10a Jornada de Recerca de l'ICS

11a Jornada de Recerca de l'IDIAP

La recerca amb grans bases de dades clíniques millora la salut

7 de juny de 2018

/ / / /

COSMOCAIXA

Vacunació antipneumocòccica en adults: estudi EPIVAC-SIDIAP

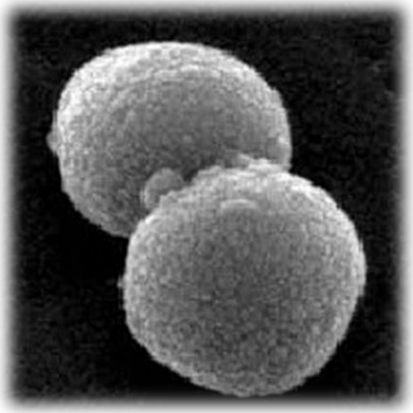
Grup de Recerca EPIVAC (*)

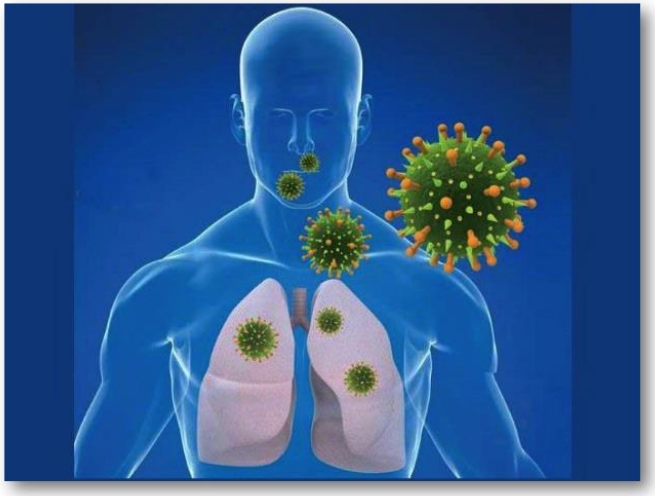
DAP Camp de Tarragona, ICS

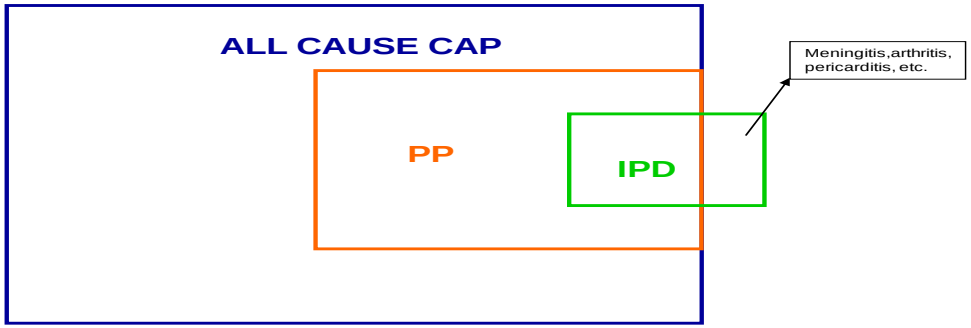
(*) GRC acreditat per l'IDIAP Jordi Gol i l'AGAUR de la Generalitat de Catalunya.

Finançat amb Beques/Ajuts IDIAP, ISCIII i PERIS

PNEUMOCOCCAL DISEASES







PNEUMOCOCCAL SEROTYPES

1[4]	2	**3**[21]	**4**[3]	5	6A, **6B**[3], **6C**[7], 6D, 6E, 6F, 6G, 6H	**7A**[1], 7C, 7D, **7F**[16]	**8**[27]	9A, **9L**[1], 9N, **9V**[2]	**10A**[6], 10B, 10C, 10F
11A, 11B, 11C, 11D, 11E, 11F	**12A**[4], 12B, **12F**[27]	13	**14**[18]	**15A**[4], **15B**[5], **15C**[2], **15F**[1]	16A, **16F**[3]	17A, **17F**[3]	18A, 18B, **18C**[1], 18F	**19A**[20], 19B, 19C, **19F**[3]	20A, 20B
21[2]	**22A**[1], **22F**[12]	**23A**[1], **23B**[9], 23F	**24A**[4], **24B**[2], **24F**[5]	25A 25F		27	28A 28F	29	
31[15]	32A 32F	33A, 33B 33C, 33D 33E, **33F**[3]	**34**[1]	35A, **35B**[5] 35C, **35F2**	36	37	**38**[2]	**39**[1]	40
41A 41F	42	43	**44**[4]	45	**46**[4]	47A 47F	48		

PNEUMOCOCCAL POLYSACCHARIDE VACCINE 23-VALENT (PPV23)

