



Viral Hepatitis Prevention Board

VHPB technical meeting

Addressing Hepatitis A in Europe in 2026 – Challenges, Strategies, and Opportunities

13-14 October 2026, Antwerp, Belgium

Hepatitis A outbreak characteristics: A comparison of regions with different vaccination strategies in Spain

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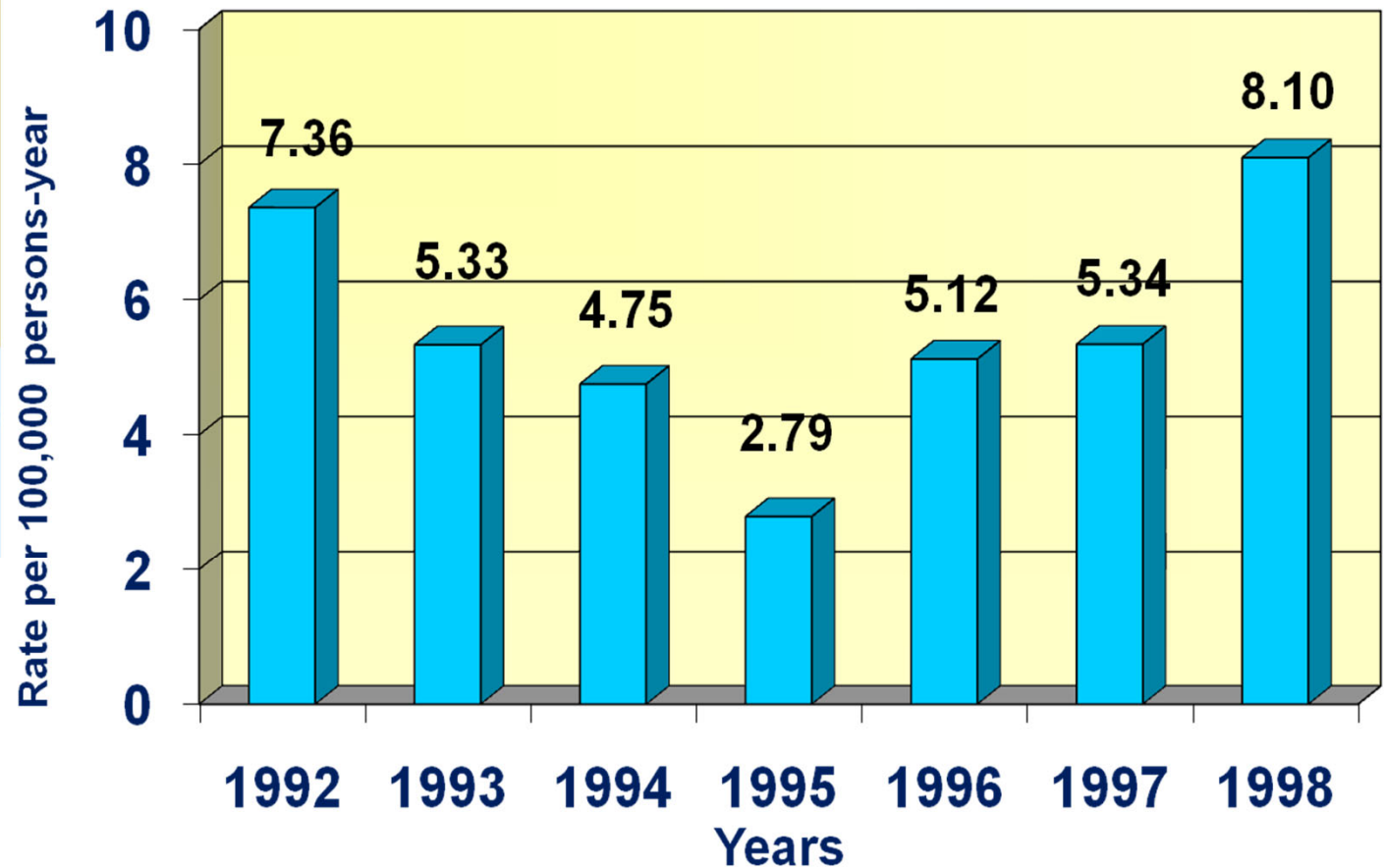


