



**STÁTNÍ ZDRAVOTNÍ ÚSTAV**  
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Co zaznělo na letošním ESPIDu:

# **Novinky ke chřipkovým vakcínám - efekt u dětí a v těhotenství**

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**Oddělení epidemiologie infekčních nemocí**

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# Porovnání závažnosti chřipky typu A a chřipky typu B u dětí

Subtype-specific Clinical Presentation, Medical Treatment and Family Impact of Influenza in Children 1–5 Years of Age Treated in Outpatient Practices in Germany During Three Postpandemic Years, 2013–2015

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**TABLE 1.** Clinical Characteristics by Influenza Type/Subtype, for 217 PCR-confirmed Preschool Influenza Patients in Pediatric Practices, 2013–2015

	Influenza Types/Subtypes				P*
	All Patients N = 217	A(H3N2) N = 122	A(H1N1) pdm2009 N = 56	B N = 39	
<b>Duration of symptoms/disease</b>					
Days with fever plus cough/rhinitis, median (IQR)†	4 (3–5)	4 (3–5)	4 (3–6)	4 (3–5)	0.286
Days with fever, median (IQR)†	4 (3–5)	4 (3–5)	4 (3–6)	5 (3–6)	0.119
<b>Severity assessments</b>					
Parent CARIFS sum score at day 3, median (IQR)§	20 (10–29)	20 (11–29)	18 (7–29)	23 (16–32)	0.128
Parent CARIFS sum score at day 6, median (IQR)§	9 (3–15)	8 (3–13)	8 (3–19)	9 (4–17)	0.651
Final categorization as moderate-to-severe, n (%)¶	188 (86.6)	100 (82.0)	52 (92.9)	36 (92.3)	0.072

Similar severity of Influenza A(H3N2), A(H1N1)pdm09 and Influenza B in duration of ARI symptoms and other severity assessments

§Sum score based on 18 items (each scored 0–3), with 0 = best possible health, 54 = worst possible health (CARIFS).<sup>27</sup>

¶Severity definition by Jain et al.<sup>16</sup> modified.

# Comparative severity of influenza A and B infections in hospitalized children

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## Introduction

Although both influenza A and B virus infections predispose children to hospitalization and a wide range of complications, influenza A viruses are conventionally thought to cause more severe illnesses than B viruses. However, when comparing the severity of influenza A and B infections in children, all outcomes should be adjusted for age because children with influenza A are generally younger than those with influenza B.

## Materials and methods

This retrospective study consisted of all children under 16 years of age hospitalized with laboratory-confirmed non-nosocomial influenza A or B infection at Turku University Hospital during a 14-year period of 1.7.2004-30.6.2018. Data on clinical presentation and outcomes, management, and duration of hospitalization were retrieved from the medical records of the children. For comparison of influenza A and B infections, the children were divided into three age groups: <3, 3-9, and 10-15 years of age.

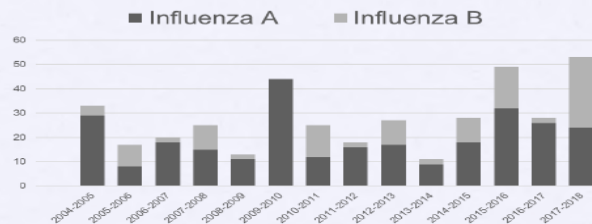


Figure. Annual distribution of influenza A and B hospitalizations during the study period

Variable	A <3 yrs (n=152)	B <3 yrs (n=39)	A 3-9 yrs (n=86)	B 3-9 yrs (n=44)	A 10-15 yrs (n=41)	B 10-15 yrs (n=29)
Highest fever (°C)	38.9	39.1	39.4	39.4	39.2	39.2
Pneumonia	21 (14%)	5 (13%)	14 (16%)	6 (14%)	9 (22%)	8 (28%)
Otitis media	47 (31%)	9 (23%)	12 (14%)	6 (14%)	2 (5%)	2 (7%)
CSF analysis	7 (5%)	4 (10%)	7 (8%)	4 (9%)	2 (5%)	3 (10%)
Blood culture	52 (34%)	14 (36%)	30 (35%)	13 (30%)	19 (46%)	12 (41%)
Antibiotic treatment	84 (55%)	22 (56%)	41 (48%)	18 (41%)	18 (44%)	14 (48%)
Intensive care	19 (13%)	8 (21%)	13 (15%)	3 (7%)	4 (10%)	6 (21%)
Mean duration of hospitalization (d)	2.2	2.2	2.5	2.1	2.2	4.4

Table. Comparison of selected outcomes between influenza A and B infections in hospitalized children in different age groups.

