economic OR socio-demographic OR socio-demographic AND (indicator OR indicators OR determinant OR determinants)) OR socio-economic position OR socio-economic position OR SEP OR Social determinants of health))*. The search query was appropriately modified for screening the other databases (detailed search queries are available upon request). Cross-linking of the studies retrieved from different databases was performed in order to remove duplicates. Bibliographies of eligible studies were eventually hand-searched to check for additional studies.

Study selection

We considered articles that provided evidence on the association between the deprivation indices or SES and influenza vaccine coverage (pandemic or seasonal) in populations at high-risk. We defined the population of interest as persons at higher risk for influenza infection or its complications, namely persons ≥65 years of age, individuals with documented comorbidities, persons with disabilities, pregnant women and HCWs. Observational studies including cross-sectional, ecological, case-control or cohort studies from any country and study setting (community or nursing home/hospital) were considered eligible. Studies that were conducted only on healthy children or adults exploring single social determinants (i.e. educational level, marital status) or other vaccine-preventable disease vaccination were considered not eligible. We further excluded cost-effectiveness and economic analyses. Finally, reviews, meta-analyses, letters and commentaries were disregarded because they did not report original data. We only included studies provided with full-text articles.

Three couples of reviewers (M.C. and F.F.; S.L. and C.d.W.; G.M. and V.V.) independently screened titles and abstracts of the retrieved articles in order to select the eligible ones. Full texts of the potentially eligible articles were subsequently retrieved and further assessed according to the reported criteria. A valid justification for exclusion was reported and any disagreements were resolved through consensus for the final inclusion.

Data extraction and synthesis

Three reviewers (V.V., M.C. and C.d.W.) independently conducted the data extraction from each article and any difference in opinion was resolved through discussion to reach consensus or in consultation with other co-authors. Data on the first author's name, year of publication, country, flu season and type of vaccination, study design, setting, study population, data source used for the ascertainment of vaccination status, influenza vaccination policy, composition of the deprivation index or SES, vaccine coverage, effect estimates (in terms of relative risks or odds ratios) with 95% CI and variables used for adjusting effect estimates were extracted. In case of multiple articles describing the same study population, we only included the most recent one. When there were missing or incomplete data, authors of the selected articles were contacted to obtain additional information. Because of the significant heterogeneity among the studies, in particular with respect to variables used to develop the deprivation indices and SES, we were not able to perform a quantitative pooling of data through meta-analysis and thus all the information from the included studies was summarized and described through a narrative synthesis.

Quality assessment

In order to assess the methodological quality of the included studies we used the Newcastle-Ottawa Quality Assessment Scale (NOS).[24] Three reviewers (S.L., F.F. and G.M.) independently evaluated each study and disagreements were resolved through discussion or in consultation with other co-authors until the consensus was achieved. The NOS uses a 'star system' and assigns up to a maximum of nine points in three perspectives: the selection of the study groups (four points); the comparability of the groups (two points) and the ascertainment of exposure or outcome of interest for case-control or cohort studies (three points), respectively. Detailed instructions for using the NOS are provided elsewhere.[25] For the cross-sectional studies included in our review, we used the already adapted NOS by Herzog et al.[26] The latter was also used to assess ecological studies. We appraised the quality of the eligible studies without excluding them a *priori* based on the result since valuable conclusions, grounded in data, might be achieved even in the studies with low methodological quality.

Results

Search results and study characteristics

The initial search of PubMed, ISI WoS, Scopus and CINAHL online databases identified a total number of 1474 studies. After removing the duplicates and reading the abstracts and titles, 124 full texts articles were selected to be assessed for further eligibility. By not fulfilling the inclusion criteria, 116 full texts were excluded, leaving 8 eligible studies to be finally included in the review. By closely inspecting the references of the included studies, we additionally identified 4 studies to be added, thus concluding a selection process with a final number of 12 studies included.[27–38] Detailed process of literature search and study selection is presented in figure 1.

