# CDC Briefing

## Regarding Booster Doses of COVID-19 Vaccines

**September 13, 2021**

## Effectiveness of mRNA COVID-19 Vaccines Against the Delta Variant Among 6M Medicare Beneficiaries 65 Years and Older

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# Executive Summary
# Key Findings

**Basic questions which require data-driven answers**

- Is vaccine effectiveness (VE) **waning** over time?
- Is VE **reduced** for the **Delta variant**?
- Does the need vary by **sub-population**?

**Project Salus provides answers to these questions**

- **VE of both mRNA vaccines appears to wane over time in this large 5.6M US-based 65 & over vaccinated cohort**
- **VE against Delta breakthrough hospitalization (57%) exceeds VE against Delta infection (33%)**
- **VE of mRNA vaccines against infection and hospitalization** in the 65 >= during Delta phase of the pandemic is **lower than previously reported in smaller studies**
- **Older age groups** (75-84 & 85 and older) **experienced further reduction in vaccine protection against hospitalization** in Salus 65 years and older cohort
- **Hospitalization rate (20% vs 32%) and death rate (2% vs 12%) of breakthrough infections lower than rates observed in Covid-19 cases in pre-vaccination pandemic phase in 2020**
- **Salus breakthrough hospitalization risk model can be applied to prioritize the over 65 population for booster vaccine**

*Graphic adapted from CDC Presentation ACIP Meeting August 30, 2021*
*Oliver, S. Framework for Booster Doses of COVID-19 Vaccines*

# Salus Platform for COVID-19 Analyses

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## VE Study Attributes

**Cohort**

20M Medicare beneficiaries nationwide with 16M individuals 65 years and older

**Exposure**

5.6M fully vaccinated with 2.7M Pfizer and 2.9M Moderna

**Period of study**

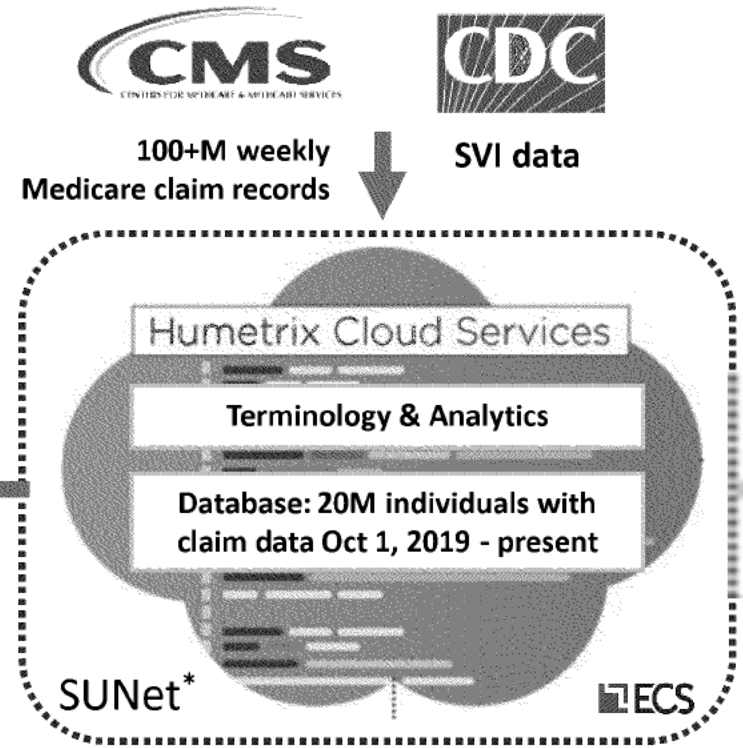
January- July 2021

**Breakthrough Key Metrics**

133K Breakthrough cases

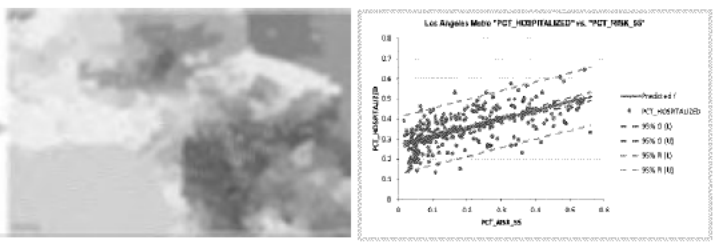
27K Breakthrough hospitalizations

8.3K requiring ICU admissions




## Other Platform Applications

Nationwide Mapping of COVID-19 Outcomes
Hospitalizations, ICU, Ventilator Rx, Deaths



Disease Risk Models with Population Risk Profiling: Severe COVID-19 risk with Validation with Hospitalization Rates

Vaccination Mapping overlaid on severe COVID-19 risk

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FDA-000005



** Medicare data and Humetrix software are hosted by SUNet, a secure unclassified US government network provided by ECS Federal*

# Salus Breakthrough Analysis Methodology and Limitations

- **Breakthrough case definition**: new COVID-19 diagnosis (by COVID-19 ICD-10 code) occurring no earlier than 2-weeks post the second vaccine dose (see appendix for more details on case definition)

- **Breakthrough analysis methodology**: to estimate weekly breakthrough cases and hospitalizations we multiplied our Medicare claim-based weekly breakthrough case counts and hospitalization counts by the corresponding weekly ratio of the claims-based vaccination rate to the CDC vaccination rate to compensate for missing COVID-19 vaccination data from Medicare claim data (Medicare claims only provide ~45% of the published CDC vaccination rate in the 65 and over age group)

- **Breakthrough data limitations**:
  - Possible overestimation of breakthrough rates due to breakthroughs clinically defined with a COVID-19 diagnosis but not confirmed by PCR or antigen test (unavailable in claim data)
  - Possible overestimation of breakthrough rates due to assuming identical breakthrough rates between individuals with claim-based vaccination data and those lacking vaccination data in their claims
  - Overestimation of breakthrough rates would lead to underestimating vaccine VE against breakthrough infections and breakthrough hospitalizations

