

ENFERMEDAD NEUMOCÓCICA INVASIVA

Mirian Domenech

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Científica Titular en el Laboratorio de Referencia de Neumococos

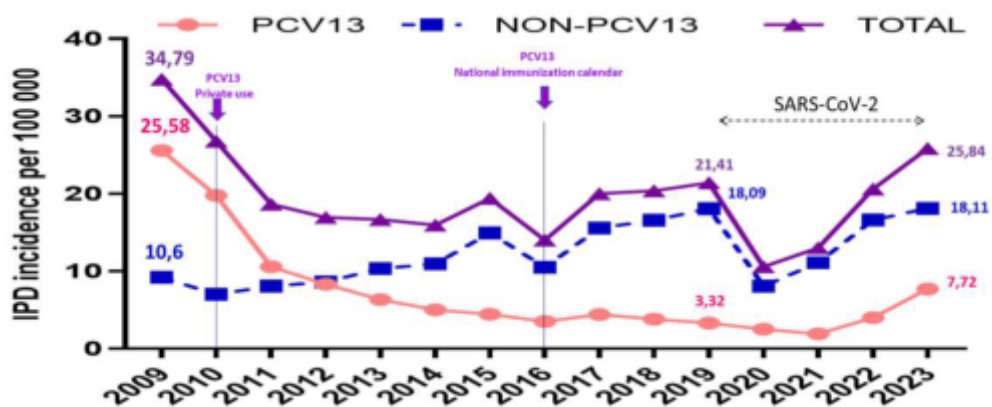
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CIBER de Enfermedades Respiratorias (CIBERES)

@miridome8



1



- La aparición del SARS-CoV-2 causó una bajada muy notable de casos de ENI por todos los serotipos en 2020
- Repunte de casos por serotipos NO-PCV13 en los últimos años con incidencias superiores al 2009
- La incidencia de casos por serotipos PCV13 en 2023 sigue aún muy por debajo de la que había en 2009 (antes de PCV13)



Laboratorio de Referencia e Investigación en Enfermedades Bacterianas Prevenibles por Vacunas

De Miguel S et al. Clin Infect Dis. 2021;ciaa1483. doi: 10.1093/cid/ciaa1483.

Pérez-García C et al. J Infect. 2024 Aug;89(2):106204. doi: 10.1016/j.jinf.2024.106204)

2

2023

Serotipos predominantes por grupo de edad

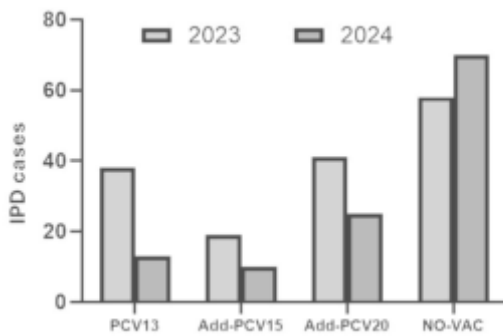
<2			2<5			5-17		
serotype	N		serotype	N		serotype	N	
24F	24	15,38	3	21	21,88	8	22	26,19
3	23	14,74	24F	15	15,63	3	14	16,67
8	13	8,33	22F	9	9,38	22F	6	7,14
15B	11	7,05	19A	8	8,33	24F	5	5,95
22F	11	7,05	15A	5	5,21	19A	4	4,76
10A	11	7,05	23B	5	5,21	19F	4	4,76
38	9	5,77	8	4	4,17	10A	3	3,57
33F	8	5,13	9N	3	3,13	6C	3	3,57
19A	5	3,21	19F	3	3,13	23A	3	3,57
16F	4	2,56	23A	3	3,13	11A	2	2,38

- < 2 años: Serotipo 24F
- 2-4 años: Serotipo 3
- ≥ 5 años: Serotipo 8

Pérez-García C* et al. J Infect. 2024 Aug;89(2):106204. doi: 10.1016/j.jinf.2024.106204)



3



- Menor número de casos en 2024 vs 2023
- Disminución importante de casos por serotipos PCV13 y adicionales de PCV15 y PCV20 en 2024

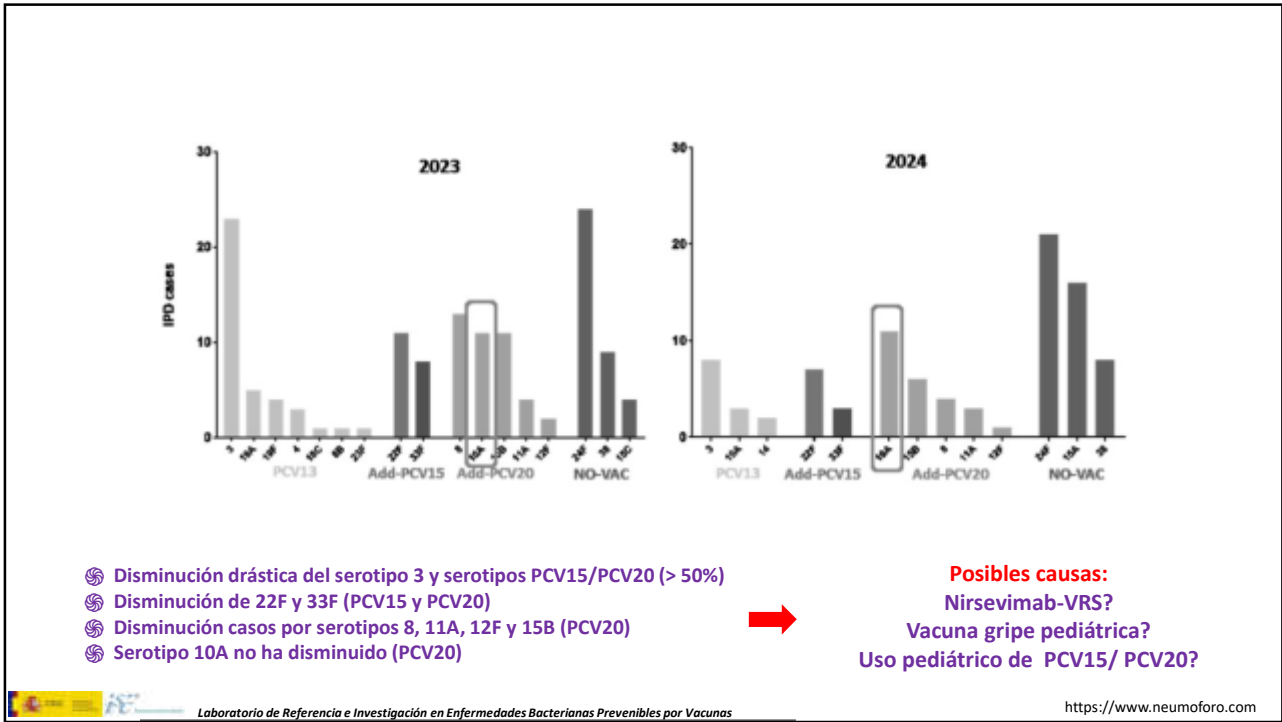
Fracción de enfermedad prevenible con PCV15 vs PCV20

En 2024
 PCV15 aumenta un 8% a PCV13
 PCV20 aumenta un 29% a PCV13

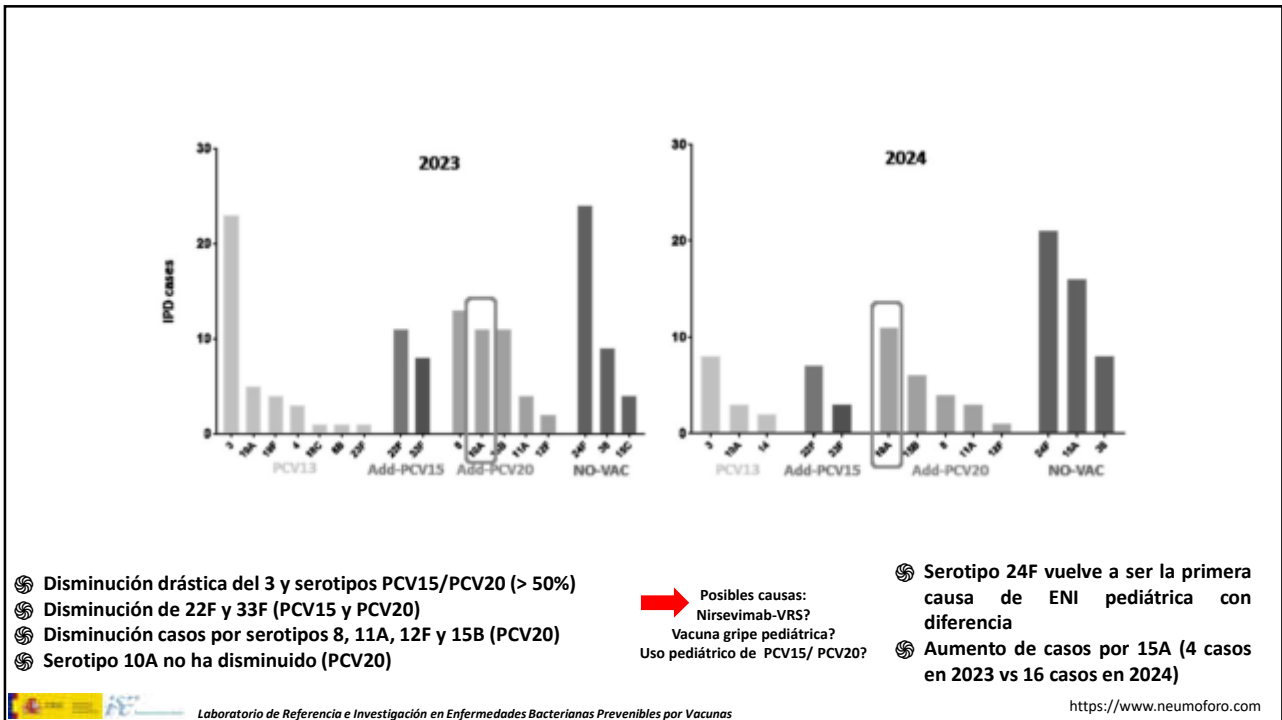


Pérez-García C* et al. J Infect. 2024 Aug;89(2):106204. doi: 10.1016/j.jinf.2024.106204)

