SARS-CoV-2 infection and immunity in Care Homes (VIVALDI study)

Dr Laura Shallcross
l.shallcross@ucl.ac.uk
• Deaths in care homes 20% higher than 5 year average

• Policy decision (31 Dec 2020) to extend vaccine dosing interval to 12 weeks

• Whole care home PCR testing programme

Source: Office for National Statistics (ONS)
So many research questions….

- What proportion of care home staff and residents have been infected with SARS-CoV-2?
- Can staff and residents be infected with SARS-CoV-2 twice?
- What are the risk factors for outbreaks and large outbreaks?
- What is the effectiveness of vaccination in preventing SARS-CoV-2 infection in care home residents?
- What is the duration of natural and vaccine-induced immunity?
CARE HOME RESIDENTS & STAFF

Serum and plasma
- Blood - baseline
- Blood – 6 weeks
- Blood – 12 weeks
- Blood – 6 months
- Blood – 12 months

PCR Testing (Pillars 2 & 1)#
- Staff: weekly (P2)
- Residents: monthly (P2)
- Outbreaks/ hospital admissions (P1)

Care Home Dataset
- Resident identifiers*
- Participating staff identifiers*
- Infection control data
- Staff turnover
- Care home characteristics
- Building layout
- Ventilation & heating

Antibody testing & cross-validation
Cellular immunity
Proteomics

LINKED RESEARCH DATASET

OUTCOMES
Hospital admissions, Mortality

# data available from March 1st; *enables linkage between datasets
Vaccine effectiveness
Aim and Analytical approach

• Aim: To estimate the relative hazards (risk) of PCR-positive infection in specific time periods following first dose vaccination, relative to unvaccinated individuals

• Residents only

• Cox regression adjusting for age, sex, local incidence of infection, care home size, residents, prior infection and clustering by care home
# Characteristics of residents and care homes

## Residents n =10,412

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>86 (80-91)</td>
</tr>
<tr>
<td>Female</td>
<td>7247 (69.6%)</td>
</tr>
<tr>
<td>Previous infection</td>
<td>1155 (11.1%)</td>
</tr>
<tr>
<td>Mean PCR tests per month</td>
<td>1.6 (1.2-2.2)</td>
</tr>
<tr>
<td>PCR positive events</td>
<td>1335/36352 (3.7%)</td>
</tr>
<tr>
<td>Symptomatic at testing</td>
<td>84/1126 (7.4%)</td>
</tr>
<tr>
<td>First vaccine dose</td>
<td></td>
</tr>
<tr>
<td>ChAdOx1</td>
<td>9160 / 10412 (88.0%)</td>
</tr>
<tr>
<td>BNT162b</td>
<td>6138 (67.0%)</td>
</tr>
<tr>
<td></td>
<td>3022 (33.0%)</td>
</tr>
</tbody>
</table>

## Care homes n=310

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>For profit</th>
<th>Not for profit</th>
<th>Independent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total bed capacity</td>
<td>228 (73.5%)</td>
<td>72 (23.2%)</td>
<td>10 (3.2%)</td>
</tr>
<tr>
<td>Date by which &gt;75% care homes started vaccination</td>
<td></td>
<td></td>
<td>Jan 19, 2021</td>
</tr>
</tbody>
</table>

**Most residents vaccinated with ChAdOx1**
- Total bed capacity: 203 (65.5%)
- Date by which >75% care homes started vaccination: Jan 19, 2021

**Most residents vaccinated with BNT162b**
- Total bed capacity: 99 (31.9%)
- Date by which >75% care homes started vaccination: Jan 7th, 2021

*Shrotri et al. Lancet Infect Dis 2021.*
### Adjusted Hazard Ratios for PCR positive infection following 1° dose vaccination

<table>
<thead>
<tr>
<th>Category</th>
<th>Testing rate per 1000 person days</th>
<th>Infection rate per 10,000 person days</th>
<th>Adjusted HR (95%CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unvaccinated</td>
<td>45.54</td>
<td>21.39</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>0-6 days</td>
<td>52.15</td>
<td>22.06</td>
<td>0.64 (0.38-1.06)</td>
<td>0.083</td>
</tr>
<tr>
<td>7-13 days</td>
<td>59.60</td>
<td>25.98</td>
<td>0.83 (0.54-1.28)</td>
<td>0.404</td>
</tr>
<tr>
<td>14-20 days</td>
<td>48.89</td>
<td>26.21</td>
<td>0.96 (0.57-1.60)</td>
<td>0.866</td>
</tr>
<tr>
<td>21-27 days</td>
<td>52.15</td>
<td>19.99</td>
<td>0.92 (0.53-1.59)</td>
<td>0.762</td>
</tr>
<tr>
<td>28-34 days</td>
<td>48.17</td>
<td>9.74</td>
<td>0.44 (0.24-0.81)</td>
<td>0.0087</td>
</tr>
<tr>
<td>35-48 days</td>
<td>74.29</td>
<td>9.36</td>
<td>0.38 (0.19-0.77)</td>
<td>0.0069</td>
</tr>
<tr>
<td>49+</td>
<td>130.55</td>
<td>14.55</td>
<td>0.49 (0.20-1.17)</td>
<td>0.108</td>
</tr>
<tr>
<td>Overall</td>
<td>54.21</td>
<td>19.91</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adjusted for age, sex, local SARS-CoV-2 incidence, care home size and clustering by care home
Cycle threshold (Ct) values for PCR positive tests, by exposure category

