Sahada aşı etkisi

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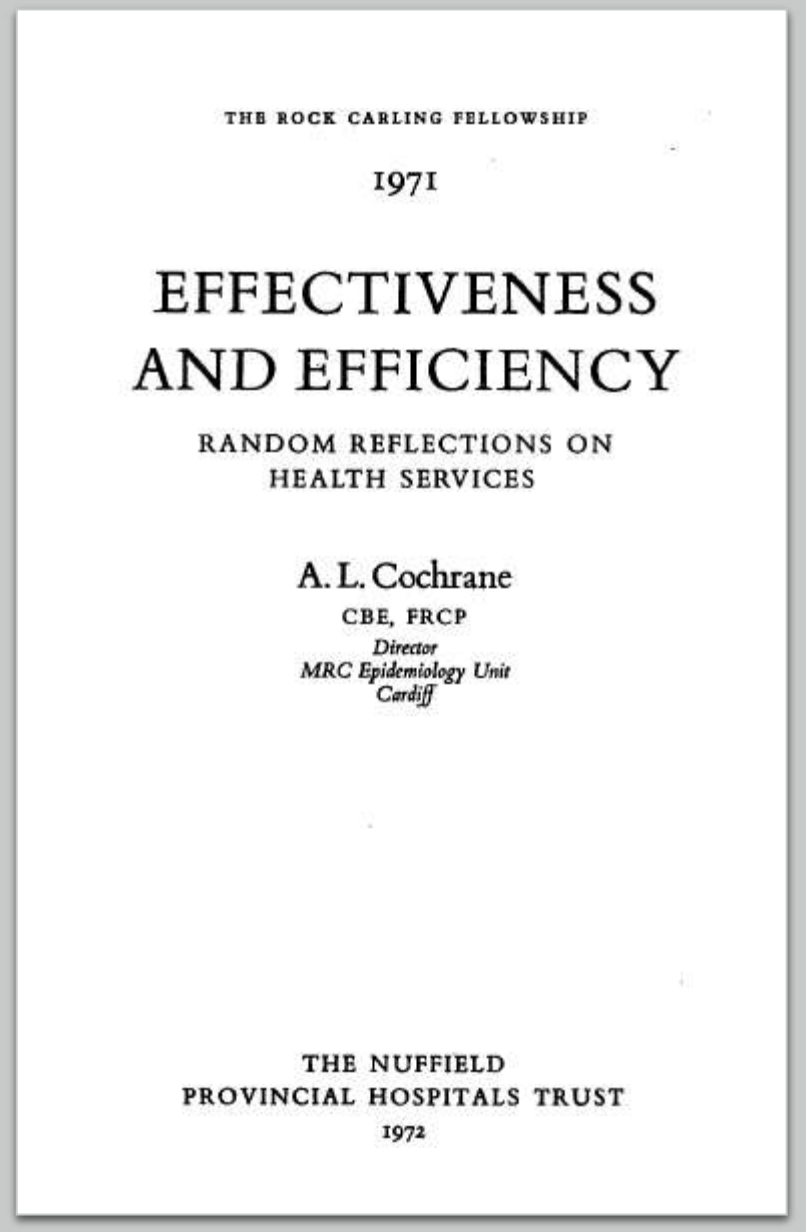


Sağlık hizmetleri müdahalelerinin test edilmesiyle ilgili üç kavram:

- **Etkinlik (Efficacy),** bir müdahalenin ideal koşullar altında zarardan çok yarar sağlama derecesidir (“İşe yarayabilir mi?”).
- **Etkililik (Effectiveness),** bir müdahalenin sağlık hizmeti uygulamasının olağan koşulları altında sağlandığında zarardan çok yarar sağlayıp sağlamadığını değerlendirir (“Pratikte işe yarıyor mu?”).
- **Verimlilik (Efficiency),** bir müdahalenin tükettiği kaynaklara göre etkisini ölçer (“Buna değer mi?”).

Etkinlik ve etkililik çalışmaları farklılıklar içerir.

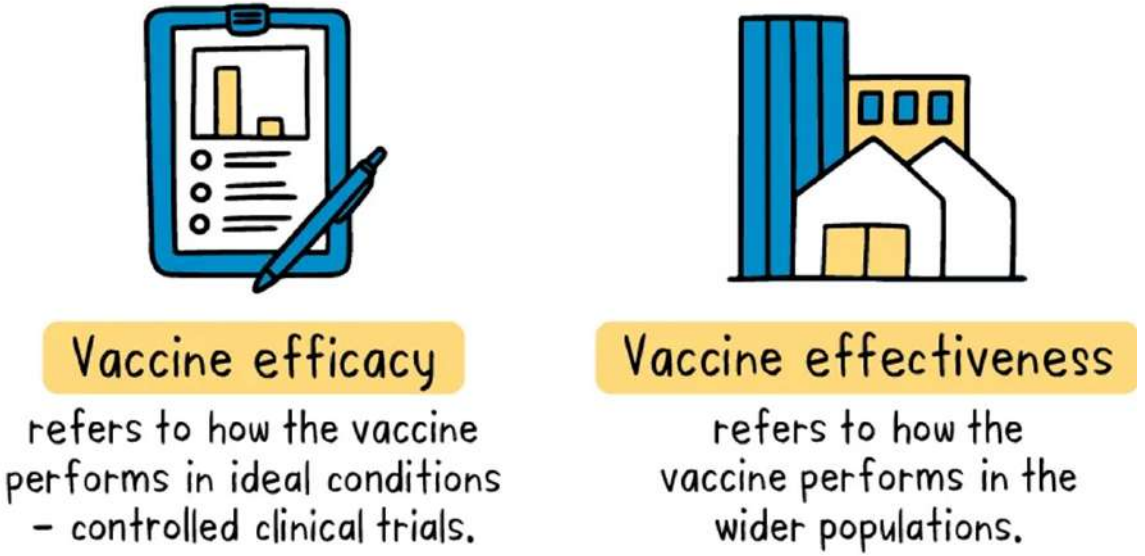
Table 1 Differences between efficacy and effectiveness studies

	Efficacy study	Effectiveness study
Question	Does the intervention work under ideal circumstance?	Does the intervention work in real-world practice?
Setting	Resource-intensive 'ideal setting'	Real-world everyday clinical setting
Study population	Highly selected, homogenous population Several exclusion criteria	Heterogeneous population Few to no exclusion criteria
Providers	Highly experienced and trained	Representative usual providers
Intervention	Strictly enforced and standardized No concurrent interventions	Applied with flexibility Concurrent interventions and cross-over permitted

Singal, A. G., Higgins, P. D., & Waljee, A. K. (2014). A primer on effectiveness and efficacy trials. *Clinical and translational gastroenterology*, *5*(1), e45. https://doi.org/10.1038/ctg.2013.13.

