Daily Contact Testing Investigations

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NHS Test and Trace is investigating using daily lateral flow assay (LFA) testing of contacts of a confirmed case, replacing quarantine for non-household contacts (and potentially also household contacts). We update work previously done to investigate these questions in November 2020 [1].

Summary

We use a household structured branching process model of infection and contact tracing.

This model best represents a general population DCT policy, akin to the Agile Lighthouse DCT pilot. The findings are not applicable to workplace or school settings, where contact tracing is not done via Test and Trace, contact patterns are different and many index cases will be identified via asymptomatic screening rather than via the symptomatic testing route as we assume here.

Looking at the effects on the growth rate of the simulated epidemics, we compare the status quo policy (10 days isolation of cases and 10 days quarantine of all contacts) to Daily Contact Testing ('DCT') policies:

- For 3, 7, 10 days of DCT
- Across different applications of the DCT policy for household versus non-household contacts
  - Household contacts quarantine only, no daily LFA testing
  - Household contacts both quarantine and LFA test daily
  - Household contacts LFA test daily and do not quarantine (i.e. the same policy for household and non-household contacts)
- With and without waiting for the results to be returned from a 'confirmatory' PCR test before tracing after a positive LFA test is received.
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We conduct sensitivity analyses to examine:

- Shorter and longer PCR testing delays and tracing delays
- Varying LFA test sensitivity
- Varying testing, isolation and quarantine adherence behaviour

Note: Here, the testing duration starts from the day that a contact is traced. The policy as implemented will result in some individuals testing for longer than their self-isolation period.

Findings

DCT compared to Status Quo, for different testing durations and household contact policies

- Assuming 100% adherence to isolation, quarantine, and daily DCT in all scenarios, **DCT policies *could* be more effective than the status quo policy for all options considered.** The most effective policy would be to both quarantine and daily LFA test household contacts, but this is only very marginally more effective with respect to median growth rates, than quarantine only of household contacts, while non-household contacts DCT and do not quarantine. **This is only if adherence is 100%.** (Fig 1)
- The importance of testing duration (3, 7 or 10 days) varies by the household contact policy adopted:
    - **Household contacts DCT, no quarantine (as for non-household contacts):**
        - **Longer durations of DCT are more effective** (Fig 1 A)
    - Household contacts DCT AND quarantine:
        - Duration of DCT makes little difference (Fig 1 B)
    - Household contacts ONLY quarantine, no DCT:
        - Duration of DCT makes little difference (Fig 1 C)
- These results imply that **duration of LFA testing in our model is more important for non-quarantining household contacts** than non-quarantining out-of-household contacts. This could be due to:
    - **Longer durations of LFA testing are required to cover the within-household epidemic** (some household contacts might not yet be infected when they start LFA testing). In our model, reflecting current isolation/quarantine policy, if a second case is suspected/detected within a household (symptoms or test), the LFA testing duration for remaining household contacts is not restarted; the original duration remains. (Cases isolate.)
    - Differences in infectious age when tested between household contacts (no tracing delay) and non-household contacts (tracing delay).