1	2	3	4	5	6A, 6B, 6C, 6D, 6E, 6F, 6G, 6H	7A, 7C, 7D, 7F	8	9A, 9L, 9N, 9V	10A, 10B, 10C, 10F
11A, 11B, 11C, 11D, 11E, 11F	12A, 12B, 12F	13	14	15A, 15B, 15C, 15F	16A, 16F	17A, 17F	18A, 18B, 18C, 18F	19A, 19B, 19C, 19F	20A, 20B
21	22A, 22F	23A, 23B, 23F	24A, 24B, 24F	25A 25F		27	28A 28F	29	
31	32A 32F	33A, 33B 33C, 33D 33E, 33F	34	35A, 35B 35C, 35F	36	37	38	39	40
41A 41F	42	43	44	45	46	47A 47F	48		

- Licensed in 1983 (serotype-coverage = 90%)
- Efficacy/effectiveness around 40-60% against IPD in immunocompetent adults
- Inadequate/poor immunogenicity in children <2 years and immunocompromised persons

PNEUMOCOCCAL CONJUGATE VACCINE 7-VALENT (PCV7)

1	2	3	**4**	5	6A, **6B**, 6C, 6D, 6E, 6F, 6G, 6H	7A, 7C, 7D, 7F	8	9A, 9L, 9N, **9V**	10A, 10B, 10C, 10F
11A, 11B, 11C, 11D, 11E, 11F	12A, 12B, 12F	13	**14**	15A, 15B, 15C, 15F	16A, 16F	17A, 17F	18A, 18B, **18C**, 18F	19A, 19B, 19C, **19F**	20A, 20B
21	22A, 22F	23A, 23B, **23F**	24A, 24B, 24F	25A 25F		27	28A 28F	29	
31	32A 32F	33A, 33B 33C, 33D 33E, 33F	34	35A, 35B 35C, 35F	36	37	38	39	40
41A 41F	42	43	44	45	46	47A 47F	48		

- T cell-dependent mode of action (adequate immune response in young children)
- Licensed in 2000 for children (serotype-coverage: 70-80%)
- Sustained effect reducing vaccine-type IPD in children and indirect effect among adults

PNEUMOCOCCAL CONJUGATE VACCINE 13-VALENT (PCV13)

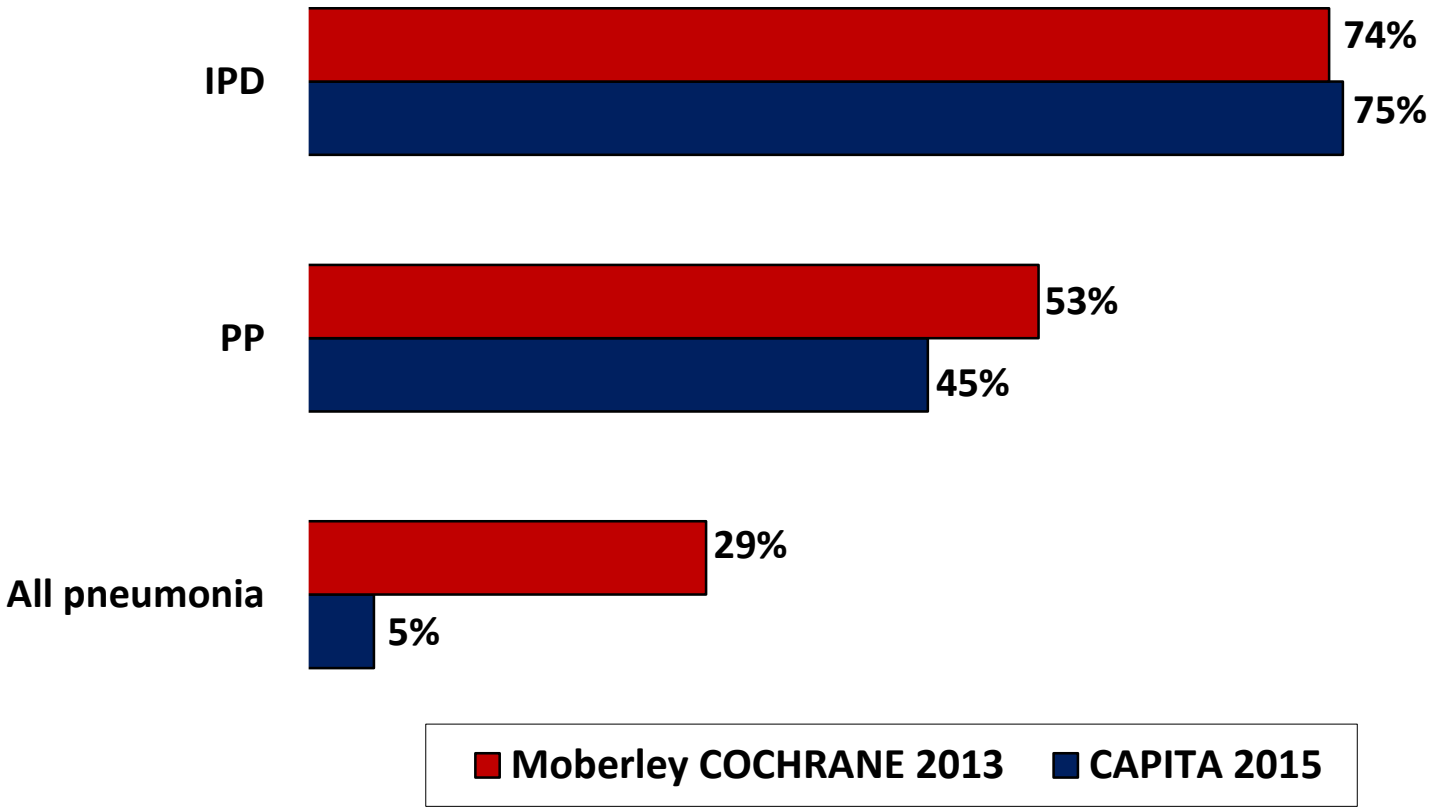
1	2		4	5	6A, 6B 6C, 6D, 6E, 6F, 6G, 6H	7A, 7C, 7D, 7F	8	9A, 9L, 9N, 9V	10A, 10B, 10C, 10F
11A, 11B, 11C, 11D, 11E, 11F	12A, 12B, 12F	13	14	15A, 15B, 15C, 15F	16A, 16F	17A, 17F	18A, 18B, 18C, 18F	19A, 19B, 19C, 19F	20A, 20B
21	22A, 22F	23A, 23B, 23F	24A, 24B, 24F	25A 25F		27	28A 28F	29	
31	32A 32F	33A, 33B 33C, 33D 33E, 33F	34	35A, 35B 35C, 35F	36	37	38	39	40
41A 41F	42	43	44	45	46	47A 47F	48		