Our search covered a wide time interval, including studies published from 2004[30] to the most recent one from 2017.[37] Eligible studies were conducted in high-income European countries, mostly in the UK,[27,29–31,35,38] France,[37] Germany[36] and in Israel[28,32] except for one study from Colombia[33] and one from Canada.[34] Most of the studies used the cross-sectional survey[27–31,33,36–38] while two were ecologic studies[34,35] and one study was case-control.[32] The study setting was represented by community in all studies, except one study that used the hospital setting.[32] Sample size varied greatly across the included studies, with the smallest sample of 806 participants[32] conducted in a hospital setting on patients with malignancies; up to the largest of more than 2.8 million individuals aged ≥ 65 years conducted in the UK.[35]

Most of the studies focussed on participants ≥60 years old,[27–31,33,35] on participants belonging to the clinical-risk groups,[32,38] and special target groups (pregnant women, people with disability, HCWs).[34,36,37] The most common method for ascertaining participants' vaccination status was by using records extracted from the national/regional vaccination databases;[27,29,34,35,37] from the general practitioner's records[30–32,38] and according to self-reporting through interviews or telephone-survey.[33,36] One study did not report the data source used for ascertaining the participants' vaccination

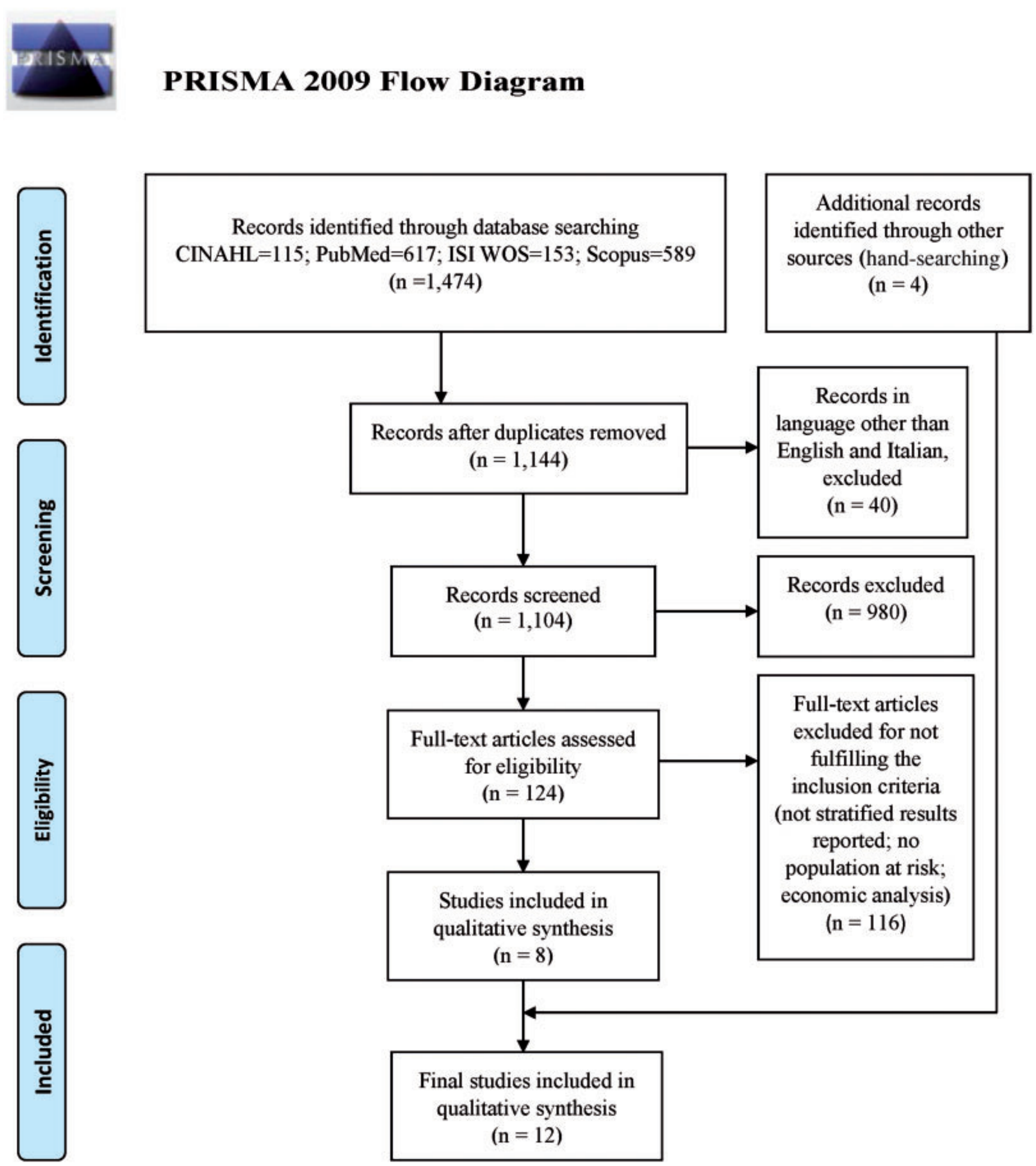

Figure 1 Flowchart depicting literature search and study selection process

status.[28] Influenza immunization was recommended and free of charge in all of the countries/regions for the individuals included in the studies, except for the population from the paper of Schwartz et al.[28] where flu vaccination at no or low cost for individuals having universal health insurance was suggested. Two studies[27,32] did not report specifications about vaccination policies for the included population. Detailed characteristics of the included studies are summarized and presented in the table 1.

Quality assessment

Overall, studies showed good quality, with two studies scoring maximum points[27,34] (Supplementary table S1). Studies demonstrated the highest scores in the exposure/outcome domain section, while the lowest points were given when evaluating the control of the confounding factors in the comparability domain. The confounding bias mostly resulted from the lack of adjustment in the multivariable models used.

Vaccine uptake

Ten studies ascertained the uptake of seasonal influenza vaccination (SIV),[27–33,35–37] with one focussing only on pandemic influenza vaccination (PIV),[34] and one on both.[38] Research expanded from 1997/98 influenza season[30] up to the season 2012/13.[33] Within each included study the vaccine uptake was reported separately for a variety of different interest groups. The highest SIV uptake was recorded by Norbury et al.