Folkhälsomyndigheten

Nyheter från forskningsvärlden –

kommande influensa-, covid-19 och RSV vacciner - kort dialog kring framtida vaccinationskampanjer, vilka vacciner blir tillgängliga…

Kari Johansen
Enheten för vaccinationsprogram

Ingen intressekonflikt - No conflict of interest

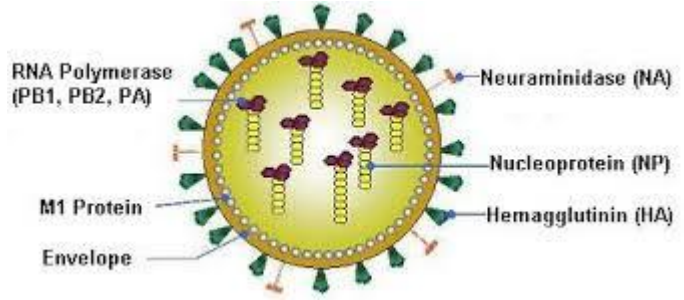
- Alla anställda vid Folkhälsomyndigheten intygar skriftligt att vi eller våra familjemedlemmar inte har några intressen i bolagen som producerar vacciner

- NB Detta är en vetenskaplig sammanställning av vacciner under utveckling och har ingen bäring på hur myndighetens framtida vaccinrekommendationer kommer att utvecklas.

Vi har några mycket spännande år framför oss

2022

Står vi inför ett paradigmskifte för influensavacciner?



Nuvarande tillverkningsplattformar – ingen av dessa tar hänsyn till innehåll av neuraminidas

- Inaktiverade (adjuvanterade eller icke-adjuvanterade)
  - Normaldos 15 µg HA
  - Hög dos 60 µg HA
- Levande attenuerade – *för barn diskuteras just nu om en av influensa B stammarna Yamagata ska tas bort då den inte cirkulerat de senaste åren (sedan mars 2020), orsaken är att den förökas hos vaccinproducenten och hos de som vaccineras**
- Rekombinant 45 µg HA

Nya tillverkningsplattformar under utveckling

- mRNA
- saRNA

Folkhälsomyndigheten

Has influenza B/Yamagata become extinct...? (Paget et al Euro Surveill.) 2022 Sep 29; 27(39): 2200753

Om mRNA-vaccinerna visas vara säkra, ge ett gott immunsvar och en god skyddseffekt i kommande prövningar…kan

- mRNA tekniken erbjuda möjligheten att ta beslut senare om vilka influensavirusstammar som ska ingå i ett uppdaterat vaccin, ca 2-3 månader istället för 6 månader – bättre match?
- mRNA-tekniken erbjuda möjligheten att inkludera både neuraminidas och hemagglutinin i till exempel oktavalenta vacciner istället för 4-valenta vacciner

Folkhälsomyndigheten

2024

- INFLUENSA
- COVID-19
- RSV

Respiratory vaccines

RSV
mRNA-1345

- Received FDA approval; launched in U.S. in July
- ACIP recommendation for all unvaccinated people ages 75+ and unvaccinated people ages 60-74 who are at increased risk
- Positive opinion from the EMA[1]; awaiting regulatory approvals in additional countries

Flu
mRNA-1010

- Engaging with regulators
- Intend to file in 2024

Next-gen COVID
mRNA-1283

- Phase 3 trial met primary efficacy endpoint, demonstrating non-inferior efficacy against COVID-19 compared to Spikevax® in participants ≥12 years
- Demonstrated higher efficacy compared to Spikevax in adults ≥18 years
- Engaging with regulators
- Intend to file in 2024

Flu/COVID combo
mRNA-1083

- Phase 3 trial met primary immunogenicity endpoints, eliciting higher immune responses against flu and SARS-CoV-2 than licensed flu and COVID vaccines in adults ≥50 years, including an enhanced flu vaccine in adults ≥65 years
- Engaging with regulators