## Results

A total of 391 (influenza A, n=279; influenza B, n=112) children were hospitalized with influenza during the study period. Overall, influenza B viruses accounted for 28.6% of all hospitalizations (Figure).

Children hospitalized with influenza A infection were significantly younger than those with influenza B infection (4.2 vs 6.4 years,  $p < 0.0001$ ). When analyzed within different age groups, no statistically significant differences were observed in any variables between children with influenza A and B infections (Table).

## Conclusions

When adjusted for age, the clinical presentation and outcomes appear to be similar between children hospitalized with influenza A and B infections. These findings underscore the importance of age as a crucial factor when analyzing clinical features of illnesses in children.

The comparable clinical severity of influenza A and B infections supports the use of quadrivalent influenza vaccines that contain both influenza B strains circulating among humans

# Očkování těhotných žen proti chřipce

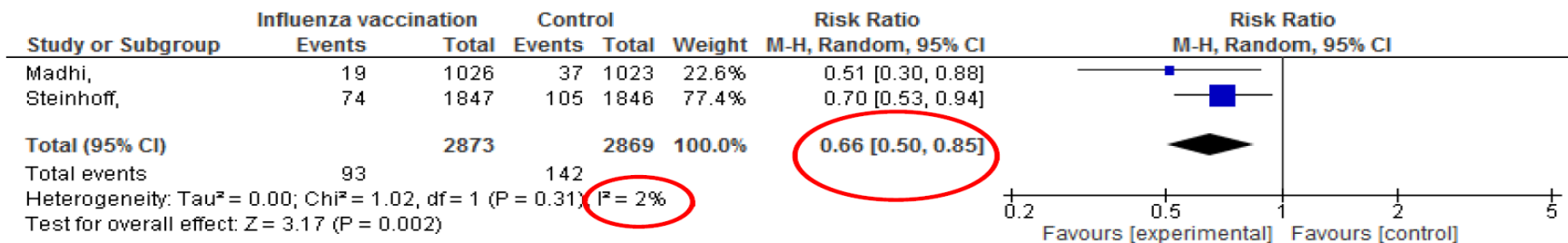
- *Pregnant women and their infants are at increased risk of morbidity and mortality due to complications from seasonal and pandemic influenza illness. Although a vaccine exists for pregnant women, no vaccine exists for infants <6 months old. This results in limited infant immunity against influenza infection. However, maternal vaccination may also confer immunity to the infant through trans-placental antibody transfer. There is growing evidence that maternal vaccination reduces infant influenza-illness burden. This systematic review aims to determine the effectiveness of maternal influenza vaccination during pregnancy on mother and infant.*
- *In a random-effects pooled meta-analysis of 2 RCTs maternal influenza vaccination was associated with an overall reduction of Laboratory Confirmed Influenza (LCI) in infants of 34% (95% CI: 0.5-0.85).*
- *Maternal influenza vaccination was protective against LCI infection in infants. This review supports the targeting of maternal influenza vaccination to partially reduce influenza illness in infants.*

# Očkování těhotných žen proti chřipce

## RESULTS - PRIMARY OBJECTIVE:

### Vaccine effectiveness of influenza vaccine in pregnancy on Laboratory Confirmed Influenza in infants:

5/6 RCTs protective effect



(Jarvis J. A systematic review and metaanalysis: the effectiveness of maternal influenza vaccination. ESPID Lublaň 2019)

# Vztah mezi BMI a imunitní odezvou po očkování proti chřipce u těhotných

- This study aimed to investigate the impact of body mass index (BMI) on vaccine responses following influenza vaccination during pregnancy
- *Results: Most pregnant women (72/90, 80%) demonstrated seropositive antibody titres to all three influenza vaccine strains (H1N1, H3N2 and B) following vaccination. More women were seropositive following vaccination in 2014 (39/43, 91%) compared with 2015 (19/29, 66%) and 2016 (14/18, 78%) (OR 4.1, CI 1.2-13.8; p=0.021). Seropositivity was comparable among high vs normal BMI women (22/24, 92% vs 50/68, 74%; p=0.09). High BMI women had improved odds of seroconversion for H1N1 antibodies compared with normal BMI women (OR 3.1, CI 1.1-9.5; p=0.04). Women vaccinated during their second trimester were more likely to achieve seropositivity to all 3 vaccine antigens (47/53, 88%) compared with women vaccinated during their first trimester (7/12, 58%) (OR 5.6; CI 1.3-23.3; p=0.018).*
- *Conclusions: BMI did not impair influenza vaccine responses in pregnant women and may improve seroconversion. Gestation at vaccination, irrespective of BMI, may be an important consideration for optimising vaccine protection for women and their newborns.*
- **Komentář JK:** uvedené nicméně neznamená, že bude průběh případné nemoci také stejný. Obézní těhotná může mít častěji dýchací obtíže....