[29] in the group of people aged ≥65 years and in patients with one or more chronic disease (mean =71.1%; SD =2.9) for the influenza season 2006/07, while the lowest vaccination coverage (mean =23.7%; SD =4.1) was documented in a group of people aged 18–65 years with disabilities for 2007/08 season by Bocquier et al.[37] Regarding the PIV, the mean vaccine uptake was 39.4% (SD =3.0) for the pandemic season 2009/10 in the population belonging to the clinical-risk group[38] and 49.4%, 38.9% and 66.8% in pregnant women, chronically ill people <65 years of age and HCWs, respectively.[34] Vaccine uptake in different risk groups and for the specific deprivation/SES groups are presented in table 2.

Deprivation indices and SES

Seven studies[27,29–31,34,35,38] investigated the association of deprivation indices with the influenza vaccine uptake (SIV alone n = 5, PIV and SIV n = 1, and PIV alone n = 1), and five studies[28,32,33,36,37] used the socio-economic strata to explore the same associations with the SIV uptake. Three UK studies used the Carstairs deprivation index,[29–31] two UK studies used the Townsend deprivation index,[35,38] while the remaining UK study used the Index of Multiple Deprivation (IMD) 2007.[27] The only study that used the material and social deprivation was conducted in Canada.[34] Variables included in the composition of SES varied across the studies.[28,32,33,36,37] Details are summarized and presented in table 1.

Six studies[28,29,32–34,36] used the OR as a measure of association, five[27,30,31,35,37] used the RR, while the remaining study[38] used the incidence rate ratio. Vaccine uptake was negatively associated with deprivation of the area where people were living. In the most deprived areas, subjects were less likely to be vaccinated than those from affluent areas, in people belonging to the clinical-risk group [asthma, chronic obstructive pulmonary disease (COPD), chronic heart disease, chronic kidney disease, diabetes, chronic liver disease, stroke/transient ischaemic attack, central nervous system degeneration and immunosuppression], pregnant women, HCWs[34,38] and people ≥65 years old[27,29–31,35] (table 2). These associations were reported across the included studies regardless of the vaccine type (SIV or PIV), measure of effect or different deprivation groups used as references (most deprived or least deprived category). A less obvious result was reported among the studies that investigated SES of the interest groups and their vaccine uptake. Three studies reported that the individuals from high-risk groups (in particular cancer patients and people with disability)[32,37] and those ≥65 years of age[28] belonging to the highest SES category had a higher probability of SIV uptake than those in the lowest SES category. On the other hand, Gutierrez et al.[33] concluded that persons ≥60 years of age from the upper class had lower odds for influenza vaccination (OR = 0.16; 95% CI: 0.08–0.30), compared to those from lower class. Böhmer et al.[36] also confirmed that the chance of SIV uptake was lower in persons with high SES when compared with persons with low one (OR = 0.74; 95% CI: 0.66–0.84).