Aşı etkinliği – aşı etkililiği

- **Aşı etkinliği, ideal, kontrollü koşullar altında bir aşının bir hastalığın prevalansını ne kadar iyi azalttığının bir ölçüsüdür. Başka bir deyişle, bir araştırma laboratuvarında veya yüksek düzeyde kontrollü bir çalışmada test edildiğinde bir aşının bir virüsün yayılmasını ne kadar iyi önlediğinin bir ölçüsüdür.**
- **Aşı etkililiği, "gerçek dünya" koşullarında bir aşının bir hastalığın prevalansını ne kadar iyi azalttığının bir ölçüsüdür. Başka bir deyişle, toplumda fiilen kullanıldığında bir aşının hastalığın yayılmasını ne kadar önlediğinin ölçüsüdür.**



https://www.who.int/news-room/feature-stories/detail/vaccine-efficacy-effectiveness-and-protection

CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Search | Vaccines site | Advanced Search

Vaccines & Immunizations

CDC > COVID-19 Vaccination

COVID-19 Vaccination

COVID-19 Vaccine Effectiveness Research

Real-World COVID-19 Vaccine Effectiveness in Healthcare Workers

A study funded and led by the Centers for Disease Control and Prevention (CDC) will evaluate how well COVID-19 vaccines prevent laboratory-confirmed, symptomatic COVID-19 in healthcare workers in the "real world," outside of a clinical trial. The study, currently enrolling healthcare workers at 34 sites nationwide, is one of many projects analyzing the real-world protection afforded by COVID-19 vaccines.

Vaccine Effectiveness Evaluations by Design

Select a study design below to get more information about the evaluation's name, population, outcome, protocol and participating sites.

- Prospective Cohort
- Retrospective Case-Control
- Retrospective Cohort
- Screening Method
- Test-negative prospective case control

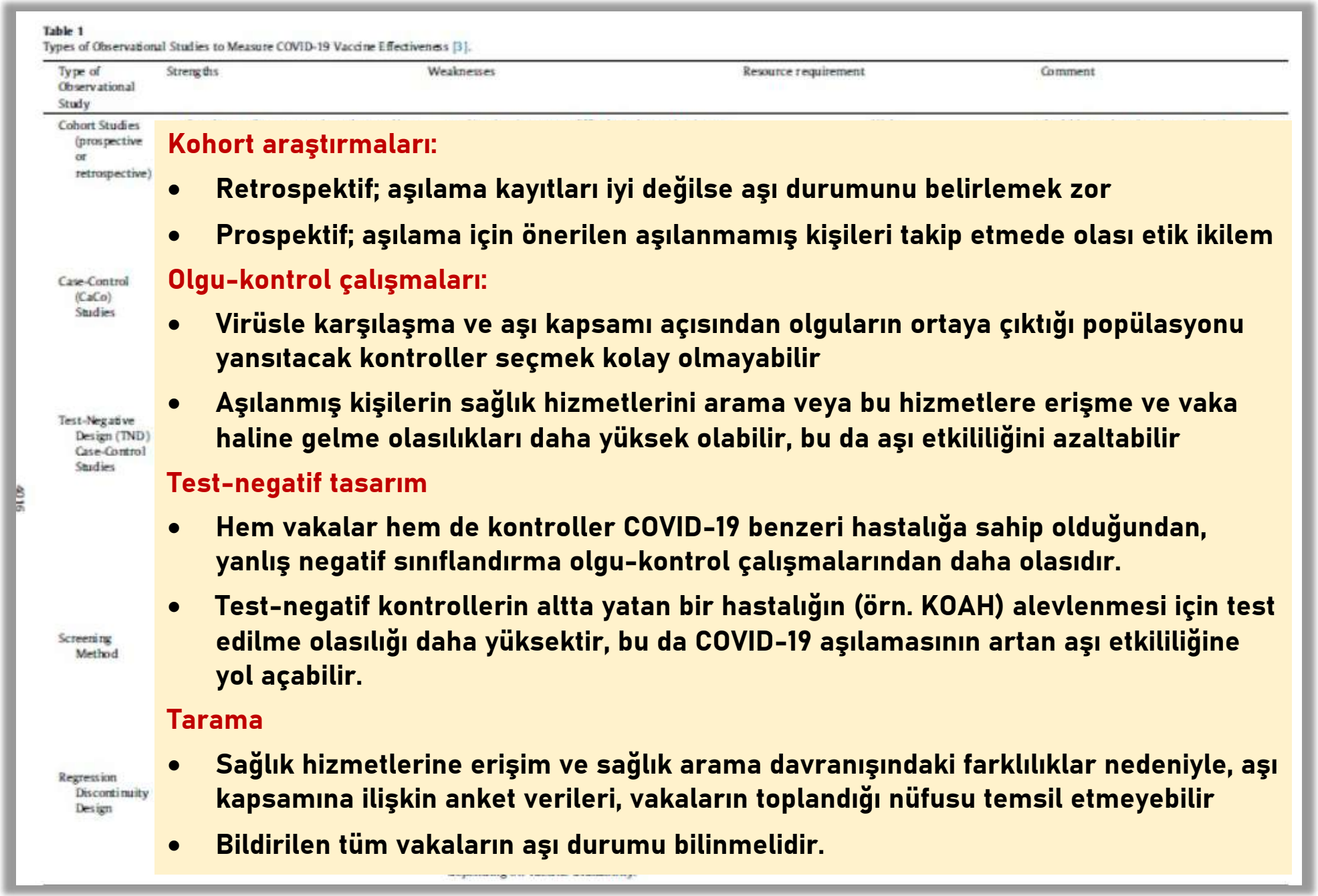


Table 1
Types of Observational Studies to Measure COVID-19 Vaccine Effectiveness [3].

