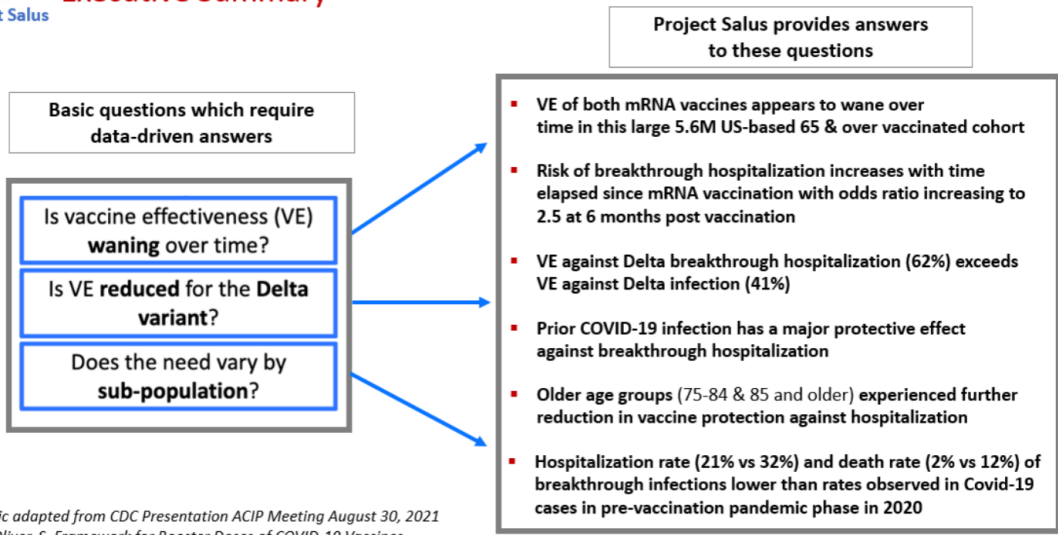




### Executive Summary



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



JAIC is the US Department of Defense Joint Artificial Intelligence Center

## Effectiveness of mRNA COVID-19 Vaccines Against the Delta Variant Among 5.6M Medicare Beneficiaries 65 Years and Older

Weekly update of September 28, 2021



Project Salus





### Salus Platform for COVID-19 Analyses

#### 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

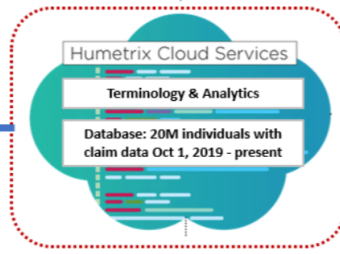
January - August 21 2021

##### Breakthrough Key Metrics

161K Breakthrough cases

33K Breakthrough hospitalizations

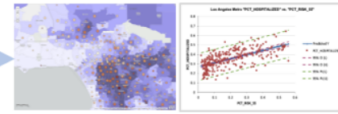
10.4K requiring ICU admissions



#### 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



### Salus Platform for COVID-19 Analyses

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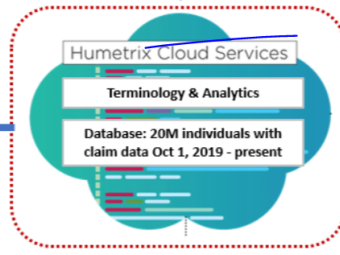
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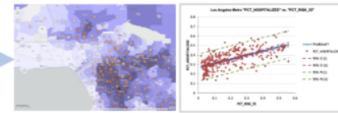
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## Salus Breakthrough Analysis Methodology and Limitations