Discussion

The results of our systematic review show that people belonging to the most deprived areas have lower influenza vaccination coverage. This evidence is consistently reported by studies included in this review that considered deprivation indices,[27,29–31,34,35,38] even though it is noteworthy to observe that they were mainly performed in the UK. Regarding the socio-economic condition, threes studies[28,32,37] reported overlapping results with respect to those addressing deprivation indices and two[33,36] reported a lower vaccination uptake in people belonging to the richest groups. Nevertheless, these two were the only studies that relied on self-reported vaccination status and did not adjust the analyses for other factors. These two aspects may undermine the robustness of their results and could suggest that overall, the evidence is more in favour of a higher vaccination uptake in wealthier people, independently of the index considered in the analyses.

Inequalities in health among groups belonging to different socio-economic conditions constitute one of the main challenges for public health,[39] as mortality and poorer self-assessments of health are substantially higher in the lower socio-economic groups.[40] Strong evidence from many studies supports an association between low SES and different health conditions. A systematic review and meta-analysis assessed the difference in HbA1c levels among people with type 2 diabetes of different SES, showing higher HbA1c levels in people of low SES as compared to people of high SES.[41] Empana et al. investigated deprivation at the individual level using a multivariable index covering socio-economic and psychosocial dimensions demonstrating an inverse relationship between increasing level of deprivation and ideal cardiovascular health as defined by the American Heart Association.[42] Another recent study showed that patients from the lowest SES had a first stroke earlier than those from the highest, showed more commonly pre-stroke disability and diabetes, and had higher adjusted risk of 1-year mortality.[43]

Socio-economic deprivation was shown to influence mortality after colorectal surgery too, with higher mortality in more deprived socio-economic groups, both in the short- and in the long-term period.[44] Also, the influenza-related hospitalization rates were found higher among persons residing in census tracts including more people living below the poverty level.[45]

The reasons why deprivation influences health status and outcomes may be found also in its relationship with the distribution of health determinants. In fact, an international comparative study conducted by Mackenbach et al. among 22 European countries showed that although inequalities in health associated with SES are present everywhere, their magnitude was highly variable, particularly for inequalities in mortality and from selected causes, suggesting that variations may be attributable to socio-economic differences in lifestyles and access to health-care.[46] With this respect, influenza vaccination uptake can be considered a health-inequality indicator and, therefore, persons living in poorer areas should be targeted for enhanced influenza vaccination outreach.[47]

The results of our systematic review, together with the evidence from the international literature, suggest that decision makers should consider the full range of determinants that may influence

Table 1 General characteristics of the included studies

First author, year	Country (city)	Study design	Study population	*N* of participants	Data source for vaccination status	Influenza vaccination policy	Composition of the deprivation index/SES
Bocquier et al., 2017[37]	France (across the country)	Cross-sectional survey (population-based)[a]	Participants aged ≥18 years with disabilities	12 396	French national survey on health and disability among people living in the community (*Enquête Handicap Santé-Ménages*)	Free of charge for people aged ≥65 years and for people in at-risk groups through vouchers	Education level, occupation and equivalized household income (EHI) per month, which incorporates household size and composition
Breeze et al., 2004[30]	UK (across the country)	Cross-sectional survey (population-based)[a]	Population aged over 74 years excluding people in long-term nursing care or with terminal illness	28 492	General practitioner's records	Recommended and free of charge for persons aged >74 years in 1998	Carstairs' deprivation index-based on four census indicators: low social class, lack of car ownership, overcrowding and male unemployment
Brien et al., 2012[34]	Canada (Montreal)	Ecologic study[a]	Residents aged 6 months or older belonging to the target groups of Canadian influenza vaccination policy	1 842 897	National Public Health Institute of Quebec	Recommended and free of charge for groups at high-risk	Material deprivation (lack of access to goods and services expressed by the proportion of persons lacking a high school diploma, the employment-to-population ratio and the average income); social deprivation (lack of social support expressed by the proportion of persons living alone, the proportion of persons separated, divorced, or widowed and the proportion of single-parent families)
Coupland et al., 2007[35]	UK (across the country)	Ecologic study[a]	Population aged ≥65 years excluding temporary residents	2 808 428	QRESEARCH primary care database v.9	Recommended for patients of all ages from selected high-risk groups. From 2000 this policy was modified to include all persons aged >64 years	Townsend score of patients' area of residence (derived from postcode)
Böhmer et al., 2011[36]	Germany (across the country)	Cross-sectional survey (population-based)[a]	Persons ≥18 years of age belonging to the target groups	21 262	'German Health Update' (GEDA) telephone-survey	Recommended and free of charge for individuals at increased risk (persons aged ≥60 years, pregnant women and persons with chronic underlying diseases, health-care workers)	Self-reported educational, income and professional status (Lampert and Kroll method)
Gutierrez et al., 2016[33]	Colombia (Bogota)	Cross-sectional survey (sample-based)[a]	Persons aged ≥60 years	2000	Self-reported influenza vaccination	Recommended and free of charge for persons ≥60 years	Home-based public services (electricity, water supply, gas, phone); income and expenses; condition of habitation: location of the area in the municipality, accessibility to public transport service
Mangtani et al., 2005[31]	UK (across the country)	Cross-sectional survey (population-based)[a]	Patients aged over 74 years from the UK Medical Research Council Trial of Assessment and Management of Older People in the Community	5572	General practitioner's records	Recommended and free of charge for persons >64 years	Carstairs' deprivation index-based on four census indicators: low social class, lack of car ownership, overcrowding and male unemployment

