

## REVIEW

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## ABSTRACT

Vaccination programmes are one of the public health measures that have the greatest impact on reducing the burden of disease, mortality and associated costs of a large number of communicable diseases. The success of vaccination is due to the use of highly effective and safe products, but also to well-functioning surveillance systems and epidemiological studies realised. Seroprevalence studies or surveys are a powerful assessment tool providing accurate information on the frequency, distribution and dynamics of communicable diseases. More than 20 years have passed since the first study was carried out in Spain, and this second seroprevalence study is essential to know the impact of vaccination programmes and the prevalence of immunity of the general population against immunopreventable diseases and other diseases of public health interest. The pathologies included in the study are: poliomyelitis, diphtheria, tetanus, pertussis, measles, rubella, mumps, varicella, invasive meningococcal serogroup C disease, hepatitis A, hepatitis B and D, hepatitis C, hepatitis E and human immunodeficiency virus (HIV) infection. Despite the current pandemic, this information can be used by technicians and decision-makers to adjust existing vaccination programmes and contribute to improving the health of the population in our country.

**Key words:** Seroprevalence, Vaccination programs, Vaccination coverage, Population surveys, Epidemiological surveillance.

## RESUMEN

2<sup>o</sup> Estudio de Seroprevalencia en España, 2017-2018.

Los programas de vacunación son una de las medidas de Salud Pública con impacto en la disminución de la carga de enfermedad, mortalidad y los costes asociados de un gran número de enfermedades transmisibles. El éxito de la vacunación se debe al uso de productos muy efectivos y seguros, pero también al buen funcionamiento de los sistemas de vigilancia y a la realización de estudios epidemiológicos. Los estudios o encuestas de seroprevalencia son una herramienta potente de evaluación que ofrece información precisa de la frecuencia, distribución y dinámica de las enfermedades transmisibles. Han pasado más de veinte años desde el primer estudio realizado en España, y este segundo estudio de seroprevalencia es fundamental para conocer el impacto de los programas de vacunación y la prevalencia de inmunidad de la población general frente a las enfermedades inmunoprevenibles y otras de interés para la Salud Pública. Las patologías incluidas en el estudio son: poliomiélitis, difteria, tétanos, tosferina, sarampión, rubéola, parotiditis, varicela, enfermedad meningocócica invasora por serogrupo C, hepatitis A, hepatitis B y D, hepatitis C, hepatitis E e infección por virus de la inmunodeficiencia humana (VIH). A pesar del momento pandémico actual, disponer de esta información puede servir a técnicos y decisores para ajustar los programas de vacunación existentes y contribuir a la mejora de la salud de la población en nuestro país.

**Palabras clave:** Seroprevalencia, Programas de vacunación, Coberturas de vacunación, Encuestas poblacionales, Vigilancia epidemiológica.

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## RELEVANCE OF THE STUDY

Vaccination programmes are one of the public health measures that have had the greatest impact on reducing the burden of disease, mortality and associated costs of a large number of communicable diseases, achieving major milestones in recent decades in the control, elimination and eradication of some diseases, which have prevented millions of deaths worldwide<sup>(1)</sup>.

The success of vaccination is due to the use of highly effective and safe products, but also to well-functioning surveillance systems and epidemiological studies. These studies make it possible to continuously evaluate programmes and adapt vaccination policy to the reality of each context by identifying the most susceptible population groups, anticipating future epidemiological scenarios<sup>(2,3)</sup>.

Seroprevalence studies or surveys are a powerful assessment tool providing accurate information on the frequency, distribution and dynamics of communicable diseases. They are cross-sectional studies in representative samples of the population, in which the prevalence of markers of infection and immune protection are determined by obtaining a blood sample. They are particularly useful for understanding the immune status of immunopreventable diseases and others whose surveillance system is not very reliable or whose epidemiology is changing, hence the importance of repeating them periodically in order to detect changes<sup>(4)</sup> and to apply their results more accurately in decision-making.