- Marketed in 2010 to replace PCV7 in children (after serotype replacement phenomenum)
- Licensed in 2012 for use in adults (after immunogenicity studies)
- Efficacy of 46% against vaccine-type IPD among Netherlands elderly (RCT CAPITA, 2014)

RECOMENDACIONES PARA LA VACUNACIÓN ANTINEUMOCÓCICA EN ADULTOS SEGÚN GENERALITAT/MINISTERIO DE SANIDAD, CDC Y SOCIEDADES PROFESIONALES

	Generalitat/Ministerio de Sanidad	CDC	Sociedades Profesionales
15-64 años			
Inmunocompromiso y/o otras condiciones de alto riesgo (fistulas, asplenia, fístulas LCR, implante coclear)	VNC13 + VNP23	VNC13 + VNP23	VNC13 + VNP23
Inmunocompetentes con ciertas patologías crónicas o factores de riesgo (enfermedad pulmonar o cardiaca crónica, diabetes, alcoholismo y tabaquismo)	VNP23	VNP23	VNC13
Inmunocompetentes sin factores de riesgo	No vacunación antineumocócica	No vacunación antineumocócica	No vacunación antineumocócica
>65 años			
Inmunocompromiso y/o otras condiciones de alto riesgo (fistulas, asplenia, fístulas LCR, implante coclear)	VNC13 + VNP23	VNC13 + VNP23	VNC13 + VNP23
Inmunocompetentes con ciertas patologías crónicas o factores de riesgo (enfermedad pulmonar o cardiaca crónica, diabetes, alcoholismo y tabaquismo).	VNP23	VNC13 + VNP23	VNC13
Inmunocompetentes sin factores de riesgo	VNP23	VNC13 + VNP23	VNP23

COMPARISON EFFICACY/EFFECTIVENESS PPV23 *vs* PCV13



- Moberley S, et al. Vaccines for preventing pneumococcal infection in adults. Cochrane Database Syst Rev. 2013;1:CD000422.
- Bonten MJ, et al. Polysaccharide conjugate vaccine against pneumococcal pneumonia in adults. N Engl J Med. 2015; 372: 1114-25.

EPIVAC-SIDIAP Cohort Study

Nom del projecte:

Efectivitat clínica de la vacunació antipneumocòccica conjugada versus polisacárida en adults de Catalunya: estudi de cohorts de base poblacional.

Ref study protocol:

Vila-Córcoles A, Ochoa-Gondar O. Evaluating Clinical Effectiveness of 13-Valent and 23-Valent Pneumococcal Vaccination among People Over 50 Years in Catalonia: The EPIVAC Cohort Study. J Respir Med Lung Dis. 2018; 3 (1): 1032

EPIVAC-SIDIAP Cohort Study. OBJECTIVE

To investigate clinical effectiveness of anti-pneumococcal vaccination (PCV13 and PPV23) in preventing hospitalisation for pneumococcal disease (IPD/PP), all-cause pneumonia and death among adults over 50 years in Catalonia.

