Mitä kansainväliset järjestöt suosittelevat 4. koronarokoteannoksista ?

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Terveyden ja hyvinvoinnin laitos

ECDC:n suositus 11.7.2022

- At the moment, there is no clear epidemiological evidence to support administrating a second booster dose in immunocompetent individuals below 60 years of age, unless they have medical vulnerabilities. ECDC and EMA will continue to closely follow vaccine effectiveness and epidemiological data and will update advice accordingly.
- EMA is working towards the possible approval of adapted vaccines in September. However, given the current epidemiological situation and forecasts, it is important to use the currently available vaccines now and not wait until adapted vaccines are available.
- In anticipation of the next expected wave in the autumn and winter seasons, countries should plan the rollout of further additional booster doses to be administered to population groups at risk of severe disease (e.g. those aged above 60 years and the medically vulnerable) in early autumn (provided sufficient time has elapsed since the administration of the previous booster dose), possibly combining campaigns for vaccination against COVID-19 and influenza.
- If adapted vaccines show increased neutralisation against Omicron variants of concern, indicating a possible higher protection against infection and transmission, the vaccination of healthcare workers and people working at long-term care facilities should also be considered for the autumn/winter rollout to provide both direct and indirect protection.

WHO EURO:n ETAGE suositus 12.7.2022

…the combination of waning SARS-CoV-2 immunity against infection and to some extent severe disease, changing mixing patterns and the potential emergence of a new SARS-CoV-2 variant may lead to one or more upsurges in SARS-CoV-2 activity in the upcoming months, which may be co-incident with influenza (and indeed other acute respiratory viruses such as RSV) leading to significantly increased pressure on health care systems.

Protection of the most vulnerable people in society will continue to be of primary importance in the upcoming autumn season. To provide additional protection, minimize the risk of severe disease, hospitalization and death from COVID-19 and maximize the resilience of health care provision, countries should:

- administer a second booster dose to moderately and severely immunocompromised individuals aged 5 years and above and their close contacts (for immunocompromised persons a second booster dose is the fifth dose of COVID-19 vaccine that should be administered after the extended 3-dose primary vaccination series and the first booster dose);
- consider providing a second booster dose as a precautionary measure in a range of possible scenarios, including potential waning long-term immunity against severe disease, to the following individuals: residents and staff of long-term care facilities // older adults (age specific cut-off should be defined by countries based on local COVID-19 epidemiology) // health care workers // pregnant women // other patient groups at high risk of severe COVID-19 outcomes defined by countries based on local COVID-19 epidemiology

WHO SAGEn suositus 18.8.2022
Rationale for a second booster

In the context of the Omicron variant, waning of VE was documented as relatively minor against severe disease and significant and rapid against symptomatic illness. A recent systematic review and meta-regression assessing VE over time since vaccination, examined data from 3 December 2021 to 21 April 2022 during an Omicron-dominant period (BA.1). Using random-effects meta-regression, the mean change in effectiveness was estimated 1–4 months after the first booster vaccination (i.e. third dose). The booster dose increased VE against all outcomes initially. Over time the decrease in effectiveness against severe disease was found to be 5% (95% CI: 2–9) 1–4 months after booster vaccination, and 8% (95% CI: 4–14) when projected to 6 months after booster vaccination. In contrast, against symptomatic disease, there was a decrease in VE over time of 24% (95% CI: 20–29) 1–4 months after the booster vaccination, and of 29% (95% CI: 18–41) when projected to 6 months (4).

The rationale for a second booster is to restore and possibly enhance protection. In some countries, second booster doses are currently being offered (i.e. fourth doses to older adults and fifth doses to immunocompromised persons) (5-7). Because these doses have been administered relatively recently, data are limited on the additional protection they confer in terms of the duration of VE, and may differ by vaccine platform

To reduce the risk of severe disease, deaths and disruption to health services, WHO recommends that countries consider a second booster dose for the following population groups:

i) all older persons (age specific cut-off should be defined by countries based on local COVID-19 epidemiology);

ii) all persons with moderately and severely immunocompromising conditions;

iii) adults with comorbidities that put them at higher risk of severe disease;

iv) pregnant women; and

v) health workers.

