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Original article

Temporal patterns and potential missed opportunities in pneumococcal vaccination among adults with diabetes: A population-based cohort study

Jacopo Lenzi [a,*], Marco Montalti [b,c], Zeno Di Valerio [d], Valeria Frassineti [e], Paolo Benetti [a,e], Rossella Messina [a], Simona Rosa [a], Andrea Casadei [b], Maria Pia Fantini [f], Paolo Di Bartolo [b,g], Davide Gori [a], Giulia Silvestrini [e]

[a] Department of Biomedical and Neuromotor Sciences, University of Bologna, Via San Giacomo 12, 40126 Bologna, BO, Italy
[b] Department of Medical and Surgical Sciences, University of Bologna, Via Giuseppe Massarenti 9, 40138 Bologna, BO, Italy
[c] Rubicone and Cesena–Valle del Savio Health Districts, Romagna Local Health Authority, Via San Lorenzino 23, 47521 Cesena, FC, Italy
[d] Department of Epidemiology of the Lazio Regional Health Service, Local Health Authority "Roma 1", Via Cristoforo Colombo 112, 00147, Rome, RM, Italy
[e] Department of Public Health, Romagna Local Health Authority, Via Fiume Montone Abbandonato 134, 48121 Ravenna, RA, Italy
[f] Alma Mater Professor, University of Bologna, Via Luigi Zamboni 33, 40126 Bologna, BO, Italy
[g] Diabetology Unit, Romagna Local Health Authority, Via Fiume Montone Abbandonato 134, 48121 Ravenna, RA, Italy

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ABSTRACT

Pneumococcal vaccination is recommended for adults with diabetes because of their increased risk of pneumococcal disease, yet uptake remains suboptimal. This population-based retrospective cohort study assessed temporal patterns and factors associated with first recorded pneumococcal vaccination among adults with diabetes in the Romagna Local Health Authority, Italy, using linked administrative healthcare databases. We included 77,138 individuals (57,113 prevalent and 20,025 incident cases) followed through June 30, 2024. Monthly coverage was estimated using a person-time approach; time to vaccination and associated factors were examined using Kaplan–Meier, Cox, and competing-risks methods.

Coverage increased from 7.2% in January 2017 to 28.0% in June 2024 but remained below 30%, with the largest monthly gains occurring during influenza vaccination seasons. In the incident cohort, the estimated cumulative probability of vaccination was 4.4% at one year, 12.6% at three years, and 34.8% at seven years, without a marked early increase after cohort entry. Age showed the strongest association with uptake, peaking at 60–69 years. Foreign citizenship was associated with markedly lower uptake, while associations with sex and comorbidity were more modest; comorbidity-related estimates were attenuated or reversed when death was treated as a competing event. Contextual factors showed limited associations.

Recorded pneumococcal vaccination was low and delayed. The temporal pattern was compatible with incomplete integration into diabetes care pathways and suggested potential missed opportunities for timely vaccination, although the responsible mechanisms could not be distinguished. Systematic assessment at predefined healthcare contacts should be evaluated to reduce vaccination delays.

1. Introduction

Adults with diabetes are at increased risk of pneumococcal disease, including bacteremia and pneumonia [1,2]. This elevated vulnerability underpins longstanding recommendations for pneumococcal vaccination in national and international guidelines [3,4]. Despite this strong clinical rationale, uptake among adults with diabetes remains suboptimal in many settings [5–7].

Current international immunization strategies increasingly place adult vaccination within a life-course approach and efforts to strengthen resilient primary healthcare systems [8]. Within this approach, adults with chronic conditions are a key target population because they often require additional or adapted recommendations beyond routine age-based schedules [3,4]. Recent policy changes following introduction of the 20-valent pneumococcal conjugate vaccine (PCV20) have simplified adult schedules in some programs by allowing a single PCV20 dose

* Corresponding author.
E-mail address: jacopo.lenzi2@unibo.it (J. Lenzi).

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instead of sequential conjugate–polysaccharide vaccination [9,10]. Diabetes-targeted pneumococcal vaccination nevertheless remains an example of risk-based adult immunization whose delivery requires healthcare systems to identify eligible individuals through clinical information, record vaccination status, communicate recommendations, and offer vaccination during routine care [4,5]. Yet coverage in risk groups remains incompletely monitored, leaving uncertainty about how recommendations are implemented in practice [5].

In Italy's decentralized National Health Service, national plans define eligibility and free-of-charge entitlement, while regions and Local Health Authorities (LHAs) translate these recommendations into operational arrangements that may vary across territories and over time. Throughout the study period, national policy provided for active offer to the annual cohort turning 65 and free-of-charge pneumococcal vaccination for adults with diabetes regardless of age [3,11].

Most evidence on pneumococcal vaccination in high-risk populations remains cross-sectional. A U.S. claims-based cohort of adults newly diagnosed with chronic conditions found that uptake remained low for several years after diagnosis and increased with healthcare encounters [12], but longitudinal population-based evidence remains scarce. In particular, little is known about the timing of vaccination relative to key points in diabetes care, such as diagnosis, routine follow-up, or specialist visits, or about the pathways through which later vaccination occurs. These questions matter because the public health value of risk-based vaccination depends not only on formal recommendations but also on their systematic translation into routine care for people with chronic conditions [8,13].

Understanding uptake as a dynamic process, rather than a static outcome, may reveal delays, missed opportunities, and inequities that aggregate coverage estimates cannot capture. Evidence from other settings indicates that vaccination uptake reflects the interaction of healthcare access, repeated healthcare contact, structural barriers, and individual attitudes [6,12–14]. Disparities have also been reported across sociodemographic groups, including by sex, socioeconomic status, and migration background, even within universal healthcare systems [5–7,15]. These patterns underscore the value of population-level longitudinal analyses that jointly characterize temporal dynamics and individual- and contextual-level determinants.

The aim of this study was to assess pneumococcal vaccination uptake among adults with diabetes in a large population-based cohort, focusing on its temporal dynamics and determinants. By integrating time-to-event analyses with the evaluation of individual and contextual factors, we sought to characterize how uptake unfolds in routine practice and inform strategies for stronger integration into chronic care pathways.

2. Methods

2.1. Study population and data sources

The study population was identified through deterministic linkage of administrative healthcare databases from Romagna's LHA (Emilia-Romagna Region, Italy), covering approximately 1.12 million residents. Individual-level data from multiple sources were linked using unique patient identifiers to construct a comprehensive longitudinal dataset.

The following data sources were used:

(i) the regional population registry (*Anagrafe assistiti*), including all individuals covered by the Italian National Health Service;
(ii) the exemptions database, recording fee exemptions for chronic conditions, including diabetes (code 013);
(iii) hospital discharge records (*Schede di dimissione ospedaliera*), containing information on each hospital discharge from public and accredited private hospitals, with diagnoses and procedures coded according to the ICD-9-CM classification;
(iv) outpatient pharmaceutical dispensing databases, capturing medications dispensed through community pharmacies or directly by healthcare facilities, classified according to Anatomical Therapeutic Chemical (ATC) codes; and
(v) the mortality registry, providing dates and causes of death coded according to ICD-10.

Two cohorts of adults with diabetes were defined: a prevalent cohort and an incident cohort.

2.1.1. Prevalent cohort

The prevalent cohort included all individuals aged ≥18 years, resident in Romagna's LHA, alive on January 1, 2017, and meeting at least one of the following criteria [16]:

(i) an active exemption for diabetes (code 013);
(ii) at least one hospital discharge between January 1, 2014 and December 31, 2016 with a primary or secondary diagnosis of diabetes mellitus (ICD-9-CM 250.xx), excluding admissions related to pregnancy, childbirth, and puerperium (MDC 14); or
(iii) at least two dispensations of antidiabetic medications (ATC codes A10A or A10B) within a 365-day period during the same time window.