- **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



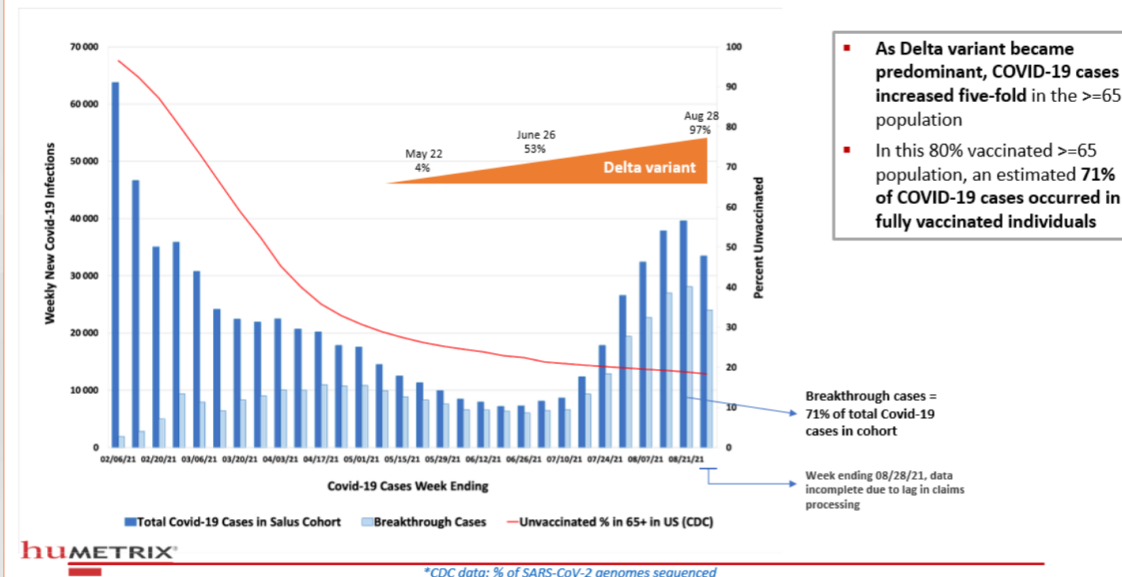
## Key Breakthrough vs. Pre-Vaccination COVID-19 Metrics

Among 5.6M fully vaccine immunized Salus cohort members aged 65 and older (2.7M Pfizer and 2.9M Moderna), as of September 10, 2021:

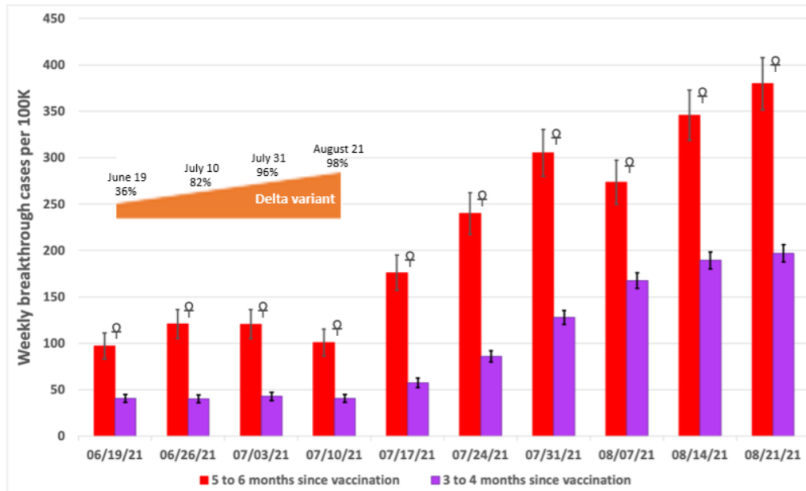
- **2.9% cumulative breakthrough rate**
- **21% hospitalization rate** in breakthrough infections, reduced by one third of 32% hospitalization rate March – December 2020
- **31% breakthrough hospitalizations include ICU care**, equivalent to 32% ICU rate March – December 2020
- **2.1% death rate** in breakthrough infections, reduced six-fold from 12% death rate March – December 2020