1. EMA: European Medicines Agency

moderna

RSV Vaccine and mAb Snapshot

TARGET INDICATION: P =PEDIATRIC M =MATERNAL E =ELDERLY

	PHASE 1	PHASE 2	PHASE 3	MARKET APPROVED
LIVE-ATTENUATED/ CHIMERIC	Blue Lake (E) PIV5/RSV Codagenix, LID/NIAID/NIH (P) RSV Pontificia Universidad Catolica de Chile (P) BCG/RSV — Inactive SIIPL, St. Jude Hospital (P) SeV/RSV — Inactive	Blue Lake (P) PIV5/RSV Meissa Vaccines (P) RSV	Sanofi, LID/NIAID/NIH (P) RSV	
PROTEIN-BASED • PARTICLE • SUBUNIT	NIH/ NIAID/VRC (E M) RSV F Protein Virometix VLP Clover Biopharma RSV F Protein	Advaccine Biotechnology (P E) RSV G Protein Daiichi Sankyo (E) Protein ? Icosavax (E) RSV/hMPV VLP		GlaxoSmithKline (E) RSV F Protein Pfizer (E) RSV F Protein Pfizer (M) RSV F Protein
NUCLEIC ACID	Innorna (E) RNA	Moderna (M P) RNA Sanofi (E) RNA	Moderna (E) RNA	
RECOMBINANT VECTORS				
IMMUNO-PROPHYLAXIS	Gates MRI (P) Anti-F mAb	Trinomab Biotechnology (P) Anti-F mAb	Merck (P) Anti-F mAb	Astra Zeneca, Sanofi (P) Nirsevimab Astra Zeneca (P) Palivizumab

UPDATED: April 25, 2024

Indicates Change

https://www.path.org/resources/rsv-vaccine-and-mab-snapshot/

PATH

US ACIP rekommenderade i juni, 2024 …

- Vaccine recommendations
- There are three RSV vaccines licensed for use in adults ages 60 years and older in the United States: GSK's AREXVY, Moderna's mRESVIA, and Pfizer's ABRYSVO. For additional details on the recommendations of the Advisory Committee on Immunization Practices (ACIP) for RSV vaccination, see Adult RSV ACIP Vaccine Recommendations.
- CDC recommends a single dose of RSV vaccines for:
- All adults ages 75 and older
- Adults ages 60-74 who are at increased risk of severe RSV disease

Regulatory Decisions

Tivdak (US)	2L mCC	✓
Xtandi (EU)	nmCSPC (EMBARK)	✓
Beqvez (US)	Gene Therapy for Hemophilia B	✓
Durveqtix (EU)	Gene Therapy for Hemophilia B	✓
Emblaveo (EU)	Multidrug-Resistant Infections	✓
Prevenar 20 Peds (EU)	Pneumococcal Infection Vaccine	✓
Velsipity (EU)	Ulcerative Colitis	✓
Talzenna (EU)	1L mCRPC*	✓
Comirnaty JN.1 (EU)	COVID-19 Vaccine	✓
RSV Act-O-Vial	RSV Vaccine	✓

Phase 3 Readouts

ABRYSVO OA Second Season	RSV Vaccine	✓
ABRYSVO Adult 18-59 yrs at High Risk	RSV Vaccine	✓
Fordadistrogene Movaparvovec	Gene Therapy for Ambulatory Duchenne Muscular Dystrophy	✓
Giroctocogene Fitelparvovec	Gene Therapy for Hemophilia A	✓
Adcetris	r/r DLBCL	✓
Adcetris	Newly diagnosed cHL	✓

mCC=metastatic Cervical Cancer; nmCSPC=non-metastatic Castration-Sensitive Prostate Cancer; mCRPC= metastatic Castration-Resistant Prostate Cancer; r/r DLBCL= Cancer; NSCLC=Non-small Cell Lung Cancer; MM= multiple myeloma; cHL=classical Hodgkin lymphoma; OA=Older Adult; *in combination with Xtandi

[✓] completion [✓] completed; didn't m

Pipeline: *phase 2*

Immunology

Dupixent[A]	IL4/IL13 mAb	Ulcerative colitis
itepekimab[A]	IL33 mAb	Bronchiectasis
amlitelimab	OX40L mAb	Alopecia areata
		Asthma
		Hidradenitis suppurativa
		Systemic sclerosis
rilzabrutinib	BTK inhibitor	Asthma
		Chronic spontaneous urticaria
		IgG4-related disease
frexalimab[B,1]	CD40L mAb	Systemic lupus erythematosus
SAR441566	Oral TNFR1 signaling inhibitor	Psoriasis
		Rheumatoid arthritis
lunsekimig[2]	IL13/TSLP Nanobody VHH	Asthma
eclitasertib[D,3]	RIPK1 inhibitor	Ulcerative colitis
SAR444656[E,4]	IRAK4 degrader	Atopic dermatitis
		Hidradenitis suppurativa
SAR442970	TNFa/OX40L Nanobody® VHH	Hidradenitis suppurativa
duvakitug[F,5]	TL1A mAb	Crohn's disease
		Ulcerative colitis