INTRODUCTION: RECOMMENDATIONS FOR HEPATITIS A VACCINATION IN SPAIN

1995 → Vaccination of risk groups

- ◆ International travellers to regions of endemic disease
- ◆ Homosexual men
- ◆ Users of intravenous drugs
- ◆ Sewage workers
- ◆ Patients receiving factor VIII concentrates
- ◆ Exposed to non-human primates
- ◆ Staff of day-care centres
- ◆ Staff of institutions for developmentally disabled persons
- ◆ People >30 years old with chronic liver disease
- ◆ People infected by hepatitis C virus

INTRODUCTION: REPORTED MORBIDITY OF HEPATITIS A. CATALONIA, 1992-1998



Domínguez et al. Vaccine 2008; 26: 1737-41

INTRODUCTION: RECOMMENDATIONS FOR HEPATITIS A VACCINATION IN CATALONIA

1995 → Vaccination of risk groups with Hepatitis A vaccine

1999 → Universal vaccination of preadolescents with combined Hepatitis A+B vaccine

Comparative Study > Med Clin (Barc). 1999 Mar 27;112(11):406-8.

[Changes in seroepidemiology of hepatitis A virus infection in Catalonia in the period 1989–1996. Implications for new vaccination strategy]

[Article in Spanish]

M Bruguera ¹, L Salleras, P Plans, J Vidal, E Navas, A Domínguez, J Batalla, J L Taberner, J Espuñes

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Abstract

Background: The aim of this study was to investigate the prevalence of the risk factors of hepatitis A virus infection (HAV) in a representative sample of a Catalanian population obtained from 1995 to 1996 and the changes in the prevalence of this infection over the period of 1989–1996.

INTRODUCTION: RATIONALE FOR HEPATITIS A UNIVERSAL VACCINATION IN CATALONIA

- **Limited impact of selective vaccination of risk groups**
- **Immediate impact of universal vaccination on clinical cases**
- **Potential of mass vaccination to eliminate the disease**
- **Combined A+B vaccine available**
- **Well-established hepatitis B vaccination program of preadolescents in schools**
- **Low cost of the program**
- **Acceptable efficiency of the program**

INTRODUCTION: EFFICIENCY OF THE INCORPORATION OF HEPATITIS A VACCINE AS A COMBINED HEPATITIS A+B VACCINE

 Length of protection: 25 years. Cohort of 67,441 pre-adolescent vaccinated at 12 years and followed for 25 years. Discount rate: 5%

Cost of vaccination program	336,567 €
Cost of hepatitis A without vaccination	995,096 €
Cost of hepatitis A with vaccination	124,821 €
Benefit of vaccination program	870,275 €
Net present value	+533,708 €
Cost-benefit ratio	2.58

Incremental cost of vaccine* : 1.98 euros

***[cost of combined hepatitis A+B vaccine] - [cost of hepatitis B vaccine]**

INTRODUCTION: WHO RECOMMENDATIONS, 2022

- ◆ People travelling to areas of intermedia of high endemicity
- ◆ Men who have sex with men
- ◆ Those in at-risk occupations
- ◆ People who inject drugs
- ◆ People who experience homelessness
- ◆ Migrants
- ◆ Refugees
- ◆ Incarcerated persons
- ◆ Patients with chronic liver disease
- ◆ People living with HIV



There is little evidence that high-risk groups vaccination efforts are successful in reducing hepatitis A in the general population.

INTRODUCTION: WHO RECOMMENDATIONS, 2022

In outbreak situations: single-dose hepatitis A vaccination is recommended, **taking into account the epidemiology and feasibility of rapidly implementing a well target vaccination programme.** It is most likely to be successful:

- ◆ When the outbreak involves a small self-contained community or a well defined population.
- ◆ When vaccination is started early in the course of the outbreak.
- ◆ When high coverage of those likely to be affected can be achieved.

UNIVERSAL VACCINATION IN MIDDLE-INCOME COUNTRIES, WHO 2022

- ◆ Single-dose schedules were demonstrated to be cost-saving.
- ◆ 2-dose-schedules were shown to be only cost-effective.
- ◆ Universal vaccination was more cost-effective than targeted or regional vaccination programmes.
- ◆ Higher endemicity, lower cost of vaccine and longer seroprotection assumptions resulted in improved cost-effectiveness.



