

1 Background

- 1.1 Previous papers from SCWG have provided scientific advice on testing strategy to reduce transmission in care homes, recommendations on mask use and face coverings in care home settings, what factors should influence the decision of whether to allow visitors, what should or could determine the prioritisation of available testing capacity and finally what factors should drive the dynamic assessment of risk. Multiple interventions have now been implemented in care homes nationwide including testing and isolation on discharge from hospital, IPC training and free PPE supplies for the winter period, cohorting of residents and of staff, wage payment of staff to encourage self isolation, visiting policies and daily operational data reporting through Capacity Tracker.
- 1.2 To maximise the effectiveness of interventions key outstanding questions remain to determine the relative risk of each of four routes of ingress of infection to the care home (hospital discharge, staff, visitor (professional or domestic) and community admissions) as well as the route of transmission within care homes once infection has entered, for which more detailed genomic studies are critical.
- 1.3 New work relating to unpaid carer risks and wider care user groups eg learning disabled (LD), supported housing environments has also been requested from the SCWG.

2 Revised approach

- 2.1 Much of the information needed to support current policy to reduce morbidity and mortality in care settings is unpublished. The SCWG has therefore convened an expert virology, epidemiology and microbiology symposium to align initial unpublished findings across all domains and to support information exchange. The initial meeting on 21/09/20 included input from colleagues in academia, PHE/Easter Six study & Hospital discharge study, COG UK/East of England study, UCL/Vivaldi study and HPS/Scottish Care Homes Study. Supplementary a work-stream understanding hospital discharge impacts on care homes is underway with PHE and the Wales/SAIL care pathway research group. A number of these studies are adding additional research questions as relevant risk factors are confirmed eg environmental risks questionnaire for care homes has been added to the Vivaldi study.
- 2.1 Combined, the studies look at temporal, spatial, geographical and serological characteristics of outbreaks, analysis of specific risk groups (particularly in care workers), routine case detections and risk factors, and future planned bespoke studies. Key summary findings from these studies can be found at Annex1.

3 Methodological considerations for virology studies

Methodological considerations make interpretation of current results challenging.

- Sampling bias. Who is selected for testing and which samples get sequenced may in turn result in a biased sample therefore what is highlighted might be what is most observable rather than most important. It is important to be mindful of this when comparing different studies. Care homes where richer data are available may be different to those with less data. For example, less testing might have been carried out on homes that had smaller or more drawn out outbreaks.
- It is difficult to analyse causality in the context of a rapidly changing environment. Researchers have noted in different studies that testing and intervention policy was changing during the first wave as different measures were introduced on visiting / general lockdown / enhanced PPE. Therefore, outcomes may not reflect causation or current risks.
- The quality of the data may affect the ability to deliver retrospective research studies. Issues around processing that affect the performance of viral sequencing have meant that some potentially useful data has been lost. However, a new Vivaldi study proposes to look at retrospectively combining the Vivaldi 2 cohort study data with HES data, ONS deaths, FSHC data. All studies highlighted that genomic data need to be analysed alongside detailed epidemiological data, creating a need for better linkage, multidisciplinary working and rapid overcoming of governance issues.
- In preparation for the second wave more data will be collected and linked. For example to explore in more detail the variation in seroprevalence that has been observed. It may be that certain areas have had higher density of testing, which may therefore be more conducive to further analysis. Future studies should plan for both retrospective and prospective analyses and should be strategically aligned, prioritised with clear protocols on investigations and coordination. An assessment of seroprevalence of residents before the second wave, and the selection of care homes to track outcomes in detail based on current status would be a benefit.