<table>
<thead>
<tr>
<th>Vaccination status</th>
<th>Samples</th>
<th>Mean Ct value (SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unvaccinated</td>
<td>552</td>
<td>26.55 (6.57)</td>
<td>-</td>
</tr>
<tr>
<td>0-27 days</td>
<td>411</td>
<td>25.91 (7.38)</td>
<td>0.158</td>
</tr>
<tr>
<td>28 + days</td>
<td>107</td>
<td>31.29 (8.71)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Key findings

• In residents, first dose vaccination provides substantial protection against new infection for at least 7 weeks

• Vaccinated individuals who become infected with SARS-CoV-2 may be less likely to spread infection compared to unvaccinated individuals who become infected

• Both vaccines protect against the α (B.1.1.7) variant, but efficacy against other VOCs is uncertain

• Further work is required to evaluate the effectiveness of the 2nd dose and the duration of immunity
Duration of immunity
Can staff and residents with SARS-CoV-2 antibodies be infected twice?

- Studies in healthcare workers (Oxford, SIREN, UCLH)
- No large scale studies in care home residents
- Immune responses may be impaired in older adults (immune-senescence)

- Partnered with Four Seasons Healthcare
- Blood sampling in 100 care homes (June/July; Aug/Sep; Oct/Nov)
- Blood samples tested for COVID-19 antibodies
Number of PCR positive tests in staff and residents from care homes participating in VIVALDI March 2020-Jan 2021

Study follow-up period

First infection
Seroprevalence and risk of PCR-positive infection

In an average 4 week period between Oct 2020 and Feb 2021

6.9% antibody-negative residents will get COVID-19

<1% of antibody-positive residents will get COVID-19

Adjusted HR for PCR-positive infection in antibody-positive versus antibody-negative residents is 0.15 (95% CI: 0.05-0.44)

Krutikov et al. Lancet Healthy Longevity 2021
We don’t know the date of index infection which makes it difficult to make inferences about waning immunity.

Interval between last antibody test and last relevant PCR test:
- Control: 0-49 days
- Reinfected: 0-49 days, 50-74 days, 75-180 days
Spike antibody titres post vaccination are higher in staff and residents who have had natural infection.

*Tut et al. The Lancet Healthy Longevity; In press*
Key findings

• Residents and staff with antibodies are substantially less likely to develop PCR-positive infection for up to 10 months following their primary infection

• The magnitude of vaccine-induced antibody response (Dose 1) is higher in individuals with natural immunity

• Investigating immune correlates of protection is challenging due to limited sample size and poor quality data on the date of primary infection

• Estimating waning immunity following vaccination is likely to be easier as the vaccination date is well recorded (although loss to follow-up problematic)
Next steps
Challenges and priorities over the next 6-12 months

• Vaccination coverage: influenza and SARS-CoV-2
• How to monitor waning immunity & vaccine effectiveness against VOCs
  - Antibodies
  - PCR
  - Cellular immunity
  - Viral sequencing
• Balancing the need to prevent infection ingress against the negative impact on staff, residents, and relatives of restrictive disease control measures e.g.
  - Visitor restrictions
  - Testing
  - Masks etc.
• Surveillance systems (data + testing)
Acknowledgements

UCL
- Maria Krutikov
- Tom Palmer
- Andrew Hayward
- Andrew Copas
- Maddie Shrotri
- Chris Fuller
- Borscha Azmi
- Pablo Medina
- Sarah Walker

DHSC
- Alasdair Donaldson
- Aidan Irwin-Singer
- Jane Cummings
- John Hatwell
- David Pearson

University of Birmingham
- Paul Moss
- Gokhan Tut
- Rachel Bruton

Other
- Daniel Davis (Palantir)
- Gemma (Palantir)
- Mark Marshall (NHSE)
- Jeremy Farrar (Wellcome Trust)
- Jamie Lopez-Bernal (PHE)
- Susan Hopkins PHE
- Abraham Roodt (TDL)
- James Robson (FHSC)
- Haydn Williams (FSHC)

This work was funded by the UK Department of Health and Social Care. The views expressed in this presentation and associated publication are those of the authors and not necessarily those of the UK Department of Health and Social Care.