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



## 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% CI

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

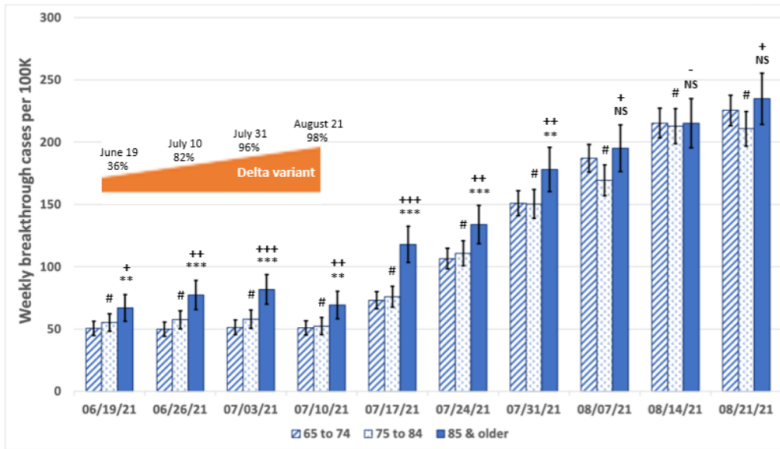
## Age Distribution of Vaccinated Groups in the 65 Years and Older Cohort

Vaccinee Group		
<b>5-6 months post vaccination</b>		
age groups	65 to 74	24%
	75 to 84	33%
	85 & older	43%
<b>3-4 months post vaccination</b>		
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?



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

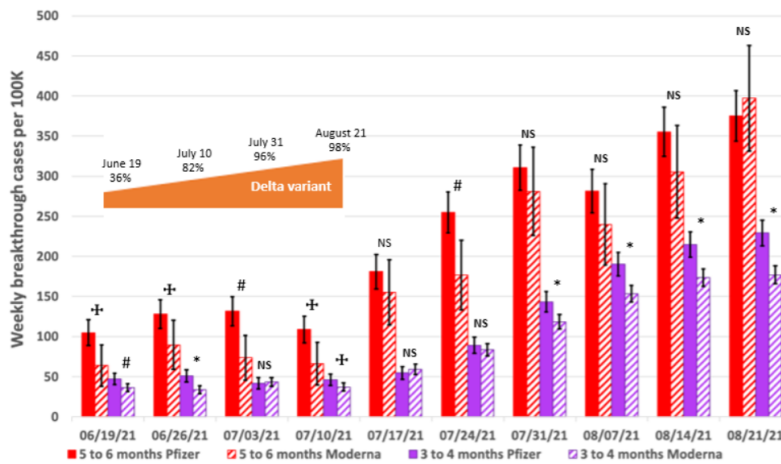


- Age has a minor contribution to the reduced vaccine protection seen in the group vaccinated 5-6 months ago

	Over 85 > 75 to 84	Over 85 > 65 to 74	75 to 84 > 65 to 74
P < 0.001	+++	***	none
P < 0.01	++	**	none
P < 0.05	+	none	none
P > 0.05	-	NS	#



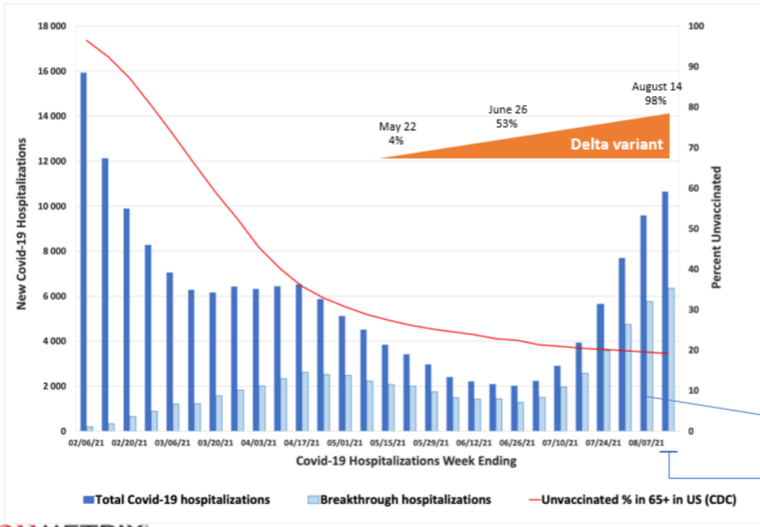
## Are There Differences in Waning Effectiveness Between Pfizer-BioNTech and Moderna Vaccines in the 65 Years and Older Cohort?