WHO supports a flexible approach to homologous versus heterologous vaccination schedules, for both primary series and booster doses.

Heterologous boosters should be implemented with careful consideration of current vaccine supply, vaccine supply projections, and other access considerations, alongside the potential benefits and risks of the specific products being used.

Vaccine effectiveness against Omicron lower than for other variants and declines over time

Infection/ Symptomatic disease

- **Primary series VE lower than pre-Omicron variants,** and significant waning
- **1st Booster dose VE with temporary restoration** of protection but with waning

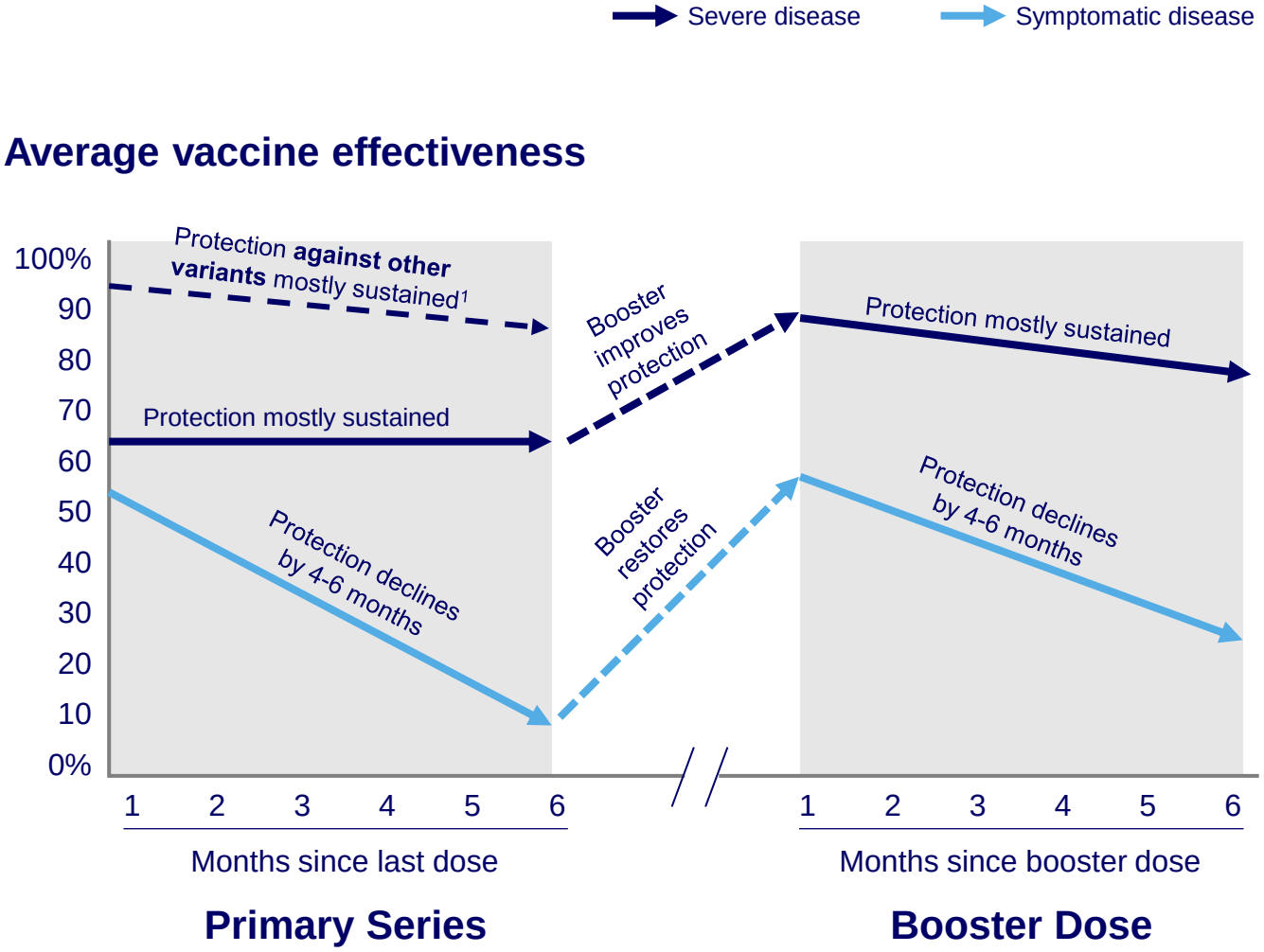
Severe disease/hospitalization

- **Primary series VE lower than pre-Omicron variants**, with **minimal** waning
- **1st Booster dose improves protection** above primary series and has only a 5 percentage point decline over first 4 months

2nd booster dose

- **Increase in protection against infection and severe disease compared to 3rd dose**
- Absolute risk reduction and/or gain in VE needs to be further defined
- **Limited data**, with limited follow up time

Average vaccine effectiveness



1. Approximation based on results for Pfizer-BioNTech vaccine from Duration of effectiveness of vaccines against SARS-CoV-2 infection and COVID-19 disease by Feiken D et al. (https://doi.org/10.1016/S0140-6736(22)00152-0), in which all studies were carried out before the omicron variant began circulating.

Source: From systematic review and meta-regression by Higdon M et al, in press.

Mitä tiedämme suojatehosta maailmalla ?

- Rokotusten suojatehoa yksinään on haasteellista arvioida, koska niin moni on saanut infektion / sairastanut koronan
- Hybridi-immuniteetti antaa laajemman suojan kuin rokote yksin

Sosiaali- ja terveydenhuollon ammattilaisten rokotukset

- WHO EURO ja WHO SAGE suosittelevat sotelaisille 4. annoksia, annosväli 3-6 kk (EURO) tai 4-6 kk (SAGE)