- ◆ Hepatitis A vaccine should be introduced into national schedule on the basis of: increasing trend over time of hepatitis A disease (older children, adolescents, adults).
- ◆ Changes in the endemicity from high to intermediate.
- ◆ Considerations of cost-effectiveness.

Article

Hepatitis A Outbreak Characteristics: A Comparison of Regions with Different Vaccination Strategies, Spain 2010–2018

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Citation: Domínguez, A.; Varela, C.; Soldevila, N.; Izquierdo, C.; Guerrero, M.; Peñuelas, M.; Martínez, A.; Godoy, P.; Borràs, E.; Rius, C.; Torner, N.; Avellón, A.M.; Jesús, C.; PREVICET Working Group on Viral Hepatitis. *Vaccines* 2021; 9: 1214.

Abstract: We compared the cumulative incidence and characteristics of hepatitis A outbreaks in two groups of Spanish autonomous regions according to whether a universal or risk group vaccination strategy was followed. Outbreaks between 2010 and 2018 were analyzed. The cumulative incidence

OBJECTIVE



To compare the cumulative incidence and characteristics of hepatitis A outbreaks during 2010-2018 in two groups of Spanish autonomous regions or cities according to the universal or risk-group hepatitis A vaccination strategy.

-Catalonia (universal vaccination in 1999) and Ceuta (universal vaccination in 2000) → whole population: 7,481,683 inhabitants.

-Castile and Leon, Community of Valencia, Madrid, Murcia and Navarre (risk-group strategy) → whole population: 15,894,677 inhabitants.

METHODS (I)

- Hepatitis A outbreak reported between 2010 and 2018
- **Outbreak definition** → two or more hepatitis A cases that were epidemiologically linked if at least one case was laboratory confirmed.
- **Laboratory confirmation** → Detection of immunoglobulin M (IgM) antibody to hepatitis A virus.



METHODS (II)

→ For each outbreak the following variables were collected:

- Year (clinical onset of first case)**
- Transmission (common source /person-to- person)**
- Setting**
- Outbreak caused by imported case**
- Number of exposed, affected, hospitalized**
- Immunoglobulin/ vaccine recommended to exposed**
- Number of exposed receiving IG or vaccine**

→ In person to person outbreaks: risk factor of the index case

METHODS (III)