(Clarke M. Associations between body mass index and vaccine responses following influenza vaccination during pregnancy. ESPID Lublaň 2019)





# Vztah mezi BMI a imunitní odezvou po očkování proti chřipce u těhotných

## Results

- 96 women were enrolled and vaccinated.
- A quarter of participants (24/96, 25%) had BMI  $\geq 30$  kg/m<sup>2</sup>.
- Pre- and post vaccination blood samples were obtained for 90/96 participants (94%).

		BMI <30 kg/m <sup>2</sup> n=72	BMI $\geq 30$ kg/m <sup>2</sup> n=24
Height	Mean m (SD)	1.64 (0.07)	1.65 (0.06)
Weight	Mean kg (SD)	67.8 (8.9)	100.2 (18.1)
BMI	Median kg/m <sup>2</sup> (range)	25.7 (17.9-29.7)	36.9 (30.2-49.2)
Year	2014/2015/2016	30/25/17	14/7/3
Age	Median years (IQR)	30 (27.0-32.5)	26.5 (31-33)
Gestational age at vaccination	Median weeks (IQR)	22 (14-29.5)	21.5 (15-26.5)
Interval between pre and post blood sample	Median days (IQR) ^	29 (28-35)	28 (27.5-36)

^ missing 6 - participants did not have post vaccination blood drawn (BMI<30 kg/m<sup>2</sup> n=66)

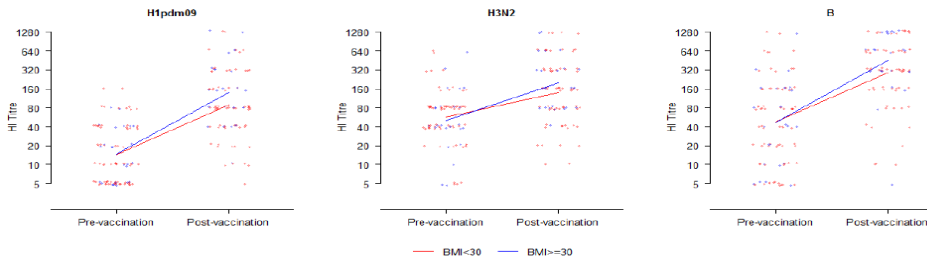
The University of Adelaide

(Clarke M. Associations between body mass index and vaccine responses following influenza vaccination during pregnancy. ESPID I ublaň 2019)



# Vztah mezi BMI a imunitní odezvou po očkování proti chřipce u těhotných

## Results – HI Titres



### Influenza vaccines composition

FluA-H1 (2014: A/California/07/2009; 2015: A/California/07/2009; 2016: A/California/07/2009)  
 FluA-H3 (2014: A/Texas/50/2012; 2015: A/Switzerland/9715293/2013; 2016: A/Switzerland/9715293/2013)  
 Flu B (2014: B/Massachusetts/2/2012; 2015: B/Phuket/3073/2013; 2016: B/Phuket/3073/2013)

## Results - seroconversion

- Seroconversion defined as a four fold rise in titre between day 0 and day 28
- More obese than non-obese women demonstrated H1N1 seroconversion (19/24, 79% vs 36/66, 55%  $\chi^2$  p=0.034).

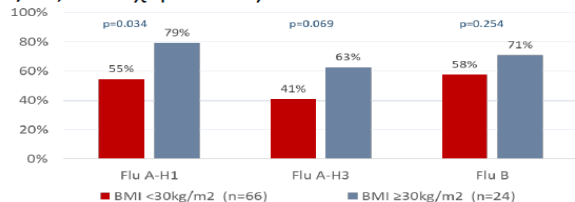


Figure: Percentage demonstrating seroconversion (≥4-fold rise in titre) following influenza vaccination by BMI category

## Results - seropositivity

- Seropositivity defined as HI Titre ≥ 40
- Overall, most pregnant women (72/90, 80%) demonstrated seropositive antibody titres to all three influenza viruses (H1N1, H3N2 and B) following vaccination