# COVID-19 Case Definitions

- **COVID-19 case definition**: COVID-19 ICD-10-CM code U071 found in any claim type. Date of diagnosis based on first claim with U071. Note: 29% have either a COVID-19 PCR or antigen test in a claim.
- **COVID-19 breakthrough infection definition**: COVID-19 diagnosis more than 2 weeks after second dose of mRNA vaccine or single dose of J&J vaccine with no COVID-19 ICD-10 code U071 between first and second dose of mRNA vaccine. Note: 36% of breakthrough cases have either a COVID-19 PCR or antigen test in a claim.
- **COVID-19 hospitalization definitions**: (1) Inpatient claim with primary admitting diagnosis ICD-10-C code U071 with data of admission within 14 days after COVID-19 diagnosis or date of discharge within 10 days of post hospitalization COVID-19 diagnosis OR (2) Carrier claim with ICD10 code U071 and place of service code = 21 and date of service either 14 days after COVID-19 diagnosis or 10 days before COVID-19 diagnosis.
- **COVID-19 associated death definitions**: (1) Inpatient claim patient discharge status code = 41 (expired in facility) OR (2) MBSF file Date of Death are within 60 days of COVID-19 diagnosis. 85% of COVID-19 deaths using this definition occurred within 30 days and 72% within 20 days of COVID-19 diagnosis

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# Key Breakthrough vs. Pre-Vaccination COVID-19 Metrics

**Among 5.6M fully vaccine immunized Salus cohort members aged 65 and older** (2.7M Pfizer and 2.9M Moderna), as of August 6th, 2021:

- **2.3% cumulative breakthrough rate**
- **20% hospitalization rate** in breakthrough infections, reduced by one third of 32% hospitalization rate March – December 2020
- **34% breakthrough hospitalizations include ICU care,** equivalent to 32% ICU rate March – December 2020
- **2.2% death rate** in breakthrough infections, reduced six-fold from 12% death rate March – December 2020

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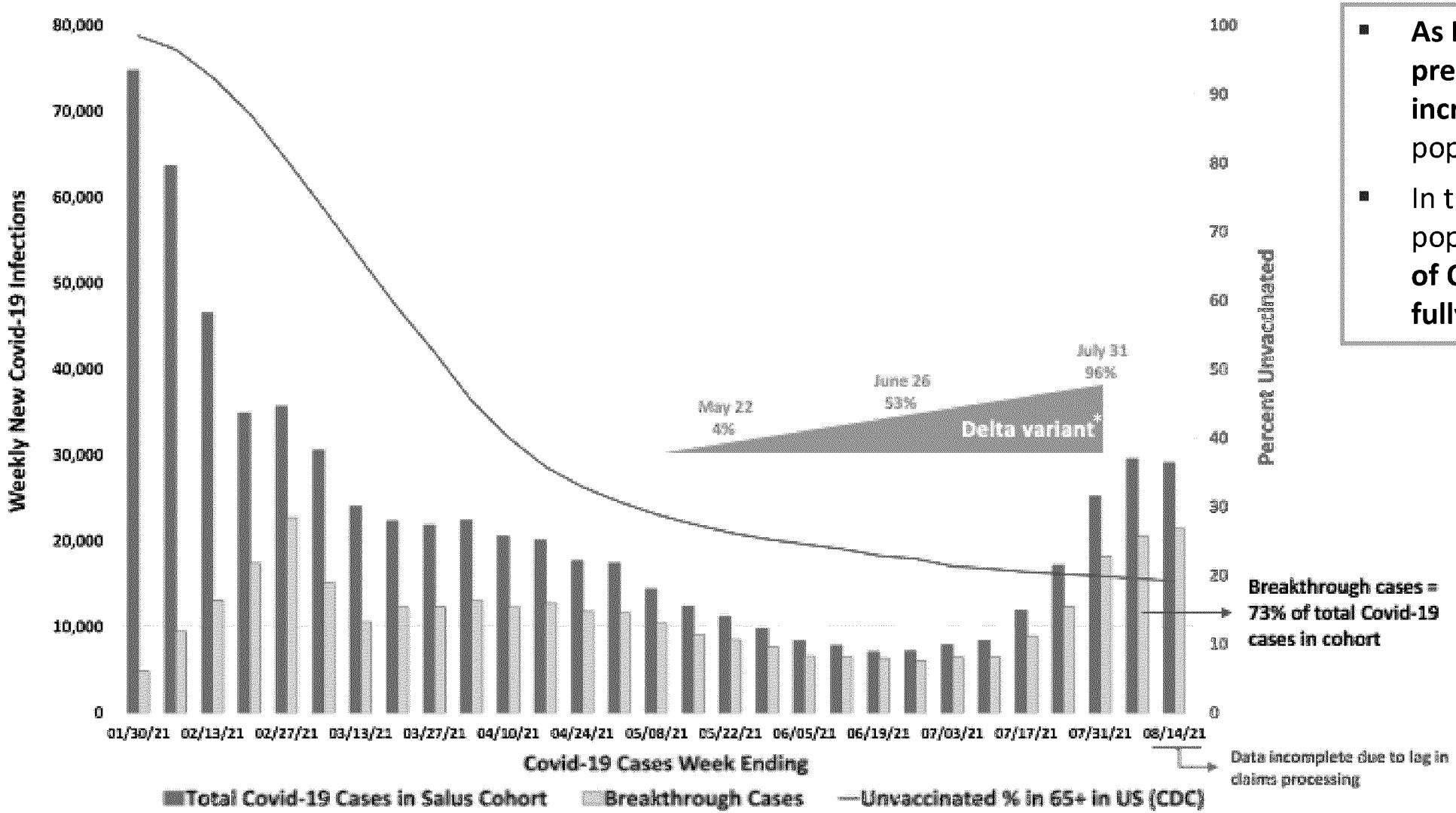
# Total & Breakthrough Cases in the 65 Years and Older Salus Cohort




- **As Delta variant became predominant, COVID-19 cases increased five-fold** in the >=65 population
- In this 80% vaccinated >=65 population, an estimated **73% of COVID-19 cases occurred in fully vaccinated individuals**