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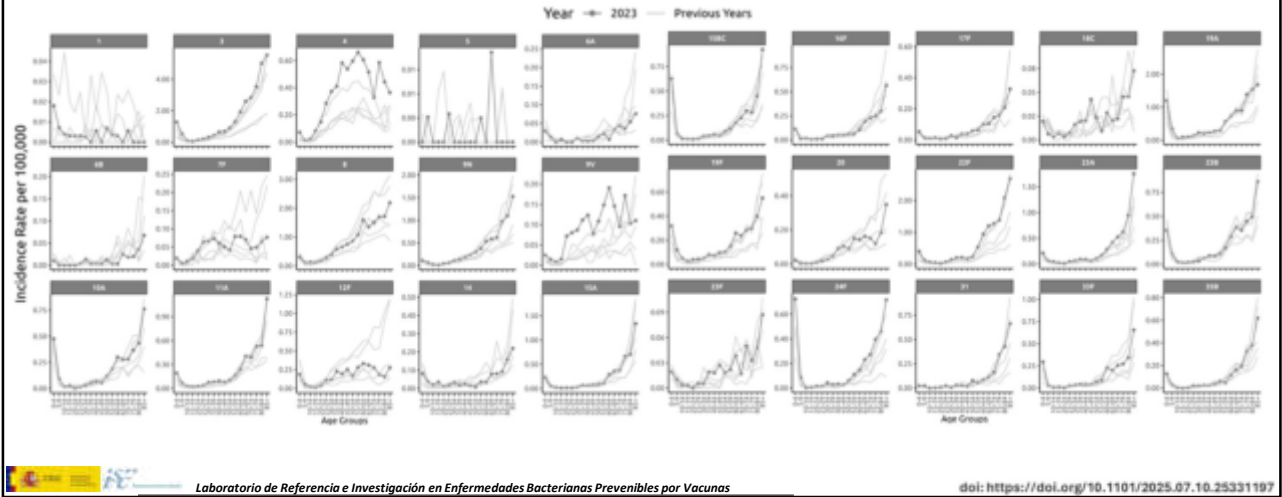


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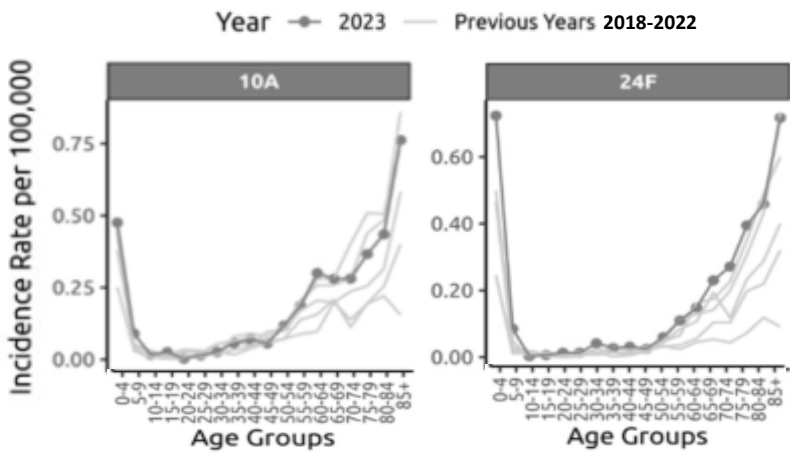


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Incidencia de ENI por serotipo, estratificada por edad

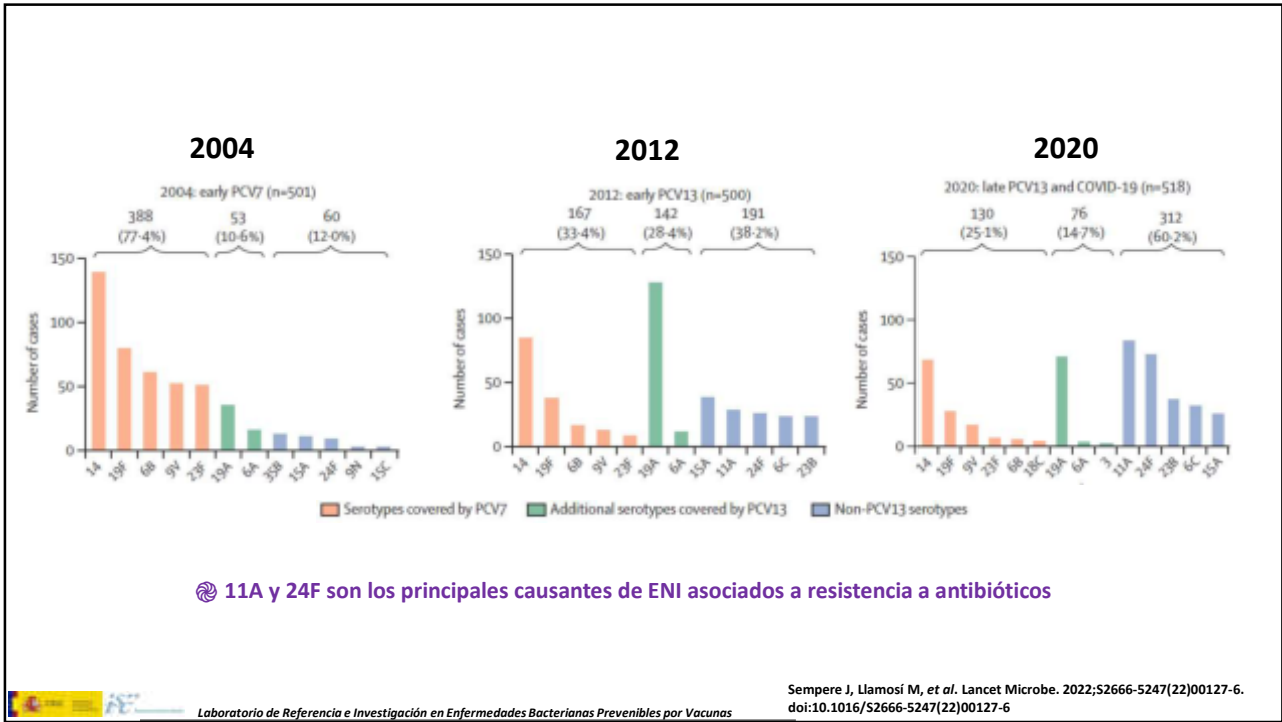


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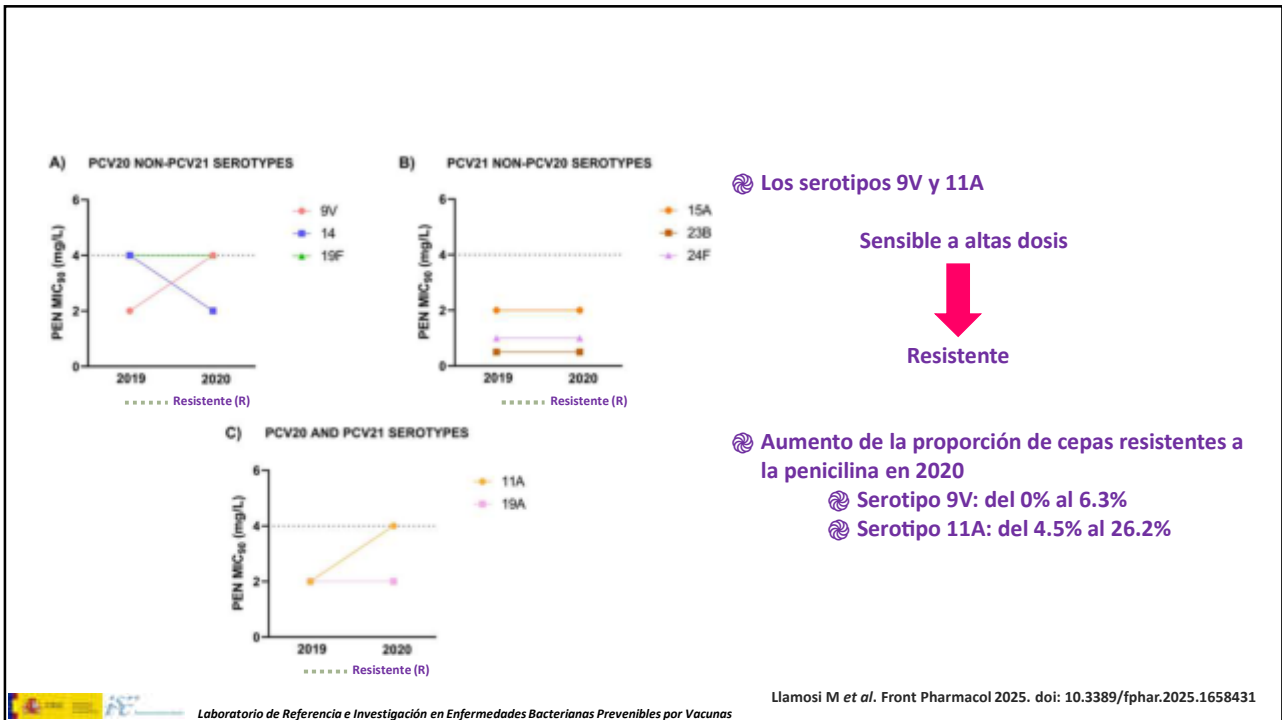


