

Supplementary material for:

A cost-minimisation analysis: comparison of acellular versus whole-cell hexavalent paediatric vaccination strategies in Argentina

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Table S1. Argentine historical data

	2021 [1, 2]		2022 [3, 4]		2023 [5, 6]		Average	
	n	%	n	%	n	%	n	%
Birth data								
Argentine population	45,808,747	100.0	46,234,830	100.0	46,654,581	100.0	46,232,719	100.0
Live births registered	529,794	100.0	495,295	100.0	460,902	100.0	495,330	100.0
Live births registered >37 weeks	483,084	91.2	450,220	90.9	417,581	90.6	450,295	90.9
Live births registered <37 weeks	46,710	8.8	45,075	9.1	43,321	9.4	45,035	9.1
Live births registered <37 weeks and ≥1500g	41,037	7.7	39,125	7.9	37,851	8.2	39,338	7.9
Live births registered <37 weeks and <1500g	5,673	1.1	5,950	1.2	5,470	1.2	5,698	1.2
Vaccination rates (wP Pentavalent)								
1 st dose	NR	87.6	NR	89.9	NR	80.5	NR	86.0
2 nd dose	NR	84.1	NR	87.9	NR	76.0	NR	83.0
3 rd dose	NR	81.2	NR	83.8	NR	68.8	NR	78.0
Booster	NR	75.7	NR	74.2	NR	63.3	NR	71.0

Abbreviations: NR: not reported

Table S2. Vaccine distribution across public and private sectors

Scheme	1st dose, 2 months of age		2nd dose, 4 months of age		3rd dose, 6 months of age		Booster dose, 15 months of age	
	Percentage	n	Percentage	n	Percentage	n	Percentage	n
Public sector*	94.0	465,611	94.0	465,611	94.0	465,611	94.0	465,611
Private sector*	6.0	29,720	6.0	29,720	6.0	29,720	6.0	29,720
Public sector-vaccination coverage	86.0	400,425	82.7	384,905	77.9	362,866	71.1	330,894
≥37 weeks' gestation	90.9	364,018	90.9	349,909	90.9	329,874	90.9	300,809
<37 weeks' gestation and ≥1,500 g	7.9	31,801	7.9	30,568	7.9	28,818	7.9	26,279
†<37 weeks' gestation and <1,500 g (pentavalent + IPV)	0.6	2,303	0.6	2,214	0.6	2,087	1.2	3,806
†<37 weeks' gestation and <1,500 g (all hexavalent)	0.6	2,303	0.6	2,214	0.6	2,087	0.0	0
Private-sector vaccination coverage	100.0	29,720	100.0	29,720	100.0	29,720	100.0	29,720
≥37 weeks' gestation	90.9	27,018	90.9	27,018	90.9	27,018	90.9	27,018
<37 weeks' gestation and ≥1,500 g	7.9	2,360	7.9	2,360	7.9	2,360	7.9	2,360
<37 weeks' gestation and <1,500 g	1.2	342	1.2	342	1.2	342	1.2	342

*The ministry of health in Argentina acquires and distributes vaccines for the National Immunization Program for 94% of the covered population regardless of their healthcare affiliation (i.e. both the public and social security sectors), the administration of which is free, with the exception of those in the private insurance sector who account for rest (6%).

†Coverage disaggregated for the current scheme. Both groups 3 and 4 shown in the table all received hexavalent vaccine in the alternative scheme.

Abbreviations: IPV: inactivated polio vaccine.

Table S3. Adverse events reported after administration of vaccines containing either whole-cell pertussis or acellular pertussis components (%)

Adverse events (Decker et al)	1 st dose		2 nd dose		3 rd dose	
	wP	aP	wP	aP	wP	aP
Fever 100.1 to 101°F (37.8°C to 38.38°C)	24.3	2.3	28.8	12.8	27.8	15.2
Fever 101.1 to 102°F (38.39°C to 38.89°C)	3.0	0.8	3.9	0.8	7.3	2.3
Fever >102°F (38.89°C or higher)	0.0	0.0	1.4	0.8	2.6	0.0
Redness 1 to 20 mm	40.8	13.5	41.6	24.1	44.4	25.8
Redness >20 mm	8.6	0.8	6.1	1.5	3.2	3.0
Swelling 1 to 20 mm	23.2	7.5	26.6	16.5	30.1	14.4
Swelling >20 mm	16.5	0.8	9.5	0.8	5.6	3.8
Moderate pain	17.6	2.3	12.6	3.0	12.0	3.8
Severe pain	9.7	0.0	6.1	0.0	3.8	0.0
Moderate irritation	16.8	3.8	16.5	6.0	12.6	4.5
Severe irritation	3.8	0.8	7.0	0.8	4.7	0.8
Somnolence	43.5	28.6	31.0	14.3	24.6	14.4
Anorexia	19.5	7.5	16.5	4.5	14.3	12.1
Vomiting	7.0	3.0	4.5	1.5	5.3	3.8