To ensure complete observability of healthcare utilization and minimize misclassification due to migration or temporary loss of registration, individuals were required to be continuously present in the population registry from January 1, 2014 to December 31, 2016. In the absence of direct information on residential mobility, continuity was assessed through presence in the registry on January 1 of each year.

Follow-up for the prevalent cohort started on January 1, 2017.

2.1.2. Incident cohort

The incident cohort included individuals aged ≥18 years, resident in the study area, who were newly identified as having diabetes between January 1, 2017 and December 31, 2023, based on the first occurrence of at least one of the following criteria [16]:

(i) assignment of a diabetes exemption (code 013);
(ii) hospital discharge with a diagnosis of diabetes mellitus (ICD-9-CM 250.xx, excluding MDC 14); or
(iii) the second dispensation of antidiabetic medication (ATC A10A or A10B) within a 365-day period.

The index date was defined as the earliest occurrence of these events.

2.1.3. Follow-up

To ensure complete observability of follow-up, all participants were required to remain registered in the study area while alive and under observation. Continuity was assessed through presence in the population registry on January 1 of each subsequent calendar year through 2023. Death ended follow-up and was not treated as loss of registry continuity. In the absence of direct information on residential mobility, these annual registry checks were used as a proxy for continued residence. Individuals residing in Montecopiolo or Sassofeltrio—municipalities transferred from the Marche Region to the Province of Rimini in 2021 and lacking complete historical data over the study period—were excluded.

All individuals were followed from cohort entry until June 30, 2024 or death, whichever occurred first. Follow-up duration ranged from a maximum of approximately 7.5 years for prevalent cases to a minimum of 6 months for incident cases entering the cohort at the end of 2023, and could be shorter in the event of early death.

2.2. Covariates

A set of individual and contextual variables potentially associated with pneumococcal vaccine uptake was considered.

2.2.1. Individual characteristics

Baseline characteristics assessed at cohort entry included sex, age, citizenship, and municipality of residence. Changes in residence within the study area during follow-up were not considered.

Comorbidity burden was measured using the Charlson Comorbidity Index [17], derived from hospital discharge records using ICD-9-CM codes and categorized as 0, 1, and $\geq$ 2 conditions to improve interpretability and avoid sparse categories. Comorbidities were identified from the index hospitalization (when applicable) and from all hospitalizations occurring in the two years preceding cohort entry, using a two-year look-back period consistent with previous studies based on administrative data [18–20]. Diabetes-related conditions were excluded from the score.

Alternative comorbidity measures, including Elixhauser-based scores and the Modified Chronic Disease Score (M-CDS) [21–24], were also explored in descriptive analyses and preliminary models but were not retained in multivariable analyses due to limited additional discriminative value and distributional imbalances in the study population.

In addition, diabetes-related complications were identified using ICD-9-CM diagnosis and procedure codes from hospital discharge records in the same two-year look-back period (see Supplementary Table S1 in the Appendix) [25].

A proxy indicator of potentially unstable metabolic control was defined, in the incident cohort only, as exclusive treatment with insulin and analogues (ATC code A10A) during the first six months after cohort entry.

2.2.2. Contextual characteristics

Contextual variables were defined at the municipality level using official classifications from the Italian National Institute of Statistics (Istat). These included altitude zone (inland mountain, inland hill, coastal hill, or plain) and degree of urbanization (city, towns and suburbs, or rural area), based on population density and spatial contiguity criteria defined within the European statistical framework.

2.3. Pneumococcal vaccination

At study onset, the 2017–2019 National Immunization Plan recommended pneumococcal vaccination both for the annual cohort turning 65 and for adults with diabetes irrespective of age. It identified seasonal influenza vaccination as an appropriate co-offer opportunity but also specified that pneumococcal vaccination could be administered independently at any time of year [11]. Emilia-Romagna adopted this framework in April 2017 [26]. The 2023–2025 national and regional plans retained both eligibility pathways, updated adult conjugate vaccine recommendations, and placed greater emphasis on provider networks and integration within chronic care pathways [3,27]. In May 2024, near the end of follow-up, a regional agreement formalized and strengthened year-round delivery and general practitioner participation [28]. Because operational implementation was determined at regional, LHA, and local service levels, the timing and intensity of these arrangements could vary across territories and over time.

Information on pneumococcal vaccination was obtained from the regional vaccination registry. The authorized extract covered all pneumococcal vaccine administrations recorded across Romagna's LHA from January 1, 1997, through June 30, 2024, including administrations occurring before cohort entry. Records before January 1, 1997 were not available for analysis. Because a 23-valent pneumococcal polysaccharide vaccine had been authorized in Italy in 1992 [29], administrations occurring between 1992 and 1996 could not be captured.

The analytic extract contained the administration date for each pneumococcal vaccination record and a general pneumococcal classification. Although the source information systems contain additional fields, vaccine formulation, brand, and administration setting were not sufficiently complete and uniform across provinces and calendar years for reliable longitudinal analysis. These fields were not included in the authorized extract, in accordance with data-minimization requirements and restrictions intended to limit re-identification risk. Dates of subsequent pneumococcal vaccine administrations were available, but without reliable formulation information they could not be classified as completion of the sequential or repeat-dose schedule recommended at the time. Individual-level linkage to separate influenza or COVID-19 vaccination data was not authorized under the approved study protocol. Consequently, co-administration, delivery within seasonal vaccination campaigns, and vaccination behavior for other vaccines could not be assessed.

Vaccination history was reconstructed using the date of first recorded pneumococcal vaccine administration. Thus, the analyses assessed initiation of recorded pneumococcal vaccination, defined as receipt of at least one recorded dose, rather than vaccine-specific uptake, completion of the recommended schedule, or vaccine-specific protection. This first-recorded-dose definition provided a consistent measure across calendar years and cohorts, but necessarily combined individuals vaccinated under different contemporaneous formulations and recommendations. Vaccinations occurring before cohort entry were used to define baseline vaccination status, whereas vaccinations during follow-up were analyzed as time-to-event outcomes.

2.3.1. Vaccination coverage

For descriptive analyses, pneumococcal vaccination coverage was derived from the same first-dose definition. Individuals contributed as unvaccinated until their first recorded pneumococcal vaccine administration and as vaccinated thereafter; those with a recorded dose before cohort entry were considered vaccinated at baseline.

2.4. Statistical analysis

2.4.1. Population size

This population-based retrospective cohort study included all eligible individuals identified through administrative databases; therefore, no formal sample size calculation was performed.

2.4.2. Temporal trends in vaccination coverage

Monthly pneumococcal vaccination coverage was estimated from January 1, 2017 to June 30, 2024 using a person-time approach.

For each month, the denominator was defined as the total person-time under observation, accounting for cohort entry and censoring due to death. The numerator was defined as the person-time covered by vaccination, with individuals contributing time from the date of vaccination onwards for the remainder of follow-up. An illustrative example of the monthly person-time calculation is provided in Supplementary Box S1.

This approach appropriately weights each individual's contribution according to time under observation within each month and accounts for the cumulative nature of vaccination status over time. Vaccinations occurring before cohort entry were considered at baseline. Monthly coverage estimates for 2024 did not include individuals with a first administrative record of diabetes in that same year, as cohort enrollment was restricted to December 31, 2023.