Type of Observational Study	Strengths	Weaknesses	Resource requirement	Comment
Cohort Studies (prospective or retrospective)				
Case-Control (CaCo) Studies				
Test-Negative Design (TND) Case-Control Studies				
Screening Method				
Regression Discontinuity Design				

Kohort araştırmaları:

- **Retrospektif; aşılama kayıtları iyi değilse aşı durumunu belirlemek zor**
- **Prospektif; aşılama için önerilen aşılanmamış kişileri takip etmede olası etik ikilem**

Olgu-kontrol çalışmaları:

- **Virüsle karşılaşma ve aşı kapsamı açısından olguların ortaya çıktığı popülasyonu yansıtacak kontroller seçmek kolay olmayabilir**
- **Aşılanmış kişilerin sağlık hizmetlerini arama veya bu hizmetlere erişme ve vaka haline gelme olasılıkları daha yüksek olabilir, bu da aşı etkililiğini azaltabilir**

Test-negatif tasarım

- **Hem vakalar hem de kontroller COVID-19 benzeri hastalığa sahip olduğundan, yanlış negatif sınıflandırma olgu-kontrol çalışmalarından daha olasıdır.**
- **Test-negatif kontrollerin altta yatan bir hastalığın (örn. KOAH) alevlenmesi için test edilme olasılığı daha yüksektir, bu da COVID-19 aşılamasının artan aşı etkililiğine yol açabilir.**

Tarama

- **Sağlık hizmetlerine erişim ve sağlık arama davranışındaki farklılıklar nedeniyle, aşı kapsamına ilişkin anket verileri, vakaların toplandığı nüfusu temsil etmeyebilir**
- **Bildirilen tüm vakaların aşı durumu bilinmelidir.**

Araştırma tasarımları aşı etkililiği sonuçlarını etkiler!

Patel MK, Bergeri I, Bresee JS, *et* al. Evaluation of post-introduction COVID-19 vaccine effectiveness: Summary of interim guidance of the World Health Organization. Vaccine. 2021 Jul 5;39(30):4013-4024.

Aşı etkililiği tahminleri her zaman geçerli olmayabilir!

Potential Reasons for Vaccine Effectiveness (VE) estimates that are different from vaccine efficacy results [3].

VE estimate valid	VE estimate not valid
• Population being studied has different VE for epidemiologic or biological reasons • Vaccine mishandling • Systematic error in vaccine administration • Problems with vaccine batch • Waning immunity resulting in lower VE • Different outcome or schedule is being evaluated from clinical trial • Vaccine less effective due to mutations in SARS-CoV-2 virus • Contribution of vaccine associated enhanced disease (VAED) (especially severe disease outcome) • Prevalence of prior infection in population different from that of efficacy study	• Error in implementation (e.g. enrollment of persons not meeting case definition, poor specimen collection/handling) • Biases • Unmeasured or incompletely controlled confounders • Chance finding; more likely with small sample size

Patel MK, Bergeri I, Bresee JS, *et* al. Evaluation of post-introduction COVID-19 vaccine effectiveness: Summary of interim guidance of the World Health Organization. Vaccine. 2021 Jul 5;39(30):4013-4024.

STROBE

Strengthening the reporting of observational studies in epidemiology

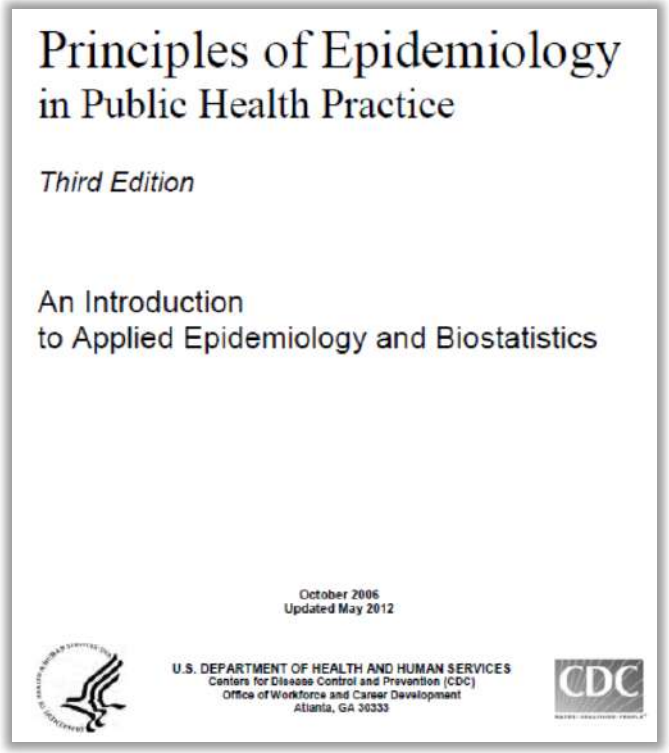
Table 4
Strengthening the reporting of observational studies in epidemiology (STROBE) checklist [30]and recommended additional elements for reporting COVID-19 vaccine effectiveness studies* [3].

Section/Topic	STROBE Item no.	STROBE	COVID-19 VE studies
TITLE AND ABSTRACT			
Title/abstract	1	• Indicate the study's design with a commonly used term in the title or the abstract • Provide in the abstract an informative and balanced summary of what was done and what was found	• Specify study design (e.g., case-control, TND or cohort) • Report vaccine type(s), outcome, target vaccine groups evaluated, study location, VE and 95% confidence intervals
INTRODUCTION			
Background/	2	Explain the scientific background and rationale for the	• Mention efficacy results from pivotal clinical trial that led to
DISCUSSION			
Key results	18	Summarize key results with reference to study objectives	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision.Discuss both direction and magnitude of any potential bias	• Specifically discuss potential biases affecting COVID-19 VE studies, including health-seeking bias, misclassification bias, diagnostic bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	• Explain potential differences in study VE from efficacy in relevant clinical trials (e.g., different target group, different outcome, immunization system factors)
Generalizability	21	Discuss the generalizability (external validity) of the study results	• Was baseline seroprevalence different from other settings? Predominant viral variant found in other settings?

Aşı etkinliği/etkililiği nasıl hesaplanır?

Aşı etkinliği/etkililiği = Risk farkı (Aşılanmamış gruptaki risk – aşılanmış gruptaki risk)

Aşılanmamış gruptaki risk


Principles of Epidemiology
in Public Health Practice

Third Edition

An Introduction
to Applied Epidemiology and Biostatistics

October 2006
Updated May 2012

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention (CDC)
Office of Workforce and Career Development
Atlanta, GA 30333

CDC

Vaccine efficacy or vaccine effectiveness

Vaccine efficacy and vaccine effectiveness measure the proportionate reduction in cases among vaccinated persons. Vaccine efficacy is used when a study is carried out under ideal conditions, for example, during a clinical trial. Vaccine effectiveness is used when a study is carried out under typical field (that is, less than perfectly controlled) conditions.