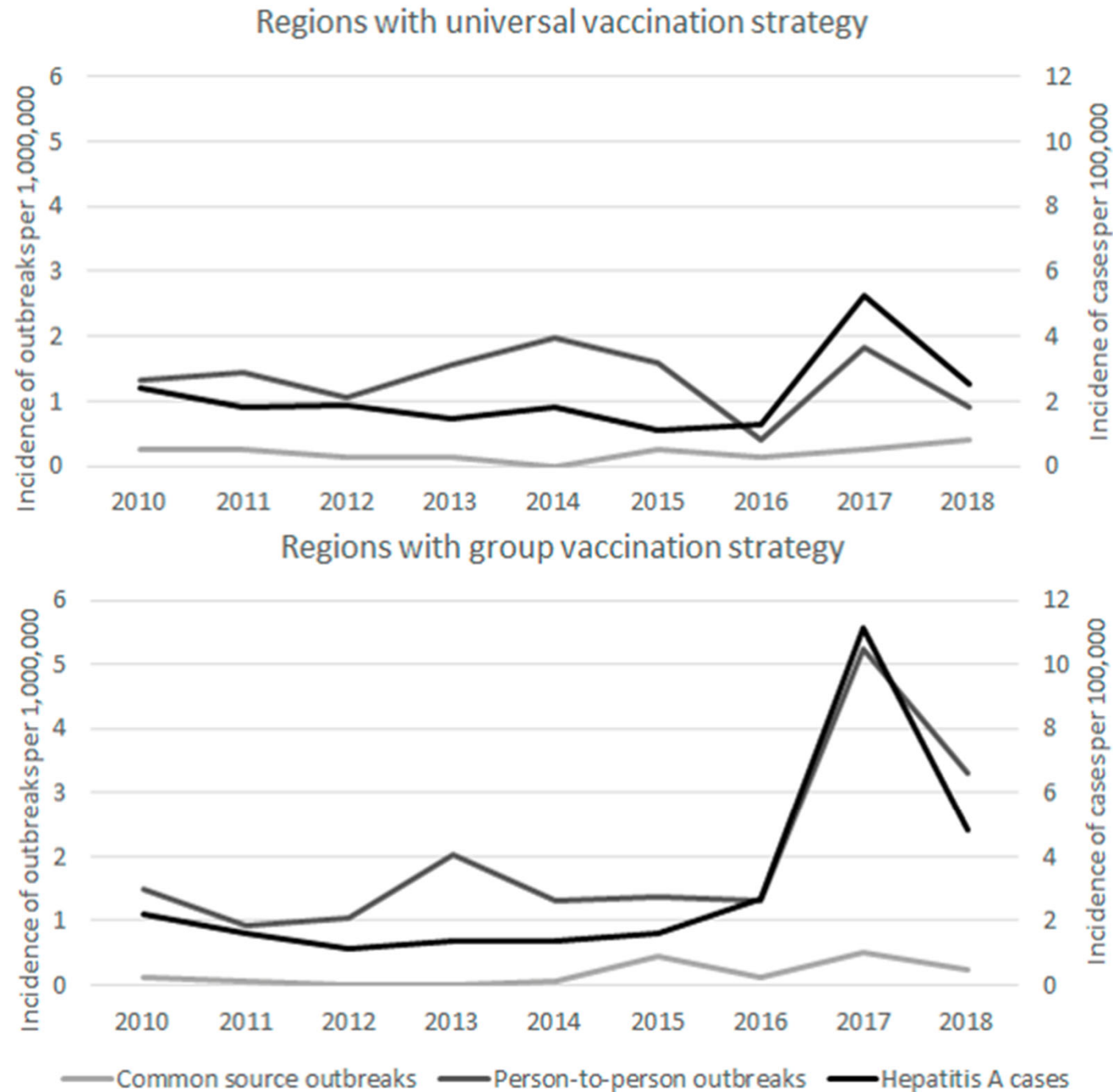
- Cumulative incidence rates of outbreaks per 1,000,000 persons were calculated for the two groups.
- Rate ratios of cumulative incidence rates and their 95%CI were calculated.
- Crude and adjusted odds ratio (OR) and their 95% confidence intervals were estimated using logistic regression.
- Adjusted OR were calculated using a multivariable logistic regression model after adjusting for significant variables in the bivariate analysis in the characteristics of outbreaks model and for the variables age and sex in the characteristics of the first case model.

RESULTS

Number and cumulative incidence rate per million inhabitants of hepatitis A in regions with different vaccination strategies. Spain, 2010–2018

	Universal vaccination N=120	Risk group vaccination N=330	Rate ratio (95% CI)	<i>P</i> value
Outbreak incidence	16.04	20.75	0.77 (0.62-0.95)	0.01
Transmission mode				
Common source	14 (1.87)	25 (1.57)	1.19 (0.60-2.28)	0.60
Person-to-person	92 (12.30)	290 (18.24)	0.67 (0.53-0.85)	0.001
Setting				
Family/household	93 (12.43)	266 (16.74)	0.74 (0.58-0.94)	0.01
School	7 (0.94)	23 (1.45)	0.65 (0.26-1.46)	0.31
Restaurant/facility canteen	0 (0)	8 (0.50)	0.12 (0.01-2.16)	0.19
Leisure facility/summer camp	1 (0.13)	2 (0.13)	1.06 (0.04-13.97)	0.96
Community/other/various	6 (0.80)	26 (1.64)	0.49 (0.18-1.14)	0.10
Other closed facilities	0 (0)	3 (0.19)	0.30 (0.02-5.87)	0.63
Imported outbreak	52 (6.95)	68 (4.28)	1.62 (1.13-2.33)	0.01

Annual incidence rate of hepatitis A cases and hepatitis A outbreaks according to transmission mode by vaccination strategy. Spain, 2010–2018



Characteristics of hepatitis A outbreaks in regions with different vaccination strategies. Spain, 2010–2018