2.4.3. Uptake of pneumococcal vaccination

Time to first recorded pneumococcal vaccination was analyzed using Kaplan–Meier failure functions, with follow-up censored at death, to estimate the cumulative probability of vaccination over time. This analysis was restricted to the incident cohort, excluding individuals vaccinated before cohort entry. Follow-up was truncated at 7 years to

avoid instability in the tail of the distribution.

Associations between covariates and time to vaccination were estimated using Cox proportional hazards models, with hazard ratios (HRs) and 95% confidence intervals (CIs) as measures of association, including both prevalent and incident cohorts. Follow-up started at cohort entry and ended at vaccination, death, or June 30, 2024, whichever occurred first. Individuals vaccinated before cohort entry were excluded.

Calendar-period effects were not formally estimated in the Cox models. Because time since cohort entry was used as the analysis time scale, calendar time changed during follow-up and was determined by entry date and elapsed follow-up; it was also closely related to cohort definition and potential follow-up duration. Secular changes were therefore examined separately through the monthly coverage analysis rather than represented by a fixed baseline covariate.

Robust standard errors clustered at the municipality level were used to account for potential within-area correlation [30]. The proportional hazards assumption was assessed using Schoenfeld residuals [31]. Given the large sample size, minor deviations from proportionality were interpreted in light of their magnitude and epidemiological plausibility.

Sensitivity analyses were conducted using competing-risks regression [32], treating death as a competing event, to assess whether associations with vaccination uptake changed when death before vaccination was explicitly accounted for.

As a further sensitivity analysis addressing possible differential under-ascertainment of vaccination history by citizenship, the Kaplan–Meier analysis was repeated among Italian citizens in the incident cohort, and the Cox model was repeated after restricting the full study population to Italian citizens.

All analyses were performed using Stata 18 (StataCorp. 2023. *Stata Statistical Software: Release 18*. College Station, TX: StataCorp LLC). A two-sided p-value $\leq$0.05 was considered statistically significant.

2.5. Ethics approval

The study was approved by the Ethics Committee of the Romagna Area (*Comitato etico della Romagna*, C.E.ROM.) on January 23, 2025 (protocol no. 491/2025; study ID 3867).

Authorization to conduct the study was subsequently granted by the LHA through a formal resolution of the Medical Director (no. 1214, April 16, 2025), in accordance with institutional procedures for observational research.

All analyses were performed on pseudonymized data in compliance with Article 9 of the General Data Protection Regulation (EU 2016/679). Under applicable regulations, informed consent was not required, as the data were collected for healthcare management and research purposes and informing individual subjects would have been impracticable or would have required a disproportionate effort.

The study was conducted in accordance with the Declaration of Helsinki and relevant national data protection regulations.

3. Results

3.1. Study population and follow-up

The study population included a total of 77,138 adult individuals with diabetes residing in Romagna's LHA, identified through deterministic linkage of administrative healthcare databases.

Of these, 57,113 (74.0%) belonged to the prevalent cohort as of January 1, 2017, while 20,025 (26.0%) were included in the incident cohort, with entry between January 1, 2017 and December 31, 2023.

Participants were followed until June 30, 2024. Median follow-up was 7.49 years (interquartile range [IQR]: 5.82–7.49) in the prevalent cohort and 4.42 years (IQR: 2.90–5.94) in the incident cohort. Total follow-up amounted to 446,611 person-years.

During the study period, 19,115 deaths were recorded (24.8% of participants; 95% CI: 24.4–25.1), corresponding to a mortality rate of 4.28 deaths per 100 person-years (95% CI: 4.22–4.34).

3.2. Population characteristics

Sociodemographic and clinical characteristics of the study population are presented in Table 1. Overall, 52.5% of individuals were male. Median age at cohort entry was 70 years (IQR: 60–78), with higher values among prevalent compared with incident cases (71 vs. 66 years). The full age distribution is shown in Appendix (Supplementary Fig. S1).

Most individuals resided in lowland areas (85.2%) and in municipalities with intermediate levels of urbanization. The distribution across provinces was relatively balanced, with 35.9% residing in Ravenna, 36.4% in Forlì–Cesena, and 27.7% in Rimini. The most represented health districts corresponded to the provincial capitals.

Foreign citizenship accounted for 3.8% of the overall population and 5.9% of the incident cohort. The most represented citizenships were Albanian (19.6%), Moroccan (11.9%), Romanian (11.7%), and Ukrainian (7.6%), together accounting for 50.8% of foreign citizens; the full distribution is shown in Supplementary Fig. S2.

Comorbidity indices were strongly skewed toward lower categories. According to the Charlson Comorbidity Index (2005 version), 84.5% of individuals had a score of 0, while 87.4% had a Moore's Elixhauser score $\leq$ 0. The M-CDS had a median value of 3 (IQR: 2–6).

Previous diabetes-related complications were documented in 2.2% of patients. Among incident cases, a proxy indicator of unstable metabolic control was identified in 2.0% of individuals.

3.3. Temporal trends in pneumococcal vaccination coverage

Temporal trends in pneumococcal vaccination coverage are shown in Fig. 1, with detailed monthly estimates overall and by sex, age group, and citizenship provided in Appendix (Supplementary Table S2).

Between January 2017 and June 2024, pneumococcal vaccination coverage increased from 7.2% to 28.0%. The overall trend was upward but non-linear, characterized by stepwise increases interspersed with periods of relative stability.

Coverage first rose in late 2017 and exceeded 10% in January 2019. Across study years, the largest month-to-month increases generally clustered between October and January, coinciding with the usual influenza vaccination campaigns. This seasonal concentration was most pronounced between late 2019 and early 2021, when coverage increased from approximately 11% to over 19%. A further increase to around 22% occurred during 2021–2022, followed by slower but sustained growth during 2023–2024, reaching the highest value at the end of follow-up.

Despite this upward trajectory, overall coverage remained below 30% throughout the study period.

3.4. Uptake of pneumococcal vaccination in the incident cohort

The cumulative probability of vaccination in the incident cohort is shown in Fig. 2 using a Kaplan–Meier failure function. The event was the first recorded pneumococcal vaccination after cohort entry, and follow-up was truncated at seven years.

The estimated cumulative probability increased gradually throughout follow-up, without a marked early increase after cohort entry. At one year after cohort entry, it was 4.4%, increasing to 8.3% at two years and 12.6% at three years. It reached 22.4% at five years, 27.4% at six years, and 34.8% at seven years.

3.5. Determinants of pneumococcal vaccination uptake

Results from the multivariable Cox proportional hazards model are reported in Table 2.

Age at cohort entry showed the strongest association with vaccination uptake, with a clear gradient relative to the reference group (18–39

Table 1
Sociodemographic and clinical characteristics of the study population with diabetes in the Romagna Local Health Authority, overall and by cohort (prevalent cohort as of January 1, 2017 and incident cohort through December 31, 2023).