Vaccine efficacy/effectiveness (VE) is measured by calculating the risk of disease among vaccinated and unvaccinated persons and determining the percentage reduction in risk of disease among vaccinated persons relative to unvaccinated persons. The greater the percentage reduction of illness in the vaccinated group, the greater the vaccine efficacy/effectiveness. The basic formula is written as:

$$\frac{\textit{Risk among unvaccinated group} - \textit{risk among vaccinated group}}{\textit{Risk among unvaccinated group}}$$

OR: *1 – risk ratio*

Aşı etkinliği/etkililiği nasıl hesaplanır?

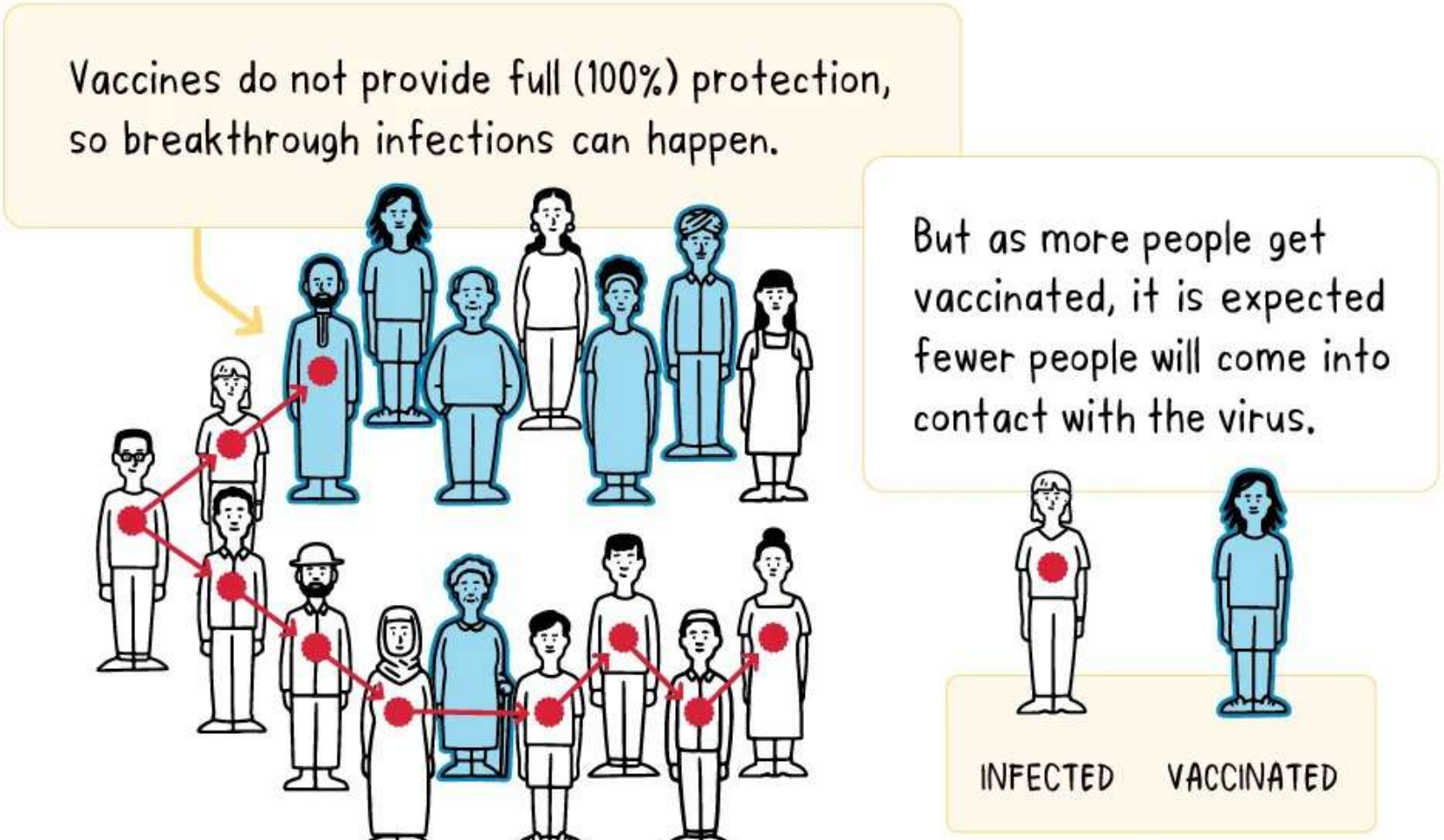
Aşı etkinliği/etkililiği = Risk farkı (Aşılanmamış gruptaki risk – aşılanmış gruptaki risk)

Aşılanmamış gruptaki risk

AŞI	HASTALIK		TOPLAM
	Var	Yok	
Var	80	720	800
Yok	80	120	200
TOPLAM	160	840	1.000

Aşılı grupta Risk	= 80/800	= %10
Aşısız grupta Risk	= 80/200	= %40
AŞI ETKİLİLİĞİ	= (40-10)/40	= %75
RİSK ORANI	= 0,1/0,4	= %25
AŞI ETKİLİLİĞİ	= 1-0,25	= %75

Sahada aşı etkililiği



Aşı etkililiği çalışmalarına gereksinim var.

- Faz 3 randomize kontrollü çalışmalar, birincil sonlanım noktaları olarak semptomatik hastalığa karşı %50-95 arasında değişen COVID-19 aşı etkinliğine ilişkin umut verici sonuçlar sağladı ve aşılar için acil kullanım izni ile sonuçlandı.
- Bununla birlikte;
  - **klinik deneyler sırasındaki kısa takip süresi**,
  - **katı uygunluk ölçütleri**,
  - ortaya çıkan **yeni endişe verici varyantlar** ve
  - **pandeminin değişen epidemiyolojisi**

  göz önüne alındığında, aşı performansıyla ilgili birçok soru hala yanıtsızdır.
- Aşı etkililiği çalışmaları, aşının gerçek dünya koşullarında kullanıldığında enfeksiyon ve hastalıkları azaltma üzerindeki etkisini anlamamıza yardımcı olmaktadır.