- ECDC:n 11.7.2022 suositus on alisteinen varianttiräätälöityjen rokotteiden saatavuudella: *If adapted vaccines show increased neutralisation against Omicron variants of concern, indicating a possible higher protection against infection and transmission, the vaccination of healthcare workers and people working at long-term care facilities should also be considered for the autumn/winter rollout to provide both direct and indirect protection.*

Varianttiräätälöidyt valmisteet

- Varianttivalmisteiden EMA myyntilupien ja saatavuuden aikatauluista:

  EMA aloittanut kesäkuun puolivälissä rullaavaan arvioinnin sekä Modernan että BioNTech/Pfizerin omikron BA.1 räätälöidyistä bivalenteista rokotteista

  - EMA:n päätöksiä odotetaan syyskuun alussa, myyntilupakomitea kokoontuu 1.9.2022
  - Rokotetoimitukset Suomeen alkavat pian myyntiluvan jälkeen
    - BA.1 variantti bivalenttirokote sekä Pfizer että Moderna
    - BA.4/5 Pfizer – myyntiluvan ja toimituksen aikataulut vielä osin auki

OBS! FDA ilmoitti kesäkuussa, ettei se tule hyväksymään BA.1 räätälöityjä, vaan BA.4/BA.5 räätälöityjä rokotteita, ennakkotieto myyntiluvasta ~15.9

UK lääkeviranomainen MHRA hyväksyi 15.8.2022 Modernan bivalentin rokotteen (alkuperäinen + BA.1)

- In each dose of the booster vaccine, ‘Spikevax bivalent Original/Omicron’, half of the vaccine (25 micrograms) targets the original virus strain from 2020 and the other half (25 micrograms) targets Omicron.
- The MHRA’s decision is based on data from a clinical trial which showed that a booster with the bivalent Moderna vaccine triggers a **strong immune response against both Omicron (BA.1) and the original 2020 strain**. In an exploratory analysis the bivalent vaccine was also found to generate **a good immune response against the Omicron sub-variants BA.4 and BA.5**.
- Safety monitoring showed that the side effects observed were the same as those seen for the original Moderna booster dose and were typically mild and self-resolving, and no serious safety concerns were identified.

https://www.gov.uk/government/news/first-bivalent-covid-19-booster-vaccine-approved-by-uk-medicines-regulator