	All	Prevalent	Incident
	(n = 77,138)	(n = 57,113)	(n = 20,025)
Sex			
Male	40,520 (52.5%)	30,227 (52.9%)	10,293 (51.4%)
Female	36,618 (47.5%)	26,886 (47.1%)	9732 (48.6%)
Age at cohort entry, years			
Mean [SD]	68.4 [13.5]	69.8 [13.1]	64.5 [14.0]
Median [IQR]	70 [60–78]	71 [62–79]	66 [56–75]
Age group at cohort entry, years			
18–29	798 (1.0%)	450 (0.8%)	348 (1.7%)
30–39	1503 (1.9%)	873 (1.5%)	630 (3.1%)
40–49	4618 (6.0%)	2830 (5.0%)	1788 (8.9%)
50–59	11,505 (14.9%)	7437 (13.0%)	4068 (20.3%)
60–69	19,368 (25.1%)	14,022 (24.6%)	5346 (26.7%)
70–79	22,707 (29.4%)	17,673 (30.9%)	5034 (25.1%)
80–89	14,111 (18.3%)	11,647 (20.4%)	2464 (12.3%)
≥90	2528 (3.3%)	2181 (3.8%)	347 (1.7%)
Citizenship			
Italian	74,184 (96.2%)	55,341 (96.9%)	18,843 (94.1%)
Foreign	2954 (3.8%)	1772 (3.1%)	1182 (5.9%)
Province of residence			
Ravenna	27,692 (35.9%)	21,109 (37.0%)	6583 (32.9%)
Forlì–Cesena	28,058 (36.4%)	20,684 (36.2%)	7374 (36.8%)
Rimini	21,388 (27.7%)	15,320 (26.8%)	6068 (30.3%)
Health district of residence			
Ravenna	14,116 (18.3%)	10,782 (18.9%)	3334 (16.6%)
Lugo	7550 (9.8%)	5844 (10.2%)	1706 (8.5%)
Faenza	6026 (7.8%)	4483 (7.8%)	1543 (7.7%)
Forlì	13,331 (17.3%)	9776 (17.1%)	3555 (17.8%)
Cesena–Valle del Savio	8581 (11.1%)	6386 (11.2%)	2195 (11.0%)
Rimini	14,617 (18.9%)	10,609 (18.6%)	4008 (20.0%)
Riccione	6771 (8.8%)	4711 (8.2%)	2060 (10.3%)
Rubicone	6146 (8.0%)	4522 (7.9%)	1624 (8.1%)
Altitude zone of municipality of residence			
Inland mountain	1263 (1.6%)	962 (1.7%)	301 (1.5%)
Inland hill	7928 (10.3%)	5833 (10.2%)	2095 (10.5%)
Coastal hill	2262 (2.9%)	1581 (2.8%)	681 (3.4%)
Plain	65,685 (85.2%)	48,737 (85.3%)	16,948 (84.6%)
Degree of urbanization of municipality of residence			
City	28,699 (37.2%)	21,306 (37.3%)	7393 (36.9%)
Towns and suburbs	37,151 (48.2%)	27,467 (48.1%)	9684 (48.4%)
Rural area	11,288 (14.6%)	8340 (14.6%)	2948 (14.7%)
CCI (2005 version)			
Mean [SD]	0.3 [1.0]	0.3 [1.0]	0.4 [1.1]
Median [IQR]	0 [0–0]	0 [0–0]	0 [0–0]
CCI category (2005 version)			
0	65,206 (84.5%)	48,395 (84.7%)	16,811 (84.0%)
1	5079 (6.6%)	3563 (6.2%)	1516 (7.6%)
≥2	6853 (8.9%)	5155 (9.0%)	1698 (8.5%)
CCI category (2011 version)			
0	67,954 (88.1%)	50,345 (88.1%)	17,609 (87.9%)
1	1840 (2.4%)	1378 (2.4%)	462 (2.3%)
≥2	7344 (9.5%)	5390 (9.4%)	1954 (9.8%)
Moore's ECI category			
≤0	67,405 (87.4%)	49,933 (87.4%)	17,472 (87.3%)
1	85 (0.1%)	62 (0.1%)	23 (0.1%)
≥2	9648 (12.5%)	7118 (12.5%)	2530 (12.6%)
van Walraven's ECI category			
≤0	66,012 (85.6%)	48,945 (85.7%)	17,067 (85.2%)
1	130 (0.2%)	90 (0.2%)	40 (0.2%)
≥2	10,996 (14.3%)	8078 (14.1%)	2918 (14.6%)
M-CDS			
Mean [SD]	4.2 [4.0]	4.3 [4.0]	3.7 [3.9]
Median [IQR]	3 [2–6]	3 [2–6]	2 [2–5]
M-CDS category			
0–1	12,874 (16.7%)	8101 (14.2%)	4773 (23.8%)
2	22,285 (28.9%)	16,347 (28.6%)	5938 (29.7%)
3–4	15,936 (20.7%)	12,375 (21.7%)	3561 (17.8%)
5–6	10,763 (14.0%)	8294 (14.5%)	2469 (12.3%)
7–9	6967 (9.0%)	5570 (9.8%)	1397 (7.0%)
≥10	8313 (10.8%)	6426 (11.3%)	1887 (9.4%)
Previous diabetes-related complications			
No	75,415 (97.8%)	55,798 (97.7%)	19,617 (98.0%)
Yes	1723 (2.2%)	1315 (2.3%)	408 (2.0%)
Unstable metabolic control (proxy)			
No	–	–	19,623 (98.0%)
Yes	–	–	402 (2.0%)

Note: Unstable metabolic control was assessed in the incident cohort only (see Section 2.2.1).
Abbreviations: SD, standard deviation; IQR, interquartile range; CCI, Charlson Comorbidity Index; ECI, Elixhauser Comorbidity Index; M-CDS, Modified Chronic Disease Score.

years). The hazard of vaccination increased markedly from the 40–49 age group (HR 1.66; 95% CI: 1.38–2.01) and peaked among individuals aged 60–69 years (HR 7.30; 95% CI: 6.17–8.65), with slightly attenuated but still elevated estimates in older age groups.

Among individual-level factors, female sex was associated with lower vaccination uptake compared with males (HR 0.84; 95% CI: 0.81–0.86), while foreign citizenship was also associated with markedly lower uptake (HR 0.48; 95% CI: 0.43–0.54). Belonging to the incident cohort was associated with higher uptake (HR 1.69; 95% CI: 1.62–1.75).

Comorbidity, measured by the Charlson Comorbidity Index, was positively associated with vaccination uptake, with a graded increase in hazard for score 1 (HR 1.22; 95% CI: 1.15–1.31) and ≥ 2 (HR 1.28; 95% CI: 1.20–1.36), whereas previous diabetes-related complications showed no association.

Contextual factors (i.e., health districts and municipality-level characteristics) showed limited associations overall, with effect sizes close to unity despite some statistically significant heterogeneity.

In analyses restricted to the incident cohort, unstable metabolic control was associated with higher vaccination uptake (HR 1.45; 95% CI: 1.14–1.83).

In competing-risks models treating death as a competing event, estimates for sex, citizenship, cohort, health district, and contextual variables were broadly consistent with the main Cox model, whereas associations for very old age and indicators of clinical complexity were attenuated or reversed (Supplementary Table S3). These discrepancies are interpreted in Supplementary Box S2 as reflecting the dual role of clinical complexity: greater healthcare contact may increase opportunities for vaccination, while higher mortality reduces the cumulative opportunity to be vaccinated.

Restriction to Italian citizens yielded virtually unchanged cumulative-probability estimates and adjusted Cox associations (Supplementary Tables S4 and S5).

4. Discussion

In this large population-based study of adults with diabetes in Romagna's LHA, pneumococcal vaccination coverage remained below 30% despite gradual improvement. Among incident cases, first vaccination did not concentrate soon after cohort entry but accumulated over several years. This pattern did not indicate consistent assessment and offer at predefined moments of diabetes care and was compatible with incomplete integration into chronic care pathways. This low uptake is notable given the increased pneumococcal disease risk in diabetes [1,2], longstanding recommendations [3,4], universal health coverage, free-of-charge vaccination for eligible risk groups, and formally structured preventive programs.