*CDC data: % of SARS-CoV-2 genomes sequenced*

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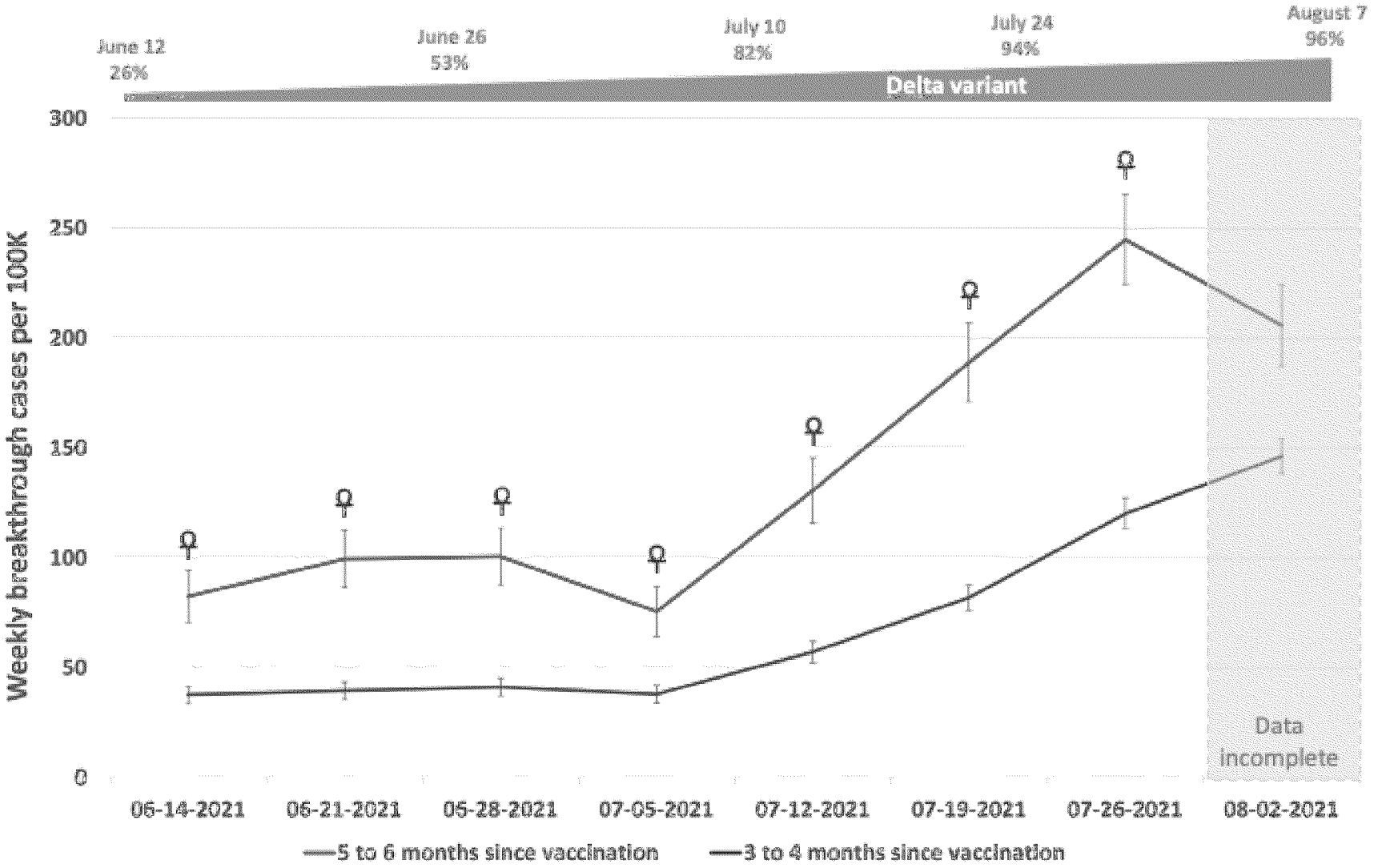
# Is mRNA Vaccine Effectiveness Against Delta Breakthrough Infection Waning Over Time in 65 Years and Older Salus Cohort?




- **Breakthrough infection rates 5-6 months post vaccination are twice as high** as 3-4 months post vaccination

95% C.I.

♀ Breakthrough infection rates 5-6 months since vaccination > 3-4 months since vaccination
P< 0.001

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# Age Distribution of Vaccinated Groups in the 65 Years and Older Cohort

| Vaccinee Group | | |
|---|---|---|
| **5-6 months post vaccination** | | |
| age groups | 65 to 74 | 24% |
| | 75 to 84 | 33% |
| | 85 & older | 43% |
| **3-4 months post vaccination** | | |
| age groups | 65 to 74 | 51% |
| | 75 to 84 | 35% |
| | 85 & older | 14% |

- **Could higher proportion of 85 years and older members in first vaccinated group explain reduced VE?**

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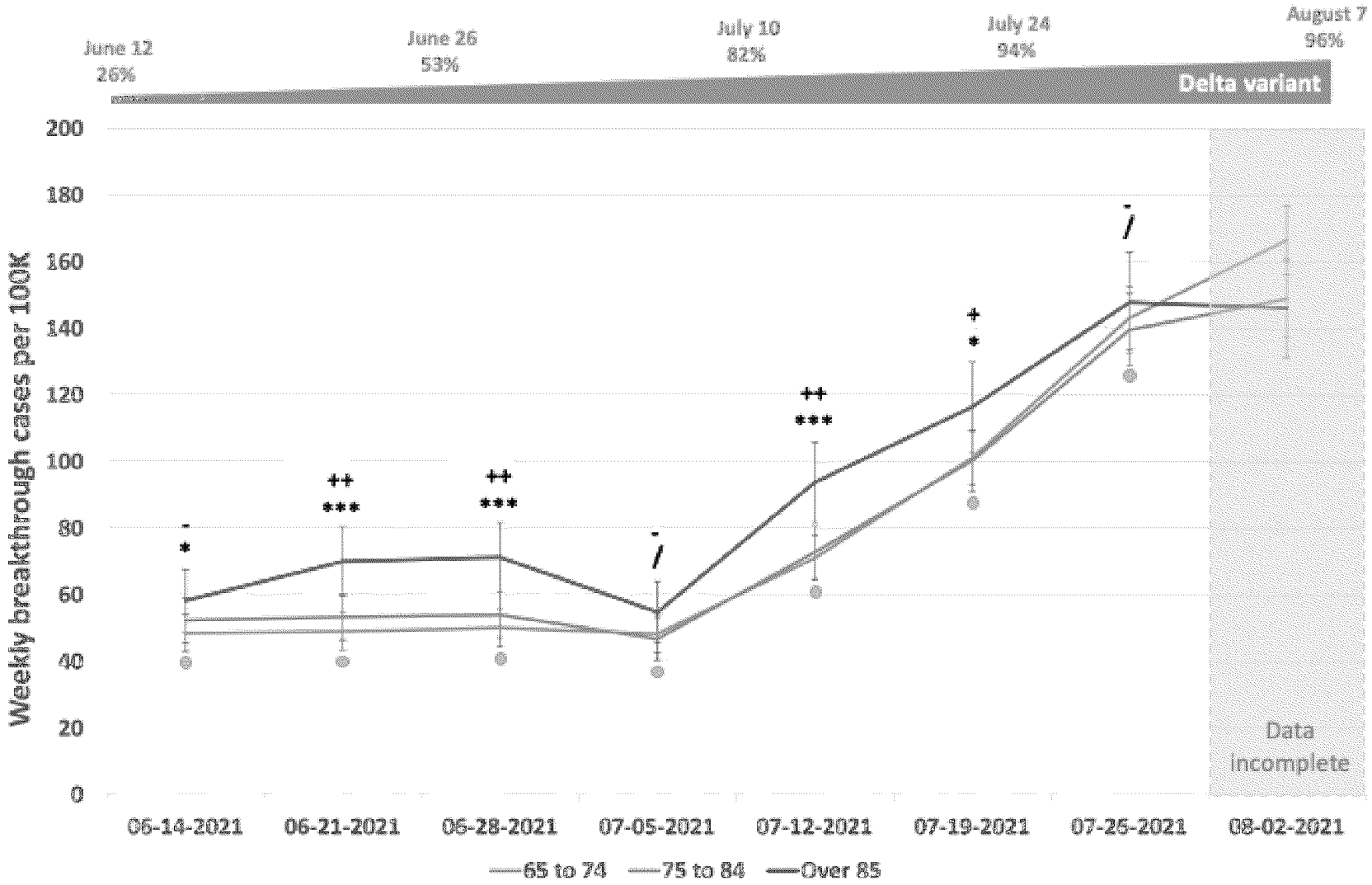
# Does Age Affect Vaccine Effectiveness Against Breakthrough Infections in the 65 Years and Older Cohort?