... considering the debate about current PCV13/PPV23 recommendations, vaccination effectiveness will be assessed according to baseline risk strata of study subjects:

- **High-risk**: asplenia and/or immunocompromising conditions
- **Medium-risk**: immunocompetent subjects with certain chronic diseases/risk conditions
- **Low-risk**: immunocompetent subjects without risk conditions

EPIVAC-SIDIAP Cohort Study. DESIGN

- **Population-based prospective cohort study**

  (funded by grants from IDIAP, ISCIII and PERIS)

- **Involving 274 primary care centres and 68 reference hospitals**

- **In Catalonia**

EPIVAC-SIDIAP Cohort Study. STUDY POPULATION/COHORT

- All persons aged 50 years or older
- Assigned to any of the 274 Primary Care Centres of the Institut Català de la Salut
- Registered in SIDIAP
- Sistema d'Informació per al Desenvolupament de la Investigació en Atenció Primària
- At January 1, 2015 (first day of follow-up)

SAMPLE SIZE:

2,025,730 (77%) of the total 2,617,336 inhabitants over 50 years in Catalonia

EPIVAC-SIDIAP Cohort Study. DATA SOURCES

- **TO ESTABLISH STUDY COHORT**:

  Sistema d'Informació per al Desenvolupament de la Investigació (IDIAP), which compiles clinical data contained in primary care “e-CAP” records.

- **TO CAPTURE STUDY EVENTS**:

  Hospital discharge data (CMBD) of 68 Catalonian hospitals will be used

EPIVAC-SIDIAP Cohort Study. END-POINTS

- **Hospitalisation from:**
  - **Invasive Pneumococcal Disease**
  - **Pneumococcal Pneumonia**
  - **All-cause pneumonia**

- **Death from:**
  - **Invasive Pneumococcal Disease**
  - **Pneumococcal Pneumonia**
  - **All-cause pneumonia**
  - **All-cause death**

EPIVAC-SIDIAP Cohort Study.

STUDY VARIABLES

- **EXPOSURE**: Vaccination status (according to e-CAP data) for both PPV23 and PCV13 will be as a time-varying condition given some individuals can receive the vaccine after the study start.

- **COVARIABLES**: Age, sex, influenza vaccine status, history of previous IPD/pneumonia, presence of chronic pulmonary/respiratory disease, chronic heart disease, diabetes mellitus, chronic liver disease, immunodeficiency/HIV infection, asplenia, chronic renal disease, bone marrow transplantation, recent cancer or immunosuppressive therapy, alcoholism, smoking and influenza vaccination status.

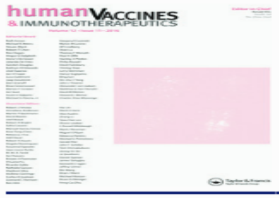
EPIVAC-SIDIAP Cohort Study. ANALYSIS

- **Cox Regression models for time-varing covariables will be used to evaluate the association between PCV13/PPV23 and the risk of each outcome adjusted for age, sex and major comorbidities/underlying risk conditions.**

- **Suplementary stratified analyses focused on age subgroups and baseline risk strata:**
  - Immunocompromised
  - Immunocompetent with other risk conditions

EPIVAC-SIDIAP Cohort Study.

BASELINE ANALYSIS: VACCINATION COVERAGES



Human Vaccines & Immunotherapeutics

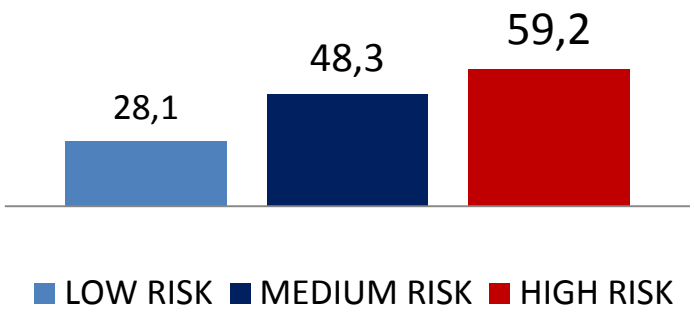
Taylor & Francis

ISSN: 2164-5515 (Print) 2164-554X (Online) Journal homepage: http://www.tandfonline.com/loi/khvi20

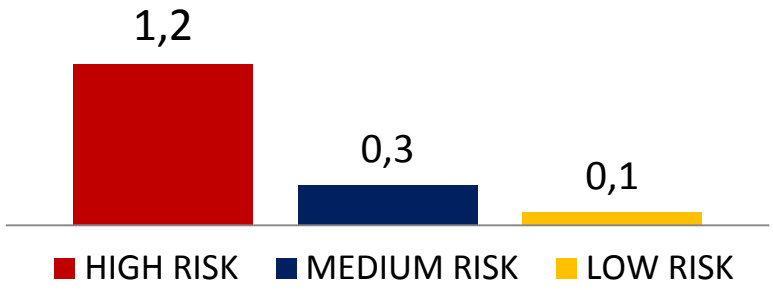
Pneumococcal vaccination coverages among low-, intermediate-, and high-risk adults in Catalonia