- Waning immunity are seen with both Pfizer-BioNTech and Moderna vaccines during Delta phase of the pandemic
- Moderna vaccine offers better protection than Pfizer vaccine for individuals vaccinated 4 months prior for weeks ending after July 31

Breakthrough infection rate Pfizer > Moderna	
P < 0.001	*
P < 0.01	#
P < 0.05	+/-
P > 0.05	NS

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

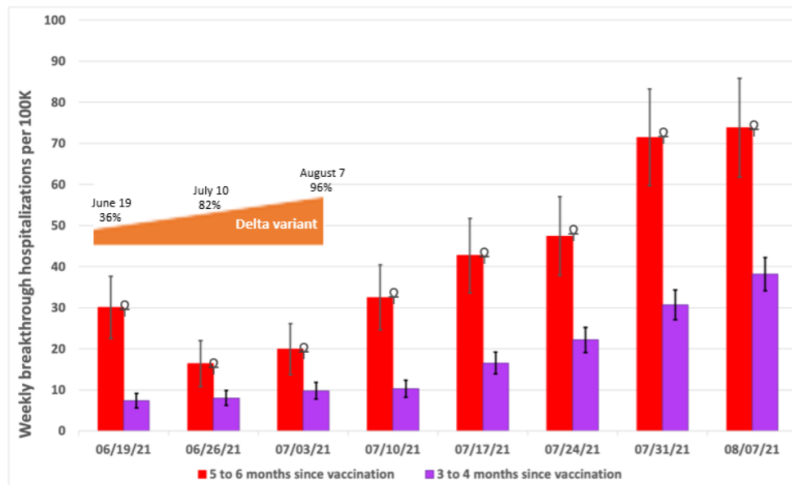


- As Delta variant surged to over 50% in June, COVID-19 hospitalizations more than doubled, reversing the prior trend of decreasing hospitalizations since April
- In this 80% vaccinated 65+ population, an estimated 60% of COVID-19 hospitalizations occurred in fully vaccinated individuals in the week ending August 7th

60% of COVID-19 hospitalizations are in vaccinated individuals

On 08/14/21, data incomplete due to lag in claims processing

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



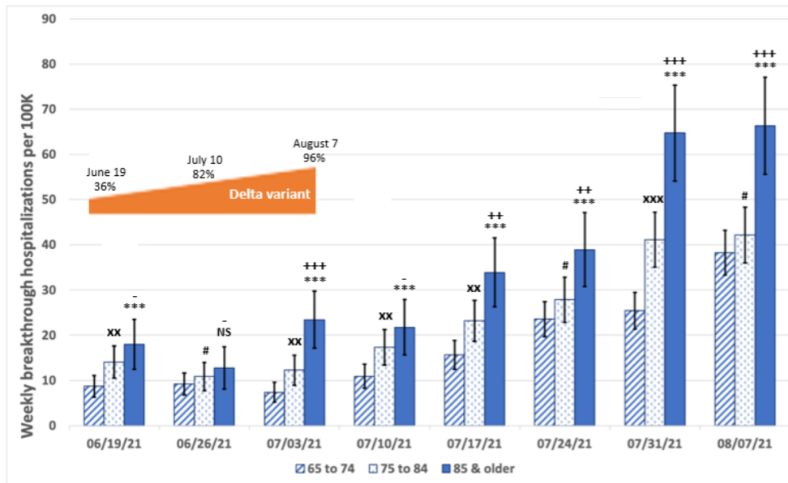
- VE against breakthrough hospitalization is significantly lower 5-6 months post vaccination than 3-4 months post vaccination

95% CI

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



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



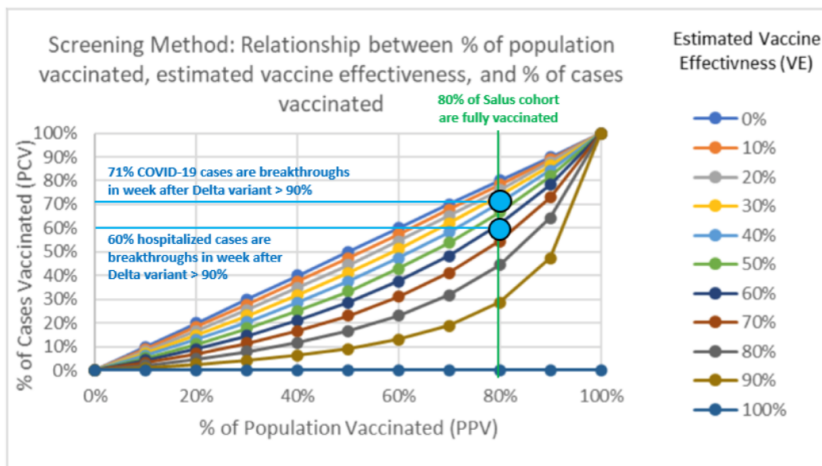
Older age associated with increased breakthrough hospitalization rates