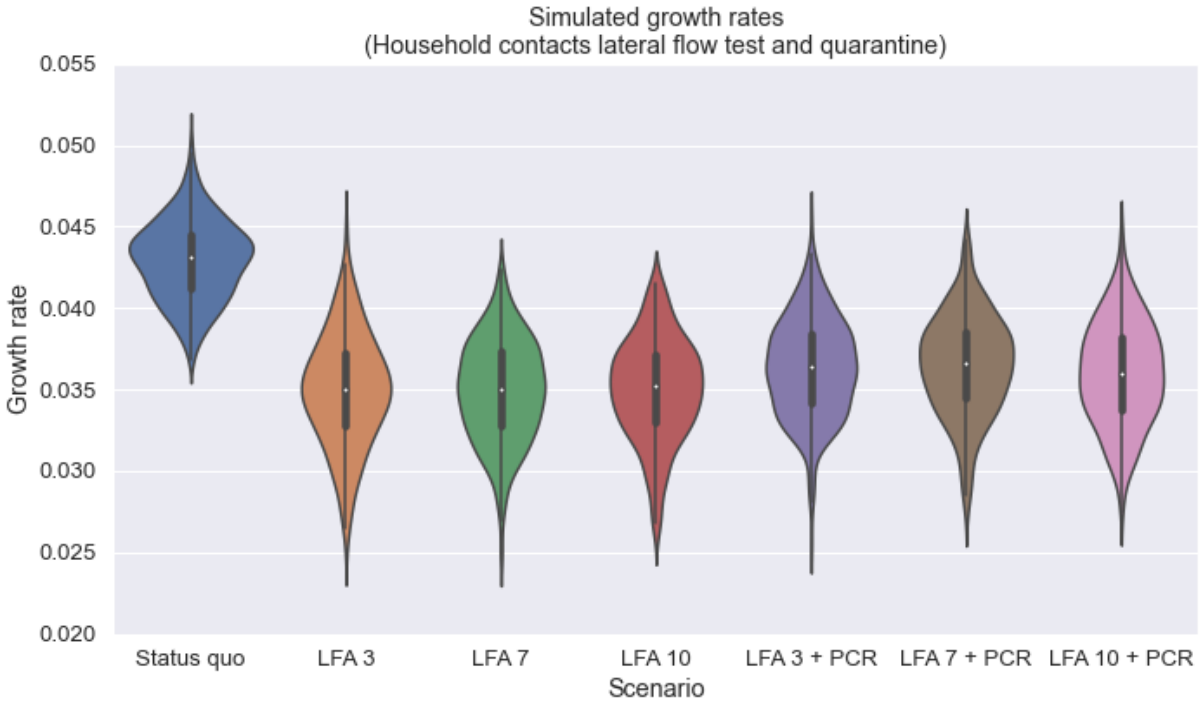
Effects of requiring a confirmatory PCR positive test to initiate contact tracing

- For all household contact policies and DCT durations, **requiring a confirmatory PCR test to initiate tracing of contacts from those testing positive on an LFD test reduced effectiveness** (assuming a test taken to results received delay drawn from the same distribution as for symptomatic PCR testing). (Fig 1)

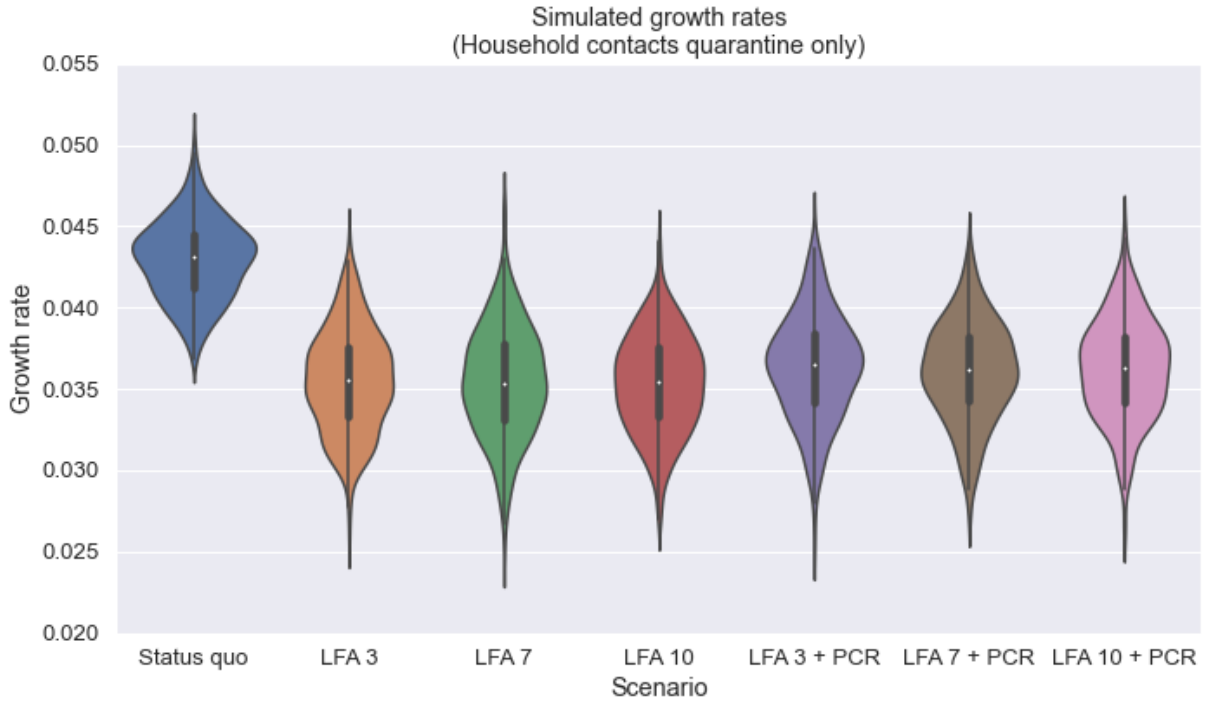
Figure 1. Comparison of TTI policies and effects of confirmatory PCR tests required to initiate tracing, assuming 100% adherence:

