**Reducing risks for coronavirus transmission in the home – can we do more to reduce ‘viral load’?**

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*Word count 1797*

*Paul Little and co-authors argue that although there is no direct evidence of the importance of the size of the infecting dose of virus (‘viral load’) for COVID-19, other sources of evidence suggest viral load is probably important and that simple evidence-based interventions may help to reduce the risks from infection transmission. Future public health effort could focus on supporting the implementation of public health advice to reduce viral load in order to reduce transmission risks in the community, particularly between family members, but also for those going into homes to care for vulnerable individuals.*

***The context***

High infections rates among health workers have been attributed to more frequent contact with infected patients, and higher infecting doses of the virus (the ‘viral load’), leading to demands for better personal protection equipment (PPE). Whilst direct evidence of viral load for COVID-19 is limited, other evidence suggests viral load is probably important and that simple evidence-based interventions may reduce the risks from infection transmission.

**Transmission in the home and community**

The government ‘stay at home’ policies aim to reduce spread between households to flatten the peak infection rate. To reduce the incidence and severity of illness, and reduce mortality and healthcare demands, effective interventions to reduce the viral load should be promoted - particularly for reducing transmission between household members caring for affected individuals, and in those supporting or caring for vulnerable individuals in the community.

Most people with Covid-19 are cared for at home, increasing the likely exposure of household members. The long incubation and high pre-symptomatic infectivity makes transmission between family members a particular risk: modelling of viral shedding in 94 COVID-19 patients and 77 transmission pairs suggests that the highest viral load is at or just before symptoms onset, with 44% of transmission occurring before symptoms (preprint: doi: <https://doi.org/10.1101/2020.03.15.20036707>).

The level of PPE for health workers is not likely to be available nor practical for members of the community. Public health advice recommends isolation of symptomatic household members - but this can be very difficult, particularly in small flats with shared facilities. Motivation may not be high enough if members of the public are sceptical about reducing transmission in the home and unaware that the illness of other family members may be more severe if they do not reduce the level of exposure. Greater awareness of this risk may be vital in order to motivate family members to pay sufficient attention to protecting themselves despite their concern for sick family members.

The medical community is commendably reluctant to make recommendations in the absence of an evidence-base. An expert team who reviewed the evidence for viral load <https://www.cebm.net/covid-19/sars-cov-2-viral-load-and-the-severity-of-covid-19/>

concluded that until the evidence is more conclusive ‘As our grandfathers used to say, when you do not know what is going on, do nothing’. However, the precautionary principle would suggest attempting to reduce the viral load from exposure to symptomatic household members, given little risk of harm from doing so.

Since it is difficult to get good dose response data it may be prudent not to treat absence of direct evidence in the pandemic as evidence of absence, particularly given evidence from other viral infections from both animal and human models, and trial evidence for reducing the transmission among families in non-pandemic years.

***Viral load: plausible but difficult to measure***

It is intuitive that viral load should influence the incidence and severity of disease. The main problem to confront in measuring the viral load in vivo is that measuring the viable infecting dose of the virus is extremely difficult in practice: contemporary measures of viral density, viability and viral contamination cannot easily be made. Establishing the relationship between infecting dose and the likelihood of developing disease is therefore very difficult. The challenge of establishing the infecting dose is complicated by environmental contamination - and it seems likely by analogy with MERS-COV that environmental contamination with COVID-19 is high (1), supported by recent case reports of extensive environmental contamination from patients with COVID-19 (2).