🌀 En el grupo de edad < 5 años los serotipos 10A y 24F presentan mayores tasas de incidencia en 2023 que en los años previos

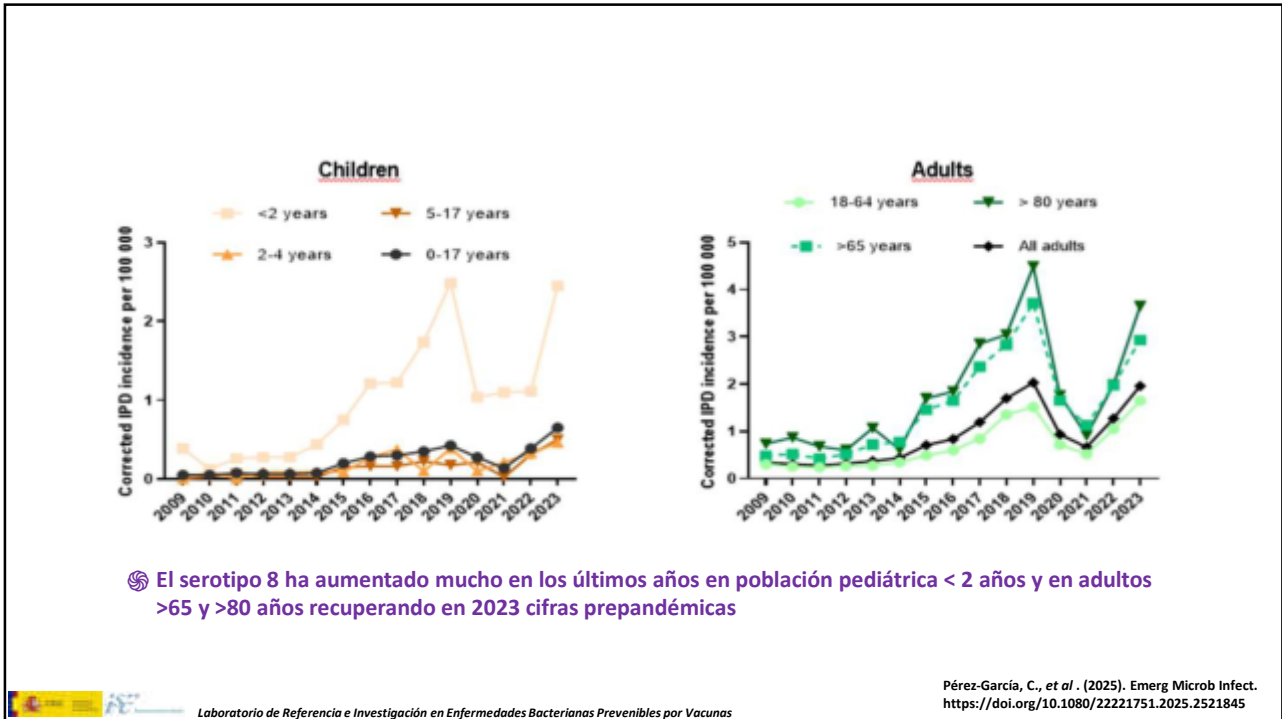
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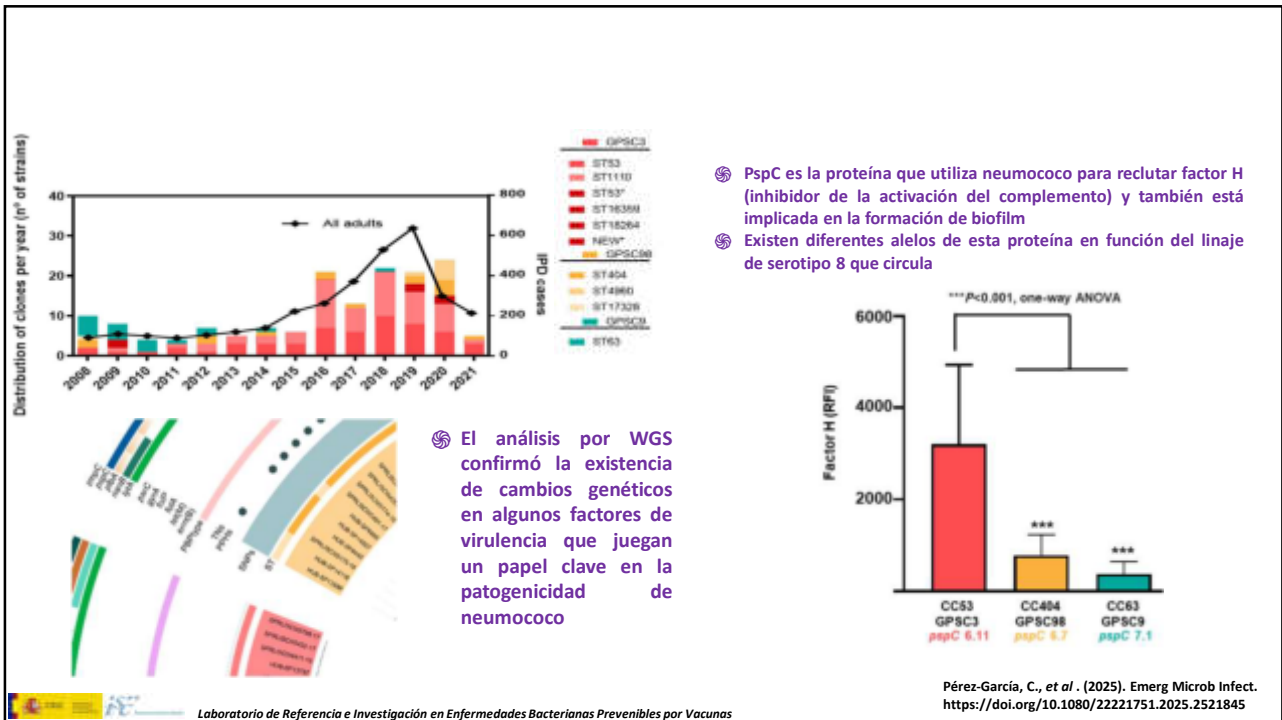
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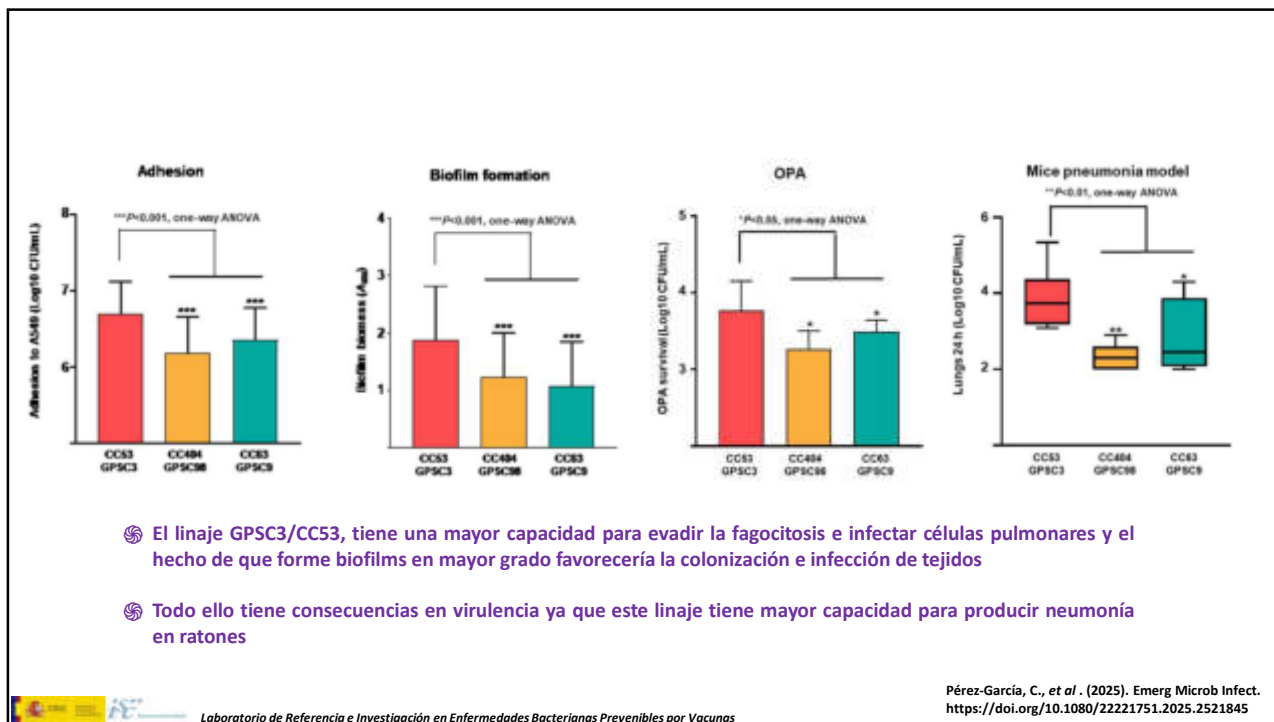