	Universal vaccination N=120	Risk group vaccination N=330	Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Transmission mode						
Common source	14 (13.2%)	25 (7.9%)	1.76 (0.88-3.54)	0.11	1.54 (0.64-3.68)	0.34
Person-to-person	92 (86.8%)	290 (92.1%)	Ref.		Ref.	
Setting						
Family/household	93 (86.9%)	266 (81.1%)	Ref.		Ref.	
School	7 (6.5%)	23 (7.0%)	0.87 (0.36-2.10)	0.76	1.67 (0.54-5.18)	0.37
Restaurant/facility canteen	0 (0%)	8 (2.4%)	-		-	
Leisure facility/summer camp	1 (0.9%)	2 (0.6%)	1.43 (0.13-15.96)	0.77	2.03 (0.15-27.44)	0.59
Community/Other/Several	6 (5.6%)	26 (7.9%)	0.66 (0.26-1.65)	0.37	0.73 (0.23-2.31)	0.59
Other closed facilities	0 (0%)	3 (0.9%)	-		-	
Imported outbreak						
Yes	52 (65.0%)	68 (28.7%)	4.62 (2.69-7.91)	<0.001	3.88 (2.13-7.09)	<0.001
No	28 (35.0%)	169 (71.3%)	Ref.			
No. of exposed people* , median (range)	5 (2-422)	5 (2-35240)		0.24		0.77
No. of affected people , median (range)	2 (2-218)	2 (2-88)		0.52		0.22
No. of hospitalized cases[†] , median (range)	0 (0-5)	1 (0-47)		<0.001		0.07
IG recommended to exposed people						
Yes	21 (31.3%)	16 (32.7%)	0.94 (0.43-2.07)	0.88	2.16 (0.67-6.97)	0.20
No	46 (68.7%)	33 (67.3%)	Ref.		Ref.	
Vaccine recommended to exposed people						
Yes	81 (92.0%)	230 (95.0%)	0.60 (0.23-1.59)	0.31	0.44 (0.11-1.71)	0.23
No	7 (8.0%)	12 (5.0%)	Ref.		Ref.	
No. of exposed people administered IG[‡] , median (range)	0 (0-68)	0 (0-80)		0.79		0.76
No. of exposed people administered vaccine[§] , median (range)	3 (0-482)	3 (0-672)		0.36		0.11

IG: immunoglobulin; Information was not available in *87, [†]27, [‡]285, [§] 222 outbreaks

Characteristics of common source and person-to-person hepatitis A outbreaks in regions with different vaccination strategies. Spain, 2010–2018

	Universal vaccination N=120	Risk group vaccination N=330	Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value
COMMON SOURCE OUTBREAKS						
Setting						
Family/household	12 (92.3%)	20 (87.0%)	-		-	
Restaurant/facility canteen	0 (0%)	3 (13.0%)	-		-	
Community/Other/Several	1 (7.7%)	0 (0%)	-		-	
Imported outbreak	7 (53.8%)	10 (47.6%)	1.28 (0.32-5.13)	0.72	1.67 (0.33-8.47)	0.53
No. of exposed people, median (range)	5 (2-38)	5 (2-400)		0.92		0.82
No. of affected people, median (range)	2 (2-38)	2 (2-31)		0.59		0.49
No. of hospitalized cases, median (range)	0 (0-5)	1 (0-16)		0.38		0.65
PERSON-TO-PERSON TRANSMISSION OUTBREAKS						
Setting						
Family/household	71 (86.6%)	233 (80.3%)	Ref.		Ref.	
School	6 (7.3%)	22 (7.6%)	0.90 (0.35-2.29)	0.82	1.69 (0.65-6.59)	0.22
Restaurant/facility canteen	0 (0%)	5 (1.7%)	-		-	
Leisure facility/summer camp	1 (1.2%)	2 (0.7%)	1.64 (0.15-18.36)	0.69	2.39 (0.18-32.34)	0.51
Community/Other/Several	4 (4.9%)	25 (8.6%)	0.53 (0.18-1.56)	0.25	0.44 (0.10-2.04)	0.29
Other closed facilities	0 (0%)	3 (1.0%)	-		-	
Imported outbreak	36 (62.1%)	54 (26.2%)	4.61 (2.49-8.52)	<0.001	4.38 (2.29-8.35)	<0.001
No. of exposed people, median (range)	5 (2-422)	5 (2-473)		0.44		0.46
No. of affected people, median (range)	2 (2-218)	2 (2-88)		0.58		0.71
No. of hospitalized people, median (range)	0 (0-3)	1 (0-47)		<0.001		0.03