A. DCT scenarios include daily LFA testing and no quarantine for ALL contacts including household contacts

B. DCT scenarios include daily LFA testing for ALL contacts, only household contacts also quarantine.



C. DCT scenarios include daily LFA testing and no quarantine for non-household contacts, household contacts only quarantine



Sensitivity analyses: testing and tracing delays, LFA test sensitivity, adherence to LFA testing, quarantine and isolation and uptake of testing if symptomatic

- Parameters having the greatest effects on reducing effectiveness of the DCT strategies included:
    - Lower adherence to quarantine
    - Probability of reporting an infection and testing among symptomatic untraced cases
    - Uptake of isolation
- Testing and tracing delays, within the range examined, had a relatively small effect (increased delays led to increased growth rate)
- We found little effect of varying the LFD test sensitivity by multiplying the curve by a varied constant. This could be due to the ability of a false negative test to be quickly identified by a repeat test, particularly given in two of the three examined household contact policies, the duration of LFA testing was relatively unimportant (ie there are redundant tests). This should be interpreted with caution as we do not model individual viral load trajectories, so sensitivity each day is dependent only on infectious age and not correlated within individuals.
- Uptake and adherence to LFA testing (uptake at all, propensity to miss tests, daily missed test probability) showed little effect. This is likely because:
    - In the model, symptomatic testing is still operating and traced contacts who develop symptoms report their infections and test on PCR.
    - One missed test could be made up relatively quickly.

  This should not be interpreted as indicating that uptake and adherence in DCT schemes will be unimportant in practice. It is likely in practice that there will be correlations in non-adherence across some behaviours (eg reporting symptoms and taking up lateral flow testing), and our initial sensitivity analysis relies on several assumptions we have not yet had the chance to vary - further work is required to extend this. For example, those who do not uptake DCT may do so because they prefer self-isolation, whereas currently in the model uptake of DCT is independent of uptake of isolation or testing. It would be helpful to consider specific trade-offs, definitions of uptake/adherence and assumptions to explore further.

Caveats

Our model does not reflect transmission associated with B.1.1.7 or other variants due to uncertainties in specifying within versus between household transmission and what an unconstrained growth rate would be. There is no immunity in the model; the population is not finite. We do not model repeat contacts outside of the household or clustering of outside household contacts. Our findings should not be considered as predictions but rather are illustrative of the anticipated relative effectiveness of different strategies and with different specified assumptions.

We do not consider here social and economic harms associated with false positive tests, or changes to the numbers of individuals required to isolate for different strategies.

Methods

Model structure

We use a household branching process model of infection and contact tracing, used and described previously [1,2]. The model increments along discrete time-steps of one day, progressing both the infection transmission and the tracing processes. Each day, nodes make outside and within household contacts parameterized using the Polymod study[3], stratified by household size, distributed as per the UK population in 2018. To reflect changes in behaviour and physical distancing policies, we scale the proportion of outside-household contacts made. The distribution of secondary cases is modeled as an overdispersed negative binomial distribution (parameters as Table 1, does not reflect B.1.1.7).

We do not model repeat contacts. The model does not reflect any population immunity.

Analyses

We compare the proposed daily LFA testing of contacts policy described above to the status quo policy: untraced symptomatic individuals report their infection after a symptom reporting delay and a given proportion (defined by the infection reporting probability) seek a PCR test. They then test with a sensitivity modelled as a function of infectious age. Contact tracing is modelled with a set of testing delays, tracing delays and a tracing success probability informed by, but not formally fit to, the tracing delay distribution of non-household contacts and the testing delay distribution as routinely collected and reported by Test and Trace since the post holiday period (post Jan 8 2021). Self-isolation of self-reported cases lasts 10 days from symptom onset and contacts of a case quarantine for 10 days either from symptom onset of the first household case for within-household contacts, or 10 days post-infection date, assumed to be last exposure, for contacts of non-household cases.