More than 20 years have passed since the first study was carried out in Spain and in this period of time new vaccines and several modifications in the vaccination schedule have been introduced<sup>(5,6)</sup>. For this reason, this second seroprevalence study makes a very important contribution to the knowledge of the prevalence of

immunity of the general population against immunopreventable diseases by providing information on the impact of vaccination programmes. In addition, other diseases of public health importance have been included in the study.

The pathologies included in the study are: poliomyelitis, diphtheria, tetanus, pertussis, measles, rubella, mumps, varicella, invasive meningococcal serogroup C disease (IMD), hepatitis A, hepatitis B and D, hepatitis C, hepatitis E and human immunodeficiency virus (HIV) infection.

Although the results of this study are published at a time when the current COVID-19 pandemic is in turmoil, they will undoubtedly help in making decisions on the most appropriate strategies to be applied to improve the health of the population.

The full study is available at:

[https://www.msbs.gob.es/profesionales/saludPublica/prevPromocion/vacunaciones/comoTrabajamos/docs/EstudioSeroprevalencia\\_EnfermedadesInmunoprevenibles.pdf](https://www.msbs.gob.es/profesionales/saludPublica/prevPromocion/vacunaciones/comoTrabajamos/docs/EstudioSeroprevalencia_EnfermedadesInmunoprevenibles.pdf)

## METHODS

The 2<sup>nd</sup> Seroprevalence Study in Spain is a cross-sectional descriptive observational study, with a similar design to the study carried out in 1996, in order to allow comparison of the results. It was conducted in the Spanish resident population aged 2 to 80 years, using two-stage cluster sampling, with an initial theoretical sample size of 10,000 people.

In addition, each person who agreed to participate in the study also answered the questions in a questionnaire specifically designed to ascertain opinions about vaccination and preventive measures, as well as risk factors, and to collect various socio-demographic variables of interest. Furthermore, all participants between

2 and 30 years of age were asked for their vaccination records.

The methodological details of this study were published in *Revista Española de Salud Pública*<sup>(7)</sup> and can be found in:

[https://www.msbs.gob.es/biblioPublic/publicaciones/recursos\\_propios/resp/revista\\_cdrom/VOL93/C\\_ESPECIALES/RS93C\\_201904021.pdf](https://www.msbs.gob.es/biblioPublic/publicaciones/recursos_propios/resp/revista_cdrom/VOL93/C_ESPECIALES/RS93C_201904021.pdf)

## RESULTS AND CONCLUSIONS

A total of 10,223 extractions were performed and 10,073 questionnaires were collected. Sociodemographic variables, history and exposures of interest, vaccination and disease history, and knowledge related to health problems and preventive activities were characterised, mainly in relation to vaccine-preventable diseases and vaccines. A high percentage of favourable responses to vaccination and knowledge of preventive measures were found to be higher in younger age groups. The vaccination coverage rates documented in the vaccination booklets received was high and consistent with the schedules in force according to age groups.

The most relevant findings for each of the diseases investigated are shown below:

– **Measles:** A decline in the population with protective antibody titres has been observed from the age group 10-15 years up to 30-39 years (cohorts born between 1978 and 2002), being more pronounced in the group 20-29 years (born between 1988 and 1997), which may be due to the loss of serological protection as time passes since vaccination with the second MMR dose, possibly due to the absence of contact with the wild virus. The need for further medium and long-term vaccination strategies will need to be assessed in certain population groups depending on their likelihood of exposure.

– **Rubella:** Population immunity to rubella virus is above 95% in all age groups, higher in females. This shows the maintenance of immunity conferred by vaccination, even if it was done in childhood. The high immunity of the population ensures the maintenance of rubella elimination in Spain.

– **Mumps:** The seroprevalence of antibodies to mumps is high between 2 and 14 years of age. Thereafter, immunity begins to decline, increasing in those over 30 years of age. This reflects, on the one hand, the loss of immunity over time since vaccination and, on the other hand, the better persistence of immunity by natural infection in cohorts born before 1978, although it is also possible that the use of Rubini strain vaccines may have some effect that is difficult to pinpoint in this study.