Rare diseases

rilzabrutinib	BTK inhibitor	Warm autoimmune hemolytic anemia
SAR447537[7]	AAT fusion protein	Alpha-1 antitrypsin deficiency

Neurology

oditrasertib[D,8]	RIPK1 inhibitor	MS

Oncology

Sarclisa	CD38 mAb	MM, relapsed/refractory
SAR443579[G]	Trifunctional CD123 NK cell engager	Acute myeloid leukemia

Vaccines

Fluzone HD[9]	Influenza inactivated vaccine	Flu pediatric
SP0218	Yellow fever vero cell vaccine	Yellow fever
SP0202[H]	Pneumococcal 21-valent conjugate vaccine	Pneumococcal disease
SP0230	Pentavalent meningococcal ABCWY vaccine	Meningitis
SP0256	RSV mRNA vaccine	RSV older adult

Vaccines

SP0237	Flu mRNA vaccine	Flu
SP0256	RSV mRNA combination vaccine	RSV older adult
SP0268	Acne mRNA vaccine	Acne

Flu: strengthening *leadership*

Novavax partnership:
potential for a truly differentiated flu+COVID-19 combo vaccine

Optimal protection	Combining the proven efficacy of Sanofi differentiated flu vaccine and the Novavax COVID-19 vaccine
Improved tolerability	Compared to COVID-19 mRNA-based combinations
Logistics	Refrigerator-stable across the supply chain

Additional benefit:
expanding COVID-19 US reach in 2025 by leveraging Sanofi commercial capabilities

Advancing H5 pandemic flu vaccine preparedness with phase 1/2 studies

- BARDA-sponsored egg-based protein adjuvanted vaccine study to start in Q3 2024[1]
- mRNA vaccine study to start in coming months

1. Project supported in whole or in part with federal funds from the US Department of Health and Human Services; Administration for Strategic Preparedness and Response; Biomedical Advanced Research and Development Authority (BARDA), under contract number 75A50122D00003.

GSK

03 July 2024

Issued: London, UK

For media and investors only

GSK and CureVac to restructure collaboration into new licensing agreement

GSK

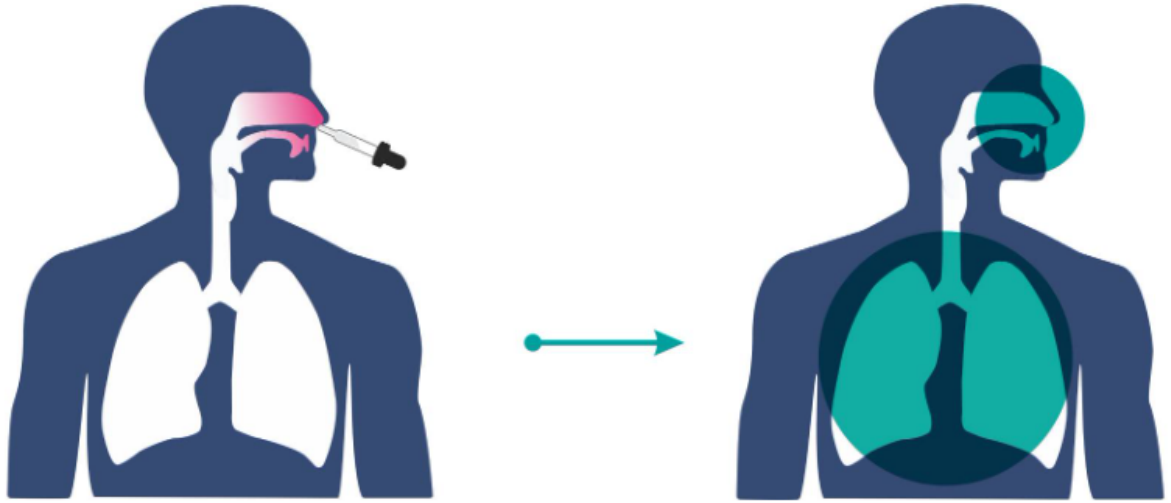
Since 2020, GSK and CureVac have worked together to develop mRNA vaccines for infectious diseases. Through this collaboration, GSK and CureVac currently have vaccine candidates for seasonal influenza and COVID-19 in phase II and avian influenza in phase I clinical development. All candidates are based on CureVac's proprietary second-generation mRNA backbone. Data generated to date for these candidate vaccines are promising and demonstrate their potential to be best-in-class new vaccines.