- **Age has a minor contribution to the reduced vaccine protection** seen in the group vaccinated 5-6 months ago
- **As Delta variant became dominant**, the modest age differences in breakthrough rates diminish

95% C.I.

| | Over 85 > 75 to 84 | Over 85 > 65 to 74 | 75 to 84 > 65 to 74 |
|---|---|---|---|
| P < 0.001 | none | *** | none |
| P < 0.01 | ++ | none | none |
| P < 0.05 | + | * | none |
| P > 0.05 | - | / | ● |

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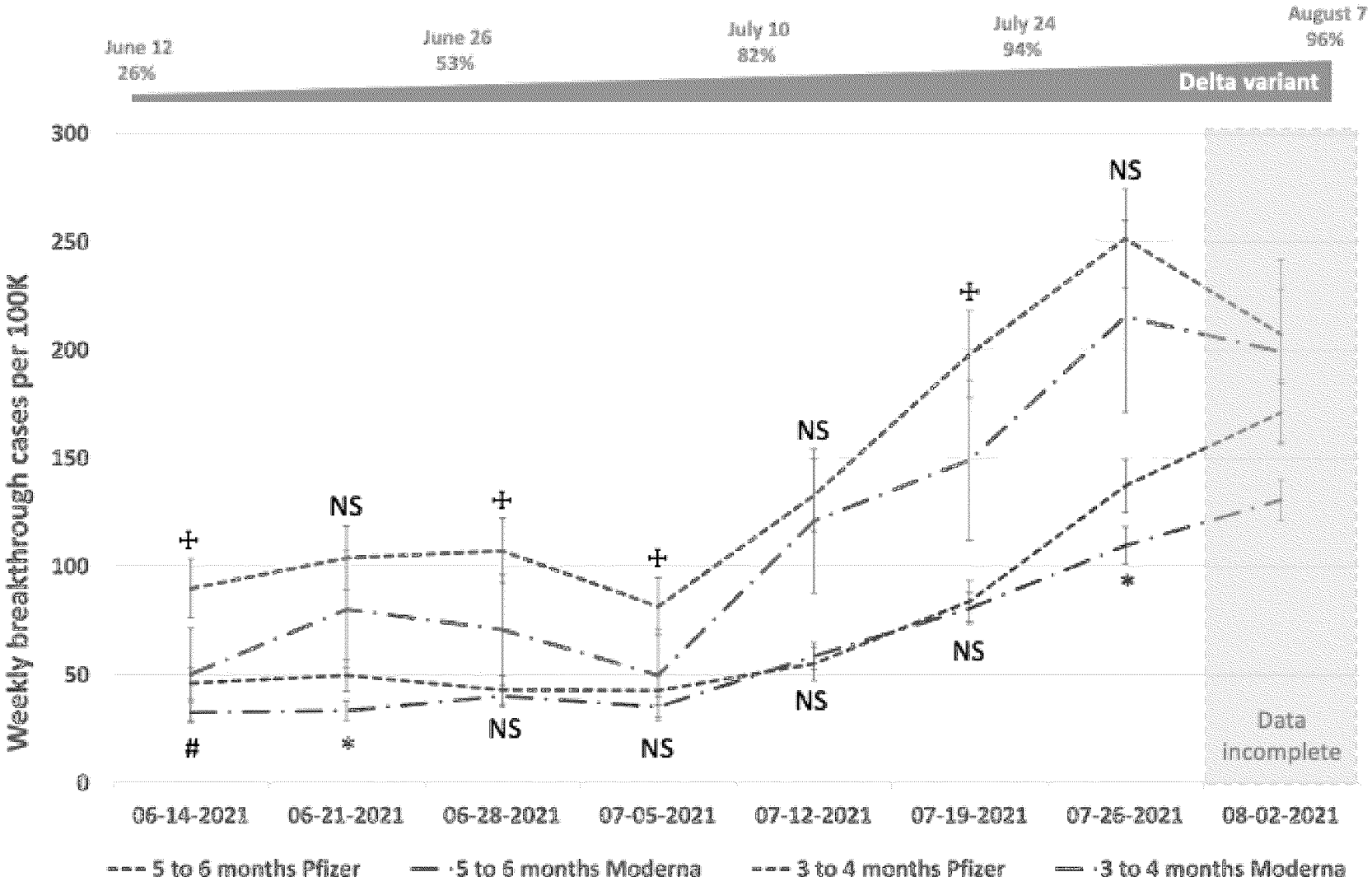
# Are There Differences in Waning Effectiveness Between Pfizer-BioNTech and Moderna Vaccines in the 65 Years and Older Cohort ?