Abbreviations: aP: acellular pertussis; wP: whole-cell pertussis

Source: Decker *et al.* 1995 [7]

Table S4. Proportion of those with adverse events who would seek medical consultation by adverse event experienced and vaccination dose (%)

Adverse events	1 st dose	2 nd dose	3 rd dose	Booster
Fever 100.1 to 101°F (37.8°C to 38.38°C)	16	18	12	9
Fever 101.1 to 102°F (38.39°C to 38.89°C)	34	32	31	27
Fever >102°F (38.89°C or higher)	50	50	48	41
Redness 1 to 20 mm	23	16	13	11
Redness >20 mm	46	45	39	33
Swelling 1 to 20 mm	19	15	15	13
Swelling >20 mm	41	43	37	34
Moderate pain	24	23	22	19
Severe pain	68	62	63	64
Severe irritation	60	74	74	74
Somnolence	65	69	71	67
Anorexia	30	29	22	16
Vomiting	45	46	41	38
Convulsions	100	97	98	100
Hypotonia-hyporesponsiveness	98	93	94	94

Source: Olivera *et al.* 2023 [8]

Table S5. Proportion of those with adverse events who would be referred to the emergency room (including those who require consultation with an emergency room specialist and hospitalisation) by adverse event experienced and vaccination dose (%)

Adverse events	1st dose	2nd dose	3rd dose	Booster
Redness 1 to 20 mm	3	0	0	0
Redness 1 to 20 mm (if premature, <37 WGA)	3	0	0	0
Redness >20 mm	20	13	13	10
Redness >20 mm (if premature, <37 WGA)	20	17	13	13
Swelling 1 to 20 mm	7	3	3	3
Swelling 1 to 20 mm (if premature, <37 WGA)	7	3	3	3
Swelling >20 mm	27	13	20	13
Swelling >20 mm (if premature, <37 WGA)	27	13	20	13
Swelling >20 mm (require ER specialist)	0	0	3	0
Swelling >20 mm (require ER specialist if premature, <37 WGA)	0	0	3	0
Swelling >20 mm (require hospitalisation after ER specialist)	3	0	0	0
Moderate pain	10	10	7	3
Moderate pain (if premature, <37 WGA)	10	10	7	3
Severe pain	67	33	57	47
Severe pain (if premature, <37 WGA)	70	37	60	53
Persistent high-pitched cry or irritability	57	40	47	40
Persistent high-pitched cry or irritability (if premature, <37 WGA)	60	47	50	40
Persistent high-pitched cry or irritability (require ER specialist)	3	0	0	0
Persistent high-pitched cry or irritability (require ER specialist if premature, <37 WGA)	3	0	0	0
Severe irritation	53	70	60	57
Severe irritation (if premature, <37 WGA)	57	70	60	57
Severe irritation (require ER specialist)	7	3	0	0
Severe irritation (require ER specialist if premature, <37 WGA)	7	3	0	0

Somnolence	73	63	60	63
Somnolence (if premature, <37 WGA)	77	67	60	63
Somnolence (require ER specialist)	3	0	0	0
Somnolence (require ER specialist if premature, <37 WGA)	3	0	0	0
Anorexia	20	10	7	3
Anorexia (if premature, <37 WGA)	27	13	10	3
Vomiting	50	50	43	37
Vomiting (if premature, <37 WGA)	50	53	47	40
Convulsions	93	93	93	90
Convulsions (if premature, <37 WGA)	93	93	93	90
Convulsions (require ER specialist)	17	0	0	0
Convulsions (require ER specialist if premature, <37 WGA)	17	0	0	0
Convulsions (require hospitalisation after ER specialist)	40	40	37	37
Hypotonia-hyporesponsiveness	100	97	97	87
Hypotonia-hyporesponsiveness (if premature, <37 WGA)	100	97	97	87
Hypotonia-hyporesponsiveness (require ER specialist)	17	0	0	0
Hypotonia-hyporesponsiveness (require ER specialist if premature, <37 WGA)	17	0	0	0