Our estimates are broadly consistent with evidence of suboptimal uptake among adults with diabetes [5]. Italian surveys have reported coverage above 40–50% [6], but self-reported pneumococcal vaccination status may be misclassified [33]. Administrative data provide more objective ascertainment, although incomplete recording remains

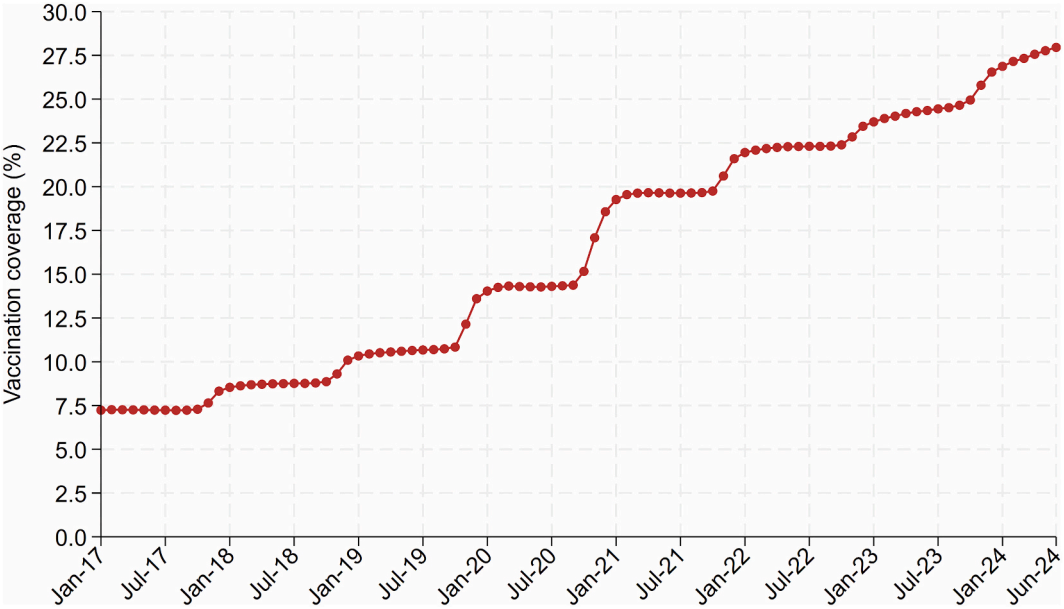

Fig. 1. Temporal trend in pneumococcal vaccination coverage among adults with diabetes in the Romagna Local Health Authority, January 2017 to June 2024.
Note: Vaccination coverage was estimated monthly as the ratio of person-days covered by vaccination to total person-days under observation in the study population.

Fig. 2. Cumulative probability of pneumococcal vaccination in the incident cohort of adults with diabetes.
Note: The curve represents the Kaplan–Meier failure function, with first recorded pneumococcal vaccination after cohort entry as the event and follow-up censored at death. The risk table reports the number of participants who were alive, under observation, and had not yet been vaccinated at each displayed time point.

possible [34]. Agreement with recent Emilia-Romagna surveillance supports the plausibility of our estimates [35]. Unlike these cross-sectional benchmarks, our longitudinal analysis documents the prolonged time to first vaccination after cohort entry.

The findings should be interpreted within a decentralized system in which national plans define eligibility and free-of-charge entitlement, while regions and LHAs organize delivery. National and regional strategies promoted proactive vaccination across primary care, specialist services, hospitals, and vaccination centers [3,27], but implementation was not governed by a single uniform pathway with predefined triggers, settings, and responsibilities throughout the study period. In the incident cohort, formal eligibility was not matched by timely recorded uptake, but the mechanism responsible cannot be identified. Subsequent vaccination may have arisen through seasonal campaigns, routine encounters, patient-initiated demand, or local arrangements.

Diabetes-based eligibility also overlapped with the annual offer to the cohort turning 65, and the registry did not identify which pathway prompted vaccination. The hazard peaked among participants aged 60–69 at cohort entry, a group including those already aged 65–69 and those aged 60–64 who became age-eligible during follow-up. Some uptake may therefore have occurred through the age-based program rather than diabetes-specific assessment. Lower HRs at older ages may reflect both the annual-cohort focus and higher competing mortality. The lower coverage in this clinically defined risk group than in regional birth-cohort programs [36] may also reflect the greater complexity of identifying and actively targeting eligible individuals through clinical rather than age information. Age should therefore be interpreted partly as a marker of program eligibility rather than solely as an individual determinant.

The calendar pattern provides additional context but not direct

Table 2
Multivariable Cox proportional hazards model: individual and contextual determinants of pneumococcal vaccination uptake.

	Hazard ratio	*p*-value	95% CI
Sex			
Male	Ref.		
Female	0.84	<0.001	0.81–0.86
Age group, years			
18–39	Ref.		
40–49	1.66	<0.001	1.38–2.01
50–59	3.37	<0.001	2.84–4.00
60–69	7.30	<0.001	6.17–8.65
70–79	4.53	<0.001	3.82–5.36
80–89	3.33	<0.001	2.80–3.97
≥90	2.90	<0.001	2.28–3.67
Citizenship			
Italian	Ref.		
Foreign	0.48	<0.001	0.43–0.54
Health district of residence			
Ravenna	Ref.		
Lugo	0.96	0.285	0.89–1.03
Faenza	1.10	0.010	1.02–1.18
Forlì	0.94	0.024	0.89–0.99
Cesena–Valle del Savio	1.13	0.001	1.05–1.21
Rimini	0.97	0.240	0.92–1.02
Riccione	1.04	0.342	0.96–1.13
Rubicone	0.90	0.006	0.83–0.97
Cohort			
Prevalent	Ref.		
Incident	1.69	<0.001	1.62–1.75
Charlson Comorbidity Index (2005)			
0	Ref.		
1	1.22	<0.001	1.15–1.31
≥2	1.28	<0.001	1.20–1.36
Previous diabetes-related complications			
No	Ref.		
Yes	1.00	0.976	0.87–1.14
Altitude zone of municipality of residence			
Inland mountain	1.14	0.051	1.00–1.30
Inland hill	0.97	0.317	0.90–1.03
Coastal hill	0.87	0.016	0.79–0.98
Plain	Ref.		
Degree of urbanization			
City	Ref.		
Towns and suburbs	0.93	0.008	0.89–0.98
Rural area	0.98	0.566	0.91–1.05

Note: The Charlson Comorbidity Index (2005 version) was categorized as 0, 1, and ≥ 2 to improve distributional balance and discriminative ability in the study population. Alternative formulations of the Charlson index and Elixhauser-based scores showed a marked concentration of subjects in extreme categories and limited representation in intermediate groups (see Table 1). The Modified Chronic Disease Score (M-CDS) was not included in the multivariable model to avoid redundancy among comorbidity measures and because it did not provide additional predictive value.
Abbreviations: CI, confidence interval.

evidence of delivery mechanisms. The first-dose outcome combined vaccinations administered under evolving formulations and schedules, so temporal changes cannot be attributed to delivery organization alone. The largest increases clustered during influenza seasons, consistent with partial campaign coupling [11,37]; however, data on individual co-administration and vaccination setting were unavailable, making this an ecological interpretation. The principal rise began in late 2019, before COVID-19 vaccination began in Italy on December 27, 2020 [38]; coverage changed little during spring and summer 2020, then resumed its rise during the 2020–2021 influenza season. COVID-19 co-administration therefore cannot explain the full increase, although pandemic-related reorganization and heightened attention to respiratory vaccination may have contributed later. More gradual subsequent growth was visible before the May 2024 agreement strengthening year-round delivery and general practitioner participation [28]. A subsequent regional circular, issued after follow-up, further harmonized adult pneumococcal access and delivery arrangements [39]. The data cannot separate the contributions of campaigns, routine encounters, provider involvement, evolving recommendations and formulations, vaccine availability, patient demand, or other local factors.