4 Key findings

- 4.1 Although staff-to-staff transmission has been observed to have been a contributory factor in specific outbreaks, it is important not to generalise to all outbreaks and emphasise one route over another without clear evidence - studies undertaken so far indicate that multiple introductions are common. Clusters of cases have been observed but many outbreaks involve cases that are spread out over a longer period, again indicating multiple introduction routes / different lineages.
- 4.2 Retrospective genomic analysis and seropositive studies in care homes therefore find **evidence for multiple routes of virus ingress to care homes, but are not systematic enough to quantify the relative frequency of different routes of ingress.** Furthermore, these studies **do not definitively rule out any mode of ingress** so staff, visitors, visiting professionals, hospital discharges and new admissions and persistent infections may all contribute to the introduction of disease.

- 4.3 The weight of evidence is stronger in some areas than others, however. Evidence of staff to staff transmission has emerged in the genomic analysis (high confidence). Weak evidence on hospital discharge and modelling the impact of visitors (see also para 6 below) does not suggest a dominant causal link to outbreaks from these sources.
- 4.4 Public Health measures that reduce community incidence could be effective in reducing ingress into care homes. In the first wave, care homes appeared to show less impact from lockdown measures, with numbers continuing to rise more than cases in the community. It is thought that greater internal infection control measures now in place will make it easier to understand where infection is coming from.
- 4.5 Asymptomatic or atypically symptomatic presentation in residents¹ and staff mean that ingress may be hidden for a number of generations of disease.
- 4.6 Sequencing community tests to understand the comparator population is critical for the future.

5 Recommendations and barriers to improve virological analysis

5.1 Future research considerations identified

- Further work on the longevity and quality of antibodies. What proportion of care homes that experienced outbreaks in the first wave have evidence of sufficient resident and staff exposure to likely reduce the risk of further outbreaks or limit their size? Does the proportion of residents and staff with antibodies reduce over time due to waning of immunity or resident and staff turnover bringing in susceptible individuals? Cohort studies following particular homes in detail will be important, such as the Easter 6 study.
- How does the physical layout of a home influence transmission? Have homes that have cohorted residents onto different floors, been able to arrest the spread of the virus? How elements of ventilation & heating impact on transmission potential.
- Surveys on behavioural aspects of controlling the virus are important, for example a qualitative study interviewing staff to get further insight into how ways of working have changed.
- Exploration of severity of outcomes and what impacts this, looking at how severity varies with different co-morbidities etc.

5.2 Barriers and opportunities identified:

- a. The structural set up of testing arrangements can have a major impact on the ability to analyse sequencing. The location for sample processing appears fixed without opportunity for dynamic decision making and sample redirection. **It is recommended that SAGE endorse processes to**

¹ Wide ranging symptomatology may be present in this population (See SAGE paper *Community case definitions for Covid-19*) and coupled with inability to express symptoms because of cognitive impairment or communication problems.

ensure COG UK and other groups can benefit from flexible rerouting of samples to specific laboratories.

- b. The ability to connect data across organisations and studies due to information governance issues.
- c. **SCWG is seeking SAGE to strongly encourage organisations, researchers and the SCWG to work collaboratively to devise the optimum approach that would balance protection of data with the facilitation of research.**
- d. It is critical moving forwards that studies build collaboratively within microbiology but also within other expertise domains to leverage knowledge and skill. Greater transparency and connectivity is needed with funders of projects to enable collaboration and linkage.
The SCWG will gather more information about ongoing and proposed research projects areas and ² seek to join up studies and disciplines in future work.
- e. It may be useful to set up a mechanism to produce analysis on a regular basis to give an up to date view of how the virus and different strains are spreading at a local / regional level.

6 Additional risk factors and modelling

6.1 Visiting

Recommendations to allow visitors to care homes within risk assessed parameters and based on local clinical judgement was made in June although many homes have continued to maintain closed doors. Isolation can however be harmful to residents, particularly where poor recognition or sensory deficit is present. Urgent work has commenced to try to develop a cost consequence model of the impact of disease ingress due to visitors (supplementary to other ingress), and the impact of stopping visitors for an extended period of isolation, using EQ-5D and ICECAP-O measures of quality of life.