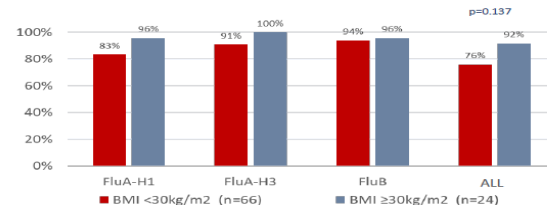


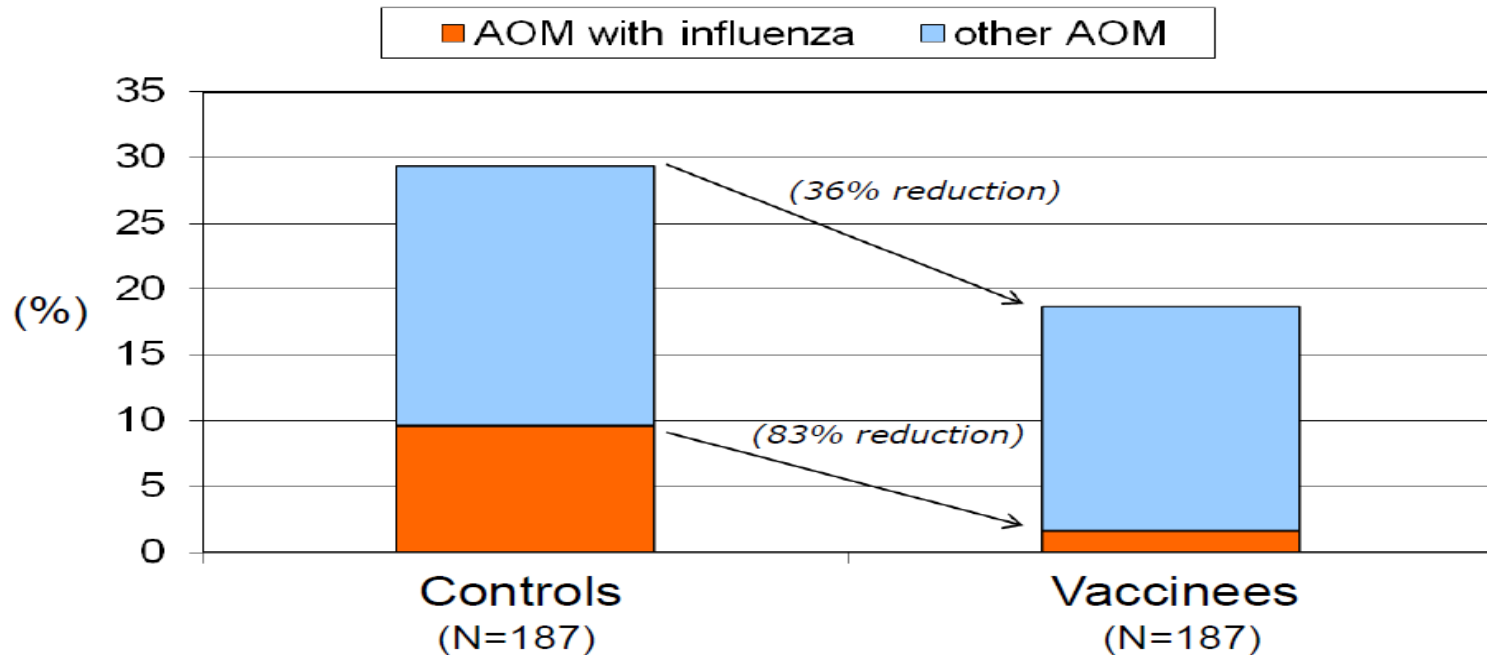
Figure: Percentage with seropositive antibody titres post influenza vaccination by BMI category

(Clarke M. Associations between body mass index and vaccine responses following influenza vaccination during pregnancy. ESPID Lublaň 2019)





# Efekt očkování proti chřipce v prevenci akutní otitis media u dětí



*Terho Heikkinen, MD; Olli Ruuskanen, MD; Matti Waris, MSc; Thedi Ziegler, PhD; Mikko Arola, MD; Pekka Halonen, MD; Am J Dis Child 1991*