***Evidence for viral load?***

**Animal models**

Although the infecting dose from a combination of droplets and environmental contamination cannot be easily measured, animal models can provide indirect evidence based on high quality experiments under controlled conditions. We are not aware of infecting dose experiments with animal models of COVID-19, but it is clear from animal models of other viral infections that variation in the infecting dose determines how many animals get infected and how severe the illness is. This is the case for both viruses not closely related to COVID-19 and those more closely related. In a model of African Swine flu virus there is a clear dose response relationship between the infecting dose and disease in the animal (3, 4). Likewise, a strong dose response effect is found in the animal model for haemopoetic necrosis virus (4). The very close cousin to SARS-COV-2 (COVID-19) is the SARS-COV-1 virus and an animal (mouse) model here also confirms the importance of dose response of several strains of the SARS-COV-1 virus. The infectivity varies between different strains of the virus which modifies the shape of the dose response curve, but, nevertheless consistent dose response relationships are observed with the severity of the infection (5, 6).

**Indirect evidence: defective viral genomes**

One of the key factors in determining how severe an infection becomes is also the extent to which defective viral genomes are produced, which effectively reduces the infecting doses during the early part of an infection by competing with non-defective genomes (7). The greater the abundance of viruses with defective genomes within an infecting inoculum, the better the clinical outcome (8): genomic analysis of viruses isolated from previously healthy people requiring admission to the intensive care unit with Influenza A infection, those not requiring intensive care, and those with fatal outcome (who also had underlying medical conditions) demonstrated that defective genomes were associated with fewer severe or fatal outcomes.

**Epidemiology of serious viral infections**

The evidence from other similar serious viral infections also suggests the infecting viral load may be important.

**Ebola**

The Ebola outbreak allowed estimation of the impact due to the strength of the infecting dose. A retrospective study was undertaken of survivors from the Kerry Town treatment centre, and included more than 933 people (those dying, those surviving and those not infected) where the severity of infecting dose was graded according to the history of exposure. The severity scale, starting with the highest first was:

* Direct contact with, or touching, the body of a person who died of Ebola virus disease;
* Direct contact with the body fluids of a patient who has Ebola virus disease with wet symptoms (that is, diarrhoea, vomiting, or bleeding);
* Direct contact with a patient with wet symptoms (eg, sharing a bed, providing care, embracing, carrying);
* Direct contact with a patient with dry symptoms (that is, without wet symptoms); Indirect contact with a patient with wet symptoms (eg, washing their clothes);
* Indirect contact with a patient with dry symptoms;
* Minimal contact (e.g., shared meals);
* No known contact.

Although there was no clear relationship with mortality, perhaps due to the mediating effect of treatment at the treatment centre, there was a very strong linear relationship with the likelihood of infection developing, ranging from 80% likelihood of getting the disease with the highest infecting dose and 10% with the lowest dose.(9)

**Viral levels in SARS-COV-1 and COVID-19**

The SARS-COV-1 is closely related to COVID-19, and during the 2003 SARS outbreak older age, comorbidities (adjusted Hazard ratio R 3.36, 95% CI 1.44–7.82) and higher initial viral levels (adjusted HR 1.21 per log10 increase in number of RNA copies per millilitre in nasopharyngeal specimens, 95% CI 1.06–1.39) were associated with worse survival (10). Viral levels 10 days after the onset of symptoms was associated with a series of poor clinical markers (Oxygen desaturation, Mechanical ventilation) and also mortality (11). Recent data from COVID-19 has shown that severe cases had viral levels 60 times higher at presentation than mild cases(12). Whilst it is more complicated to interpret this data since the levels of virus once the disease has started will be in part a function of the immune response of the patient, the size of the initial viral load is likely to be a contributing factor, allowing immune defences to be more easily over-run.

**Influenza**

The difference in case fatality rates in the three waves of the ‘Spanish’ Flu pandemic of 1918-19 can be explained by the number of simultaneous contacts a susceptible person has with infected individuals (i.e. the more contact the higher the infectious doses)(13). However, in a detailed study modelling influenza virus transmission within households in 2008-2012, infectivity was proportional to viral load but viral load alone provided a poor fit to the models(14). Clearly from this evidence and the above evidence in SARS-COV-1 we need to better understand the relationship between infecting dose and other prognostic factors in modifying the immune response and clinical outcome (e.g. age, comorbidity etc).