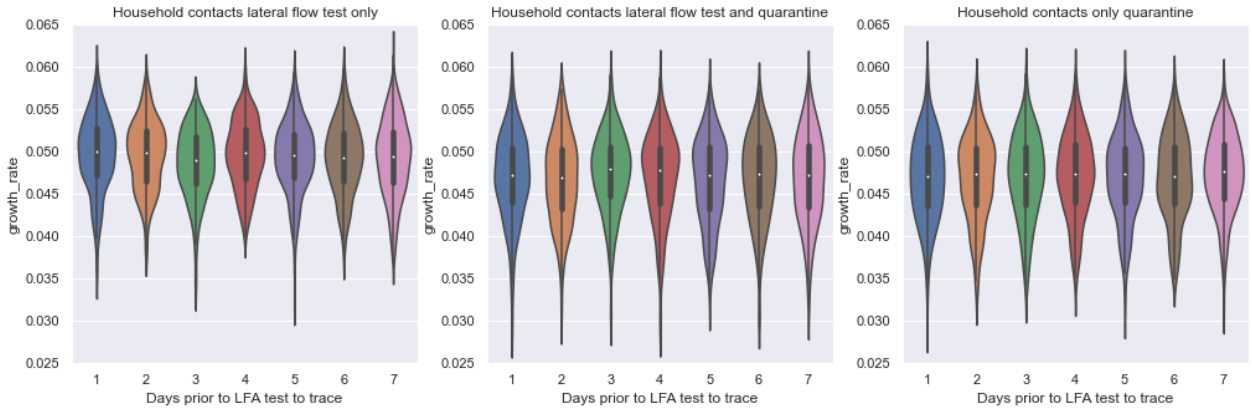
We simulate 2000 epidemics for each lateral flow testing duration and the status quo policy, running simulations for 40 days from 500 starting infections. We use log linear regression to estimate the growth rate of the epidemics between days 10 and 40.

Testing and tracing process

In the status quo policy, when an individual tests positive through a PCR test, they list contacts that occurred **2 days prior to symptom onset and 7 days post symptom onset.** With the new LFA tests, these criteria do not necessarily make sense. Some individuals will test positive prior to symptom onset, and asymptomatics who do not have a symptom onset will also test positive.
Unless specifically varied for sensitivity analysis, we use Test and Trace's policy that **contacts will be traced back 2 days prior to a positive lateral flow tes**t, including when that tracing is delayed by a confirmatory PCR test (assuming individuals isolate in the interim).

We also examine the effect of varying this between 1 and 7 days prior to the positive LFA test result, but find little difference (Fig 2).

Figure 2: Effect of varying the number of days prior to testing positive on an LFA test that contacts are traced



Lateral flow testing durations commence from the time that a contact is traced (not from the time at which they were last exposed to a case as quarantine is defined). We do not assume a postage delay in these analyses.