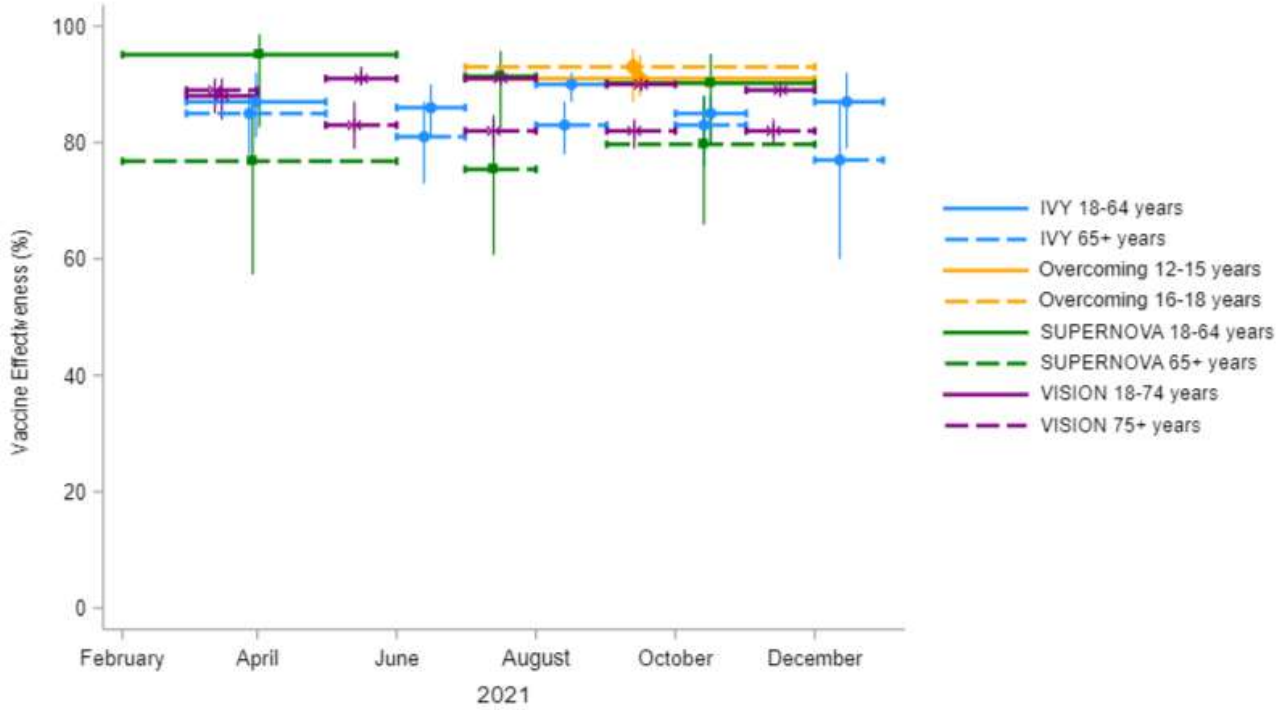
Patel MK, Bergeri I, Bresee JS, *et* al. Evaluation of post-introduction COVID-19 vaccine effectiveness: Summary of interim guidance of the World Health Organization. Vaccine. 2021 Jul 5;39(30):4013-4024.

Aşı politikasını ve aşılama programını belirlerken ‘aşı etkinliği’ çalışmalarının yanıtlarını eksik bıraktığı sorular:

- Çok yaşlı nüfusta etkinlik?
- Bağışıklığı baskılanmış kişilerde etkinlik?
- Ağır hastalıktan koruma düzeyi?
- Ölümden koruma düzeyi?
- Yeni endişe verici varyantlara karşı etkinlik?
- Aşının doz sayısına göre etkinlik?
- Aşının doz aralıklarına göre etkinlik?

Primary Series Vaccine Effectiveness Against Hospitalization Among People Ages 12 Years and Older by Age Group (All Studies)

Vaccine effectiveness was lower among adults ages 65 years and older compared to people younger than 65 years of age.



https://covid.cdc.gov/covid-data-tracker/#vaccine-effectiveness

UK Health Security Agency

«Aşının farklı durumlara karşı (ağır hastalık, ileriye doğru bulaşma, nüfusun farklı alt grupları, farklı varyantlar vb.) etkinliğini ve ayrıca koruma süresini anlamak için uygulama sonrası gerçek dünya verileriyle aşı etkililiği çalışmalarına ihtiyaç vardır.»

COVID-19 vaccine surveillance report

Week 6

10 February 2022

Figure 1. Vaccine effectiveness against symptomatic disease by period after the second and booster doses for Delta (black squares) and Omicron (grey circles) for a) recipients of 2 doses of Astrazeneca (ChAdOx1-S) vaccine as the primary course and Pfizer (BNT162b2) or Moderna (mRNA-1273) as a booster; b) recipients of 2 doses of Pfizer vaccine as the primary course and Pfizer or Moderna as a booster, and c) 2 doses of Moderna as a primary course and Pfizer or Moderna as a booster