The adjusted associations complement the temporal findings but do not identify delivery mechanisms. Given the large sample, estimates were interpreted according to magnitude and consistency rather than statistical significance alone: differences were largest for age and citizenship, more modest for sex and comorbidity, and generally close to unity for contextual factors. Higher uptake among participants with greater comorbidity or unstable metabolic control was consistent with healthcare contact creating more opportunities for vaccination [13]. Competing-risk analyses, however, attenuated or reversed the comorbidity associations, consistent with a shorter window for vaccination before death among clinically complex individuals. Repeated healthcare contact and gradual changes in awareness or perceived benefit over the course of diabetes may both contribute to delayed uptake [40,41].

The sex difference in uptake was modest and should be interpreted cautiously. Its direction differs from some European pneumococcal studies [5,7] and from broader evidence that women often use outpatient and preventive services more frequently [42]. The finding may reflect unmeasured differences in provider recommendation, perceived risk, competing priorities, or pathway-specific delivery rather than lower healthcare engagement overall. The larger disparity by citizenship is an important equity signal, but foreign citizenship is a heterogeneous administrative marker rather than a measure of migration history, socioeconomic position, language proficiency, legal status, or culture. It may encompass barriers to access, communication, and engagement [15], but does not identify a single mechanism or a narrowly defined intervention target.

Overall, low uptake should not be attributed to patient hesitancy alone. Individual demand and the organization of delivery may both contribute, but their relative roles cannot be determined [13,14]. The prolonged delays point to potential missed opportunities and support evaluating systematic vaccination assessment at diagnosis, routine follow-up, and specialist encounters. Recent adult policies include PCV20-based single-dose options [9,10] and PCV21 as an alternative higher-valency conjugate vaccine [43], with emerging economic evaluations of age- and risk-based PCV21 use [44]. These innovations may reduce logistical barriers. However, formulation changes alone are unlikely to close the coverage gap without effective delivery arrangements capable of reaching clinically eligible adults. Longitudinal uptake data can help align vaccine innovation with implementation strategies [5,8].

4.1. Strengths and limitations

This study has several strengths. It combined a large population-based cohort, near-complete resident coverage, and deterministic linkage of administrative databases. The longitudinal design characterized both monthly coverage and time to first vaccination, showing how uptake accumulated after entry into the target population rather than providing only a static estimate. The person-time approach also accounted for staggered cohort entry and death during follow-up.

Several limitations should be considered. Administrative data lacked education, socioeconomic position, health literacy, smoking, frailty, functional dependence, previous vaccination behavior, vaccine attitudes, and detailed information on care organization or provider practices. Residual confounding is therefore likely, and adjusted HRs should be interpreted as associations rather than causal effects or direct measures of healthcare organization. Citizenship was available only as a binary administrative variable and should not be interpreted as a direct measure of migration history or related social conditions. Differential under-ascertainment of vaccinations received outside the regional information system cannot be excluded; however, restriction to Italian citizens did not materially alter the findings. Vaccine formulation and brand, completion of contemporaneous sequential or repeat-dose

schedules, administration setting, and linkage to other vaccination records were not available for reliable analysis because historical completeness was uneven and greater granularity and linkage were not included under the approved data-minimization framework. The outcome therefore measured initiation of recorded pneumococcal vaccination, not schedule adherence or vaccine-specific protection, and calendar changes may reflect formulations, recommendations, campaigns, provider practices, supply, logistics, or local implementation. Disease duration was not directly measured, and residual differences between prevalent and incident cases may remain. Diabetes complications and comorbidities were identified mainly from hospital data, potentially missing conditions managed exclusively in outpatient care, although this approach captures more severe clinical profiles.

5. Conclusion

In this large population-based study, pneumococcal vaccination uptake among adults with diabetes remained suboptimal over time, despite clear clinical indications and an organized, universal healthcare setting. Vaccination did not concentrate soon after entry into the diabetes cohort but accumulated over several years. This pattern did not indicate consistent assessment and offer at predefined moments of care and was compatible with incomplete integration into chronic care pathways. The prolonged delays suggest potential missed opportunities for timely vaccination, although the data could not determine the mechanisms responsible.

Formal recommendations were therefore not matched by timely uptake in routine practice. Studies incorporating provider- and patient-level information are needed to distinguish the contributions of care organization, provider recommendation, vaccine access, and patient acceptance. Systematic assessment at predefined healthcare contacts should be evaluated as a strategy to reduce vaccination delays in high-risk populations.

Declaration of generative AI and AI-assisted technologies in the manuscript preparation process

During the preparation of this work, the authors used ChatGPT (OpenAI) to support language refinement, improve clarity and structure of the text, and enhance overall coherence and conciseness. The tool was also used to assist in identifying potential logical inconsistencies and improving the organization of arguments. All content was critically reviewed, revised, and validated by the authors, who take full responsibility for the final manuscript.

CRediT authorship contribution statement

Jacopo Lenzi: Writing – original draft, Visualization, Supervision, Project administration, Methodology, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Marco Montalti:** Writing – review & editing, Validation, Investigation, Conceptualization. **Zeno Di Valerio:** Writing – review & editing, Validation, Investigation, Conceptualization. **Valeria Frassineti:** Supervision, Software, Investigation, Data curation. **Paolo Benetti:** Software, Investigation, Data curation. **Rossella Messina:** Validation, Supervision, Project administration. **Simona Rosa:** Validation, Supervision, Methodology. **Andrea Casadei:** Writing – review & editing, Investigation. **Maria Pia Fantini:** Validation, Supervision, Conceptualization. **Paolo Di Bartolo:** Validation, Supervision. **Davide Gori:** Writing – review & editing, Validation. **Giulia Silvestrini:** Writing – review & editing, Validation, Supervision, Project administration, Conceptualization.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2026.129063.

Data availability

The data supporting the findings of this study are not publicly available due to legal and ethical restrictions. The data consist of pseudonymized individual-level health records derived from administrative healthcare databases and are subject to strict data protection regulations under the General Data Protection Regulation (EU 2016/679) and institutional policies of the Romagna Local Health Authority (*AUSL Romagna*), which is the data controller.

Data cannot be shared outside the authorized research environment, as this would violate the conditions under which access was granted. Aggregated data supporting the findings are available from the corresponding author upon reasonable request.

References

[1] Thomsen RW, Hundborg HH, Lervang H-H, Johnsen SP, Schønheyder HC, Sørensen HT. Risk of community-acquired pneumococcal bacteremia in patients with diabetes: a population-based case-control study. Diabetes Care 2004;27(5):1143–7. https://doi.org/10.2337/diacare.27.5.1143.

[2] Shea KM, Edelsberg J, Weycker D, Farkouh RA, Strutton DR, Pelton SI. Rates of pneumococcal disease in adults with chronic medical conditions. Open Forum Infect Dis 2014;1(1):ofu024. https://doi.org/10.1093/ofid/ofu024.