Abbreviations: ER: emergency room; WGA: weeks' gestation age at birth

Source: Olivera *et al.* 2023 [8]

Table S6. Proportion of those with adverse events who would need follow-up by adverse event experienced and vaccination dose (%)

Adverse events	1 st dose	2 nd dose	3 rd dose	Booster
Fever 100.1 to 101°F (37.8°C to 38.38°C)	63	47	30	33
Fever 100.1 to 101°F (37.8°C to 38.38°C) (if premature, <37 WGA)	67	50	33	33
Fever 101.1 to 102°F (38.39°C to 38.89°C)	60	53	50	53
Fever 101.1 to 102°F (38.39°C to 38.89°C) (if premature, <37 WGA)	67	60	53	53
Fever >102°F (38.89°C or higher)	43	57	57	60
Fever >102°F (38.89°C or higher) (if premature, <37 WGA)	57	60	60	60
Redness 1 to 20 mm	47	53	53	50
Redness 1 to 20 mm (if premature, <37 WGA)	47	53	53	50
Redness >20 mm	67	70	53	50
Redness >20 mm (if premature, <37 WGA)	73	70	60	53
Redness >20 mm (require specialist)	3	0	0	0
Redness >20 mm (require specialist if premature, <37 WGA)	3	0	0	0
Swelling 1 to 20 mm	47	63	50	43
Swelling 1 to 20 mm (if premature, <37 WGA)	47	63	50	43
Swelling >20 mm	67	63	60	53
Swelling >20 mm (if premature, <37 WGA)	67	67	60	53
Moderate pain	43	47	43	40
Moderate pain (if premature, <37 WGA)	43	47	43	40
Moderate pain (require specialist)	3	0	0	3
Moderate pain (require specialist if premature, <37 WGA)	3	0	0	3
Severe pain	40	57	57	40
Severe pain (if premature, <37 WGA)	43	60	57	47
Severe pain (require specialist)	7	0	0	3

Severe pain (require specialist if premature, <37 WGA)	7	0	0	3
Persistent high-pitched cry or irritability	53	57	60	40
Persistent high-pitched cry or irritability (if premature, <37 WGA)	53	57	60	40
Severe irritation	47	33	47	47
Severe irritation (if premature, <37 WGA)	47	33	47	47
Somnolence	40	40	37	30
Somnolence (if premature, <37 WGA)	40	40	37	30
Anorexia	50	50	50	53
Anorexia (if premature, <37 WGA)	53	50	53	57
Vomiting	53	43	57	57
Vomiting (if premature, <37 WGA)	55	43	57	60
Vomiting (require specialist)	0	0	0	0
Vomiting (require specialist if premature, <37 WGA)	3	0	0	0
Convulsions	73	40	33	40
Convulsions (if premature, <37 WGA)	73	40	33	40
Convulsions (require specialist)	20	10	0	7
Convulsions (require specialist if premature, <37 WGA)	20	17	0	10
Hypotonia-hyporesponsiveness	53	43	37	33
Hypotonia-hyporesponsiveness (if premature, <37 WGA)	53	43	37	33
Hypotonia-hyporesponsiveness (require specialist)	7	20	0	7
Hypotonia-hyporesponsiveness (require specialist if premature, <37 WGA)	13	20	0	7

Abbreviations: WGA: weeks' gestation age at birth

Source: Olivera *et al.* 2023 [8]

Table S7. Proportion of those with adverse events who would require nonsteroidal anti-inflammatory drugs by adverse event experienced and vaccination dose (%)