- **Waning immunity are seen with both Pfizer-BioNTech and Moderna** vaccines during Delta phase of the pandemic

95% C.I.

* Breakthrough infection rate Pfizer-BioNTech > Moderna
P < 0.001

\# Breakthrough infection rate Pfizer-BioNTech > Moderna
P < 0.01

‡ Breakthrough infection rate Pfizer-BioNTech > Moderna
P < 0.05

**NS** Breakthrough infection rate Pfizer-BioNTech > Moderna
P > 0.05

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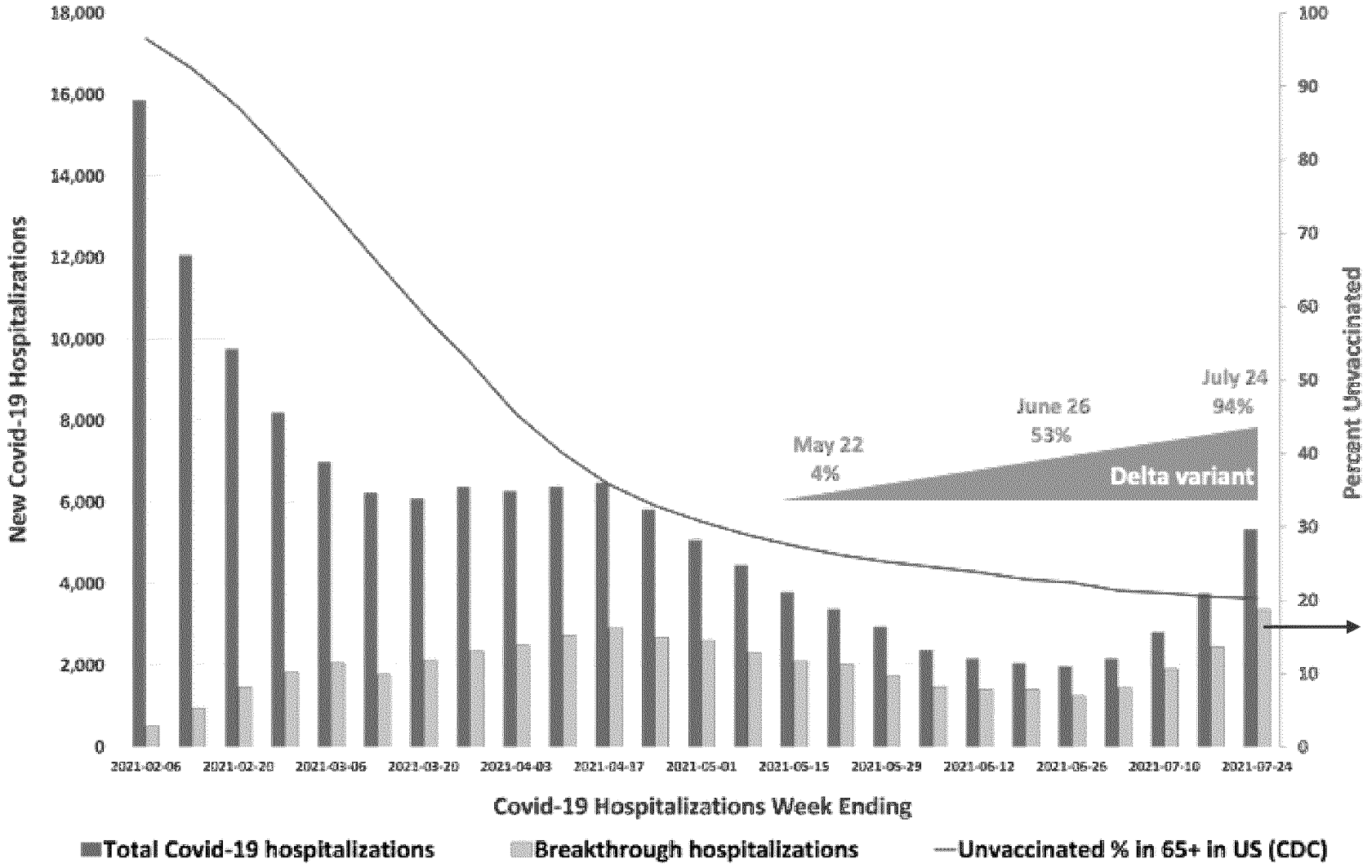
# Total & Breakthrough Hospitalizations in the 65 Years and Older Cohort




- **As Delta variant surged to over 50% in June, COVID-19 hospitalizations more than doubled, reversing the prior trend of decreasing hospitalizations since April**
- In this 80% vaccinated 65+ population, an estimated **63% of COVID-19 hospitalizations occurred in fully vaccinated individuals in the week of July 24th**