– **Poliomyelitis:** The prevalence of neutralising antibodies to poliovirus types 1 and 3 is very high in all age groups, ensuring the level of susceptible population below the 15% required to prevent transmission in case of introduction of these viruses. These results ensure that the population immunity target is met to contribute to the eradication of polio.

– **Diphtheria:** The seroprevalence of protective diphtheria antibodies increases with age up to 30 years. It declines significantly thereafter, probably due to the loss of immunity over time. Evidence shows that high childhood vaccination coverage contributes to limiting secondary transmission and the maintenance of population-wide chains of transmission after importation of cases. Additionally, improving tetanus vaccination with combined tetanus-diphtheria (Td) vaccines in the older population may also contribute to improving diphtheria immunity.

– **Tetanus:** High prevalence of protective levels of tetanus antibodies is observed in children under 50 years of age, declining

significantly thereafter, especially after the age of 60 years. It is necessary to raise awareness, both among the population and health personnel, of the need for vaccination in the elderly, where a significant proportion of susceptible people are found.

– **Pertussis:** Seroprevalence results indicate that circulation of *Bordetella pertussis* occurs in all age groups.

– **Varicella:** The introduction of the vaccine in the vaccination schedule is reflected in the increase of antibody seroprevalence in the youngest age group (2-5 years), compared to previous studies. It is still too early to observe the effect of childhood vaccination in the other age groups.

– **Invasive meningococcal disease (serogroup C):** The seroprevalence of protective antibodies to serogroup C IMD is close to 75% in cohorts that have benefited from routine vaccination in adolescence (12-16 years of age). In addition, longer-lasting immunity and greater protection is shown in these age groups.

– **Hepatitis A:** A high proportion of susceptible people is observed in the general population. However, it is shown that almost 5% of children aged 2-5 years have immunity that lasts until the age of 19 years, which is probably acquired after natural exposure to HAV in early childhood. This situation of HAV infection in childhood and increased susceptibility in the adult population highlights the importance of epidemiological surveillance in case identification and rapid intervention in outbreaks to limit possible spread.

– **Hepatitis B and D:** The prevalence of HBV infection has decreased significantly since the previous study in 1996. The prevalence of active HBV infection and of women carrying HBsAg is also very low. The prevalence of hepatitis D in HBsAg carriers is similar to other studies in

our setting. The seroprevalence of anti-HBs antibodies shows two peaks, reflecting the routine vaccination carried out in Spain, which started in adolescents and was later shifted to childhood. All these results reflect the success of the hepatitis B vaccination programme.

– **Hepatitis C:** HCV infection results indicate that the level of infection prevalence in Spain is low, especially in terms of prevalence of active infection. Prevalence is higher in men and in people born outside Spain. Background records of blood exposure were frequent. The undiagnosed fraction of HCV infection was 14.3% for the presence of antibodies and 29.4% for active infection, although the methodology used to identify history could overestimate it.

– **Hepatitis E:** The results of seroprevalence of antibodies to hepatitis E virus obtained in this study are higher than the estimates made so far in our country. They also suggest ongoing transmission with increased past exposure and persistence of antibodies in those who have been exposed to HEV. The low number of detected cases of acute infection seems to indicate that HEV infection in our country goes undetected in its subclinical or asymptomatic forms.

– **HIV infection:** The overall prevalence of HIV infection obtained in this study is lower than other estimates. The characteristics of the population studied, with under-representation of the most exposed population groups, may justify obtaining a lower estimate than that of the general population. The prevalence according to age and sex, in addition to the undiagnosed fraction, is in the range of other estimates made in our setting.

In conclusion, this second seroprevalence study provides valuable information, after 20 years, on the impact of vaccination programmes and on the immune status of the general population against immunopreventable

diseases and other diseases of major public health importance. Despite the current pandemic, this information can be used by technicians and decision-makers to adjust existing vaccination programmes and contribute to improving the health of the population in our country.

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