Hipra

Från hipra.com:

- **“HIPRA will have a COVID-19 vaccine adapted to the JN.1 variant, aligning with the new EMA and WHO recommendations for this autumn**
- **It is the only vaccine developed and manufactured 100% in Europe and will be available in single-dose format**
- **The company is manufacturing the first batches at its production centers in Spain**
- The adapted **recombinant protein adjuvanted vaccine** will be available in **single-dose format**. Among other advantages, this presentation facilitates logistics and administration by healthcare personnel, thus helping to improve vaccination coverage rates. ”

Nya Covid-19 vacciner – skydd mot infektion och transmission möjlig?



- Likely to prevent infection and transmission
- Likely to prevent disease

- The nasal route has excellent potential for vaccination due to the organized immune systems of the nasal mucosa.
- Non-invasive, Needle-free.
- Ease of administration – does not require trained health care workers.
- Elimination of needle-associated risks (injuries and infections).
- High compliance.
- Scalable manufacturing – able to meet global demand.

COVID-19 BBV154 NASAL VACCINE TRIAL

Intranasala covid-19 vacciner kanske skyddar mot infektion och inte bara mot allvarlig sjukdom och död

npj | vaccines

www.nature.com/npjvaccines

ARTICLE OPEN

Check for updates

Phase III Pivotal comparative clinical trial of intranasal (iNCOVACC) and intramuscular COVID 19 vaccine (Covaxin®)

Chandramani Singh[1], Savita Verma[2], Prabhakar Reddy[3], Michael S. Diamond[4], David T. Curiel[5], Chintan Patel[6], Manish Kumar Jain[7], Sagar Vivek Redkar[8], Amit Suresh Bhate[9], Vivek Gundappa[10], Rambabu Konatham[11], Leelabati Toppo[12], Aniket Chandrakant Joshi[13], Jitendra Singh Kushwaha[14], Ajit Pratap Singh[15], Shilpa Bawankule[16], Raches Ella[17], Sai Prasad[17], Brunda Ganneru[17], Siddharth Reddy Chiteti[17], Sreenivas Kataram[17] and Krishna Mohan Vadrevu[17]✉

One of the most preferable characteristics for a COVID-19 vaccine candidate is the ability to reduce transmission and infection of SARS-CoV-2, in addition to disease prevention. Unlike intramuscular vaccines, intranasal COVID-19 vaccines may offer this by generating mucosal immunity. In this open-label, randomised, multicentre, phase 3 clinical trial (CTRI/2022/02/40065; ClinicalTrials.gov: NCT05522335), healthy adults were randomised to receive two doses, 28 days apart, of either intranasal adenoviral vectored SARS-CoV-2 vaccine (BBV154) or licensed intramuscular vaccine, Covaxin®. Between April 16 and June 4, 2022, we enrolled 3160 subjects of whom, 2971 received 2 doses of BBV154 and 161 received Covaxin. On Day 42, 14 days after the second dose, BBV154 induced significant serum neutralization antibody titers against the ancestral (Wuhan) virus, which met the pre-defined superiority criterion for BBV154 over Covaxin®. Further, both vaccines showed cross protection against Omicron BA.5 variant. Salivary IgA titers were found to be higher in BBV154. In addition, extensive evaluation of T cell immunity revealed comparable responses in both cohorts due to prior infection. However, BBV154 showed significantly more ancestral specific IgA-secreting plasmablasts, post vaccination, whereas Covaxin recipients showed significant Omicron specific IgA-secreting plasmablasts only at day 42. Both vaccines were well tolerated. Overall reported solicited reactions were 6.9% and 25.5% and unsolicited reactions were 1.2% and 3.1% in BBV154 and Covaxin® participants respectively.