Adverse event	1 st dose	2 nd dose	3 rd dose	Booster
Fever 100.1 to 101°F (37.8°C to 38.38°C)	100	100	100	93
Fever 101.1 to 102°F (38.39°C to 38.89°C)	97	100	100	97
Fever >102°F (38.89°C or higher)	100	97	100	100
Redness 1 to 20 mm	60	60	47	40
Redness >20 mm	60	60	60	63
Swelling 1 to 20 mm	47	43	37	40
Swelling >20 mm	40	50	37	50
Moderate pain	93	87	87	87
Severe pain	87	90	83	80
Persistent high-pitched cry or irritability	63	67	73	60
Severe irritation	73	57	53	53
Somnolence	7	10	7	13
Anorexia	3	13	20	13
Vomiting*	7	7	3	10
Convulsions*	10	20	27	33
Hypotonia-hyporesponsiveness	13	10	7	7

*Regarding other medication, antiemetics in the case of vomiting are indicated in 40%, 53%, 53% and 57% for each of the doses, respectively. In the case of seizures, benzodiazepines are indicated by 620%, 20%, 10% and 13% for each of the doses, respectively.

Source: Olivera *et al.* 2023 [8]

Table S8. Comprehensive cost inputs

Variables	Arg\$	US\$	Source
Cost of analgesics/antipyretics			
Ibuprofen suspension: 2% suspension 2 g/100ml (Pfizer)	5,903.86	4.37	Kairos.
Ibuprofen suspension: FEBRATIC Ped. 2% (Roemmers)	4,258.44	3.66	Kairos.
Ibuprofen suspension. PEDIATRIC ACTRON 2% Oral (Bayer)	4,600.00	3.95	Kairos.
Mean cost of ibuprofen suspension	4,648.35	3.99	
Cost of antiemetics			
Metochlopramide: RELIVERAN for CHILDREN 2 mg/ml. Oral drops x20ml (Gador)	6,939.56	5.96	Kairos.
Metoclopramide: Vannier 5 mg /ml. Oral Drops x 20ml. (Vannier)	6,020.57	5.17	Kairos. :
Metochlopramide: Gastrocalm 2 mg/ml. Oral Drops x 20ml. (Medisol)	5,400.00	4.64	Kairos.
Mean cost of antimetic drops	6,116.25	5.25	
Cost of paediatric outpatient visit			IQVIA Argentina. Unit Costs and Health Events Base
Average paediatric outpatient medical consultation in the public sector	6,525.83	5.60	
Average paediatric outpatient consultation for Provincial social security organizations	10,743.51	9.22	
Average paediatric outpatient medical consultation under National Social Security Schemes	11,867.80	10.16	
Average paediatric outpatient medical consultation in the private sector	13,472.62	11.56	
Weighted average paediatric outpatient visit	9,343.30	8.02	
Cost of paediatric emergency room visit			IQVIA Argentina. Unit Costs and Health Events Base
Average paediatric emergency medical consultation in the public sector	11,906.96	10.22	
Average cost of paediatric emergency medical consultation for Provincial Social Security Organizations	18,643.51	16.00	
Average cost of paediatric emergency medical consultation for National Social Security Organizations	20,393.61	17.51	
Average paediatric emergency medical consultation in the private sector	20,437.03	17.54	
Weighted average paediatric Emergency Room visit	16,263.40	13.96	
Cost of day of hospitalisation in paediatric ward			IQVIA Argentina. Unit Costs and Health Events Base
Average cost of stay in paediatric ward in the public sector	56,177.14	48.22	
Average cost of stay in paediatric ward for Provincial Social Security Organizations	88,872.81	76.29	
Average cost of hospitalisation in paediatric ward for National Social Security Organizations	554,618.59	476.07	
Average cost of stay in paediatric ward in the private sector	571,218.49	490.32	
Weighted average of 1 day of hospitalisation in the paediatric ward†	105,712.10	90.74	
Cost of aP hexavalent vaccine in the private healthcare sector			
Hexaxim (Sanofi)	209,454.02	179.79	Kairos.

Variables	Arg\$	US\$	Source
Infanrix Hexa (GSK)	204,016.96	175.1 2	Kairos.
Mean cost of aP hexavalent vaccine in the private health sector	206,740.90	177.4 6	

Note: Prices were converted from Argentine Pesos (Arg\$) into US\$ using an exchange rate of Arg\$1,165=US\$1 (May 2, 2025).