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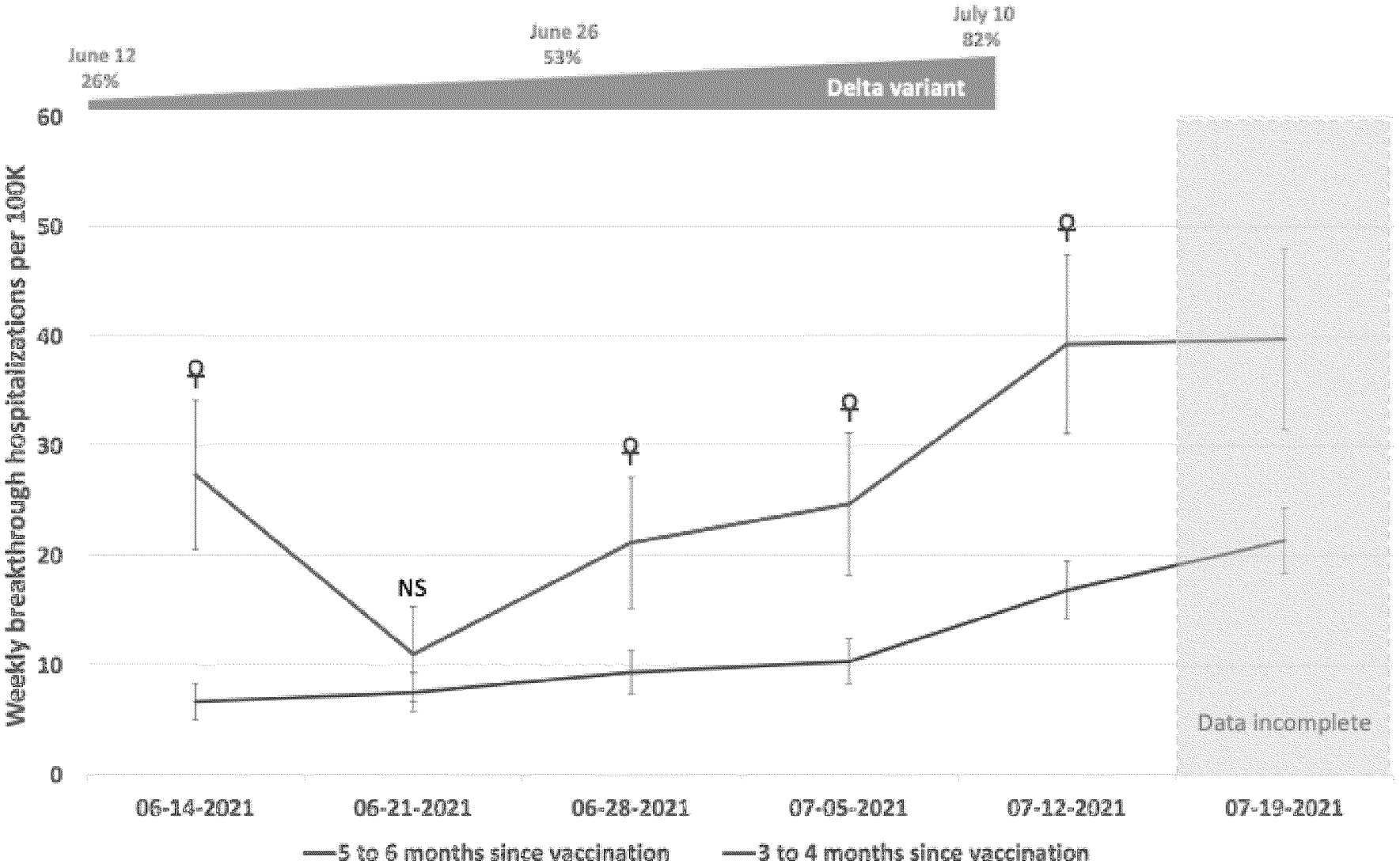
# Is Vaccine Protection Against Breakthrough Hospitalization Waning Over Time in the 65 Years and Older Cohort?




- **VE against breakthrough hospitalization is significantly lower 5-6 months post vaccination than 3-4 months post vaccination**

95% C.I.

Breakthrough hospitalization rate for 5-6 months since vaccination > 3-4 months
P< 0.001

NS Breakthrough hospitalization rate for 5-6 months since vaccination > 3-4 months
P> 0.05

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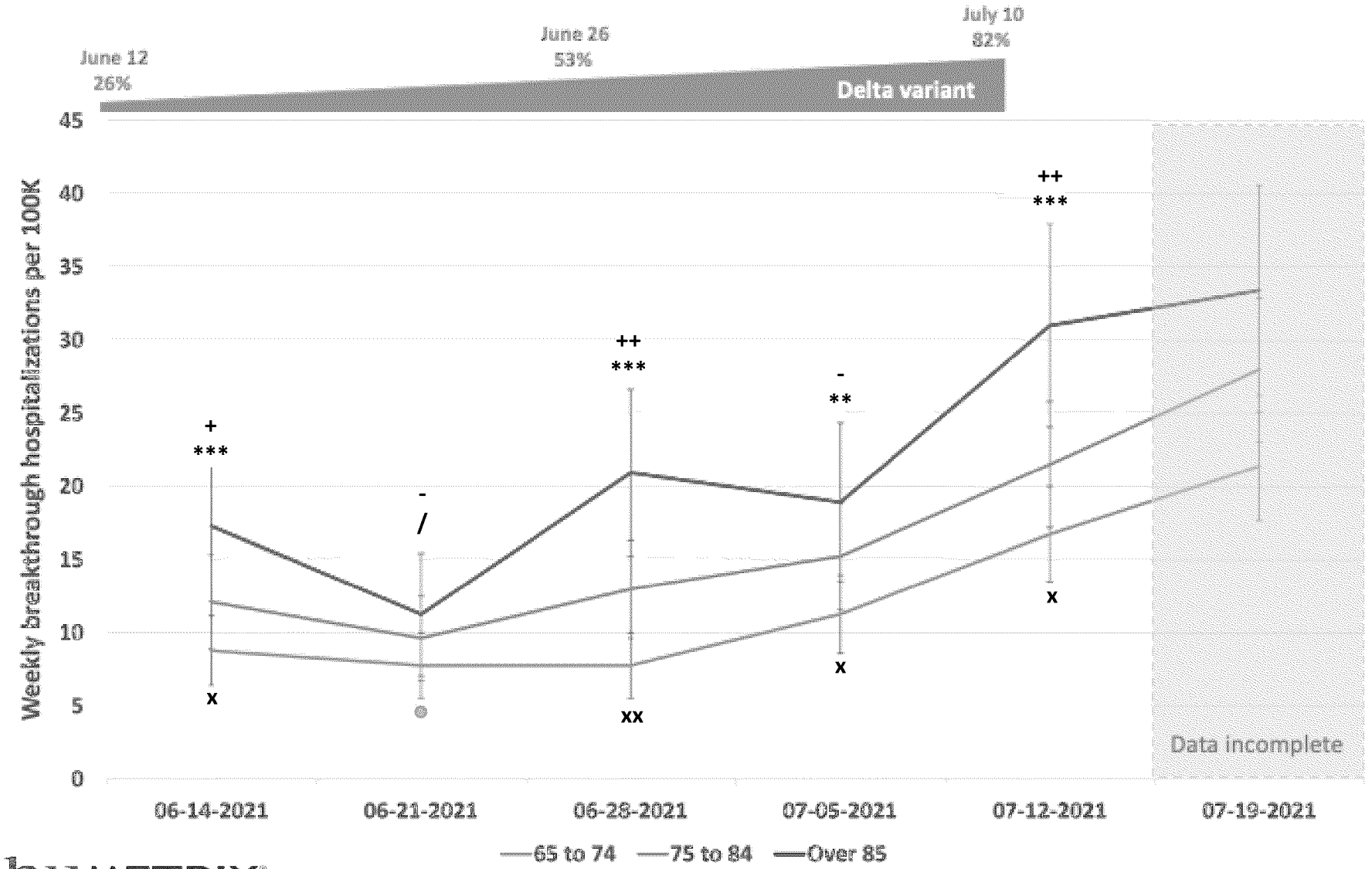
# Are there Age Differences in Vaccine Protection Against Breakthrough Hospitalizations in the 65 Years and Older Cohort?