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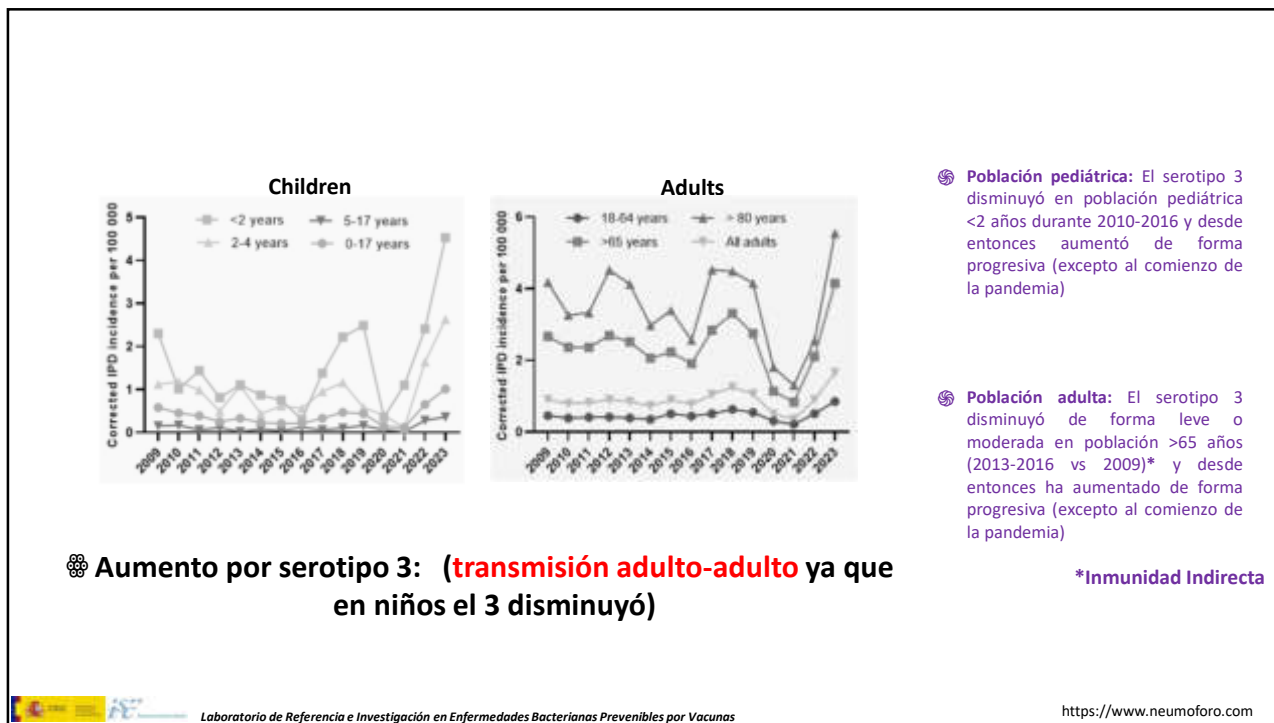
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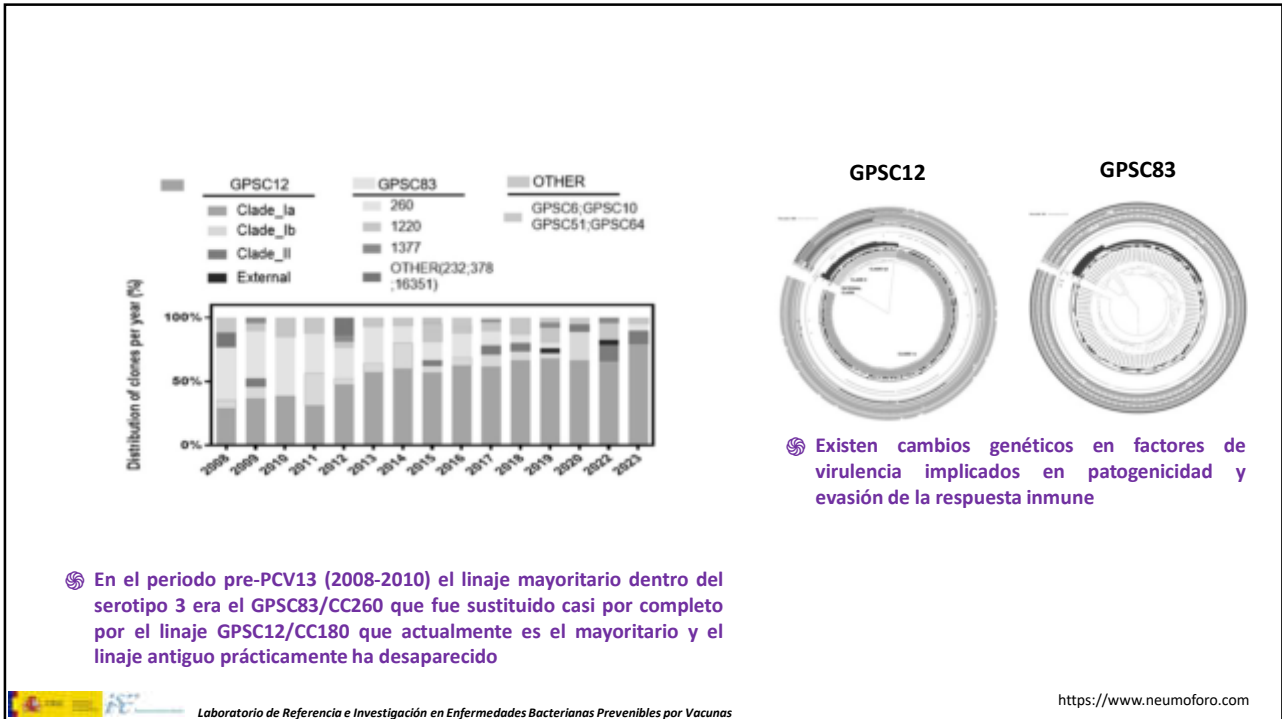
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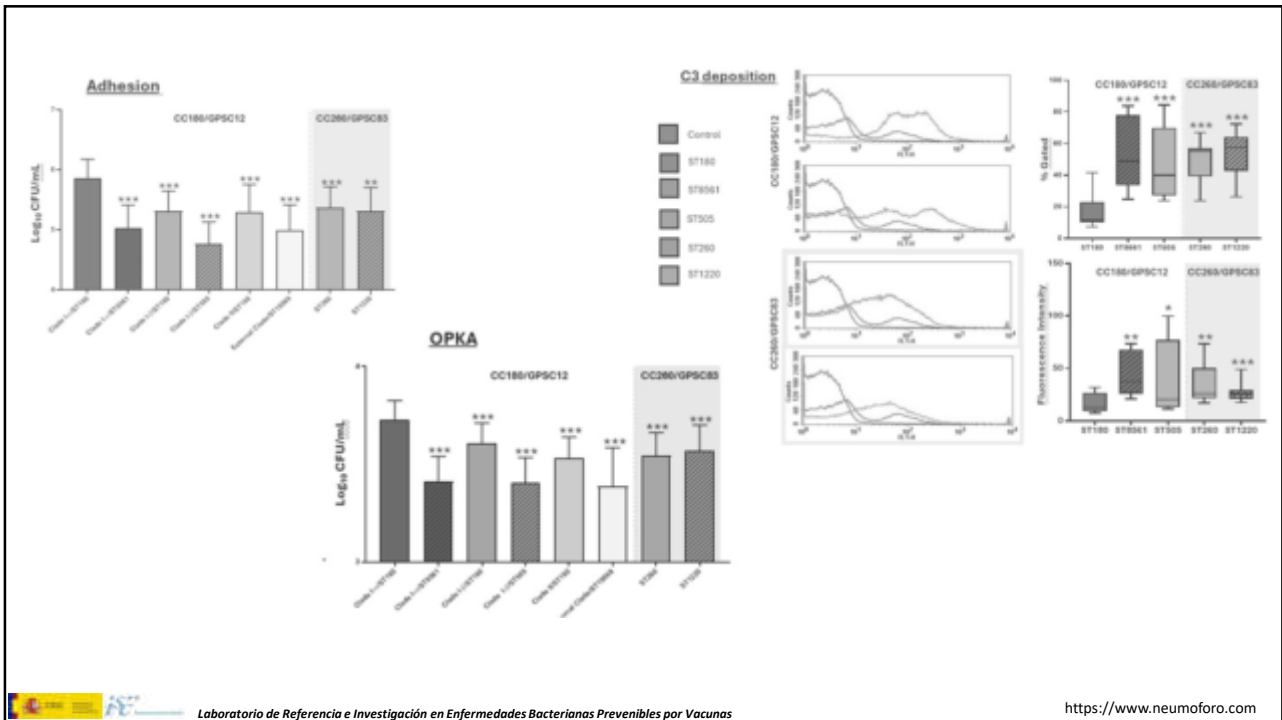
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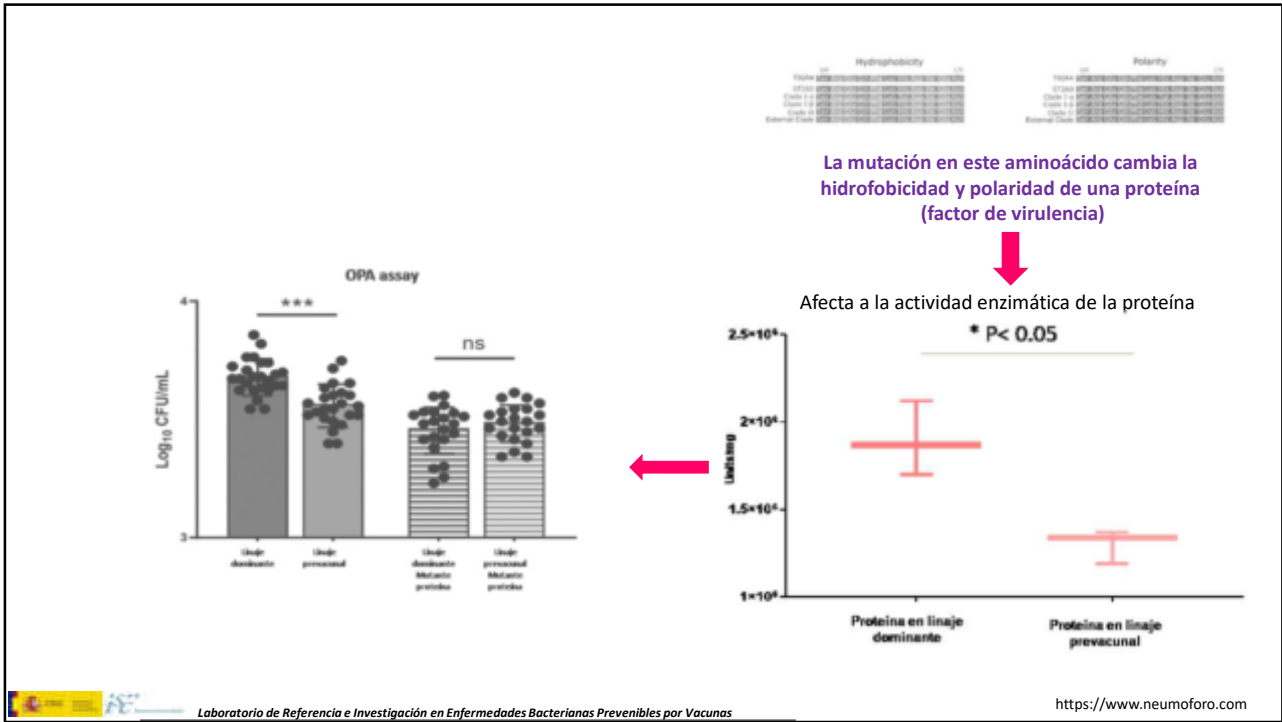