(continued)

Table 1 Continued

First author, year	Country (city)	Study design	Study population	*N* of participants	Data source for vaccination status	Influenza vaccination policy	Composition of the deprivation index/SES
Sammon et al., 2012[38]	UK (across the country)	Cross-sectional survey (population-based)[a]	Participants aged 0.5–110 years belonging to the clinical-risk groups: asthma, COPD, chronic heart disease, chronic kidney disease, diabetes, chronic liver disease, stroke/TIA, central nervous system degeneration and immunosuppression	708 609	UK General Practice Research Database (GPRD)	Recommended and free of charge vaccination with PIV for persons aged 6 months to 5 years, and with SIV for all those aged >64 years. In both age categories, the other vaccine (SIV and PIV, respectively) was only offered to people belonging to clinical-risk groups	Townsend score of patients' area of residence, or, where this was not available, the area indices of multiple deprivation (IMD) score (which incorporates four variables: unemployment (as a percentage of those aged 16 and over who are economically active); non-car ownership (as a percentage of all households); non-home ownership (as a percentage of all households) and household overcrowding)
Vinograd et al., 2014[32]	Israel (Petah Tikva)	Case-control study (sample-based nested)[b]	Patients with high-risk (metastatic solid tumours, leukaemia, including myelodysplastic syndromes, and all haematopoietic stem cell transplantation recipients) and low-risk malignancy (non-metastatic solid cancer, lymphoma and multiple myeloma)	806	Self-reported (validated by crossing with patients' electronic health records)	NR	Demographic characteristics (dependency ratio, median age, percentage of families with four or more children); education and schooling (percentage of the students studying for a bachelor's or higher degree, percentage eligible for a matriculation certificate); standard of living (level of motorization, percentage of new motor vehicles, average income per capita); labour force statistics (percentage of job seekers, percentage of salaried workers and self-employed persons earning up to minimum wage, percentage of salaried workers earning more than twice the average salary); support/pension (percentage receiving unemployment benefits, percentage receiving income supplements; percentage receiving old age pensions with income supplements)
Norbury et al., 2011[29]	Scotland (across the country)	Cross-sectional survey (population-based)[a]	People aged ≥65 years or patients belonging to the specified clinical-risk groups (CHD, diabetes, stroke or TIA, COPD, or asthma requiring treatment with inhaled corticosteroids)	685 753	Primary Care Clinical Informatics database at the University of Aberdeen and Scottish practices database	Recommended and free of charge for persons aged ≥65 years and for younger people in clinical-risk groups	Postcode-defined Carstairs deprivation score-based on four census indicators: low social class, lack of car ownership, overcrowding and male unemployment
Schwartz et al., 2013[28]	Israel (across the country)	Cross-sectional survey (population-based)[a]	All patients aged ≥65 years members of the Maccabi Health-care Services	136 944	NR	Universal national health insurance provides flu vaccinations at no or low cost	SES defined by the income quartile assigned by zip code of the patient's residence, as defined by the Israeli national census of 1995
Shah et al., 2012[27]	England and Wales (across the country)	Cross-sectional survey (population-based)[a]	Persons aged 65–104 years	387 568	The Health Improvement Network (THIN, CSD EPIC) primary care database	NR	Index of Multiple Deprivation (IMD) 2007 based on seven domains: income deprivation, employment deprivation, health deprivation and disability, education skills and training deprivation, barriers to housing and services, living environment deprivation and crime

a: Community setting.
b: Hospital setting.
NR=not reported; CHD=coronary heart disease; COPD=chronic obstructive pulmonary disease; TIA=transient ischaemic attack; GP=general practitioners; PIV=pandemic influenza vaccination; SIV=seasonal influenza vaccination.