- **Older age associated with increased breakthrough hospitalization rates**

95% C.I.

| | Over 85 > 75 to 84 | Over 85 > 65 to 74 | 75 to 84 > 65 to 74 |
|---|---|---|---|
| P < 0.001 | none | *** | none |
| P < 0.01 | ++ | ** | xx |
| P < 0.05 | + | none | x |
| P > 0.05 | - | / | ● |

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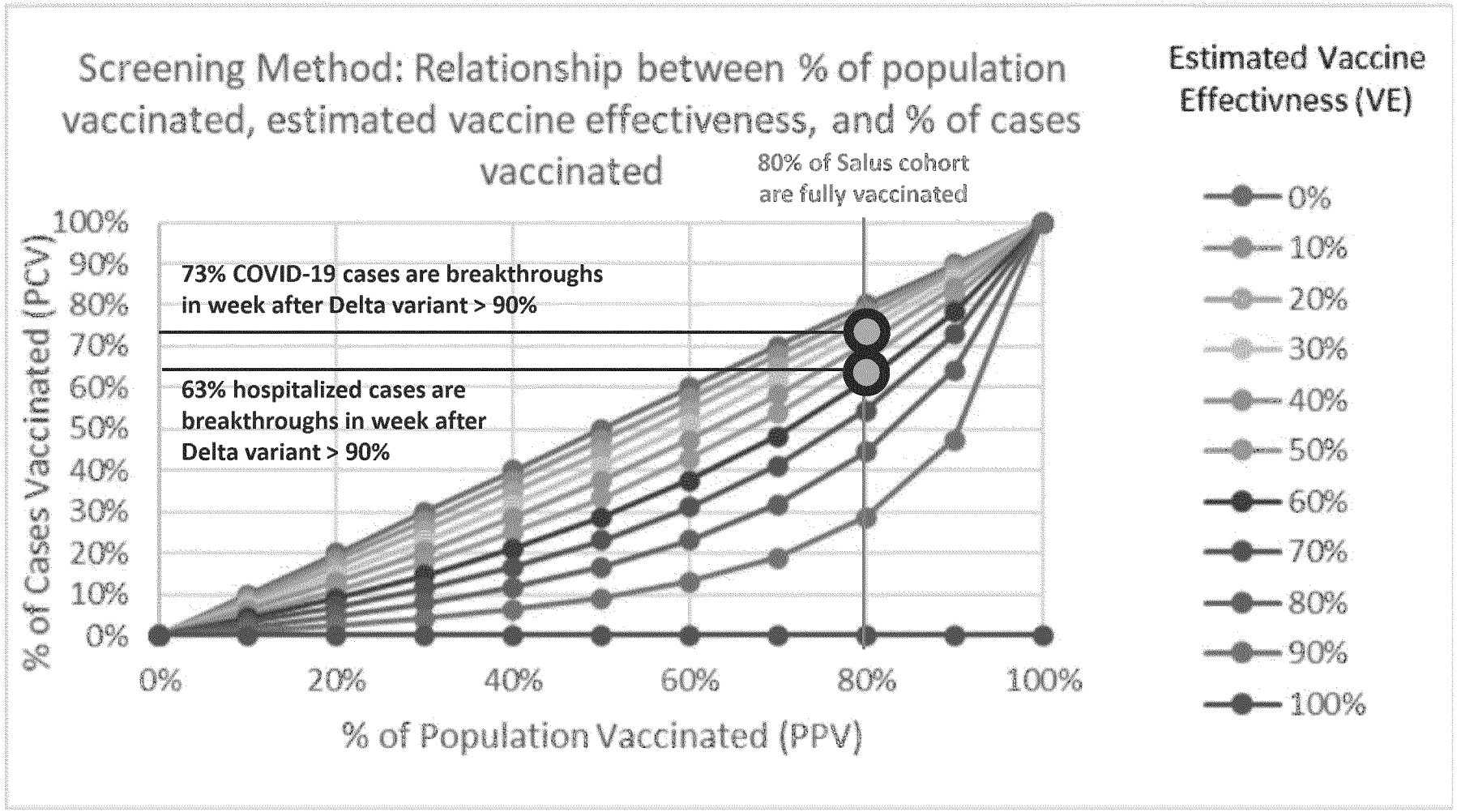
# What is the Vaccine Effectiveness Against the Delta Variant in the Salus Cohort? – Using the CDC Screening Approach




- **33% calculated VE against infection**
- **57% calculated VE against hospitalization**

**VE Screening method**

VE = 1- [(PCV/(1-PCV))((1-PPV)/PPV)]

PCV = proportion cases vaccinated

PPV = proportion population vaccinated

*Graphic adapted from CDC Presentation July 30, 2021*
*Improving communication around vaccine breakthrough and vaccine effectiveness*