[3] Conferenza Permanente per i Rapporti tra lo Stato, le Regioni e le Province Autonome di Trento e di Bolzano. Intesa 2 agosto 2023 sul "Piano nazionale di prevenzione vaccinale (PNPV) 2023–2025" e sul "Calendario nazionale vaccinale" (Rep. atti n. 193/CSR). Gazzetta Ufficiale della Repubblica Italiana; 2023. Serie Generale, n. 194, 21 agosto 2023, https://www.gazzettaufficiale.it/eli/id/2023/08/21/23A04685/SG.

[4] International Diabetes Federation Europe. IDF Europe position paper on the vaccination of people living with diabetes. https://www.eu-patient.eu/globalassets

/idf-europe-position-paper-on-vaccination-of-people-living-with-diabetes.pdf; 2021.
[5] Boey L, Bosmans E, Ferreira LB, Heyvaert N, Nelen M, Smans L, et al. Vaccination coverage of recommended vaccines and determinants of vaccination in at-risk groups. Hum Vaccin Immunother 2020;16(9):2136–43. https://doi.org/10.1080/21645515.2020.1763739.
[6] Di Valerio Z, La Fauci G, Scognamiglio F, Salussolia A, Montalti M, Capodici A, et al. Pneumococcal vaccine uptake among high-risk adults and children in Italy: results from the OBVIOUS project survey. BMC Public Health 2024;24(1):736. https://doi.org/10.1186/s12889-024-18216-3.
[7] Vila-Córcoles A, Ochoa-Gondar O, de Diego C, Satué E, Vila-Rovira A, Aragón M. Pneumococcal vaccination coverages by age, sex and specific underlying risk conditions among middle-aged and older adults in Catalonia, Spain, 2017. Eurosurveillance 2019;24(29):1800446. https://doi.org/10.2807/1560-7917.ES.2019.24.29.1800446.
[8] Lindstrand A, Mast E, Churchill S, Rahimi N, Grevendork J, Brooks A, et al. Implementing the immunization agenda 2030: a framework for action through coordinated planning, monitoring & evaluation, ownership & accountability, and communications & advocacy. Vaccine 2024;42(Suppl. 1):S15–27. https://doi.org/10.1016/j.vaccine.2021.09.045.
[9] Kobayashi M, Farrar JL, Gierke R, Britton A, Childs L, Leidner AJ, et al. Use of 15-valent pneumococcal conjugate vaccine and 20-valent pneumococcal conjugate vaccine among U.S. adults: updated recommendations of the Advisory Committee on Immunization Practices—United States, 2022. MMWR Morb Mortal Wkly Rep 2022;71(4):109–17. https://doi.org/10.15585/mmwr.mm7104a1.
[10] Wierzbowski A, Pless R, Hildebrand KJ, on behalf of the National Advisory Committee on Immunization. Summary of the NACI statement on public health level recommendations on the use of pneumococcal vaccines in adults, including the use of 15-valent and 20-valent conjugate vaccines. Can Commun Dis Rep 2023;49(2/3):81–6. https://doi.org/10.14745/ccdr.v49i23a08.
[11] Conferenza Permanente per i Rapporti tra lo Stato, le Regioni e le Province Autonome di Trento e di Bolzano. Intesa 19 gennaio 2017 sul "Piano nazionale prevenzione vaccinale 2017–2019" (Rep. atti n. 10/CSR). Gazzetta Ufficiale della Repubblica Italiana; 2017. Serie Generale, n. 41, 18 febbraio 2017, https://www.gazzettaufficiale.it/atto/serie_generale/caricaDettaglioAtto/originario?atto.codiceRedazionale=17A01195&atto.dataPubblicazioneGazzetta=2017-02-18&elenco30giorni=false.
[12] Petigara T, Zhang D. Pneumococcal vaccine coverage in adults aged 19–64 years, newly diagnosed with chronic conditions in the U.S. Am J Prev Med 2018;54(5):630–6. https://doi.org/10.1016/j.amepre.2018.01.033.
[13] Arsenault C, Ravishankar S, Lewis T, Armeni P, Croke K, Doubova SV, et al. The role of health systems in shaping vaccine decisions: insights from Italy, Mexico, the United Kingdom, and the United States. Vaccine 2025;54:127134. https://doi.org/10.1016/j.vaccine.2025.127134.
[14] Anderson KAM, Creanza N. Internal and external factors affecting vaccination coverage: modeling the interactions between vaccine hesitancy, accessibility, and mandates. PLOS Global Public Health 2023;3(10):e0001186. https://doi.org/10.1371/journal.pgph.0001186.
[15] Khuu E, Moussaoui S, Vignier N, Bonello K, Archer E. Vaccine hesitancy among migrant populations in Europe: a mixed-methods systematic review. Vaccine 2025;68:127954. https://doi.org/10.1016/j.vaccine.2025.127954.
[16] Ministero della Salute. Nuovo sistema di garanzia per il monitoraggio dell'assistenza sanitaria (Decreto 12 marzo 2019): Allegato 1. Metodologia per il calcolo degli indicatori PDTA; 2019. https://www.salute.gov.it/new/sites/default/files/imported/C_17_pagineAree_5238_4_file.pdf.
[17] Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care 2005;43(11):1130–9. https://doi.org/10.1097/01.mlr.0000182534.19832.83.
[18] Romano PS, Roos LL, Jollis JG. Adapting a clinical comorbidity index for use with ICD-9-CM administrative data: differing perspectives. J Clin Epidemiol 1993;46(10):1075–9. https://doi.org/10.1016/0895-4356(93)90103-8.
[19] Cleves MA, Sanchez N, Draheim M. Evaluation of two competing methods for calculating Charlson's comorbidity index when analyzing short-term mortality using administrative data. J Clin Epidemiol 1997;50(8):903–8. https://doi.org/10.1016/S0895-4356(97)00091-7.
[20] Sharabiani MTA, Aylin P, Bottle A. Systematic review of comorbidity indices for administrative data. Med Care 2012;50(12):1109–18. https://doi.org/10.1097/MLR.0b013e31825f64d0.
[21] Quan H, Li B, Couris CM, Fushimi K, Graham P, Hider P, et al. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. Am J Epidemiol 2011;173(6):676–82. https://doi.org/10.1093/aje/kwq433.
[22] van Walraven C, Austin PC, Jennings A, Quan H, Forster AJ. A modification of the Elixhauser comorbidity measures into a point system for hospital death using administrative data. Med Care 2009;47(6):626–33. https://doi.org/10.1097/MLR.0b013e31819432e5.
[23] Moore BJ, White S, Washington R, Coenen N, Elixhauser A. Identifying increased risk of readmission and in-hospital mortality using hospital administrative data: the AHRQ Elixhauser comorbidity index. Med Care 2017;55(7):698–705. https://doi.org/10.1097/MLR.0000000000000735.
[24] Iommi M, Rosa S, Fusaroli M, Rucci P, Fantini MP, Poluzzi E. Modified-chronic disease score (M-CDS): predicting the individual risk of death using drug prescriptions. PLoS One 2020;15(10):e0240899. https://doi.org/10.1371/journal.pone.0240899.
[25] Lenzi J, Messina R, Rosa S, Iommi M, Rucci P, Fantini MP, et al. A multi-state analysis of disease trajectories and mental health transitions in patients with type 2 diabetes: a population-based retrospective cohort study utilizing health administrative data. Diabetes Res Clin Pract 2024;209:111561. https://doi.org/10.1016/j.diabres.2024.111561.