Table 2 Reported associations between the deprivation status and influenza vaccine uptake by population subgroups

First author, year	Flu season	Type of vaccination	Population group at risk	Deprivation group[d] socio-economic strata[e]	Vaccine uptake (%)	Measures of association [OR[a]/IRR[b]/RR[c] (95% CI)]	Variables adjusted for in the model
Bocquier et al., 2017[37]	2007/08	SIV	People aged 18–65 years with disability	0–1 (lowest)[e]	24.7	Ref.	Age, gender, living with a partner, type of residence area, and for whether the respondent answered him/herself or not, number of visits to a GP in the last 12 months, and chronic disease
				2	22.7	0.92 (0.77–1.09)[c]	
				3	20	0.87 (0.72–1.04)[c]	
				4	20.9	0.93 (0.76–1.15)[c]	
				5	22.6	1.10 (0.88– 1.37)[c]	
				6	31.5	**1.51 (1.25– 1.81)**[c]	
			People aged >65 years with disability	0–1 (lowest)[e]	62.4	Ref.	Age, gender, living with a partner, type of residence area, and for whether the respondent answered him/herself or not, number of visits to a GP in the last 12 months and chronic disease
				2	62.7	1.00 (0.96–1.05)[c]	
				3	64.3	1.03 (0.97–1.09)[c]	
				4	67	1.06 (0.99–1.14)[c]	
				5	64.4	1.05 (0.96– 1.14)[c]	
				6	62.2	**1.11 (1.02– 1.21)**[c]	
Breeze et al., 2004[30]	1997/98 – 1999/00	SIV	Population aged over 74 years	Least deprived[d]	NR	Ref.	Age, gender, individual socio-economic position
				2nd quintile		1.04 (0.97–1.12)[c]	
				3rd quintile		1.01 (0.93–1.10)[c]	
				4th quintile		0.98 (0.84–1.16)[c]	
				Most deprived		**0.82 (0.72–0.94)**[c]	
Brien et al., 2012[34]	2009/10	PIV	Pregnant women	Material deprivation[d] (OR for a one-unit increase in deprivation score)	49.4	**0.83 (0.74–0.93)**[a]	Age, gender, priority group status (as a percentage of the neighbourhood population), percentage of immigrants
			Chronically ill <65 years		38.9	**1.09 (1.02–1.17)**[a]	
			Health-care workers		66.8	**0.85 (0.70–0.99)**[a]	
			Pregnant women	Social deprivation[d] (OR for a one-unit increase in deprivation score)	49.4	0.98 (0.87–1.10)[a]	Age, gender, priority group status (as a percentage of the neighbourhood population), percentage of immigrants
			Chronically ill <65 years		38.9	0.99 (0.91–1.09)[a]	
			Health-care workers		66.8	0.99 (0.85–1.17)[a]	
Coupland et al., 2007[35]	1999/00 – 2004/05	SIV	Population aged ≥65	Lowest fifth (most affluent)[d]	15.9	Ref.	Year, gender, ethnicity and rurality
				Second	NR	0.997 (0.995–1.0)[c]	
				Third	NR	**0.993 (0.990–0.996)**[c]	
				Fourth	NR	**0.986 (0.983–0.989)**[c]	
				Highest fifth (most deprived)	12.7	**0.979 (0.975–0.982)**[c]	
Böhmer et al., 2011[36]	2008/09	SIV	Persons ≥60 years, chronically ill, health-care workers	Low[e]	47.7	Ref.	Not adjusted
				Medium	43.7	**Univariate: 0.85 (0.78–0.93)**[a]	
				High	40.3	**Univariate: 0.74 (0.66–0.84)**[a]	
Gutierrez et al., 2016[33]	December 2012	SIV	Persons ≥60 years	Lower class (1–2)[e]	76.6	Ref.	NR
				Middle class (3–4)	76.1	0.89 (0.67–1.18)[a]	
				Upper class (5–6)	36.9	**0.16 (0.08–0.30)**[a]	
Mangtani et al., 2005[31]	2000/01	SIV	Patients >74 years	Least deprived[d]	69.4	Ref.	Age, gender, practice factors, health factors, smoking, marital status
				Second quintile	69.6	0.97 (0.92–1.04)[c]	
				Middle quintile	64.8	0.93 (0.86–0.99)[c]	
				Fourth quintile	70.3	1.03 (0.95–1.13)[c]	
				Most deprived	60.9	0.93 (0.81–1.07)[c]	