***Is there pragmatic evidence that could help carers reduce the number and severity of infections?***

We are aware of only one behavioural intervention proven to reduce virus transmission within households –a digital intervention, ‘Germ Defence’. This could supplement public health advice on infection control in the home since it uses behaviour change techniques to help people implement this advice, by:

* explaining the importance and benefits of reducing exposure to motivate users to restrict their exposure;
* pre-planning for how to isolate an infected household member as far as possible (e.g. by avoiding sharing areas of the home;
* personalised goal setting for increasing a range of infection control behaviours;
* changing the home environment to support new habits (e.g. improving ventilation and increasing protective behaviours such as cleaning shared surfaces);
* Problem-solving to overcome barriers.

Germ Defence was trialled in 20,066 people in the H1N1 pandemic and subsequent seasonal flu years (15) and reduced:

* the number of respiratory infections (hazard ratio 0.75, 95% confidence intervals 0.72 to 0.79);
* infection transmission among family members (0.79, 0.74 to 0.83);
* the severity of infections which developed (a modest reduction in the number of days of moderately bad illness: intervention mean 3.9 days, median 2 days vs control (mean 4.5 days; median 3 days;
* Reduced gastro-intestinal infections;
* healthcare usage in terms of GP consultations and antibiotic prescriptions.

The team has been funded by the UKRI Covid-19 call to rapidly adapt and disseminate this intervention nationally and internationally – in the past weeks it has been translated into over 20 languages for this purpose. Germ Defence is likely to limit not just the transmission of COVID-19 but also the other viruses that are still causing the majority of respiratory illnesses in the current pandemic, even in secondary care settings(16). Other viruses may also be important given recent evidence that co-infection with other viruses occurs in more than 20% of cases(17).

**Conclusion**

Care is needed when extrapolating from prior evidence, but plausibly viral load is important for COVID-19. The precautionary principle suggests that people caring for household members who are unwell should be encouraged to take key measures to reduce infecting viral load in order to reduce the incidence and severity of infection. Promoting infection control measures in the community is a government priority (https://www.gov.uk/coronavirus) and will continue to be so as ‘stay at home’ policies are lifted (<https://www.gov.scot/publications/coronavirus-covid-19-framework-decision-making/>). Public health advice could be usefully supplemented by dissemination of evidence-based behavioural interventions to reduce viral load.

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**Key messages**

Government policy is aimed at reducing transmission of SARS-COV-2 (COVID-19) between family units, but less attention has been given to the risks of transmission between family members.

There is little direct evidence for SARS-COV-2, but evidence from controlled experiments in animal models (including SARS-COV-1), viral genome studies, and observational evidence from the Ebola and 'Spanish Flu’ outbreaks suggests the infecting viral load may be important.

An intervention to reduce infecting viral loads in non-pandemic years demonstrated reduced incidence, transmission and severity of infections (the MRC PRIMIT trial, n=20066), and could be used to support public health advice to improve infection control in families.

**Contributors and sources**

The starting point for this article was the review performed by the Centre for Evidence Based Medicine (CEBM) team in Oxford, supplemented by a rapid search for relevant evidence in PubMed, and the authors’ knowledge of the wider literature.

Paul Little is a clinical GP academic with expertise in infections in primary care and the community. His research programmes are funded by the UK National Institute of Health Research (NIHR) Programme Grants for Applied Research, Health Technology Assessment programme, and the School for Primary Care Research funding streams. He was the CI of the PRIMIT trial of ‘Germ Defence’ funded by the Medical Research Council.

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Since surviving a stroke, Cathy Rice has undertaken public involvement in a wide range of health research, including the UKRI Covid-19 funded project to expand and disseminate ‘Germ Defence’.

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**Competing interests**

Professors Little and Yardley were part of the team that developed Germ Defence. All other authors except RR are part of the team that is expanding and disseminating Germ Defence for COVID-19.

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**PPI statement**

PPI collaborators (CR and JB) were involved in discussing, writing and revising this article