Angel Vila-Corcoles, Olga Ochoa-Gondar, Imma Hospital, Cinta de Diego, Eva Satué, Jordi Bladé, Xabier Ansa, Jorge A. Guzmán, Elisabet Salsench & Francisca Ramos

PPV23



PCV13



Overall PPV23 coverage = 38.8%
Overall PCV13 coverage = 0.3%

EPIVAC-SIDIAP Cohort Study

BASELINE ANALYSIS: UNDERLYING RISK CONDITIONS

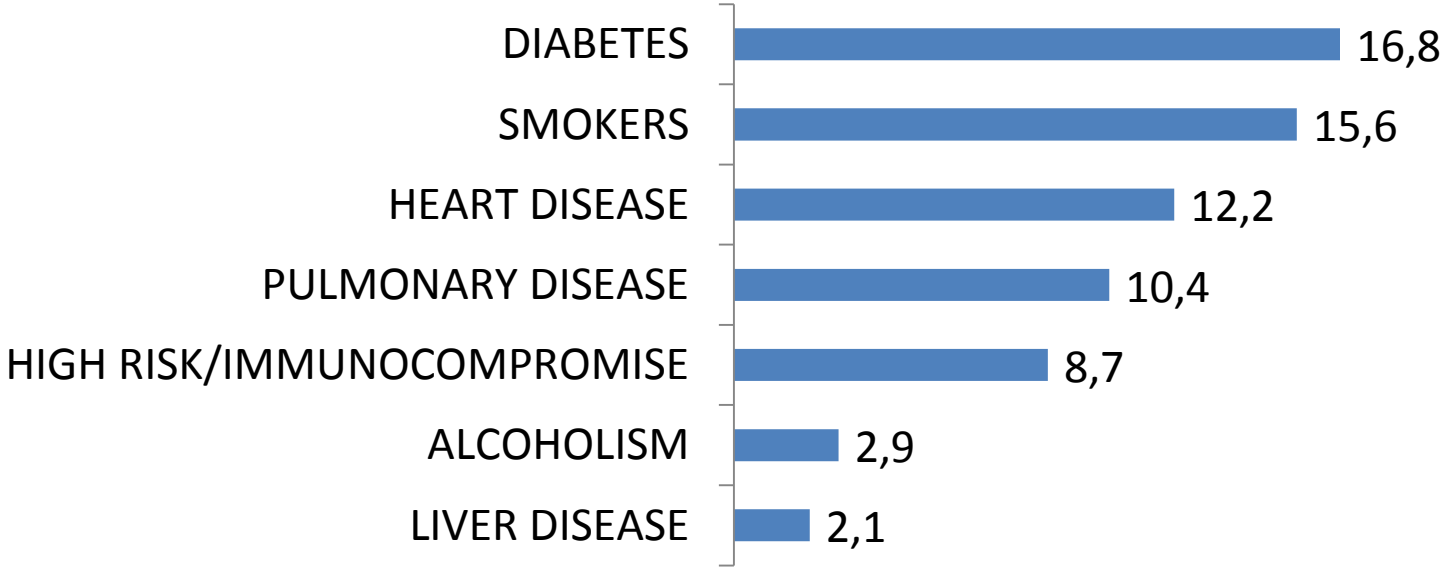
Ochoa-Gondar *et al. BMC Public Health* (2017) 17:610
DOI 10.1186/s12889-017-4529-8

BMC Public Health

RESEARCH ARTICLE Open Access

Prevalence of high, medium and low-risk medical conditions for pneumococcal vaccination in Catalonian middle-aged and older adults: a population-based study

O. Ochoa-Gondar[1,2*], I. Hospital[1], A. Vila-Corcoles[1,2], M. Aragon[3], M. Jariod[4], C. de Diego[1], E. Satue[1] and EPIVAC Study Group