Modelling studies have shown that allowing visiting has only a marginal impact on case load in a home (a median increase of 1 additional case in an outbreak of about 30 cases in a medium sized care home but this is not a significant increase given other stochastic effects). Greater confidence would be found with genomic or epidemiological confirmation of this finding but a key gap is the lack of a robust process to better characterise the impact of isolation on individuals.

6.2 Dynamic risk assessment

The tool presented in the SAGE paper of 18/06/2020 has been extended to incorporate further routes of ingress of disease and prototyped with data from Scotland suggesting an effective tool can be developed in combination with other sources of intelligence. The tool suggests testing frequency could be reduced in areas of low prevalence or smaller care homes but requires further consideration.

6.3 Excess deaths

Analysis using CQC notifications in England by SCWG and a published report on care homes in Scotland ³ shows that excess deaths have mainly been clustered in the homes that have had a Covid outbreak or death. This could signify a degree of under-diagnosis. It may also signify that deaths that would have normally taken place in hospital have occurred in care homes, possibly variable responses to outbreaks at local level due to challenges in diagnosis and control (especially in early stages without widespread support). This also suggests that changes in the way that care might have been delivered in homes since the first wave, including the introduction of visitor restrictions, doesn't appear to have affected outcomes as measured by increased mortality at this stage, however, mortality may be censored in time.

6.4 Unpaid carers and PPE

Unpaid carers (often but not always relatives) provide many millions of hours of care each week to people in England. This has probably increased during the COVID-19 pandemic. Much of this unpaid care work requires levels of proximity incompatible with physical distancing recommendations. The long incubation and high pre-symptomatic infectivity of COVID-19 makes transmission between carers and cared for a particular risk. Search of the literature reveals no direct evidence for the effectiveness of PPE for unpaid carers. Therefore we depend on generalising from evidence in health care settings.

Whether to supply PPE for unpaid carers is complex. It is highly likely that the use of masks, gloves, gowns and other PPE, together with behavioural infection control measures such as hand washing and physical distancing, will result in a decreased risk of coronavirus transmission between unpaid carers and cared for persons. The major caveat is that protective procedures must be properly instigated and consistently followed if they are to be effective. When using PPE unpaid carers should follow procedures recommended for domiciliary care workers. N95 masks offer much better protection than medical masks, and cloth masks/face covering may offer little or no protection, although giving a sense of security. Rather than it simply being a matter of the availability of PPE for carers that determines effectiveness, the behaviour of carers and cared for persons are major determinants of transmission. It is crucial that protective behaviours are implemented prior to symptom development. The behavioural evidence suggests that co-resident carers are less likely to wear PPE routinely in the home (although it should be made available to those who wish to avail of it) and physical distancing is often seen as less acceptable. As most research appears to have been conducted in relation to masks and gowns, we particularly advocate the use of this kind of PPE by unpaid carers. We also strongly advise that appropriate training and behaviour change measures must be provided using evidence based interventions such as Germ Defence.

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<https://www.medrxiv.org/content/10.1101/2020.07.09.20149583v1>

Genomics studies – key findings in each area of research

1 Easter Six Study

The Easter Six focused on six London care homes over the Easter weekend. Homes in this region were affected early in the UK epidemic, before there was full recognition of the extent of community transmission and the risks of asymptomatic transmission. Further work may look for similar findings in other areas:

- High proportion of asymptomatic infection
- Symptomatic & PCR (+) = poor outcome
- Outbreak = High rates of infection in both staff and residents
- PCR values were similar in age groups, symptomatic vs asymptomatic
- No differences in infectiousness according to symptoms/age
- >98% PCR (+) seroconvert, irrespective of symptoms
- High percentage of PCR(-) also seroconvert in outbreak settings
- Symptoms are not a useful way of screening
- No clear impact of sex or age on seroconversion –
- Majority who are seropositive make neutralising antibodies
- High levels of neutralising antibodies found.
- Recognition of an outbreak is a late signal
- PCR snapshots seriously underestimates exposure
- Staff seropositivity in the Easter 6 homes was extremely high overall, but seropositivity in a wider group of London homes with less obvious or no outbreaks was quite variable from community levels of exposure to much higher, not always associated with known outbreaks. This highlights the difficulties in understanding exposures or risks in care homes
- Risk factors for staff seropositivity were not clear.