(continued)

Table 2 Continued

First author, year	Flu season	Type of vaccination	Population group at risk	Deprivation group[d] socio-economic strata[e]	Vaccine uptake (%)	Measures of association [OR[a]/IRR[b]/RR[c] (95% CI)]	Variables adjusted for in the model
Sammon et al., 2012[38]	2009/10	PIV	Patients from the 'clinical risk group'	1 (least deprived)[d]	41.8	1.03 (0.98–1.08)[b]	Any variable found to be predictive of either SIV or PIV uptake at a significance level of *P*<0.2
				2	42	**1.04 (1.01–1.08)**[b]	
				3	40.2	Ref.	
				4	36.7	**0.92 (0.89–0.96)**[b]	
				5	34.7	**0.88 (0.83–0.93)**[b]	
				Unknown	40.7	**0.90 (0.82–0.98)**[b]	
		SIV	Patients from the 'clinical risk group'	1 (least deprived)[d]	65.8	1.04 (1.00–1.07)[b]	
				2	65.6	1.03 (1.00–1.05)[b]	
				3	62.9	Ref.	
				4	60.6	0.98 (0.95–1.00)[b]	
				5	59.5	0.98 (0.94–1.01)[b]	
				Unknown	60	**0.92 (0.85–0.98)**[b]	
Vinograd et al., 2014[32]	2010/11	SIV	Patients with cancer	5–10 (least deprived)[e]	NR	Ref.	Not adjusted
				1–4		**0.53 (0.34–0.81)**[a]	
Norbury et al., 2011[29]	2003/04	SIV	People aged ≥65 years and patients with one or more chronic disease (CHD, stroke/TIA, diabetes, asthma, COPD)	1 (affluent)[d]	72.9	Ref.	Patients' characteristics
				2	70.8	**0.92 (0.87–0.96)**[a]	
				3	68	**0.92 (0.88–0.96)**[a]	
				4	69	**0.89 (0.85–0.93)**[a]	
				5	66.3	**0.86 (0.82–0.90)**[a]	
				6	64.3	**0.79 (0.75–0.83)**[a]	
				7 (deprived)	61.2	**0.75 (0.70–0.80)**[a]	
	2006/07	SIV	People aged ≥65 years and patients with one or more chronic disease (CHD, stroke/TIA, diabetes, asthma, COPD)	1 (affluent)	75	Ref.	
				2	73.5	**0.88 (0.84–0.92)**[a]	
				3	71.4	**0.90 (0.86–0.94)**[a]	
				4	72	**0.86 (0.82–0.90)**[a]	
				5	71	**0.82 (0.78–0.86)**[a]	
				6	68.1	**0.78 (0.74–0.82)**[a]	
				7 (deprived)	66.8	**0.72 (0.68–0.76)**[a]	
Schwartz et al., 2013[28]	2008/09	SIV	Patients aged ≥65 years	Low[e]	66.6	**0.72 (0.68–0.77)**[a]	Age, gender, rural residency, socio-economic status, region of origin, immigrant status, Holocaust survivorship, number of chronic medical conditions, number of primary care visits in the past 5 years, number of days of hospitalization in the past 5 years, primary physician's region of origin and gender
				Low–mid	65.6	**0.74 (0.71–0.77)**[a]	
				Mid–high	69.5	**0.82 (0.79–0.85)**[a]	
				High	76	Ref.	
Shah et al., 2012[27]	2008/09	SIV	Population aged ≥65 years	Least deprived[d]	NR	Ref.	Age, gender, region, area deprivation, registration length, dementia/care home status and co-morbidity indicator
				2nd quintile		**0.99 (0.98–0.99)**[c]	
				3rd quintile		**0.97 (0.96–0.97)**[c]	
				4th quintile		**0.95 (0.94–0.96)**[c]	
				Most deprived		**0.93 (0.92–0.94)**[c]	

a: Odds ratio.
b: Incidence rate ratio.
c: Risk ratio.
d: Deprivation group.
e: Socio-economic strata.
Text in bold indicates statistically significant finding.
Ref.=reference; PIV=pandemic influenza vaccination; SIV=seasonal influenza vaccination; NR=not reported; CHD=coronary heart disease; COPD=chronic obstructive pulmonary disease; TIA=transient ischaemic attack; GP=general practitioners.

