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

Paul Little, Robert C. Read, Richard Amlôt, Tim Chadborn, Cathy Rice, Jennifer Bostock, Lucy Yardley

Professor Paul Little, FMedSci, Primary Care Population Sciences and Medical Education Unit, Faculty of Medicine, University of Southampton

Professor Robert C Read, FRCP, NIHR Southampton Biomedical Research Centre, University Hospital Southampton, and Faculty of Medicine, University of Southampton.

Professor Richard Amlôt, PhD, Behavioural Science Team, Emergency Response Department, Public Health England

Dr Tim Chadborn, PhD, Public Health England and Cabinet Office, UK Government

Ms Jennifer Bostock, MA, Nuffield Department of Population Health, University of Oxford

Ms Cathy Rice, BSc (no University affiliation)

Professor Lucy Yardley, PhD, Department of Psychology, University of Southampton and School of Psychological Science, University of Bristol

Corresponding author: Professor Little p.little@soton.ac.uk

*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.

**References**

1. Bin SY, Heo JY, Song MS, Lee J, Kim EH, Park SJ, et al. Environmental Contamination and Viral Shedding in MERS Patients During MERS-CoV Outbreak in South Korea. Clin Infect Dis. 2016;62(6):755-60.

2. Ong SWX, Tan YK, Chia PY, Lee TH, Ng OT, Wong MSY, et al. Air, Surface Environmental, and Personal Protective Equipment Contamination by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) From a Symptomatic Patient. Jama. 2020.

3. Niederwerder MC, Stoian AMM, Rowland RRR, Dritz SS, Petrovan V, Constance LA, et al. Infectious Dose of African Swine Fever Virus When Consumed Naturally in Liquid or Feed. Emerging infectious diseases. 2019;25(5):891-7.

4. McKenney DG, Kurath G, Wargo AR. Characterization of infectious dose and lethal dose of two strains of infectious hematopoietic necrosis virus (IHNV). Virus Res. 2016;214:80-9.

5. Roberts A, Lamirande EW, Vogel L, Jackson JP, Paddock CD, Guarner J, et al. Animal models and vaccines for SARS-CoV infection. Virus Res. 2008;133(1):20-32.

6. Roberts A, Deming D, Paddock CD, Cheng A, Yount B, Vogel L, et al. A mouse-adapted SARS-coronavirus causes disease and mortality in BALB/c mice. PLoS pathogens. 2007;3(1):e5-e.

7. Vignuzzi M, López CB. Defective viral genomes are key drivers of the virus-host interaction. Nat Microbiol. 2019;4(7):1075-87.

8. Vasilijevic J, Zamarreno N, Oliveros JC, Rodriguez-Frandsen A, Gomez G, Rodriguez G, et al. Reduced accumulation of defective viral genomes contributes to severe outcome in influenza virus infected patients. PLoS pathogens. 2017;13(10):e1006650.

9. Bower H, Smout E, Bangura MS, Kamara O, Turay C, Johnson S, et al. Deaths, late deaths, and role of infecting dose in Ebola virus disease in Sierra Leone: retrospective cohort study. BMJ (Clinical research ed). 2016;353:i2403-i.

10. Chu CM, Poon LL, Cheng VC, Chan KS, Hung IF, Wong MM, et al. Initial viral load and the outcomes of SARS. Cmaj. 2004;171(11):1349-52.

11. Hung IF, Cheng VC, Wu AK, Tang BS, Chan KH, Chu CM, et al. Viral loads in clinical specimens and SARS manifestations. Emerging infectious diseases. 2004;10(9):1550-7.

12. Xu T, Chen C, Zhu Z, Cui M, Chen C, Dai H, et al. Clinical features and dynamics of viral load in imported and non-imported patients with COVID-19. International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases. 2020.

13. Paulo AC, Correia-Neves M, Domingos T, Murta AG, Pedrosa J. Influenza infectious dose may explain the high mortality of the second and third wave of 1918-1919 influenza pandemic. PLoS One. 2010;5(7):e11655.

14. Tsang TK, Cowling BJ, Fang VJ, Chan KH, Ip DK, Leung GM, et al. Influenza A Virus Shedding and Infectivity in Households. J Infect Dis. 2015;212(9):1420-8.

15. Little P, Stuart B, Hobbs FDRea. An internet-delivered handwashing intervention to modify influenza-like illness and respiratory infection transmission (PRIMIT): a primary care randomised trial. Lancet. 2015;DOI: [http://dx.doi.org/10.1016/S0140-6736(15)60127-1](http://dx.doi.org/10.1016/S0140-6736%2815%2960127-1).

16. Liu R, Han H, Liu F, Lv Z, Wu K, Liu Y, et al. Positive rate of RT-PCR detection of SARS-CoV-2 infection in 4880 cases from one hospital in Wuhan, China, from Jan to Feb 2020. Clinica chimica acta; international journal of clinical chemistry. 2020;505:172-5.

17. Kim D, Quinn J, Pinsky B, Shah NH, Brown I. Rates of Co-infection Between SARS-CoV-2 and Other Respiratory Pathogens. Jama. 2020.

**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.

Lucy Yardley is a behavioural scientist with expertise in digital support for illness management and is leading the UKRI Covid-19 funded project to expand and disseminate ‘Germ Defence’. She is an NIHR Senior Investigator and her research programme is partly supported by NIHR Applied Research Collaboration (ARC)-West, NIHR Health Protection Research Unit (HPRU) for Behavioural Science and Evaluation, and the NIHR Southampton Biomedical Research Centre (BRC)

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’.

Robert Read is an Academic Infectious Disease Physician and Director of the NIHR Southampton Biomedical Research Centre. He is an NIHR Senior Investigator who`s research is supported by the UK Medical Research Council, European Union Innovative Medicines Initiative, the Wellcome Trust, Bill & Melinda Gates Foundation, the NIHR Global Health Programme and the NIHR Southampton Biomedical Research Cente.

Tim Chadborn has a split role as Head of Behavioural Insights and Evaluation Lead at Public Health England and Expert Analyst in the Systems Unit at the Cabinet Office

Jennifer Bostock (JB) is a public advisor to the Covid-19 Germ-Defence project, a member of the Healthcare Infection Society and led the public involvement for PIRU of the evaluation of the implementation of the UK’s Antimicrobial Resistance Strategy.

Richard Amlôt is the Head of Behavioural Science and Scientific Programme Leader within the Emergency Response Department at Public Health England. He is the PHE co-Director of the NIHR Health Protection Research Unit in Behavioural Science and Evaluation of Interventions, and a visiting Professor of Practice in the Psychology of Health Protection at King’s College London.

**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.

The Corresponding Author (Professor Little) has the right to grant on behalf of all authors and does grant on behalf of all authors, a worldwide licence (<http://www.bmj.com/sites/default/files/BMJ%20Author%20Licence%20March%202013.doc>) to the Publishers and its licensees in perpetuity, in all forms, formats and media (whether known now or created in the future), to i) publish, reproduce, distribute, display and store the Contribution, ii) translate the Contribution into other languages, create adaptations, reprints, include within collections and create summaries, extracts and/or, abstracts of the Contribution and convert or allow conversion into any format including without limitation audio, iii) create any other derivative work(s) based in whole or part on the on the Contribution, iv) to exploit all subsidiary rights to exploit all subsidiary rights that currently exist or as may exist in the future in the Contribution, v) the inclusion of electronic links from the Contribution to third party material where-ever it may be located; and, vi) licence any third party to do any or all of the above.

**PPI statement**

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