Characteristics of the first case in hepatitis A outbreaks in regions with different vaccination strategies. Spain, 2010–2018

	Universal vaccination N=120	Risk group vaccination N=330	Crude OR (95% CI)	<i>P</i> value	Adjusted OR (95% CI)	<i>P</i> value
Age						
0-14 years	68 (58.6%)	86 (47.5%)	Ref.		Ref.	
15-44 years	36 (31.0%)	78 (43.1%)	0.58 (0.35-0.97)	0.04	0.54 (0.32-0.92)	0.02
≥45 years	12 (10.3%)	17 (9.4%)	0.89 (0.40-2.00)	0.78	0.83 (0.36-1.89)	0.65
Sex						
Male	77 (67.5%)	138 (72.3%)	Ref.		Ref.	
Female	37 (32.5%)	53 (27.7%)	1.25 (0.76-2.07)	0.38	1.13 (0.66-1.95)	0.65
Born in Spain						
Yes	36 (65.5%)	51 (67.1%)	0.93 (0.45-1.93)	0.84	1.10 (0.48-2.54)	0.81
No	19 (34.5%)	25 (32.9%)	Ref.		Ref.	
Occupation						
Food handler	4 (5.1%)	6 (6.7%)	Ref.		Ref.	
Healthcare worker	0 (0%)	2 (2.2%)	-		-	
Nursery/school/high school worker	3 (3.8%)	5 (5.6%)	0.90 (0.13-6.08)	0.91	1.02 (0.14-7.56)	0.99
School/Student	70 (88.6%)	77 (85.6%)	1.36 (0.37-5.03)	0.64	1.34 (0.34-5.24)	0.68
Other*	2 (2.5%)	0 (0%)	-		-	
Hepatitis A vaccinated						
Yes	0 (0%)	1 (0.9%)	-		-	
No	84 (100%)	132 (99.2%)	Ref.		Ref.	
Men who have sex with men[†]						
Yes	5 (23.8%)	27 (67.5%)	0.15 (0.04-0.50)	0.002	0.23 (0.07-0.82)	0.02
No	16 (76.2%)	13 (32.5%)	Ref.		Ref.	
Drug user[‡]						
Yes	1 (3.0%)	0 (0%)	-		-	
No	32 (97.0%)	12 (100%)	Ref.		Ref.	

* Performing arts direction, not working, [†] Only for men aged ≥15 years, [‡] Only for persons aged ≥15 years

Characteristics of the first case in COMMON-SOURCE TRANSMISSION outbreaks in regions with different vaccination strategy. Spain, 2010–2018

	Regions with universal vaccination N=120	Regions with risk group vaccination N=330	Crude odds ratio (95% CI)	<i>P</i> value	Adjusted odds ratio (95% CI)	<i>P</i> value
Age						
0-14 years	7 (53.8%)	10 (58.8%)	Ref.		Ref.	
15-44 years	4 (30.8%)	6 (35.3%)	0.95 (0.19-4.68)	0.95	0.96 (0.19-4.80)	0.96
≥45 years	2 (15.4%)	1 (5.9%)	2.86 (0.21-37.99)	0.43	2.86 (0.21-38.04)	0.43
Sex						
Male	9 (69.2%)	12 (70.6%)	Ref.		Ref.	
Female	4 (30.8%)	5 (29.4%)	1.07 (0.22-5.14)	0.94	0.98 (0.20-4.94)	0.98
Born in Spain	7 (87.5%)	8 (53.3%)	6.12 (0.60-62.82)	0.13	6.27 (0.47-82.57)	0.16
Occupation						
Food handler	1 (11.1%)	0 (0%)	Ref.		Ref.	
School/Student	7 (11.1%)	3 (100%)	-		-	
Others*	1 (77.8%)	0 (0%)	-		-	
Hepatitis A vaccinated	0 (0%)	0 (0%)	-		-	
Men who have sex with men[†]	2 (100%)	0 (0%)	-		-	
Drug user[‡]	0 (0%)	0 (0%)	-		-	

* Not working. [†] Only for men aged ≥15 years. [‡] Only for persons aged ≥15 years

Characteristics of the first case in PERSON-TO-PERSON TRANSMISSION hepatitis A outbreaks in regions with different vaccination strategy. Spain, 2010–2018