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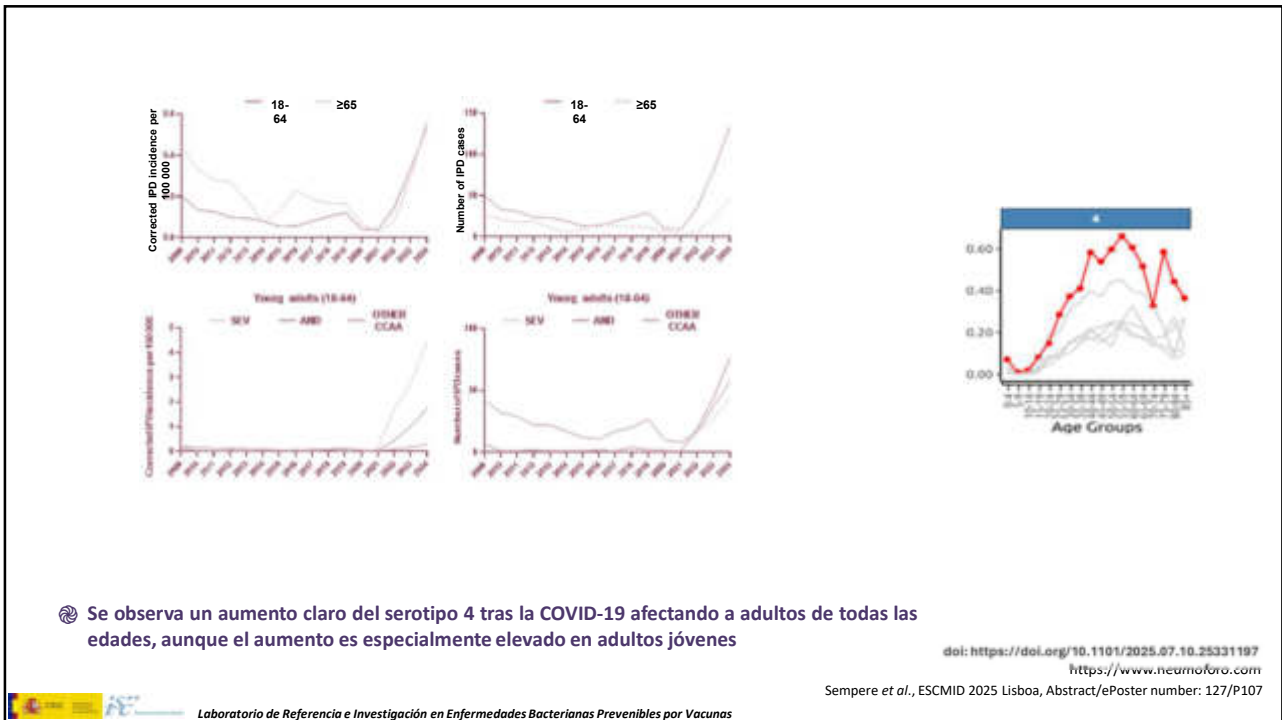
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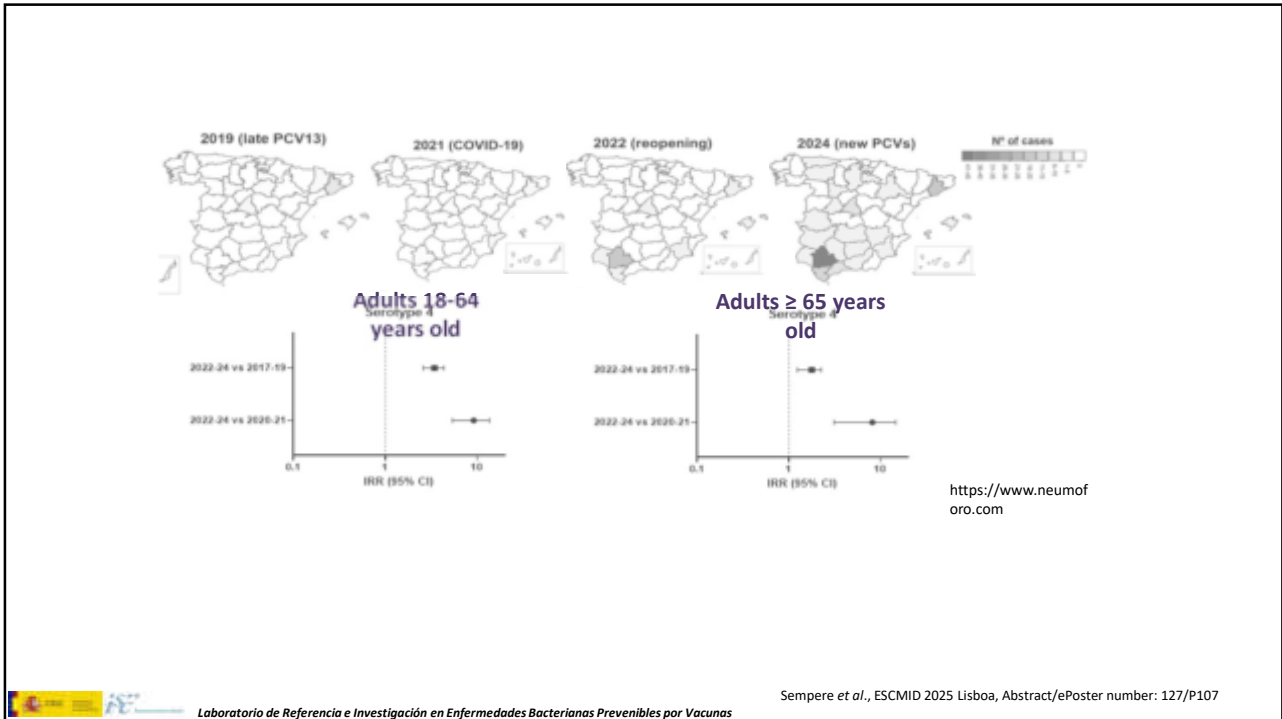
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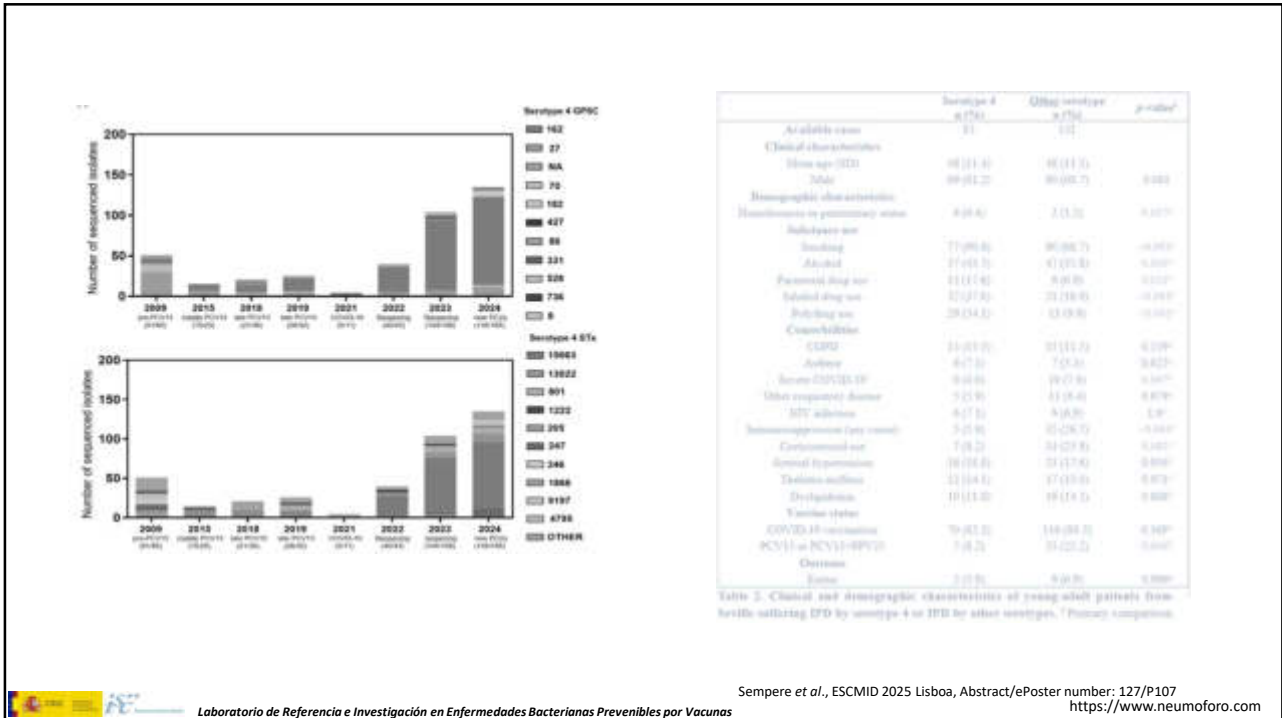
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Novedades en la interacción entre Virus y Bacterias