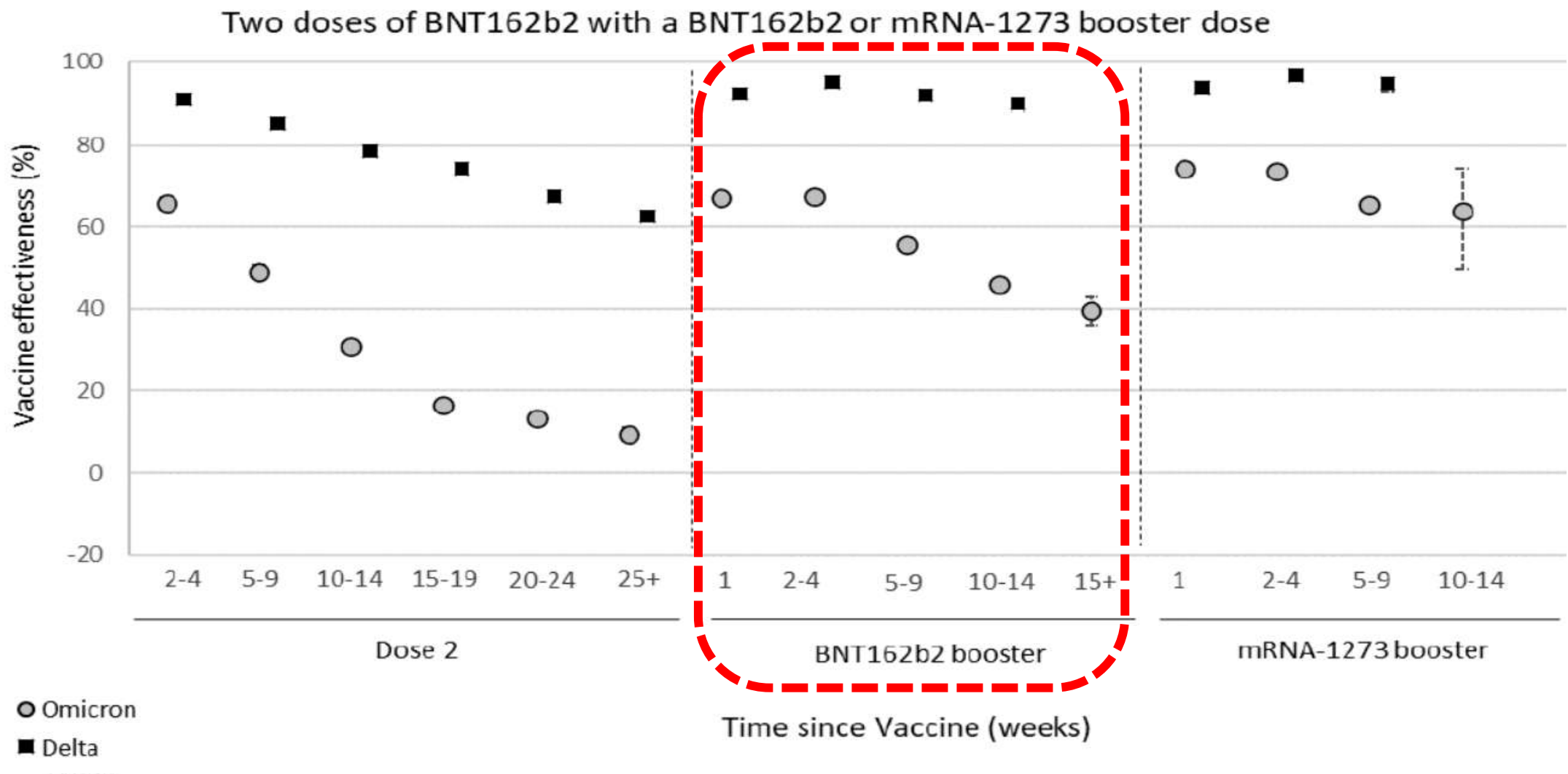
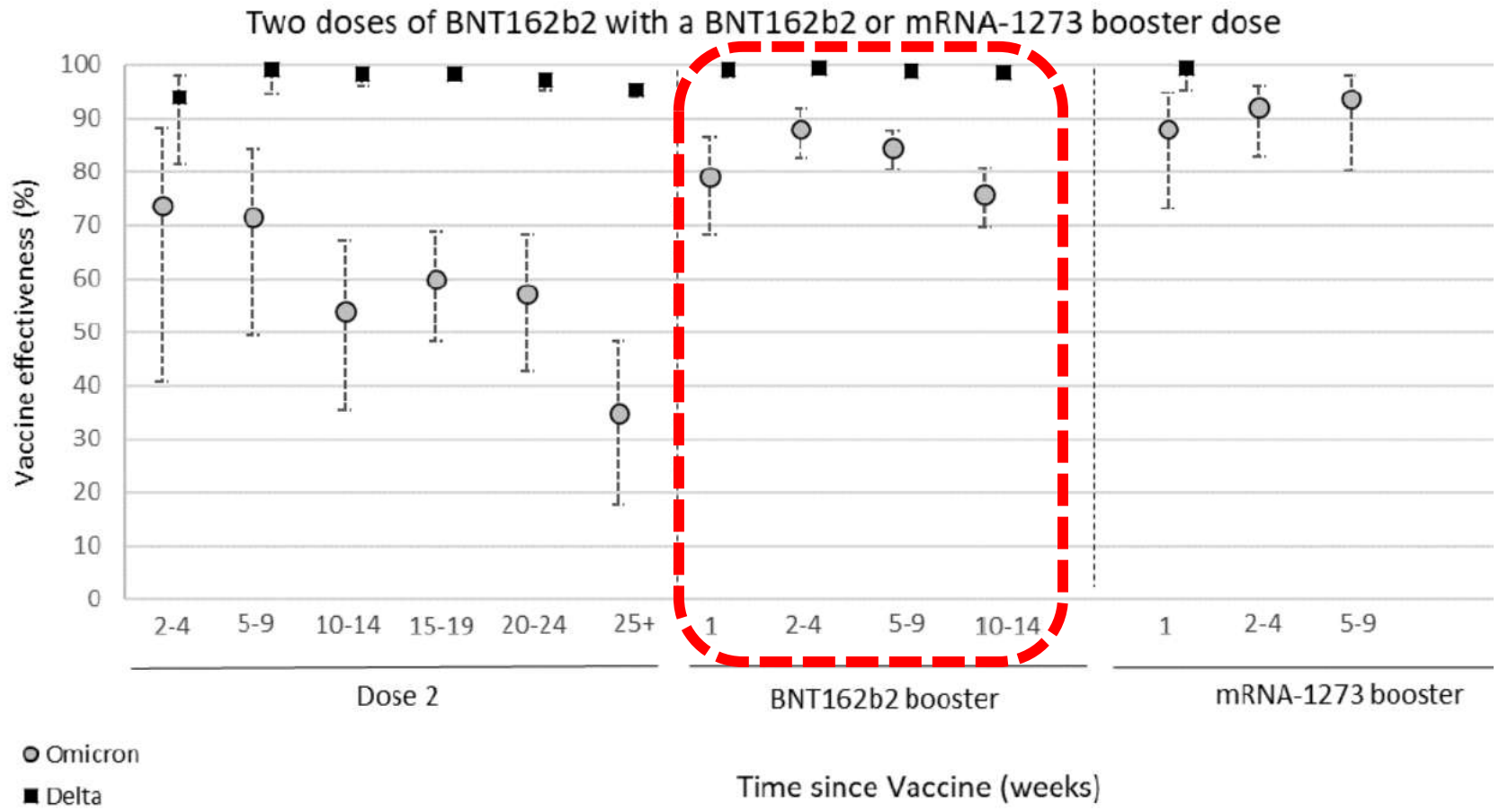


Figure 2. Vaccine effectiveness against hospitalisation by period after the second and booster doses for Delta (black squares) and Omicron (grey circles) for a) recipients of 2 doses of Astrazeneca (ChAdOx1-S) vaccine as the primary course and Pfizer (BNT162b2) or Moderna (mRNA-1273) as a booster; b) recipients of 2 doses of Pfizer vaccine as the primary course and Pfizer or Moderna as a booster



Effectiveness against mortality

High levels of protection (over 90%) are also seen against mortality with all 3 vaccines and against both the Alpha and Delta variants with relatively limited waning (6, 10, 11). Vaccine effectiveness against mortality with the Omicron variant has been estimated for those aged 50 years and older by combining the risk of becoming a symptomatic case with the risk of death among symptomatic cases in vaccinated (all vaccines combined) compared to unvaccinated individuals (Table 1). At 25+ weeks following the second dose, vaccine effectiveness was around 60% while at 2 or more weeks following a booster vaccine effectiveness was 95% against mortality.