EPIVAC-SIDIAP Cohort Study

BASELINE ANALYSIS: RISK STRATA

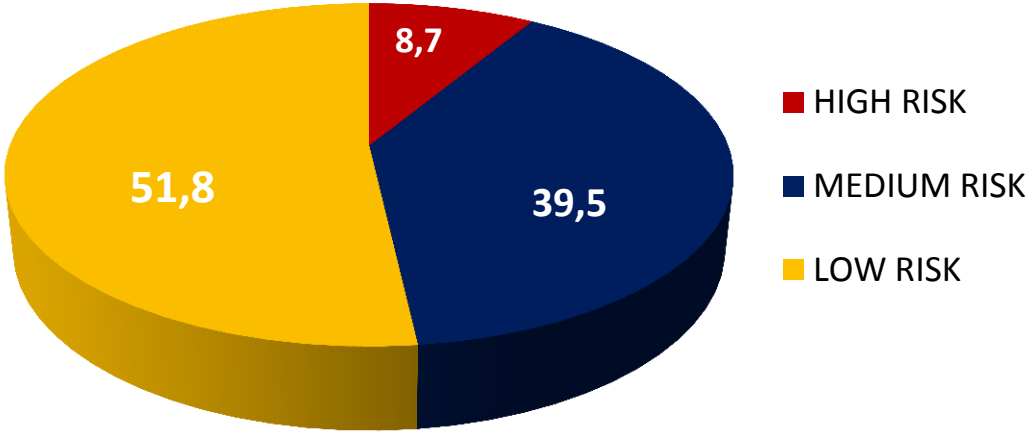
Rev Esp Salud Pública. 2017; Vol. 91; 16 de marzo e1-e8. www.msc.es/resp

ORIGINAL BREVE

Recibido: 10 de marzo de 2017
Aceptado: 15 de marzo de 2017
Publicado: 16 de marzo de 2017

ESTIMACIÓN DE LA POBLACIÓN MAYOR DE 50 AÑOS SUSCEPTIBLE DE RECIBIR LA VACUNACIÓN ANTINEUMOCÓCICA EN CATALUÑA Y ESPAÑA (*)

Angel Vila-Córcoles (1), Olga Ochoa-Gondar (1), Eva Satué (1), (1), Marc Vila-Rovira (2) y Manel Jariod (3).



The target population for pneumococcal vaccination varied between 0.2-1.9 million in Catalonia and 1.5-12.3 million in Spain (depending on distinct risk strata considered).

Cohort EPIVAC-SIDIAP . FIRST-YEAR FOLLOW-UP

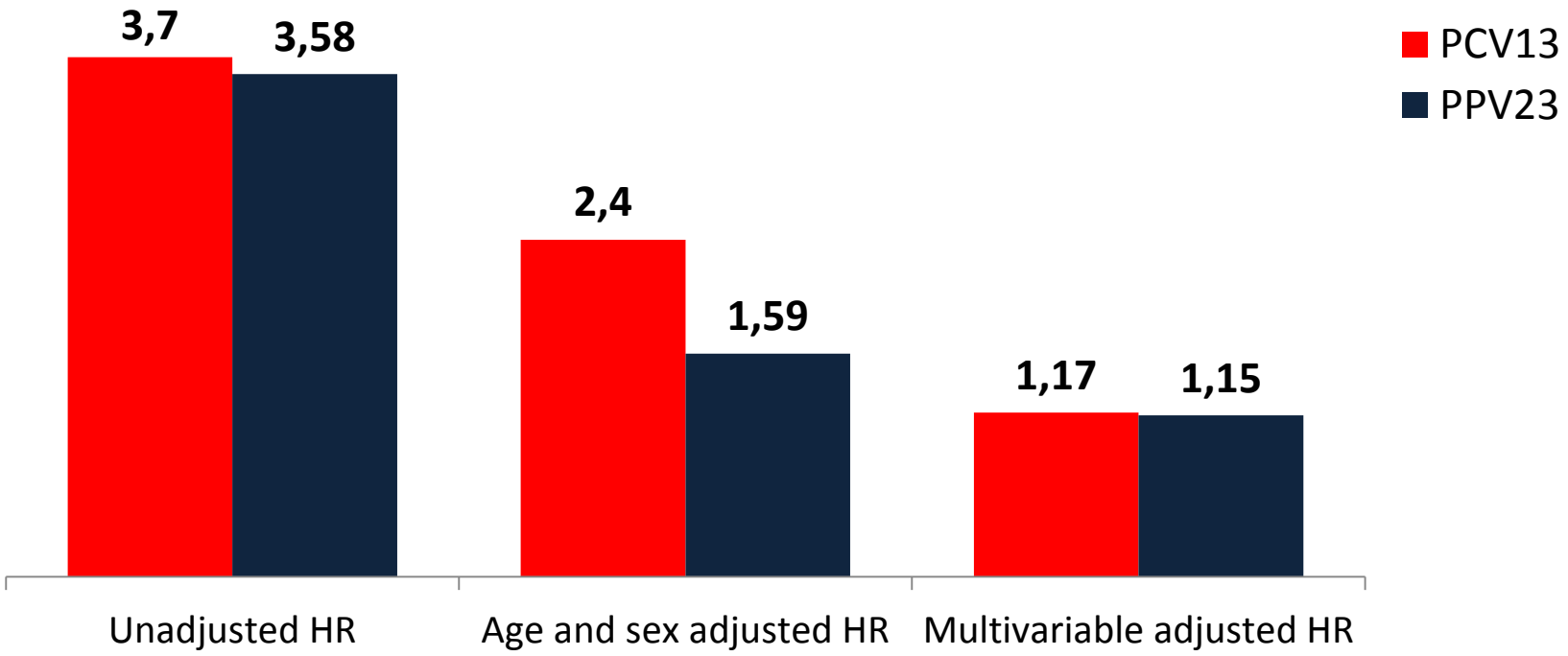
TIME FOLLOW-UP until first event/one-year (persons-year)			
PCV13 vaccinated	PPV23 vaccinated	Unvaccinated	Overall
6,913	777,477	1,206,311	1,990,701