JOSE YUSTE

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Investigador Científico

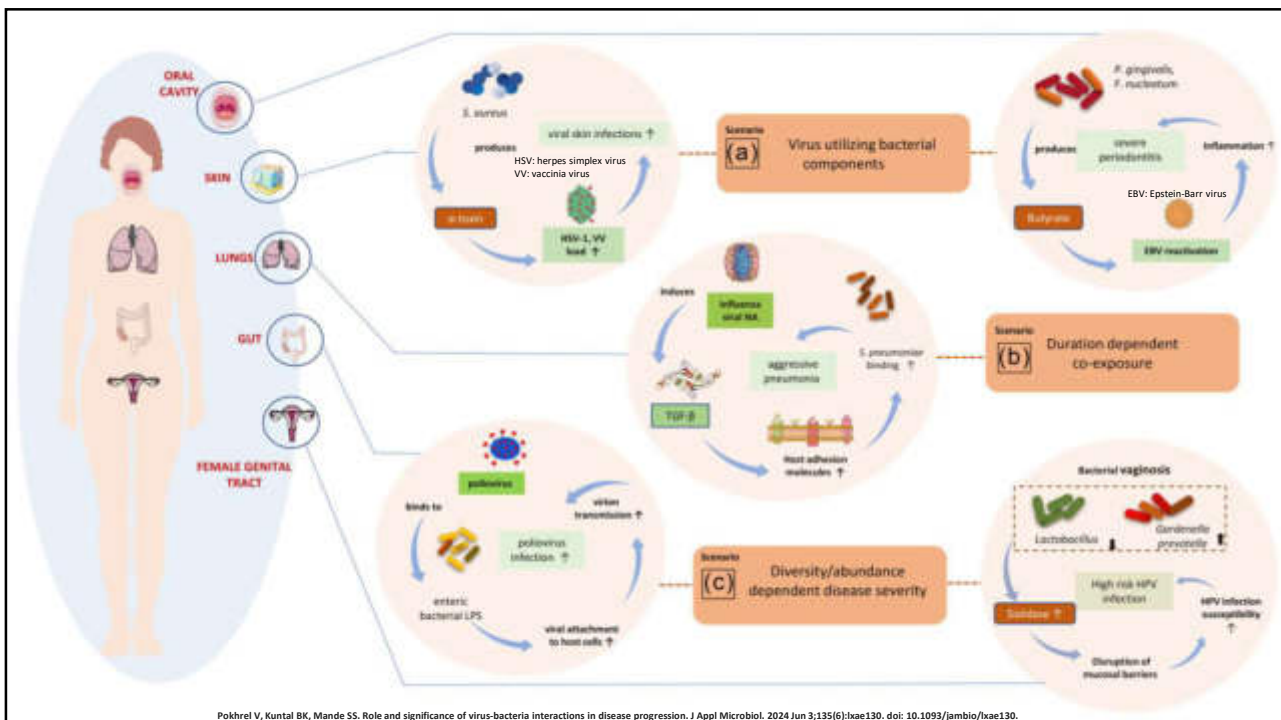
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Neumococo y su interacción con virus respiratorios

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LAS CO-INFECCIONES DE NEUMOCOCO CON VIRUS RESPIRATORIOS INCREMENTAN LA GRAVEDAD Y MORTALIDAD DE LAS NEUMONÍAS

Bacterial culture results in autopsy series involving culture of blood and pleural fluid or empyema fluid from victims of the 1918-1919 influenza epidemic.

Type of autopsy series	No. of results	No. (%) of cultures from which organism was recovered, by organism							No. growth
		Streptococcus pneumoniae	Streptococcus faecalis	Staphylococcus aureus	Diphtheria intracellulare meningitidis	Mixed pneumopathogen	Bacillus anthracis	Other bacteria	
Blood culture (n = 42)									
All military and civilian	107	399 (21.3)	377 (28.6)	68 (3.4)	168 (3)	28 (1.3)	61 (3.2)	278 (14.7)	860 (28.7)
Pleural fluid or empyema fluid culture (n = 35)									
All military and civilian	120	267 (21.3)	539 (43.3)	39 (4.7)	6 (0.6)	74 (5.9)	21 (1.7)	45 (3.6)	244 (19.6)

NOTE: The bacteria are listed by their common names in 1918. Streptococcus pneumoniae was cultured and sometimes typed with antisera into types I, II, III, IV, and V; type IV was generally regarded as consisting a number of "antigenic types." Streptococcus faecalis probably corresponds to Streptococcus pyogenes in most cases, most other are distinguished. Staphylococcus aureus from Staphylococcus albus. Bacillus anthracis observed only "Staphylococcus," which we categorized as "aerobic." The content suggested a pathogenic organism. Diphtheria intracellulare meningitidis corresponds to Neisseria meningitidis. Bacillus anthracis corresponds to Haemophilus influenzae. See Results for details about the "mixed pneumopathogen" and "other bacteria" category. Many "other" organisms were undoubtedly untyped pneumococci and streptococci. Bold type indicates percentage.

"Si la gripe condena, la co-infección (neumococo) ejecuta"

Louis Cruevilhier, 1919

Morens DM. J Infect Dis. 2008 Oct 1; 198(7): 962-970. doi: 10.1086/591708

 Laboratorio de Referencia e Investigación en Enfermedades Bacterianas Prevenibles por Vacunas

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LAS CO-INFECCIONES DE NEUMOCOCO CON VIRUS RESPIRATORIOS INCREMENTAN LA GRAVEDAD Y MORTALIDAD DE LAS NEUMONÍAS

Bacterial culture results in autopsy series involving culture of blood and pleural fluid or empyema fluid from victims of the 1918-1919 influenza epidemic.

Type of autopsy series	No. of results	No. (%) of cultures from which organism was recovered, by organism							No. (28%)
		Streptococcus pneumoniae	Streptococcus hemolyticus	Streptococcus aureus	Diphtheria-tetanus-meningitis	Mixed pneumococci	Acetab. influenzae	Other bacteria	
Blood culture (n=42)									
All military and civilian	107	99 (71%)	37 (28%)	48 (34)	149 (5)	24 (5)	41 (23)	278 (14.7)	80 (28.7)
Pleural fluid or empyema fluid culture (n=75)									
All military and civilian	120	20 (17%)	59 (49%)	39 (33%)	6 (5%)	74 (62%)	21 (18%)	45 (38%)	244 (204)

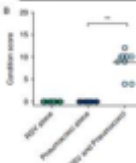
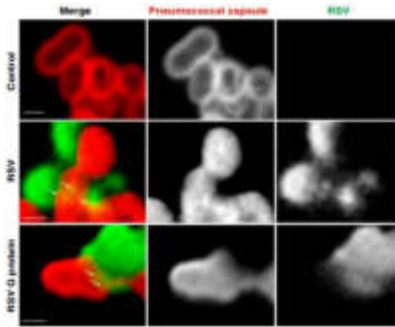
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"Si la gripe condena, la co-infección (neumococo) ejecuta"
Louis Cruveilhier, 1919

Morens DM. J Infect Dis. 2008 Oct 1; 198(7): 962-970. doi: 10.1086/591708

Respiratory Syncytial Virus Increases the Virulence of Streptococcus pneumoniae by Binding to Penicillin Binding Protein 1a A New Paradigm in Respiratory Infection

American Journal of Respiratory and Critical Care Medicine Volume 190 Number 2 | July 15 2014