## MATERIALS AND METHODS

We conducted

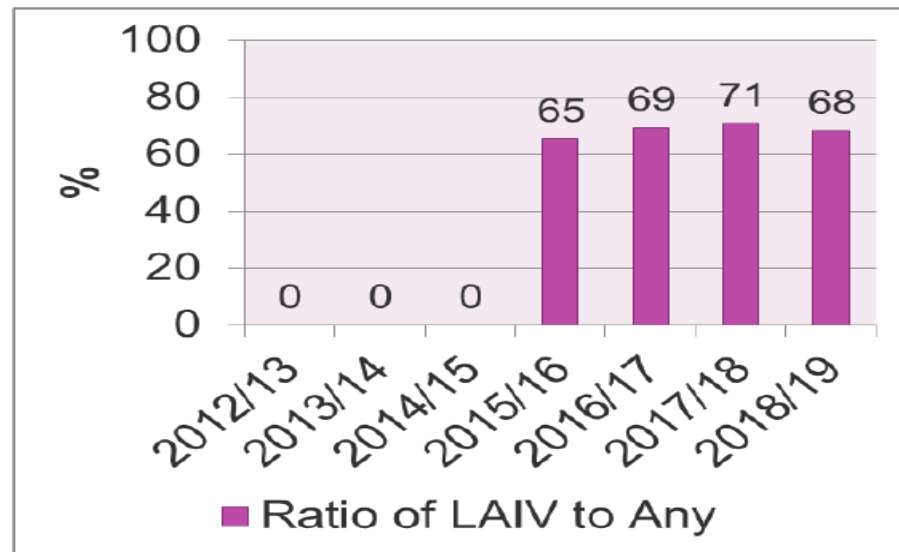
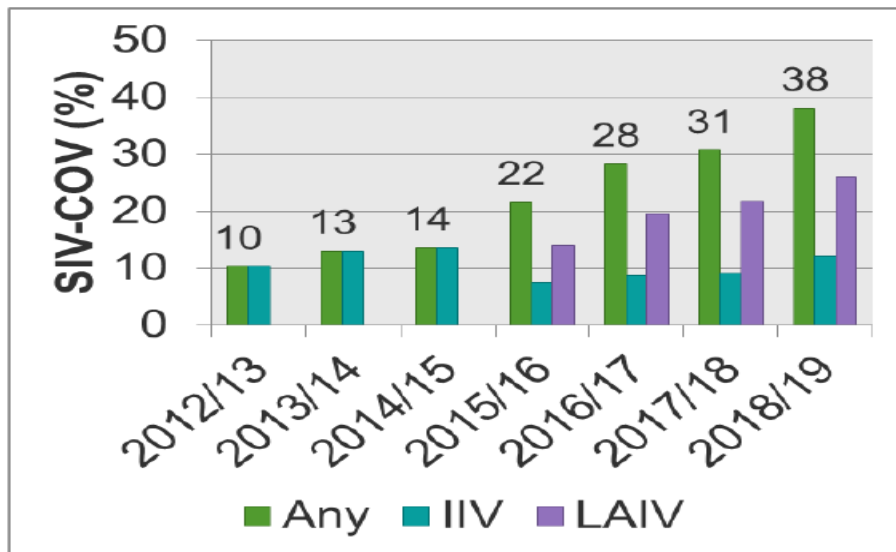
- a register-based cohort study comprising all children born 2012-2016, currently living in Finland,
- Vaccination data obtained from National Vaccination Register

The vaccination coverage (SIV-COV, proportion vaccinated)

- was calculated by vaccine type and age group and compared to previous seasons' figures