The high percentage of sero-prevalence may possibly be partly down to the fact that the Easter Six focused on London care homes. Homes in this region were affected early in the UK epidemic, before there was full recognition of the extent of community transmission and the risks of asymptomatic transmission. Therefore further work may examine whether this finding is evident in other areas.

2 East of England (COG Study):

This study included care home residents tested during the first phase of the COVID-19 pandemic in a large geographical region in the UK

- Proportion of cases from care home residents increased as general transmission decreased during lockdown. Care homes more resistant to lockdown measures

- 7406 positive samples from 6600 identified patients. 18.2% of positive cases were care home residents.
- Sampling strategy changed during and after the study meaning capturing all genomic issues is difficult.
- 1100 residents from 292 care homes. randomised sample of non-care home residents used to compare care home vs non-care home samples.
- Two care homes observed – with similar outbreaks - who shared care workers, suggesting their involvement in transmission.
- Two patterns of transmission – distinct clusters suggested multiple introductions, and outbreaks transmitted within care homes. The study is as of yet unable to distinguish if introductions travelled via hospital admissions.
- Locally, PHE are investigating specific epidemiological risks, to understand differences between introductions that filtered out and introductions causing larger outbreaks. Likely due to geographical differences and staffing ratios.
- Admissions and patient movement data as a priority could help investigate transmission data.
- Ratio of cases from care home workers to patients is 4:1. Identifying care worker characteristics and the true risk of hospital discharge transmission critical in mitigating second wave transmission.
- Mortality data comes from Cambridge University Hospital (CUH) deaths data.
- Earlier deaths likely to be missed.
- To fully explore hospital discharge to care home transmission, pillar 2 data is important.
- 40% of pillar 2 data sequencing.
- Variability of immunity between care homes mean wave 2 transmissions may not mirror wave 1 issues – care homes patients broadly have turnover between 8-10 months; thus, patient's immunity is not clear cut.

3 Whole Genome Sequence Transmission in Care Homes in Scotland

- Majority of samples have no direct link. There are a minority of samples are linked to other care homes by 1 SNP or less.
- Discrete transmission connections that link care homes. The source of such transmission is yet to be unpicked.
- Strong evidence of connection between health workers and samples in some care homes.
- Care home admissions to hospital: less in Scotland than in England
- Outbreaks are heterogenous in size, duration and pattern (some more explosive, some more drawn out including long gaps between cases in some)
- Definition of symptomatic is not clear cut as depends which symptoms are counted as COVID-related.

4 Vivaldi Study

- Vivaldi-1 Follow up survey with care home managers to assess behavioural effects.
- Vivaldi-2 primarily explores seroprevalence, began in four seasons care homes with the intention to expand beyond 4 seasons (from October 2020) to ensure study is generalisable. The study will also assess waning immunity through repeat antibody testing (3 rounds in staff and residents, a further 2 rounds in residents over 12 months)
- Additional objectives include linkage to data on hospital admissions and mortality to model importation risk following hospital discharge into care homes, and explore the impact of the pandemic on direct and indirect mortality.
- Blood samples are also being collected for analysis of cellular immunity and proteomics
- Data collection includes capture of information on symptoms at each round of PCR testing (and in the subsequent 7 days); administrative data from each care home (list of residents, dates of care home entry and exit, care home characteristics e.g staff turnover and visitor logs, and a care home manager survey to collect data on care home characteristics and building survey – including ventilation and heating.
- Poor co-morbidity data, but possible to infer from linkage to hospital datasets
- Preliminary results from antibody testing across 99 care homes indicate that 1/5 of care homes have zero sero-prevalence based, but seroprevalence varies widely,
- No clear pattern in prevalence, generally proportion of prevalence is higher in residents than staff.
- Majority of care homes have results as they expected.