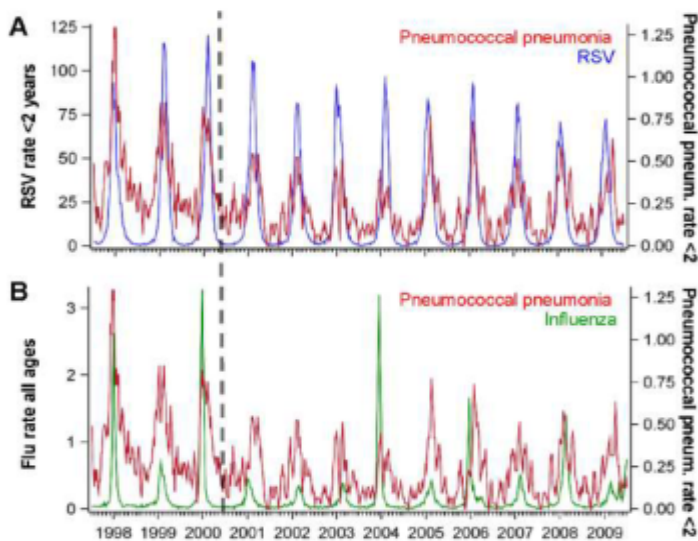


La infección por RSV favorece la infección por neumococo

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LAS CO-INFECCIONES DE NEUMOCOCO CON VIRUS RESPIRATORIOS INCREMENTAN LA GRAVEDAD Y MORTALIDAD DE LAS NEUMONÍAS




Neumococo se asocia frecuentemente a infecciones con el virus respiratorio sincitial y gripe

Weinberger DM, Klugman KP, Steiner CA, Simonsen L, Viboud C. Association between respiratory syncytial virus activity and pneumococcal disease in infants: a time series analysis of US hospitalization data. *PLoS Med.* 2015;12(1):e1001776. Published 2015 Jan 6. doi:10.1371/journal.pmed.1001776

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PROYECTO NEUMOPRETER
(NEUMOnías: PREvención y TERapias)



ANEJO: INVESTIGADORAS PRINCIPALES Y PERSONAS DEL EQUIPO DE INVESTIGACIÓN DEL PROYECTO PID2024-161579GB-I00

1. INVESTIGADORAS PRINCIPALES:	EXCLUIDA (SÍ/NO)
JOSE ENRIQUE YUSTE LOBO	NO
MIRIAM DOMENECH LUCAS	NO

2. PERSONAS QUE FIGURAN EN EL EQUIPO DE INVESTIGACIÓN:	EXCLUIDAS (SÍ/NO)
INVESTIGADORAS:	
RUTH GIL PRIETO	NO
MARIA JOSE CURRAS TURLA	NO

Instituto de Salud Carlos III

- Miriam Domenech
- Jose Yuste
- Inmaculada Casas
- Francisco Pozo
- Susana Monge

Hospital Vall de Hebrón

- Xavi Martínez
- Susana Otero

Neumococos


Virus respiratorios (gripe y VRS)

CNE-SIVIRA

Respuesta vacunal

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EFECTO INMUNOMODULADOR DE ANTIBIÓTICOS Y ANTICUERPOS ANTINEUMOCÓCICOS

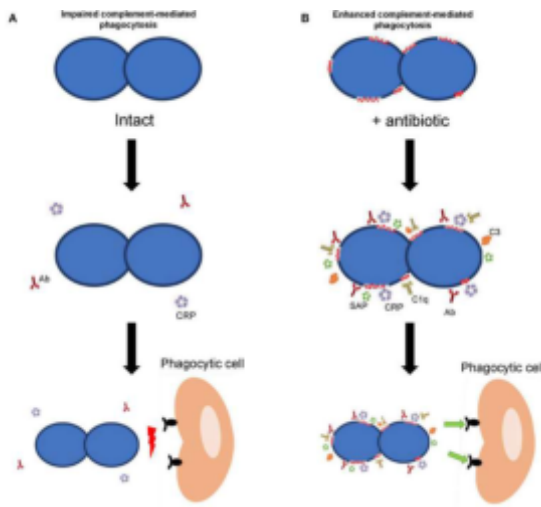


published: 20 November 2018
doi: 10.3389/fimmu.2018.02700


Combination of Antibodies and Antibiotics as a Promising Strategy Against Multidrug-Resistant Pathogens of the Respiratory Tract

Miriam Domenech^{1,2}, Julio Sempere^{1,2}, Sara de Miguel^{1,2} and Jose Yuste^{1,2*}

¹ Centro Nacional de Microbiología, Instituto de Salud Carlos III, Madrid, Spain, ² Centro de Investigación Biomédica en Red de Enfermedades Respiratorias, Madrid, Spain



La exposición a antibióticos produce daño en la envoltura bacteriana exponiendo mayor cantidad de epítopos antigénicos que permiten a los anticuerpos antineumocócicos unirse de forma más eficiente a neumococo favoreciendo la fagocitosis




INCREMENTO DE LA RESPUESTA INMUNITARIA

Domenech M, et al. Front Immunol. 2018 Nov 20;9:2700. doi: 10.3389/fimmu.2018.02700

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PROYECTO NEUMOPRETER (NEUMONías: PREvención y TERapias)



ANEXO: INVESTIGADORES PRINCIPALES Y PERSONAS DEL EQUIPO DE INVESTIGACIÓN DEL PROYECTO PID2024-161579GB-IB0


1. INVESTIGADORES PRINCIPALES:	EXCLUIDOS (SÍ/NO)
JOSE ENRIQUE YUSTE LOBO	NO
MIRIAM DOMENECH LUCAS	NO
2. PERSONAS QUE FIGURAN EN EL EQUIPO DE INVESTIGACIÓN:	EXCLUIDOS (SÍ/NO)
INVESTIGADORAS:	
RUTH GIL PRIETO	NO
MARIA JOSE CURRAS TURLA	NO

Uno de los objetivos del proyecto es la caracterización de posibles efectos sinérgicos en la infección de linajes hipervirulentos de neumococo con gripe y VRS

↓

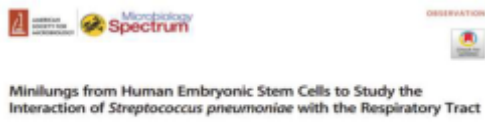
Task 1B: Synergistic infection of hypervirulent lineages with respiratory virus infection by influenza and Respiratory Syncytial Virus (RSV). People involved: JY, MD, MC, PH, JS, CP, EJV

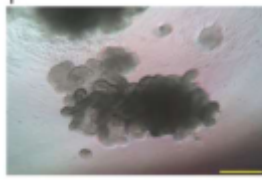
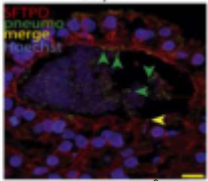
- Instituto de Salud Carlos III
 - Miriam Domenech
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 - Inmaculada Casas**
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 - Susana Monge**
- Hospital Vall de Hebrón
 - Xavi Martínez
 - Susana Otero
- Universidad Rey Juan Carlos
 - Ruth Gil Prieto
 - Angel Gil
- Hospital de Santiago de Compostela
 - María José Currás
 - Federico Martínón
- Mount Sinai (Nueva York)
 - Adolfo García Sastre
- Estancia de Covadonga Pérez García en Mount Sinai



Infecciones en modelos animales y celulares

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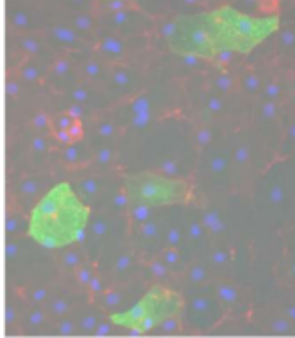



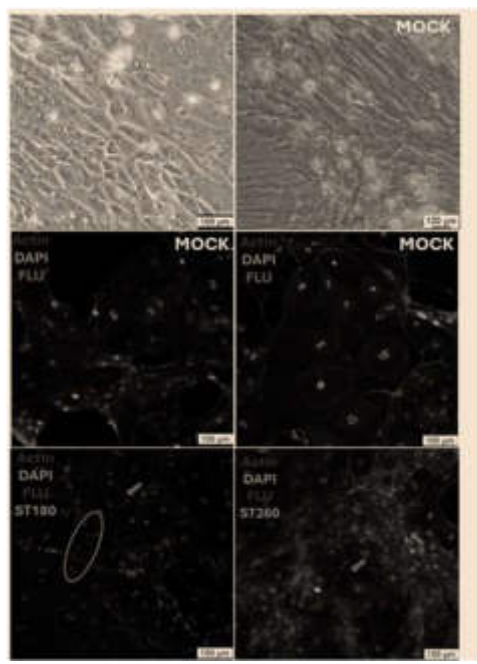
Co-infección gripe-neumo

→

Infección con VRS (sincitios en verde)

↻

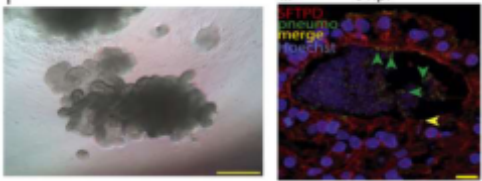




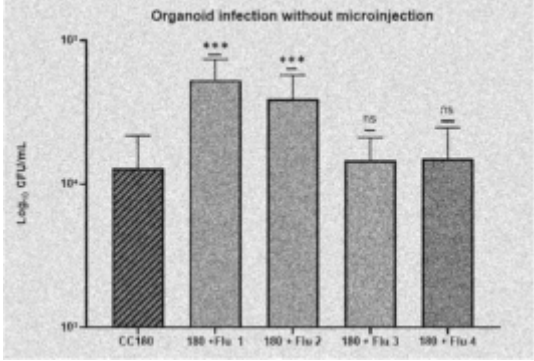
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Minilungs from Human Embryonic Stem Cells to Study the Interaction of *Streptococcus pneumoniae* with the Respiratory Tract