RESULTS: GLOBAL INCIDENCE OF STUDY EVENTS

Event	Number of cases	Incidence Rate (per 100,000 persons-year)
Invasive Disease (IPD)	447	22.4
Pneumococcal Pneumonia (PP)	1648	82.8
All-cause pneumonia	12,699	637.9
Death from IPD	45	2.3
Death from PP	81	4.1
Death from pneumonia	855	43.0
Death from any cause	47,265	2367.2

Cohort EPIVAC-SIDIAP. FIRST-YEAR FOLLOW-UP

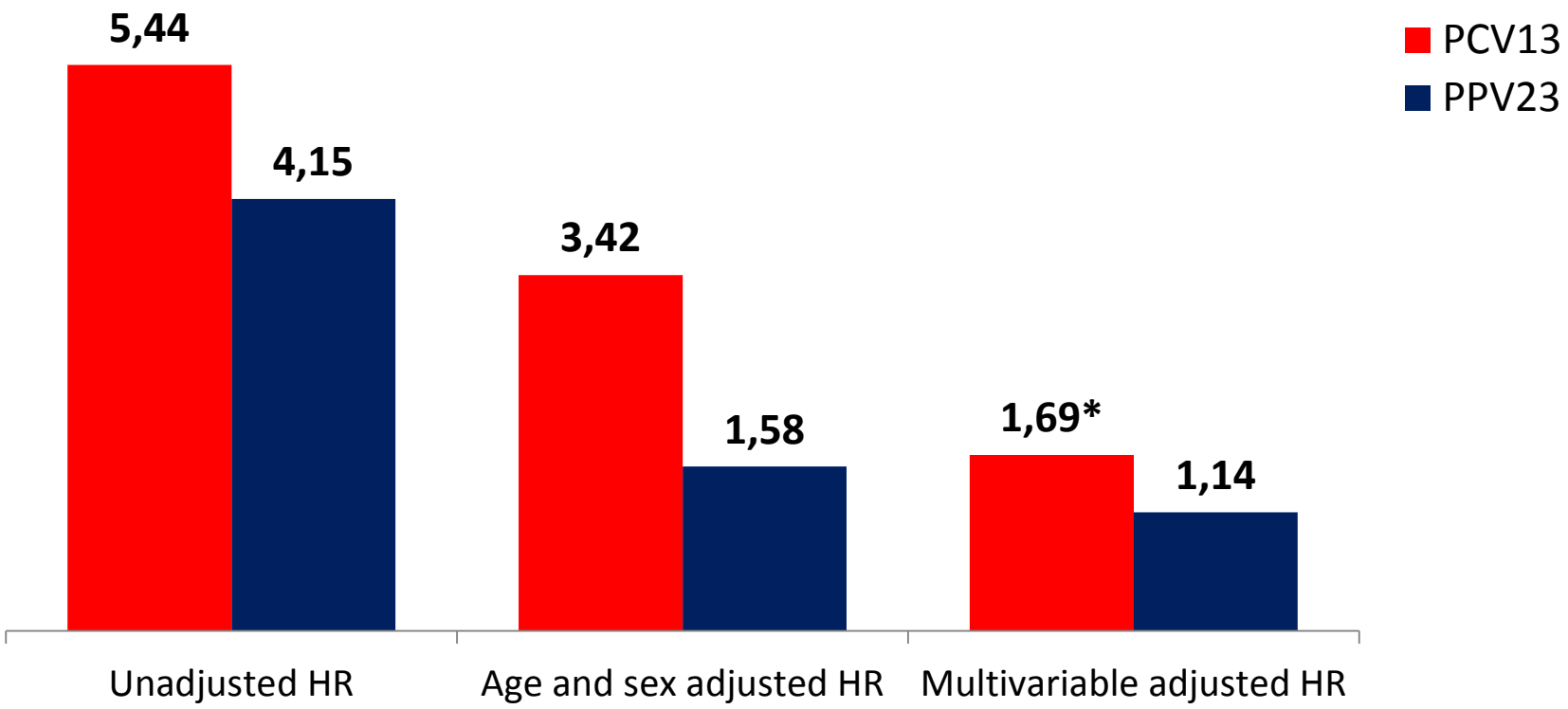
RESULTS: RISK OF PNEUMOCOCCAL PNEUMONIA ACCORDING TO PNEUMOCOCCAL VACCINE STATUS