	Regions with universal vaccination N=120	Regions with risk group vaccination N=330	Crude odds ratio (95% CI)	P value	Adjusted odds ratio (95% CI)	P value
Age						
0-14 years	52 (56.5%)	74 (46.5%)	Ref.		Ref.	
15-44 years	31 (33.7%)	69 (43.4%)	0.64 (0.37-1.11)	0.11	0.57 (0.32-1.01)	0.05
≥45 years	9 (9.8%)	16 (10.1%)	0.80 (0.33-1.95)	0.62	0.73 (0.29-1.82)	0.50
Sex						
Male	61 (67.0%)	124 (72.5%)	Ref.		Ref.	
Female	30 (33.0%)	47 (27.5%)	1.30 (0.75-2.25)	0.35	1.18 (0.65-2.13)	0.59
Born in Spain	26 (63.4%)	43 (71.7%)	0.68 (0.29-1.60)	0.38	0.75 (0.30-1.90)	0.54
Occupation						
Food handler	2 (3.4%)	6 (7.1%)	Ref.		Ref.	
Healthcare worker	0 (0%)	2 (2.4%)	-		-	
Nursery/school/high school worker	3 (5.1%)	5 (5.9%)	1.80 (0.21-15.41)	0.59	2.08 (0.22-19.59)	0.52
School/Student	53 (89.8%)	72 (84.7%)	2.21 (0.43-11.37)	0.34	2.27 (0.42-12.31)	0.34
Other §	1 (1.7%)	0 (0%)	-		-	
Hepatitis A vaccinated	0 (0%)	1 (0.9%)	-		-	
Men who have sex with men†	3 (16.7%)	27 (71.1%)	0.08 (0.02-0.34)	0.001	0.13 (0.03-0.55)	0.006
Drug user‡	1 (3.7%)	0 (0%)	-		-	

§ Performing arts direction. † Only for men aged ≥15 years. ‡ Only for persons aged ≥15 years.

What about the cost of hepatitis A outbreaks?

Article

Healthcare and Epidemiological Surveillance Costs of Hepatitis A Outbreaks in Spain in Regions with and without Universal Hepatitis A Vaccination of Children during 2010-2018

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Plans-Rubió et al. Vaccines 2024; 12: 648

Total, healthcare and epidemiological surveillance costs (EUR) per million population of hepatitis A outbreaks in Catalonia and regions without universal vaccination (UV) in 2010–2014, 2015–2018 and in the whole period

Periods	Healthcare costs (EUR) per million population			Epidemiological surveillance costs (EUR) per million population			Total costs (EUR) per million population		
	Regions without UV	Catalonia (UV)	Ratio	Regions without UV	Catalonia (UV)	Ratio	Regions without UV	Catalonia (UV)	Ratio
2010–2014	21,692.8	19,691.0	1.10	9985.1	12,182.8	0.82	31,677.9	31,873.8	0.99
2015–2018	53,807.3	18,825.5	2.86	16,186.0	7332.6	2.21	69,993.3	26,158.1	2.68
2010–2018	75,500.1	38,516.4	1.96	26,171.1	19,515.5	1.34	101,671.2	58,031.9	1.75



The total, healthcare and epidemiological surveillance costs per million population were higher in the group of regions without universal hepatitis A vaccination program of children

Epidemiological surveillance costs for the whole period were:
25.7% of total costs in regions without universal vaccination
33.6% of total costs in Catalonia with universal vaccination

CONCLUSIONS (I)

- 1. The cumulative incidence rate of outbreaks was lower in regions with a universal vaccination strategy than in regions with a risk-group vaccination strategy.**
- 2. MSM were less frequently the first case of the outbreak in regions with a universal vaccination strategy.**

CONCLUSIONS (II)

- 3. Imported outbreaks were more frequent in regions with universal vaccination.**
- 4. Cost-effectiveness studies of different hepatitis A immunization strategies taking into account the surveillance and control of outbreaks resources are needed.**

ACKNOWLEDGEMENTS

We would like to thank the collaboration of:

Reporting physicians; Technicians of Epidemiological Surveillance Units

This study was partially funded by

CIBER Epidemiología y Salud Pública (CIBERESP, Grant number ESPC07/2021), Instituto de Salud Carlos III, Spain

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Thank you!!

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