

THE LANCET Microbe

Supplementary appendix 2

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Supplement to: Sempere J, Llamosí M, Ruiz B L, et al. Effect of pneumococcal conjugate vaccines and SARS-CoV-2 on antimicrobial resistance and the emergence of *Streptococcus pneumoniae* serotypes with reduced susceptibility in Spain, 2004–20: a national surveillance study. Lancet Microbe 2022; published online August 3. [https://doi.org/10.1016/S2666-5247\(22\)00127-6](https://doi.org/10.1016/S2666-5247(22)00127-6).

SUPPORTING INFORMATION

Effect of pneumococcal conjugate vaccines and SARS-CoV-2 on antimicrobial resistance and the emergence of *Streptococcus pneumoniae* serotypes with reduced susceptibility in Spain, 2004–20: a national surveillance study

Julio Sempere†, Mirella Llamosí†, Beatriz López Ruiz, Idoia del Río, Covadonga Pérez García, Darío Lago, Mercedes Gimeno, Pilar Coronel, Fernando González-Camacho, Mirian Domenech* and Jose Yuste*

Spanish Pneumococcal Reference Laboratory, National Center for Microbiology, Instituto de Salud Carlos III, Madrid, Spain (J Sempere PhD, M Llamosí BsC, B López Ruiz AS, I del Río AS, C Pérez García BsC, D Lago BsC, F González-Camacho PhD, M Domenech PhD, J Yuste PhD), Scientific Department, Meiji Pharma Spain, Madrid, Spain (M Gimeno PhD, P Coronel hD) Department of Genetics, Physiology and Microbiology, University Complutense Madrid, Madrid, Spain (M Domenech) and CIBER de Enfermedades Respiratorias (CIBERES), Madrid, Spain (J Sempere, M Domenech, J Yuste).

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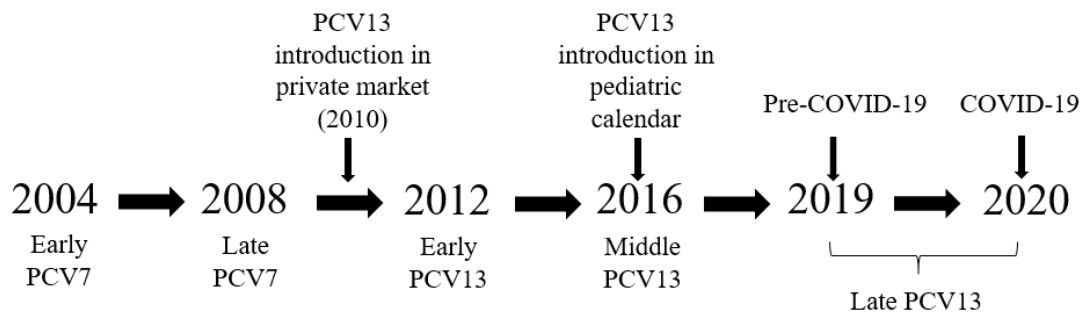


Figure S1: Timeline for the selection of clinical isolates for the period 2004-2020.

In some years, important events are remarked including periods before and after the introduction of the different pneumococcal vaccines in Spain. The years when PCV13 was included in the private market (2010) and the national pediatric vaccination calendar (2016) are mentioned to see the impact of these events in antimicrobial resistance and the year 2020 when SARS-CoV-2 appeared.

	2004 Early PCV-7	2008 Late PCV-7	2012 Early PCV-13	2016 Middle PCV-13	2019 Late PCV-13 and Pre- COVID	2020 Late PCV-13 and COVID
Total strains characterized	3169	4637	3415	2426	3154	2171
Total strains (PEN-S)	2041 (64%)	3280 (71%)	2363 (69%)	1817 (75%)	2568 (81%)	1653 (76%)
Total strains (PEN-I/R)	1128 (36%)	1357 (29%)	1052 (31%)	609 (25%)	586 (19%)	518 (24%)
Selected strains in this study (PEN-I/R)	501	498	500	500	500	518
Average age of patients	44	52	57	57	57	61
IPD isolates	289	258	206	226	381	399
Non-bacteraemic pneumonia isolates	211	240	294	274	119	119

Table S1: Distribution of pneumococcal strains per year. Data include the total number of strains characterized at the Spanish Pneumococcal Reference Laboratory per year, the number of penicillin susceptible strains (PEN-S) or with reduced susceptibility to penicillin (PEN-I/R) and the number of selected strains for this study among PEN I/R isolates. The percentage indicate the proportion of (PEN-S or PEN-I/R). The average age of hospitalized patients and the number of IPD isolates or non-bacteraemic pneumonia isolates are also included.

MIC breakpoints (mg/L)		
	S ≤	R >
Penicillin	0·06	2
Amoxicillin	0·5	1
Cefotaxime	0·5	2
Cefpodoxime	0·25	0·5
Cefixime	0·5	2
Cefditoren	0·5	2
Erythromycin	0·25	0·5
Levofloxacin	0·001	2

Table S2: Breakpoints considered for susceptible and resistant strains. We followed EUCAST guidelines. For those antibiotics without a defined breakpoint by EUCAST or CLSI such as cefixime and cefditoren, we used the same breakpoints as cefotaxime.

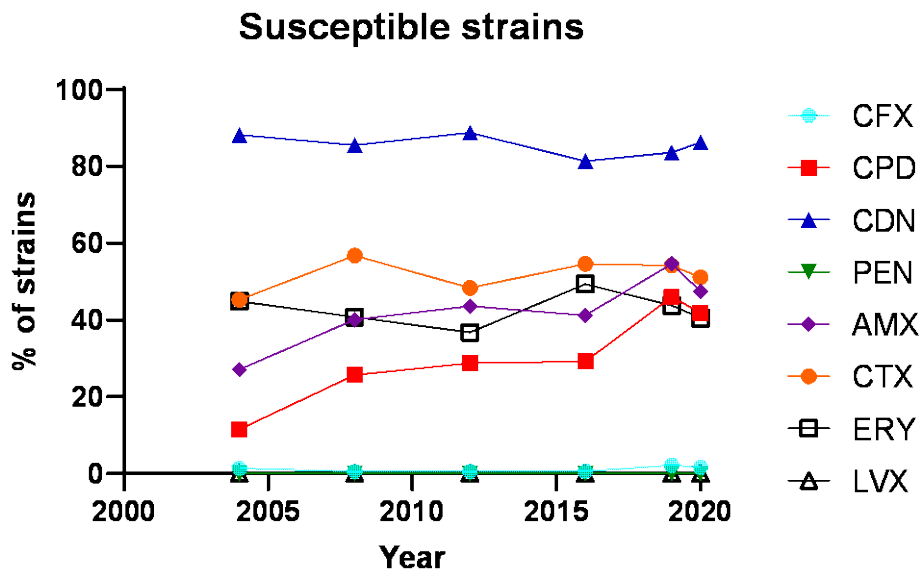


Figure S2: Evolution of susceptible strains to different antibiotics during the period 2004-2020. The antibiotics tested were CFX (cefixime), CPD (cefepodoxime), CDN (cefditoren), PEN (penicillin), AMX (amoxicillin), CTX (cefotaxime), ERY (erythromycin), and LVX (levofloxacin).