mRNA vaccinerna som givits intramuskulärt har inte kunnat skydda mot infektion

Etablerad indisk vaccin producent Bharat

Skyddseffekt bland sjukvårdspersonal i Indien 29%

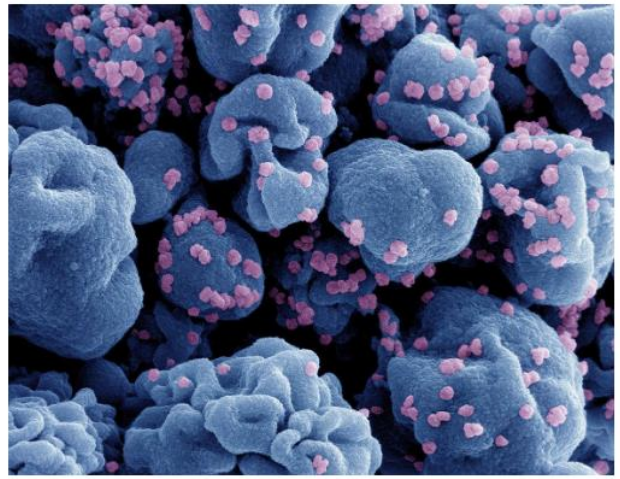
Monday, July 1, 2024

NIH-sponsored trial of nasal COVID-19 vaccine opens

Candidate vaccine could provide enhanced breadth of protection against emerging SARS-CoV-2 variants.

A Phase 1 trial testing the safety of an experimental nasal vaccine that may provide enhanced breadth of protection against emerging variants of SARS-CoV-2, the virus that causes COVID-19, is now enrolling healthy adults at three sites in the United States. The National Institutes of Health (NIH) is sponsoring the first-in-human trial of the investigational vaccine, which was designed and tested in pre-clinical studies by scientists from NIH's National Institute of Allergy and Infectious Diseases (NIAID) Laboratory of Infectious Diseases.

"The rapid development of safe and effective COVID-19 vaccines was a triumph of science, and their use greatly mitigated the toll of the pandemic," said NIAID Director Jeanne M. Marrazzo, M.D., M.P.H. "While first-generation COVID-19 vaccines continue to be effective at preventing severe illness, hospitalizations, and death, they are less successful at preventing infection and milder forms of disease. With the continual emergence of new virus variants, there is a critical need to develop next-generation COVID-19 vaccines, including nasal vaccines, that could reduce SARS-CoV-2 infections and transmission."



Colorized scanning electron micrograph of a cell (blue) infected with the Omicron strain of SARS-CoV-2 virus particles (pink), isolated from a patient sample. Image captured at the NIAID Integrated Research Facility (IRF) in Fort Detrick, Maryland. *NIAID*

pneumonia virus (MPV) as a vector to deliver a version of the SARS-CoV-2 rmation. MPV does not cause disease in humans or non-human primates but does have an affinity for epithelial cells that line the respiratory tract and may be effective in delivering vaccine to the places where natural coronavirus infections begin.

In pre-clinical non-human primate studies, MPV/S-2P was safe and well tolerated. It produced robust systemic immune responses, including SARS-CoV-2-directed antibodies, as well as local immunity in cells in the mucosal tissues lining the nose and respiratory tract. Studies in humans and animals suggest that mucosal immunity is more effective than systemic immunity in controlling replication of respiratory viruses.