health outcomes when designing public health interventions and should work toward mitigating social and health shocks to protect people already experiencing frail socio-economic condition. With this respect, the use of deprivation indices for identifying frail people could be useful, even though they show general problematic aspects that should be mentioned. Firstly, deprivation indices are useful measures to analyze health inequalities but they are constructed by several methods,[48–51] therefore it can be difficult to choose a valid and reliable index for studying different phenomena, even if they have been proven to be useful in identifying patterns of inequalities in health outcomes.[48–55] The different used methods answer to the different ways of empirically defining deprivation, namely 'any disadvantage of an individual or human group, related to the community or society to which the individual or human group belongs, and these disadvantages can be of social or material nature'.[51,52] As a consequence, measuring deprivation requires the identification of two main issues: which indicators will be used to construct a deprivation index and how to combine them. The criteria for choosing different indicators that compose deprivation indices can vary according to the theoretical approach that foreshadow the methodological development of the index.[56–58]

Two main approaches can be described: a top-down and a bottom-up approach.[57–59] In the top-down approach, the variables composing the index are chosen according to the theoretical definition of deprivation and, in some cases, according to the specific aim at the basis of the index computing without any early consideration about statistical issues. In the bottom-up approach a wide group of variables, usually covering all or the main aspects of the demographic and socio-economic characteristics of the study population, are considered and then reduced to a more manageable number through statistical means. Other important empirical aspects affecting the computing of indices are the availability of information (national census, local databases, etc.); the territorial extension of the index (i.e. computed for a nation or smaller areas) and the geographic level at which they can be computed (census tract, municipality, etc.). Finally, although widely used in public health, deprivation indices are rarely validated, except in few mainly British and Italian studies.[54,57,59–63] Validating a deprivation index means verifying whether it adequately reflects the reality being measured and this is possible, for instance, by comparison with other synthetic indicators that, at the same geographic level, describe specific aspects of the deprivation concept and for which the direction of the relationship with deprivation is well-known.[59]

All these considerations about deprivation indices should be considered among the limits of our review. Other limitations are represented by the inclusion of only published studies, which means that publication bias cannot be ruled out. Furthermore, we did not search in the grey literature and, as only studies written in English or Italian were considered, we may have missed some relevant studies published in other languages. Most of the included studies were cross-sectional survey, which can be considered as a limitation, although the information on vaccine uptake was obtained in most cases from national/regional registries and database or at least validated by crossing with patients' electronic health records. Another critical point is that the raw data were not available even after contacting the principal investigator and that groups being compared were defined according to different indices and cut-offs. Further, we did not investigate reasons for not accepting the vaccine; however, this was not the purpose of this study. A meta-analysis was not performed due to the heterogeneity in considered indices and compared groups. Nonetheless, results from multivariate analyses were shown in tables since they provided a more comprehensive and robust overview of results. In addition, our findings might not be generalizable to other populations from middle and low-income countries, since most of the included studies were conducted in high-income countries, which makes challenging the translation of the evidence into other health-care systems.

Our study also has several strengths. The thoroughness of the search strategy, the double-blind evaluation, the focus on different risk groups and the attempt to provide a comprehensive synthesis of the available evidence are definitely strengths of this study. The search, in fact, covered a wide time interval, including studies that evaluated different influenza seasons and both pandemic and seasonal influenza vaccination. In addition, influenza vaccination policies and the composition of deprivation indices/SES were explained in detail in most of the included studies. This aspect allowed us to have a good insight into the complex relationship between socio-economic and deprivation status and influenza vaccine uptake in different risk groups and across different countries/regions.

In conclusion, this systematic review, to the best of our knowledge, is the first that, through a systematic and thorough approach, focussed on the relationship between influenza vaccination uptake and deprivation and SES in populations where the influenza vaccination is recommended, highlighting the importance of strengthening interventions tailored to the different population categories.

Supplementary data

Supplementary data are available at *EURPUB* online.

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