Abbreviations: aP: acellular pertussis

Table S9. Adverse events reported after administration of vaccines containing either whole-cell pertussis or acellular pertussis components in the sensitivity analysis (%)

Adverse events (Zhang et al)	1 st dose		2 nd dose		3 rd dose		Booster	
	wP	aP	wP	aP	wP	aP	wP	aP
Fever >38°C	46.67	6.02	43.75	12.77	44.62	16.19	50.93	22.61
Redness	34.35	9.57	34.31	12.42	35.12	16.23	54.44	34.34
Swelling	41.69	11.67	42.08	18.36	44.11	27.48	39.72	30.72
Pain	21.53	7.13	45.32	7.36	38.10	7.29	81.85	34.29
Irritation	57.30	28.31	50.72	30.99	44.57	28.38	34.31	21.52
Drowsiness	29.14	15.00	18.25	9.12	17.27	12.58	23.13	12.04
Anorexia	25.89	10.36	17.64	8.98	14.19	7.95	18.5	10.21
Vomiting	8.09	6.52	6.10	3.83	4.89	4.13	3.33	3.57
Persistent acute crying	5.79	1.12	3.83	1.63	1.46	0.67	0.39	0.22

Abbreviations: aP: acellular pertussis; NR: not reported; wP: whole-cell pertussis

Source: Zhang *et al.* 2014 [9]

Table S10. Breakdown of total costs by dose in the base case analysis (US\$)

Vaccination scheme	Timepoint	AE management costs	Vaccine acquisition costs	Programmatic costs	Total costs
wP hexavalent	2 months	\$20,402,892	\$7,274,346	\$1,273,352	\$28,950,590
	4 months	\$16,148,402	\$7,196,811	\$1,223,997	\$24,569,210
	6 months	\$12,647,160	\$7,086,711	\$1,153,913	\$20,887,784
	Booster	\$10,808,077	\$6,895,321	\$1,052,243	\$18,755,641
	Total	\$60,006,532	\$28,453,189	\$4,703,504	\$93,163,225
aP hexavalent	2 months	\$8,278,145	\$13,899,097	\$1,273,352	\$23,457,574
	4 months	\$6,452,154	\$13,564,788	\$1,223,997	\$21,240,939
	6 months	\$6,696,405	\$13,090,070	\$1,153,913	\$20,940,388
	Booster	\$5,802,001	\$12,401,395	\$1,056,866	\$19,260,262
	Total	\$27,228,705	\$52,955,351	\$4,708,127	\$84,892,183

Abbreviations: aP: acellular pertussis; wP: whole-cell pertussis

Table S11. Breakdown of costs by population in the base case analysis (US\$)

Vaccination scheme	Population	Health system	AE management	Programmatic	Vaccine acquisition	Total
wP hexavalent	≥37 weeks' gestation	Public	\$52,623,082	\$4,275,863	\$6,588,593	\$63,487,538
	<37 weeks' gestation and ≥1,500 g	Public	\$4,888,323	\$373,538	\$575,578	\$5,837,439
	<37 weeks' gestation and <1,500 g	Public	\$413,874	\$33,105	\$51,008	\$497,987
	<37 weeks' gestation and <1,500 g, in Program	Public	\$553,261	\$21,001	\$4,936,681	\$5,510,939
	≥37 weeks' gestation	Private	\$1,384,968	\$0	\$14,802,149	\$16,187,114
	<37 weeks' gestation and ≥1,500 g	Private	\$125,632	\$0	\$1,317,188	\$1,442,818
	<37 weeks' gestation and <1,500 g	Private	\$17,393	\$0	\$181,995	\$199,387
	Total	Overall	\$60,006,533	\$4,703,507	\$28,453,192	\$93,163,222
aP hexavalent	≥37 weeks' gestation	Public	\$22,969,075	\$4,275,863	\$28,962,918	\$56,207,856
	<37 weeks' gestation and ≥1,500 g	Public	\$1,935,254	\$373,538	\$2,530,193	\$4,838,986
	<37 weeks' gestation and <1,500 g	Public	\$295,869	\$54,103	\$366,473	\$716,445
	≥37 weeks' gestation	Private	\$1,841,129	\$0	\$19,177,744	\$21,023,073
	<37 weeks' gestation and ≥1,500 g	Private	\$163,674	\$0	\$1,675,364	\$1,839,401
	<37 weeks' gestation and <1,500 g	Private	\$23,706	\$0	\$242,660	\$266,419
	Total	Overall	\$27,228,707	\$4,708,127	\$52,955,352	\$84,892,180