95% CI

	Over 85 > 75 to 84	Over 85 > 65 to 74	75 to 84 > 65 to 74
P < 0.001	+++	***	xxx
P < 0.01	++	none	xx
P < 0.05	+	none	x
P > 0.05	-	NS	#



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



41% calculated VE against infection

62% calculated VE against hospitalization

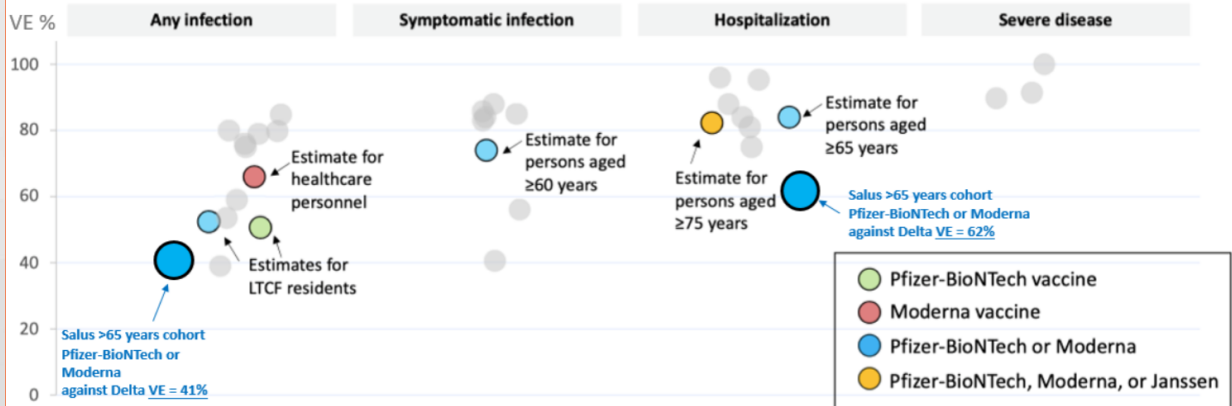
**VE Screening method**  
 $VE = 1 - \frac{PCV}{(1-PPV)}$   
 PCV = proportion cases vaccinated  
 PPV = proportion population vaccinated

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





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

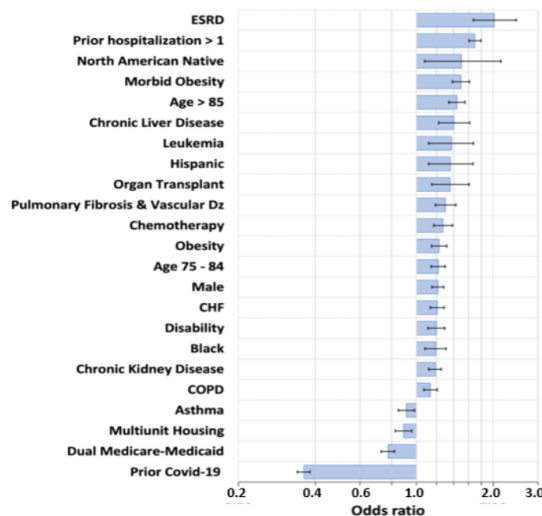


- VE of both mRNA vaccines in this 65+ cohort is lower than previously reported in smaller study sizes for both COVID-19 infection and hospitalization
- VE for mRNA vaccines is higher against hospitalization than against infection

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



## Risk Model for 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
- Prior COVID-19 infection has a major protective effect against breakthrough hospitalization
- 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