Table 1. Hazard ratios and vaccine effectiveness against mortality (all vaccine brands combined). OR = odds ratio, HR = hazards ratio, VE = vaccine effectiveness

Dose	Interval after dose	OR versus symptomatic disease	HR versus mortality	VE versus mortality
2	25+ weeks	0.93 (0.9 to 0.96)	0.45 (0.19 to 1.03)	59% (4 to 82)
3	2+ weeks	0.41 (0.39 to 0.42)	0.12 (0.06 to 0.24)	95% (90 to 98)

Table 2. Summary of evidence on vaccine effectiveness against different outcomes (a) Omicron (b) Delta (all vaccines combined)

a)

	Dose 2			Dose 3		
	0 to 3 months	4 to 6 months	Over 6 months	0 to 3 months	4 to 6 months	Over 6 months
Infection	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
Symptomatic disease	25 to 70%	5 to 30%	0 to 10%	50 to 75%	40 to 50%	Insufficient data
Hospitalisation	65 to 85%	55 to 65%	30 to 35%	80 to 95%	75 to 85%	Insufficient data
Mortality	Insufficient data	Insufficient data	40 to 70%	85 to 99%	Insufficient data	Insufficient data

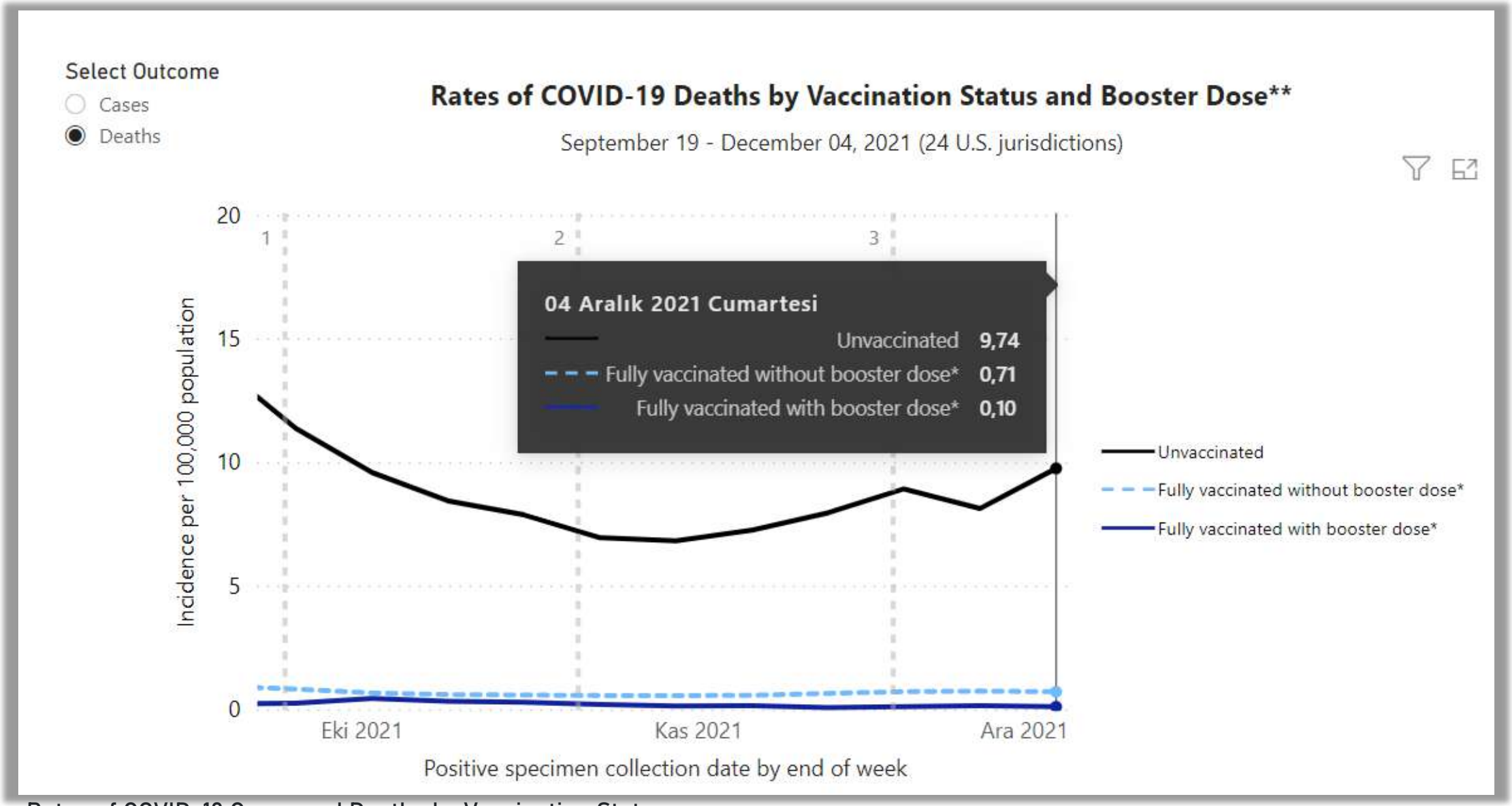
b)

	Dose 2			Dose 3		
	0 to 3 months	4 to 6 months	Over 6 months	0 to 3 months	4 to 6 months	Over 6 months
Infection	65 to 80%	50 to 65%	Insufficient data	Insufficient data	Insufficient data	Insufficient data
Symptomatic disease	65 to 90%	45 to 65%	40 to 60%	90 to 99%	90 to 95%	Insufficient data
Hospitalisation	95 to 99%	80 to 90%	70 to 85%	95 to 99%	Insufficient data	Insufficient data
Mortality	95 to 99%	90 to 95%	80 to 99%	95 to 99%	Insufficient data	Insufficient data

Table 3. Vaccine effectiveness against symptomatic disease (all vaccine brands combined) for BA.1 and BA.2. OR = odds ratio, VE = vaccine effectiveness.