Hazard Ratio (HR) are for vaccinated as compared with unvaccinated subjects

Cohort EPIVAC-SIDIAP. FIRST-YEAR FOLLOW-UP

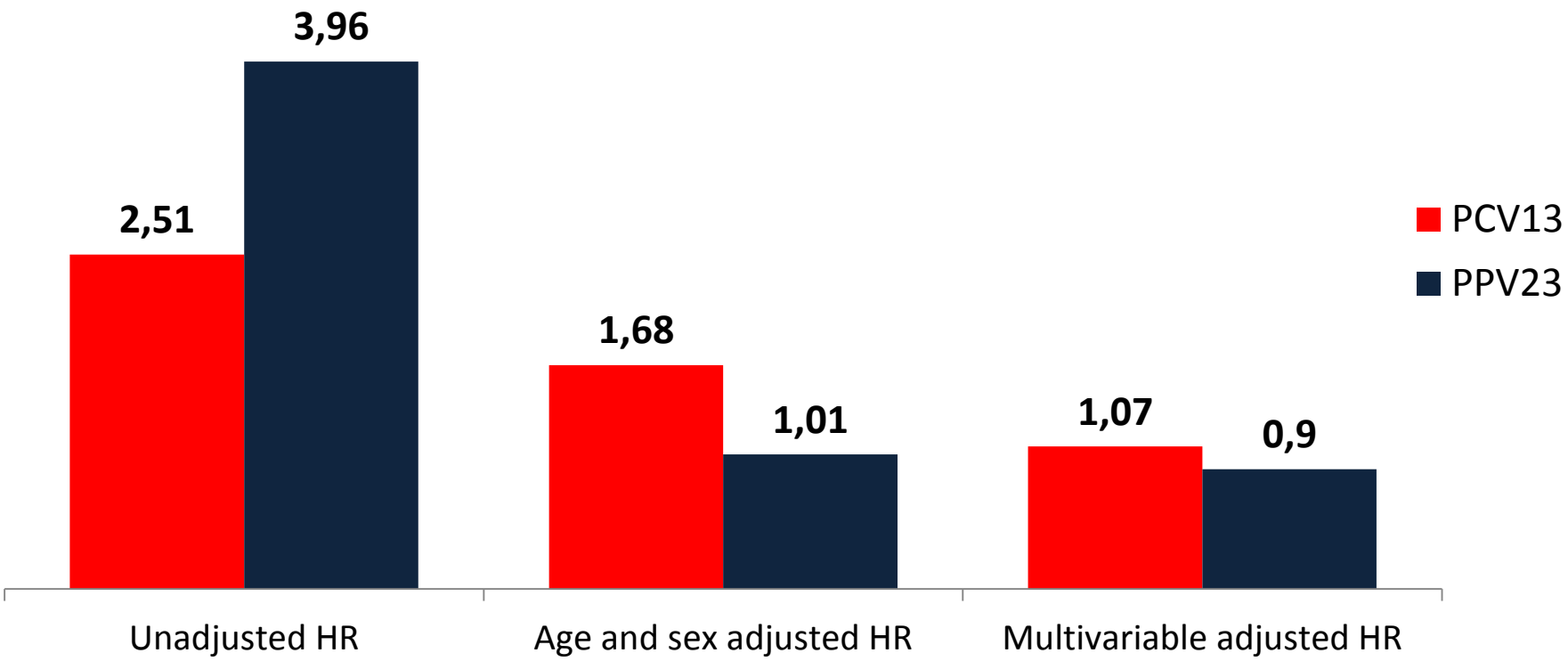
RESULTS: RISK OF ALL-CAUSE PNEUMONIA ACCORDING TO PNEUMOCOCCAL VACCINE STATUS



Hazard Ratio (HR) are for vaccinated as compared with unvaccinated subjects

Cohort EPIVAC-SIDIAP. FIRST-YEAR FOLLOW-UP

RESULTS: RISK OF ALL-CAUSE DEATH ACCORDING TO PNEUMOCOCCAL VACCINE STATUS (47,265 EVENTS)



ALL-CAUSE DEATH RATES (per 100,000 person/years)

PCV13 vaccinated = 5944 (IC95% 5385-6562) **PPV23 vaccinated** = 4348 (IC95% 4083-4627)

Unvaccinated = 1092 (IC95% 1026-1162)

CONCLUSIONS

✓ In this population-based prospective cohort study involving more than 2 million people over 50 years-old around Catalonia, clinical benefits from pneumococcal vaccination have not emerged after one-year follow-up.

✓ Our preliminary data does not exclude a possible negative/harm effect of PCV13 (increasing risk of all-cause pneumonia among PCV13 vaccinated subjects), which should be closely monitored in future studies involving more vaccinated person-time at-observation.

Generalitat de Catalunya
Departament de Salut

Institut Català
de la Salut

IDIAP
Jordi Gol

ics.gencat.cat