En första första diskussion…

- RU –

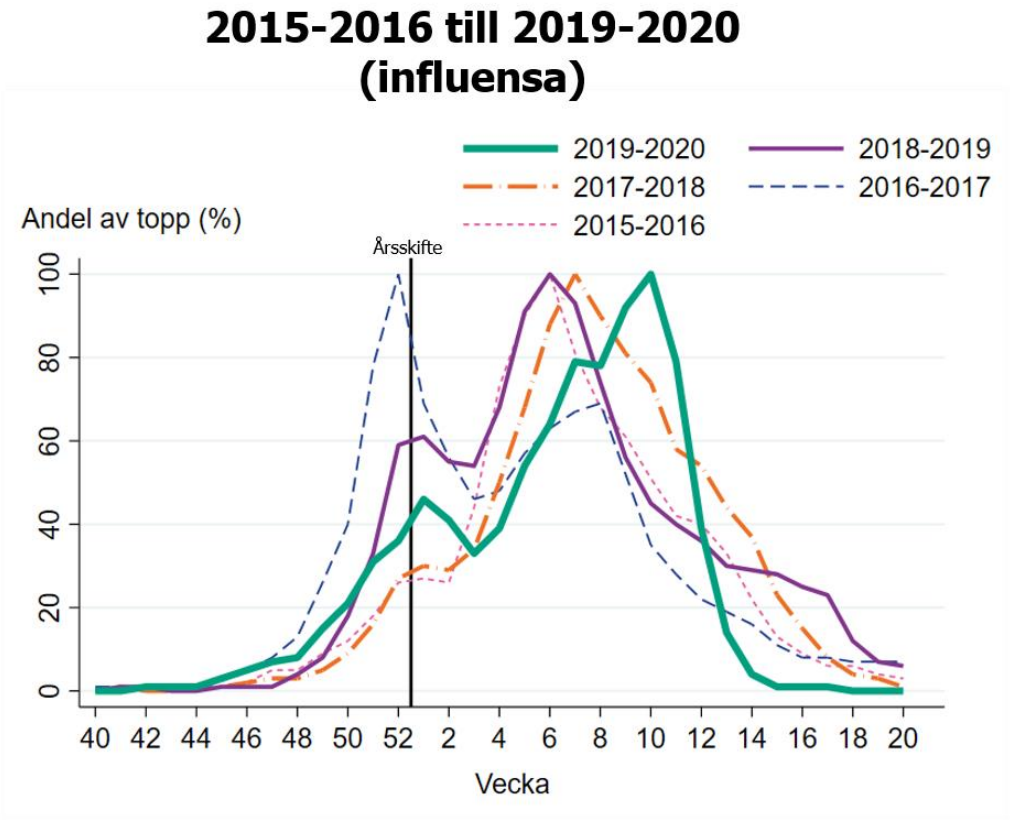
  ”Uppdraget till Folkhälsomyndigheten fokuserar på att beskriva de avväganden som

  ligger till grund för vaccinationsstart och samvaccination mot covid-19 och influensa.”

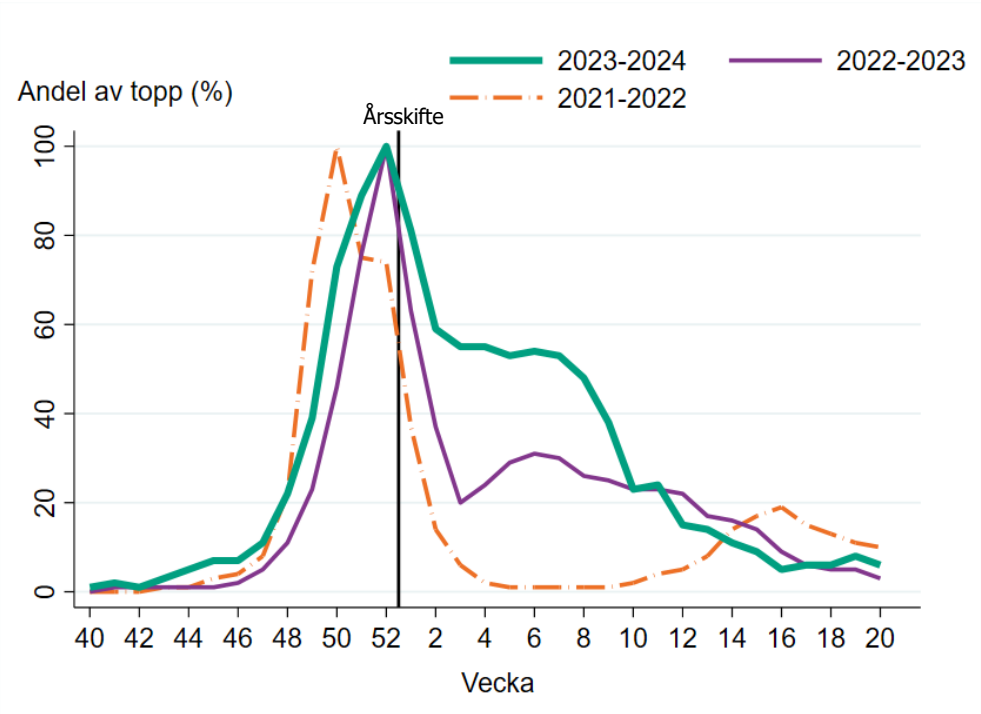
- OCH/MEN, det står nu klart att många nya vaccinprodukter förväntas bli tillgängliga över tid mot covid-19 och influensa och dessutom vacciner och monoklonala antikroppar mot RSV de kommande åren, många med en oklar skyddseffekt över tid på befolkningsnivå som påverkar när de bör ges. Vetenskapliga studier av säkerhet och effekt behövs…