Dose	Interval after dose	BA.1 (VE (95% CI))	BA.2 (VE (95% CI))
2	25 weeks and over	10% (9 to 11)	18% (5 to 29)
3	2 to 4 weeks	69% (68 to 69)	74% (69 to 77)
3	5 to 9 weeks	61% (61 to 62)	67% (62 to 71)
3	10+ weeks	49% (48 to 50)	46% (37 to 53)

High Confidence	Evidence from multiple studies which is consistent and comprehensive
Medium Confidence	Evidence is emerging from a limited number of studies or with a moderately level of uncertainty
Low Confidence	Little evidence is available at present and results are inconclusive



Rates of COVID-19 Cases and Deaths by Vaccination Status,
https://covid.cdc.gov/covid-data-tracker/#rates-by-vaccine-status

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 71
February 15, 2022

Effectiveness of Maternal Vaccination with mRNA COVID-19 Vaccine During Pregnancy Against COVID-19–Associated Hospitalization in Infants Aged <6 Months — 17 States, July 2021–January 2022

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TABLE 3. Effectiveness* of maternal 2-dose primary mRNA COVID-19 vaccination against COVID-19-associated hospitalization in infants aged <6 months, by timing of maternal vaccination during pregnancy† — 20 pediatric hospitals, 17 states,§ July 2021–January 2022

Timing of maternal vaccination during pregnancy†	No. vaccinated¶/Total (%)		Vaccine effectiveness,* % (95% CI)
	Case-infants	Control-infants	
Any time	28/176 (15.9)	65/203 (32.0)	61 (31 to 78)
Early (first 20 weeks)	17/165 (10.3)	26/164 (15.9)	32 (–43 to 68)
Late (21 weeks' gestation through 14 days before delivery)	9/157 (5.7)	38/176 (21.6)	80 (55 to 91)

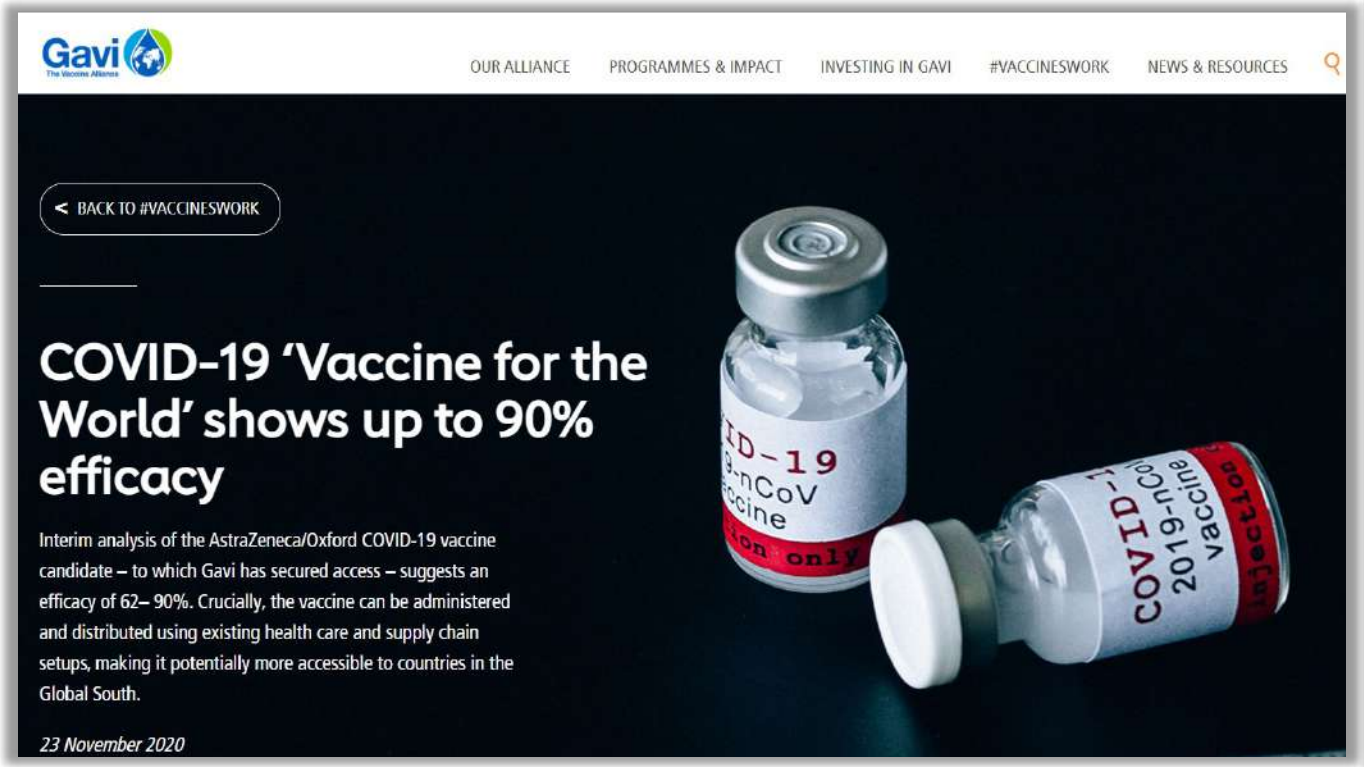
* Vaccine effectiveness estimates were based on odds of antecedent maternal vaccination during pregnancy in case-infants versus control-infants, adjusted for U.S. Census region, admission date (biweekly intervals), continuous age, sex, and race/ethnicity (non-Hispanic White, non-Hispanic Black, non-Hispanic other, Hispanic of any race, or unknown).

Incidence rates, hazard ratios, and VE of 2 doses of mRNA-1273 vaccine in preventing COVID-19 infection, hospitalization, and hospital death

Outcomes	Vaccinated (*N*=352878)		Unvaccinated (*N*=352878)		VE (95% CI)	
	Number of cases	Incidence per 1000 person-years (95% CI)	Number of cases	Incidence per 1000 person-years (95% CI)	Unadjusted	Adjusted[a]
COVID-19 infection	289	2.77 (2.47–3.11)	1144	20.20 (19.06–21.41)	85.5% (83.5–87.3%)	87.4% (85.6–89.1%)
COVID–19 hospitalization	13	0.12 (0.07–0.21)	182	3.21 (2.77–3.71)	95.8% (92.6–97.6%)	95.8% (92.5–97.6%)
COVID–19 hospital death	1	0.01 (0.00–0.07)	25	0.44 (0.30–0.65)	97.7% (83.1–99.7%)	97.9% (84.5–99.7%)

[a] Adjusted for covariates age, sex, race/ethnicity, frailty index (in quartiles), history of COVID-19 infection, history of SARS-CoV-2 molecular test, number of outpatient and virtual visits, preventive care, Medicaid, neighborhood median household income, KPSC physician/employee status, medical center area.

Bruxvoort K.J., Sy L.S., Qian L. *et* al. Real-world effectiveness of the mRNA-1273 vaccine against COVID-19: Interim results from a prospective observational cohort study. The Lancet Regional Health – Americas. 2022;6: 100134



Dikkatiniz ve sabrınız için teşekkürler ☺