Abbreviations: aP: acellular pertussis; wP: whole-cell pertussis

Table S12. Breakdown of adverse event management costs in the base case analysis (US\$)

Vaccination scheme	Timepoint	Medication	Primary care visit	ER visit	Hospitalisation	Follow-up visit	Total AE management costs
wP hexavalent	2 months	\$1,784,913	\$5,519,214	\$5,540,336	\$104,976	\$7,453,453	\$20,402,892
	4 months	\$1,707,806	\$4,306,342	\$3,122,803	\$100,968	\$6,910,483	\$16,148,402
	6 months	\$1,484,755	\$3,293,552	\$2,280,214	\$95,277	\$5,493,363	\$12,647,161
	Booster	\$1,318,428	\$2,701,141	\$1,958,918	\$87,422	\$4,742,169	\$10,808,077
	Total	\$6,295,901	\$15,820,249	\$12,902,271	\$388,644	\$24,599,468	\$60,006,532
aP hexavalent	2 months	\$387,284	\$2,111,824	\$2,553,483	\$22,713	\$3,202,841	\$8,278,145
	4 months	\$720,149	\$1,641,349	\$1,131,710	\$21,893	\$2,937,052	\$6,452,154
	6 months	\$759,817	\$1,755,873	\$1,211,241	\$20,729	\$2,948,745	\$6,696,405
	Booster	\$660,492	\$1,419,566	\$1,042,342	\$19,041	\$2,660,560	\$5,802,001
	Total	\$2,527,742	\$6,928,612	\$5,938,775	\$84,376	\$11,749,199	\$27,228,705

Abbreviations: AE: adverse event; aP: acellular pertussis; ER: emergency room; wP: whole-cell pertussis

Table S13. Breakdown of vaccine acquisition costs in the base case analysis (US\$)

Vaccination scheme	Timepoint	wP hexavalent	aP hexavalent	Total vaccine acquisition costs
wP hexavalent	2 months	\$1,950,798	\$5,323,548	\$7,274,346
	4 months	\$1,875,186	\$5,321,625	\$7,196,811
	6 months	\$1,767,816	\$5,318,895	\$7,086,711
	Booster	\$1,621,380	\$5,273,941	\$6,895,321
	Total	\$7,215,180	\$21,238,009	\$28,453,189
aP hexavalent	2 months	\$0	\$13,899,097	\$13,899,097
	4 months	\$0	\$13,564,788	\$13,564,788
	6 months	\$0	\$13,090,070	\$13,090,070
	Booster	\$0	\$12,401,395	\$12,401,395
	Total	\$0	\$52,955,351	\$52,955,351

Abbreviations: aP: acellular pertussis; wP: whole-cell pertussis

Table S14. Breakdown of healthcare resource utilisation in the public sector

Schedule	Medication administrations	First outpatient visits	Emergency consultations	Hospitalisations	Outpatient follow-up visits	Transfers	Days of absence
1st dose							
wP hexavalent	435,733	318,355	235,143	970	432,364	1,971,724	986,832
aP hexavalent	88,299	116,476	104,205	198	124,435	690,232	345,315
Difference	347,434	201,880	130,938	772	307,929	1,281,492	641,518
2nd dose							
wP hexavalent	411,598	248,170	133,341	933	383,557	2,011,022	766,001
aP hexavalent	166,370	90,276	46,056	191	161,540	595,743	298,062
Difference	245,228	157,894	87,286	742	222,017	1,415,278	467,939
3rd dose							
wP hexavalent	353,696	187,260	95,940	879	311,761	1,189,922	595,840
aP hexavalent	173,178	96,156	49,079	180	167,366	625,201	312,780
Difference	180,517	91,104	46,862	699	144,395	564,720	283,060
Booster dose							
wP hexavalent	325,308	159,406	85,530	819	279,764	1,049,401	525,519
aP hexavalent	151,609	77,174	41,928	164	144,641	527,487	263,907
Difference	173,699	82,232	43,602	655	135,123	521,914	261,612
Total							
Difference	946,879	533,110	308,687	2,868	809,464	3,783,405	1,654,129

Abbreviations: aP: acellular pertussis; wP: whole-cell pertussis

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