# Proočkovanost dětí proti chřipce ve Finsku

## RESULTS, CHILDREN AGED 2 YEARS



$N_{2018/19} = 53906$

01.05.2019

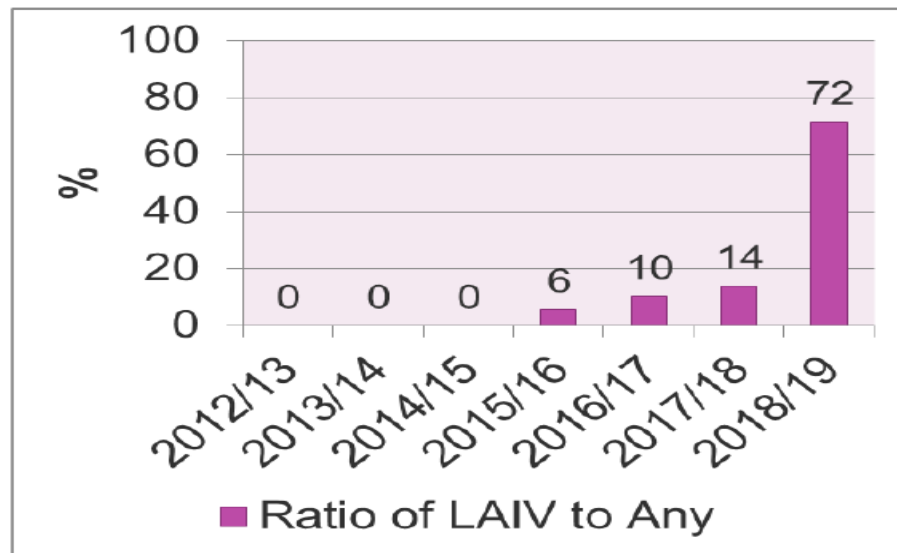
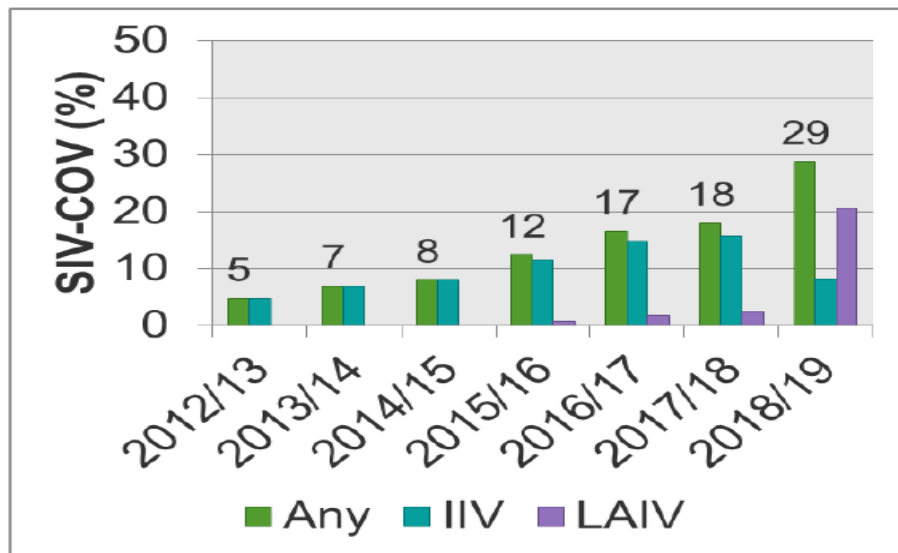
NIP INFL VACC Finland Nohynek

(Nohynek H. Seasonal influenza vaccine coverage, especially live-attenuated vaccine. Coverage, increases steadily among children in Finland according to a nationwide register based cohort study. ESPID Lublaň 2019)



# Proočkovanost dětí proti chřipce ve Finsku

## RESULTS, CHILDREN AGED 3 – 6 YEARS



$N_{2018/19} = 236804$

01.05.2019

NIP INFL VACC Finland Nohynek

(Nohynek H. Seasonal influenza vaccine coverage, especially live-attenuated vaccine. Coverage, increases steadily among children in Finland according to a nationwide register based cohort study. ESPID Lublaň 2019)



# Proočkovanost dĕtĭ proti chřĭpce ve Finsku

## CONCLUSIONS

- Seasonal influenza vaccine coverage in children in Finland is increasing steadily
- Coverage has particularly been boosted by the introduction of LAIV4
- Electronic National Vaccine Register allows for real time monitoring of vaccine coverage, and also for estimating vaccine effectiveness



01.05.2019

NIP INFL VACC Finland Nohynek

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(Nohynek H. Seasonal influenza vaccine coverage, especially live-attenuated vaccine. Coverage, increases steadily among children in Finland according to a nationwide register based cohort study. ESPID Lublaň 2019)



# Shrnutí

- Očkování těhotných žen proti chřipce má význam v prevenci onemocnění jak pro matku, tak pro novorozence, který v prvním půlroce svého života ještě nemůže být očkovan.
- Očkování dětí proti chřipce snižuje jejich nemocnost, snižuje výskyt zánětu středouší a též omezuje množství „zdrojů nákazy“ pro další skupiny obyvatel.
- Kromě klasického očkování seniorů a chronicky nemocných tudíž očkování dětí představuje další z možných strategií prevence chřipky, nicméně pro podmínky České republiky je zatím jeho významnou limitací nedostupnost vhodné vakcíny.
- Neexistence elektronické vakcinační databáze v ČR znemožňuje monitoring proočkovanosti v reálném čase a limituje kalkulaci efektivity očkování.



# Děkuji za pozornost