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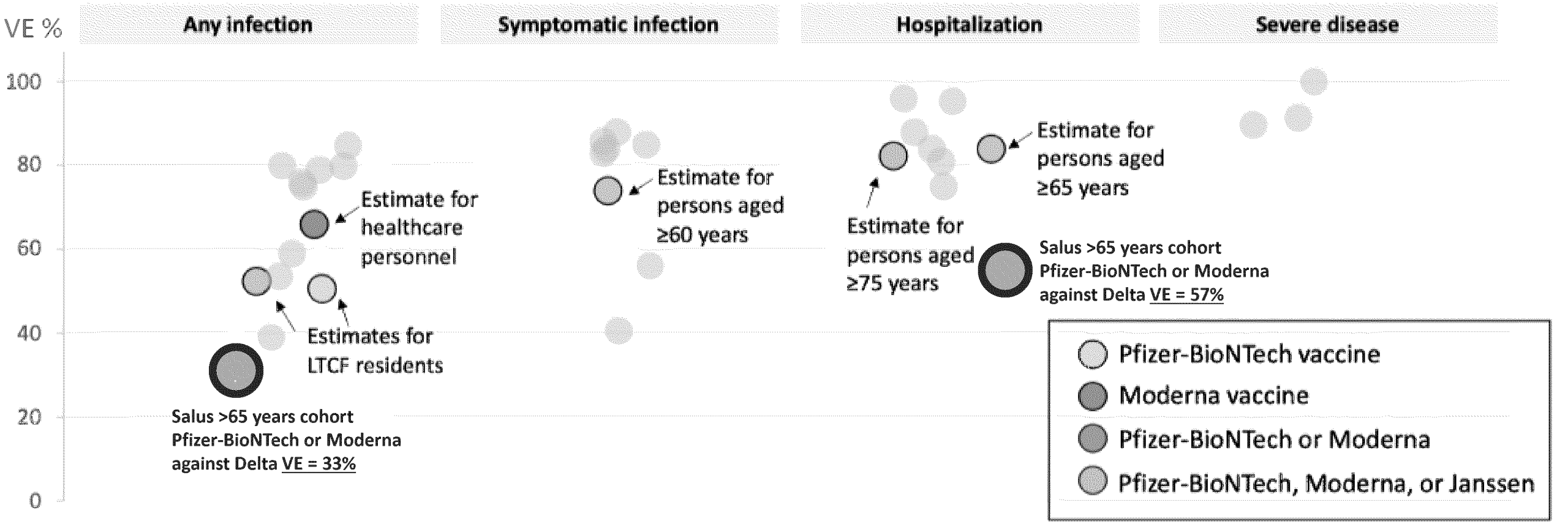
# How Does mRNA Vaccine Effectiveness in 65+ Salus Cohort with 5.6M Vaccinees Compared to Published Estimates?




- **VE of both mRNA vaccines in this 65+ cohort is lower than previously reported in smaller study sizes for both COVID-19 infection and hospitalization**
- **VE for mRNA vaccines is higher against hospitalization than against infection**

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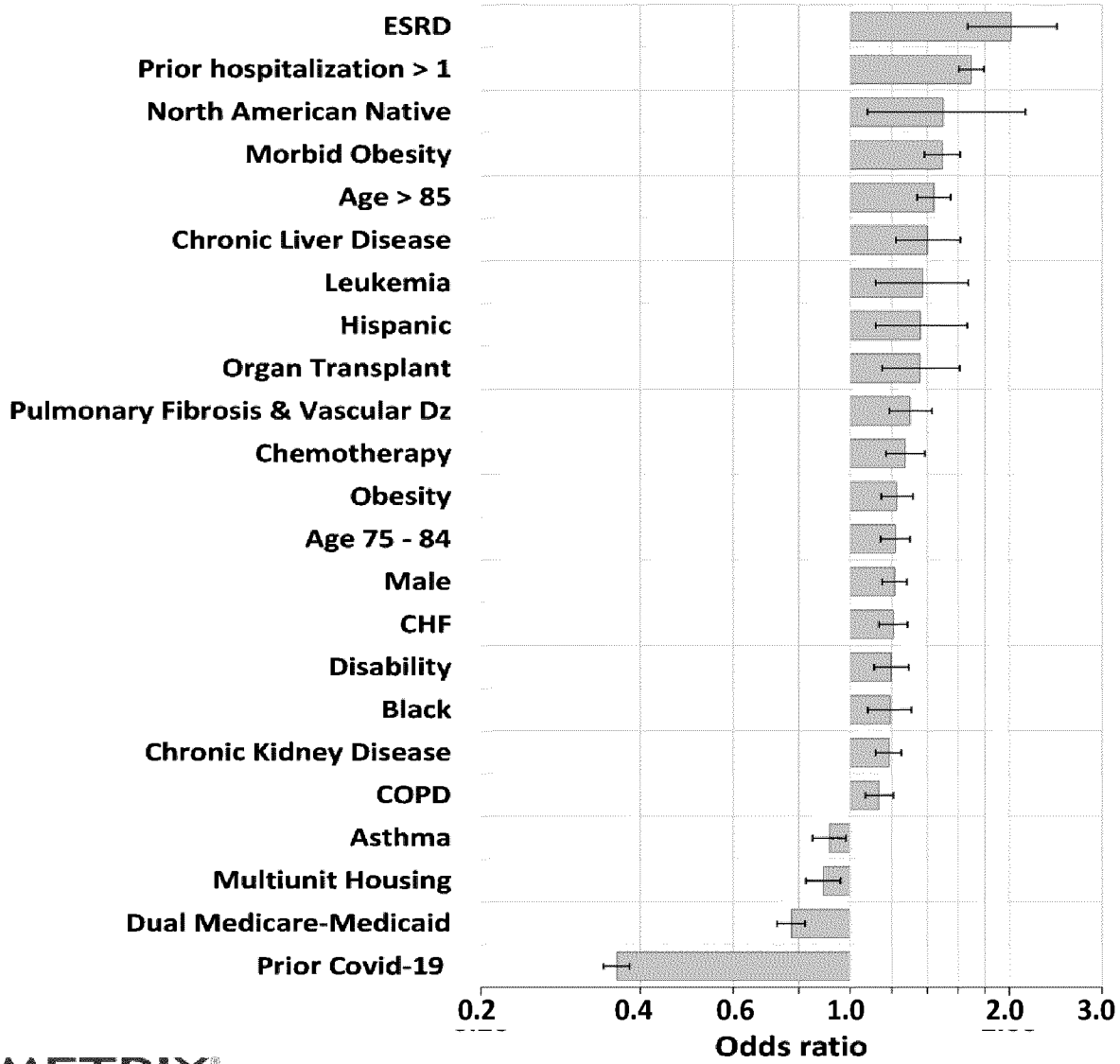
# Risk Model for Breakthrough Hospitalization




- **Prior COVID-19 infection has a major protective effect against breakthrough hospitalization**
- **Risk of breakthrough hospitalization increases with time elapsed since mRNA vaccination with odds ratio increasing to 2.5 at 6 months post vaccination**
- **There is a step up in risk in the 75-84 and again in the over 85 age categories compared to the 65-74 category**
- **Risk model can be used to stratify the over 65 population to best select those in most need of booster vaccine dose**

Logistic Regression Model performance:
AUROC 0.73, balanced accuracy 0.67

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