[26] Regione Emilia-Romagna, Giunta regionale. Deliberazione 5 aprile 2017, n. 427: Approvazione del Piano regionale di prevenzione vaccinale 2017. https://salute.regione.emilia-romagna.it/normativa-e-documentazione/leggi-atti/regionali/delibere/archivio/dgr-427-2017; 2017.
[27] Regione Emilia-Romagna, Giunta regionale. Deliberazione 12 dicembre 2023, n. 2138: Approvazione del Piano regionale dell'Emilia-Romagna per la prevenzione vaccinale 2023–2025. Bollettino Ufficiale della Regione Emilia-Romagna Telematico; 2023. n. 362, 27 dicembre 2023, https://bur.regione.emilia-romagna.it/area-bollettini/n-362-del-27-12-2023-parte-seconda/approvazione-del-piano-regionale-dellemilia-romagna-per-la-prevenzione-vaccinale-2023-2025.
[28] Regione Emilia-Romagna, Giunta regionale. Deliberazione 27 maggio 2024, n. 896: *Approvazione dello schema di verbale di intesa tra la Regione Emilia-Romagna, Direzione generale Cura della persona, salute e welfare e le Organizzazioni sindacali dei medici di medicina generale per la partecipazione alla campagna vaccinale*. Bollettino Ufficiale della Regione Emilia-Romagna Telematico; 2024. n. 191, 19 giugno 2024, https://bur.regione.emilia-romagna.it/area-bollettini/giugno-periodico-parte-seconda-2a-quindicina/approvazione-dello-schema-di-verbale-di-intesa-tra-la-regione-emilia-romagna-direzione-generale-cura-della-persona-salute-e-welfare-e-le-organizzazioni-sindacali-dei-medici-di-medicina-generale-per-la-partecipazione-alla-campagna-vaccinale.
[29] Ministero della Sanità. Autorizzazioni all'immissione in commercio di specialità medicinali per uso umano [Decreto n. 611/1992 del 27 luglio 1992: vaccino "PNEUMO 23"]. Gazzetta Ufficiale della Repubblica Italiana; 1992. Serie Generale, n. 180, 1° agosto 1992, https://www.gazzettaufficiale.it/eli/id/1992/08/01/092A3623/sg.
[30] Rogers WH. SG17: regression standard errors in clustered samples. Stata Tech Bull 1993;13:19–23. Reprinted in Stata Technical Bulletin Reprints (Vol. 3, pp. 88–94). Stata Press. https://www.stata.com/products/stb/journals/stb13.pdf.
[31] Grambsch PM, Therneau TM. Proportional hazards tests and diagnostics based on weighted residuals. Biometrika 1994;81(3):515–26. https://doi.org/10.1093/biomet/81.3.515.
[32] Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. J Am Stat Assoc 1999;94(446):496–509. https://doi.org/10.1080/01621459.1999.10474144.
[33] Mangtani P, Shah A, Roberts JA. Validation of influenza and pneumococcal vaccine status in adults based on self-report. Epidemiol Infect 2007;135(1):139–43. https://doi.org/10.1017/S0950268806006479.
[34] Amoud R, Kwong JC, Maxwell C, Tyas SL, Cooke M, Hernandez A, et al. Validation of influenza vaccination status using health administrative databases by integrating pharmacy claims and medical billing databases in Ontario, Canada. BMC Infect Dis 2025;25(1):653. https://doi.org/10.1186/s12879-025-11014-1.
[35] Regione Emilia-Romagna. *Coperture vaccinali—adulti per condizioni di rischio per patologia cronica—anno* 2024. Emissione: 15 luglio 2025. https://salute.regione.emilia-romagna.it/sanita-pubblica/vaccinazioni/report-cv-2024-soggetti-patologici-anno-2024.pdf; 2025.
[36] Regione Emilia-Romagna. Coperture vaccinali per coorte in Emilia-Romagna: Anno 2025. Emissione: maggio 2025. https://salute.regione.emilia-romagna.it/sanita-pubblica/vaccinazioni/report-coperture-vaccinali-er-2025.pdf; 2025.
[37] Regione Emilia-Romagna. Vaccinazione antinfluenzale in Emilia-Romagna: avvio della campagna 2022–2023 e possibilità di co-somministrazione con il vaccino antipneumococcico. 17 ottobre 2022. https://notizie.regione.emilia-romagna.it/comunicati/2022/ottobre/sanita-vaccinazione-antinfluenzale-in-emilia-romagna-si-parte-lunedi-24-ottobre-a-disposizione-1-milione-150mila-dosi-che-potranno-aumentare-fino-a-1-milione-380mila-obiettivo-rafforzare-ancora-l2019offerta-per-le-persone-ad-alto-rischio-di-tutte-le-eta; 2022.
[38] Ministero della Salute. Vaccine day, Speranza: "È il giorno che aspettavamo da tempo, la strada è ancora lunga". 27 dicembre 2020. https://www.salute.gov.it/new/it/news-e-media/notizie/vaccine-day-speranza-e-il-giorno-che-aspettavamo-da-tempo-la-strada-e-ancora; 2020.
[39] Regione Emilia-Romagna, Direzione Generale Cura della Persona, Salute e Welfare. Circolare n. 8/2024, Prot. 09/08/2024.0863669.U: Raccomandazioni e indicazioni per l'offerta vaccinale contro pneumococco, herpes zoster e difterite-tetano-pertosse nel soggetto adulto in Emilia-Romagna, azioni di armonizzazione dei modelli gestionali relativi all'accesso e all'erogazione delle prestazioni vaccinali e trasmissione del documento tecnico aggiornato "Raccomandazioni e offerte vaccinali per condizioni di rischio 2023–2025 – Rev.01" e del report sulle coperture vaccinali regionali – anno 2023. 9 agosto 2024, https://www.omceopr.it/wp-content/uploads/2024/08/Circolare_8-2024_-_Raccomandazioni_e_indicazioni_HZ_PNC_DTP_e_trasmissione_CV_e_Doc._Tec.pdf; 2024.
[40] Ko YM, Ko SH, Han K, Park YM, Choi JY, Kim SY, et al. Importance of awareness and treatment for diabetes in influenza vaccination coverage of diabetic patients under 65 years: a population-based study. Diabetes Metab J 2021;45(1):55–66. https://doi.org/10.4093/dmj.2019.0189.
[41] Voloshin A, Altermatt A, Wilkinson A, Gibney KB, Hill S, Kaufman J, et al. What drives vaccine uptake?—investigating the application of the health belief model through a longitudinal cohort study during the COVID-19 pandemic in Victoria, Australia. Vaccines 2025;13(10):1021. https://doi.org/10.3390/vaccines13101021.
[42] Golinelli D, Sanmarchi F, Guarducci G, Palombarini J, Benetti P, Rosa S, et al. Gender differences in healthcare utilization across Europe: evidence from the

European health interview survey. Health Policy 2025;162:105448. https://doi.org/10.1016/j.healthpol.2025.105448.

[43] Kobayashi M, Leidner AJ, Gierke R, Farrar JL, Morgan RL, Ca.pos-Outcalt D, et al. Use of 21-valent pneumococcal conjugate vaccine among U.S. adults: recommendations of the Advisory Committee on Immunization Practices—United States, 2024. MMWR Morb Mortal Wkly Rep 2024;73(36):793–8. https://doi.org/10.15585/mmwr.mm7336a3.

[44] Stoecker C, Wang Y, Leidner AJ, Cho B-H, Ward C, Kobayashi M. Cost-effectiveness of age-based and risk-based use of the new 21-valent pneumococcal conjugate vaccine among U.S. adults. Vaccine 2026;69:127940. https://doi.org/10.1016/j.vaccine.2025.127940.