Julio Sempere^{1,2}, Judite Andrea Rest^{1,2}, Isaac Chomoro-Rivera¹, Fernando González-Camacho¹, María Pilar de Lencastre^{1,2}, José Tomás¹, Alberto Zambrano¹*



Co-infección gripe neuromo



Condition	Log ₁₀ CFU/mL
CC180	~10 ^{1.2}
180 + Flu 1	~10 ^{2.8} (***)
180 + Flu 2	~10 ^{2.5} (***)
180 + Flu 3	~10 ^{1.2} (ns)
180 + Flu 4	~10 ^{1.3} (ns)

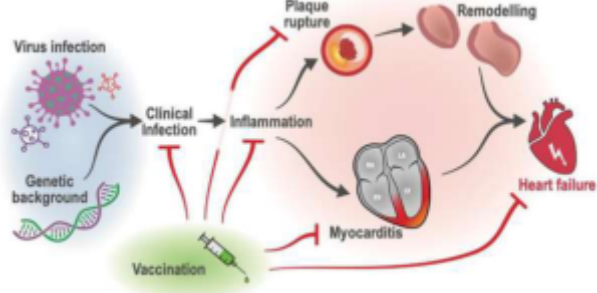
Los neumococos del linaje dominante GPSC12/CC180 producen coinfección sinérgica con determinadas variantes de gripe

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PREVENCIÓN DE LA NEUMONÍA DESDE UNA PERSPECTIVA GLOBAL: GRIPE + VRS + NEUMOCOCO + COVID-19 + TOS FERINA

Association of respiratory infections and the impact of vaccinations on cardiovascular diseases

Jessica Rademacher^{1,2}, Markus Thewissen¹, Christopher Alexander Hinze¹, Felix Buder², Michael Böhm¹, and Tobias Walte^{1,2,3}*



Importancia de prevenir neumonías en pacientes con enfermedades cardiovasculares

Conclusion

Cardiac disease has been associated with an increased risk of cardiovascular complications following acute infections, which is reduced in patients who are vaccinated. Vaccines are regarded as one of the most effective preventive measures in modern medicine. **The combination of pneumococcal and influenza vaccination had an additive effect.** All patients with cardiovascular disease should be vaccinated against influenza, pneumococcus, COVID-19, RSV, pertussis, and herpes zoster. Vaccination campaigns targeting increasing professional recommendations and public perception should be implemented in the coming years.

Rademacher J, et al. Eur J Prev Cardiol. 2024 May 11;31(7):877-888. doi: 10.1093/eurjpc/zwae016.

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PREVENCIÓN DE LA NEUMONÍA DESDE UNA PERSPECTIVA GLOBAL: GRIPE + VRS + NEUMOCOCO + COVID-19 + TOS FERINA



EUROPEAN RESPIRATORY REVIEW SERIES
S. SIMON ET AL.

The role of vaccination in COPD: influenza, SARS-CoV-2, pneumococcus, pertussis, RSV and varicella zoster virus

Susanne Simon¹, Oana Joaen¹, Tobias Welte^{1,2,3} and Jessica Rademacher^{1,3}

Number 7 in the Series "Non-pharmacological interventions in COPD: state of the art and future directions" Edited by Geert M. Verleden and Wim Janssens

¹Department of Respiratory Medicine and Infectious Disease, Hannover Medical School, Hannover, Germany; ²Biomedical Research in Endstage and Obstructive Lung Disease, Member of the German Center for Lung Research, Hannover, Germany;

Corresponding author: Tobias Welte (Welte.Tobias@mh-hannover.de)

Importancia de prevenir neumonías en pacientes con EPOC

Vaccination strategies

Vaccines are regarded as one of the most effective preventive measures in modern medicine. All patients with COPD should be vaccinated against influenza, pneumococcus, COVID-19, pertussis and HZV, if they have not already received these vaccinations. Table 3 summarises the currently licensed vaccines, as well as their indication, efficacy and side-effects. Vaccination rates in COPD patients are mostly far behind the recommended strategies. Patients and resident doctors often complain about lack of recommendation, knowledge, misunderstanding and high expenses. Official recommendations vary from country to country and sometimes from region to region. A periodic assessment of practice performance could help to evaluate adherence rates to recommended vaccines. It would have the advantage of ensuring adherence to standards of care, identifying barriers to vaccination, developing strategies for improving vaccination adherence and optimising vaccine delivery to targeted patients. In order to improve vaccination coverage, we need better tools and better education to inform and motivate treating physicians.

Points for clinical practice

- Infectious disease prevention through immunisation is a cornerstone prophylactic measure against exacerbations but there is much room for improvement.
- Expert opinion: in addition to standard vaccinations, all COPD patients should be vaccinated by:
 - yearly high-dose or adjuvanted quadrivalent influenza vaccine
 - a single-dose PCV23
 - two doses of recombinant zoster vaccine
 - basic immunisation and booster against SARS-CoV-2 by mRNA vaccines.
- Awareness of vaccinations should be improved in physicians and patients with COPD.

Simon S, et al. Eur Respir Rev. 2023 Sep 6;32(169):230034. doi: 10.1183/16000617.0034-2023.

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PREVENCIÓN DE LA NEUMONÍA DESDE UNA PERSPECTIVA GLOBAL: GRIPE + VRS + NEUMOCOCO + COVID-19 + TOS FERINA



Protect Yourself with Vaccines if You Have Diabetes

Which vaccines are recommended?

VACCINE	AGE
COVID-19 (and booster)	≥ 6 months old and older
Influenza B	<ul style="list-style-type: none"> ≥ 65 years old or younger* ≥ 18 years old and older (especially)**
Pneumococcal Diphtheria, tetanus, pertussis (Tdap)	<ul style="list-style-type: none"> ≥ 16-64 years old ≥ 18 years old and older (especially with your diabetes care team)
RSV (Respiratory Syncytial Virus)	<ul style="list-style-type: none"> ≥ 16-64 years old ≥ 65 years old and older (especially with your diabetes care team)
Shingles (Zoster)	<ul style="list-style-type: none"> ≥ 50 years old and older ≥ 18 years old and older (especially with your diabetes care team)
Whooping Cough (Diphtheria, tetanus, pertussis)	<ul style="list-style-type: none"> ≥ 16-64 years old ≥ 65 years old and older (especially with your diabetes care team)
Measles (MMR)	<ul style="list-style-type: none"> ≥ 12 years old and older ≥ 18 years old and older (especially with your diabetes care team)

→ Vacuna frente a COVID-19

→ Vacuna frente a gripe

→ Vacuna frente a neumococo

→ Vacuna frente a VRS

→ Vacuna frente a tos ferina

Importancia de prevenir neumonías en pacientes con DIABETES

https://professional.diabetes.org/sites/dpro/files/2024-10/SRI-ProtectYourselfwithVaccines-Patient_10_30.pdf?_gl=1*17kgn3m*_gcl_au*MTgwMDMyMDA1OC4xNzMwODgzMjE5*_ga*MTcwMzQ3NjE0NC4xNzMwODgzMjE5*_ga_QDP2V81FZ*MTczMDg4MzIxMS4xLjAuMTczMDg4MzIxMS4xNjE0NC4xNzMwODgzMjE5

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PREVENCIÓN DE LA NEUMONÍA DESDE UNA PERSPECTIVA GLOBAL: GRIPE + VRS + NEUMOCOCO + COVID-19 + TOS FERINA

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Review Article
Respiratory Syncytial Virus Vaccination Recommendations for Adults Aged 60 Years and Older: The NeumoExperts Prevention Group Position Paper

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VACCINATION GUIDE AGAINST COMMUNITY ACQUIRED PNEUMONIA IN ADULTS 2024

SHOULD BE VACCINATED	FLU	PCV20	COVID-19	PERTUSSIS	RSV
• Age 65 and older (immunocompetent conditions)	✓	✓	✓	✓	✓
• Older than 60 years	✓	✓	✓	✓	✓
• Adults with chronic respiratory, cardiovascular and immune conditions, long-term care facilities and shared living spaces	✓	✓	✓	✓	✓
• Underlying conditions and long-term care facilities	✓	✓	✓	✓	✓
• Social Settings: <ul style="list-style-type: none"> • Workplaces • Healthcare facilities • Homes • Long-term care 	✓	✓	✓	✓	✓
• Hospitalization and long-term care facilities	✓	✓	✓	✓	✓
• Pregnancy	✓	✓	✓	✓	✓
• Adults with immunocompromised conditions	✓	✓	✓	✓	✓
• Adults from 18 to 59 years	✓	✓	✓	✓	✓

KEY QUESTIONS

Should I get vaccinated? Yes, if you are 65 years or older, or older than 60 years and have a chronic condition, live in a long-term care facility, or are pregnant.

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Fig. 1. Vaccination guide against community acquired pneumonia in adults (aged 18 years) (continued from Table 1). Source: authors' modification.

Redondo E, et al. Arch Bronconeumol. 2024 Mar;60(3):161-170. English, Spanish. doi: 10.1016/j.arbres.2024.01.004.