Tidigare influensatoppar sedan covidpandemin

Före/fram till pandemin (fem säsonger)

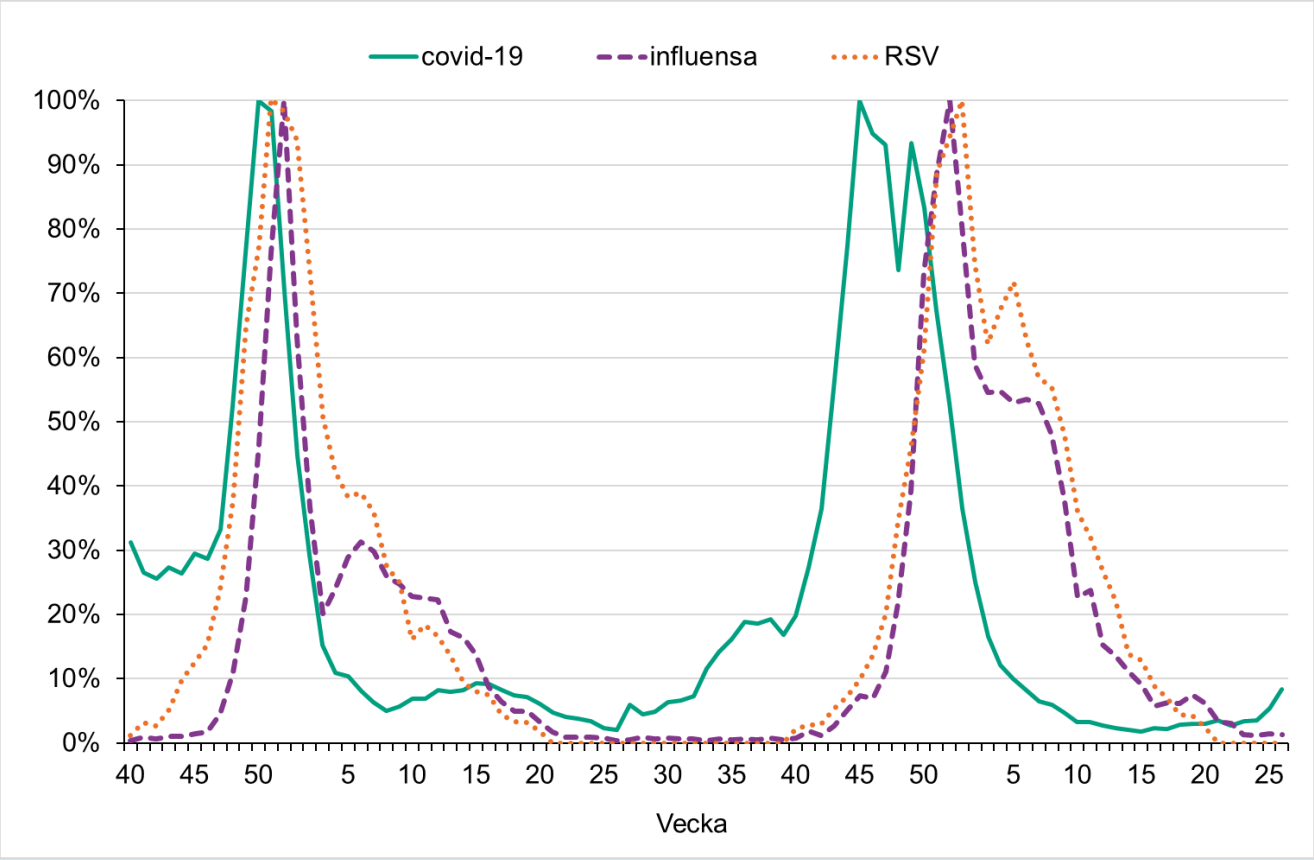


Under/efter pandemin (sedan hösten 2021):



2022-2023 och 2023-2024

- 2022-2023: gemensamma toppar i december 2022
- 2023-2024: tidigare topp för covid-19, samtidiga toppar för influensa och RS-virus



Paneldiskussion

- Johanna Rubin, bitr enhetschef och barnläkare, enheten för vaccinationsprogram
- AnnaSara Carnahan, epidemiolog, enheten för smittskyddssamordning och övervakning av säsongsvirus