Test route and sensitivity

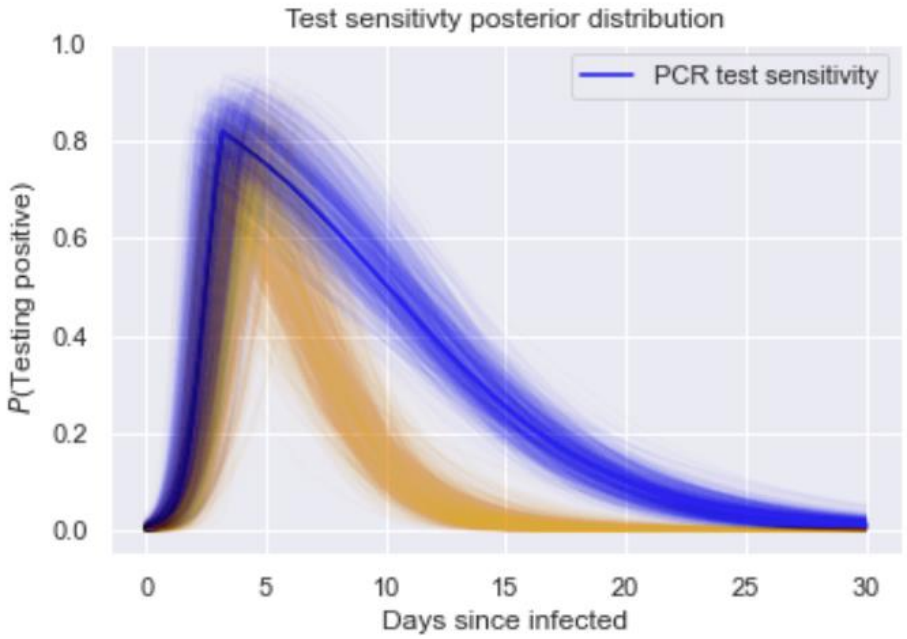
We assume that all untraced symptomatic cases who report their symptoms test using PCR. For traced cases who are currently undergoing LFA testing, we vary whether or not they will book a PCR if they develop symptoms - the rationale behind this is that false negative lateral flow assay tests may deter symptomatic cases from booking a test. We do not assume any asymptomatic testing in the model other than of contacts (i.e. all index cases in chains are symptomatic). We assume that if traced individuals develop symptoms, and are not currently being lateral flow tested, then they always book a PCR - the rationale being that they should be on the lookout for symptoms since they know they have been exposed.

We model PCR test sensitivity and LFA test sensitivity as functions of time since infection. We model these based on studies of healthcare workers and previous assessments of LFA test sensitivity [4, 5], Figure 3.

We vary the sensitivity of the LFA test using a constant multiplier (Table 2 below).

We do not model individual viral trajectories, which would require scaling of both test sensitivity and infectivity, and the exact relationship between viral load and infectiousness is currently not known.

Figure 3: PCR and LFA test sensitivity based on MCMC samples as a function of time since infection



Parameters

Models are parameterised as Table 1.

We have not formally fit specific testing and tracing distributions but have chosen distributions that reflect recent performance via examination of the Test and Trace data for simulations where these are not parameters that are varied (note for tracing delays we are interested only in non-household contacts).

Table 1: Unvarying parameter values

Parameter	**Values**
Growth Rate (pre-interventions or contact reductions)	0.22 per day (doubling time around 3 days) [6]
Incubation period	Gamma (shape=3.019, scale=1.6 days) [7]
Generation time	Weibull (mean=5, var=1.9^2 days) [8]

Household Size Distribution	(1: 0.29, 2: 0.35, 3: 0.15, 4: 0.14, 5: 0.05, 6: 0.02)
Household secondary attack rate	25% [9,10]
Overdispersion of secondary cases distribution	0.32
Proportion asymptomatic	0.2 [11]
Relative infectivity of asymptomatics	0.35 [11]
Number of social contacts per day	Polymod (within and outside household proportions, by household size) [3]
Reduction in global contacts per day due to physical distancing	60%
Onset to isolation and PCR test booking among untraced symptomatic individuals	Gamma (mean = 2.62, sd = 2.38) [7, data from Singapore]

Table 2: Parameters values that are varied

Parameter	**Default Value**	**Range varied for sensitivity analyses**
PCR testing delay (test to result and tracing)	Specimen to report delay, Poisson distribution, mean 1.2 days (consistent with non-household contacts as reported by Test and Trace in mid January 2021)	Poisson, Mean 0.8 - 2.5 days
Contact tracing delay	Exponential distribution mean 1.2 days (consistent with non-household contacts as reported by Test and Trace in mid January 2021)	Exponential, Mean 0.8 - 2.5 days

Probability of successfully tracing a contact	0.7 (consistent with non-household contacts as reported by Test and Trace in mid January 2021)	Uniform, 0.5 - 0.9
Probability that an untraced symptomatic infected individual reports their symptoms and seeks a test	0.25 (consistent with surveys about testing behaviour [12, 13])	Uniform, 0.2 - 0.3
Probability that individuals take up 10 days self-isolation and 10 days quarantine in the status quo policy model.*	1	Uniform, 0.6 - 1
Probability that individuals take up LFA testing under DCT policies.	1	Uniform, 0.6 - 1
Propensity for imperfectly adhering to quarantine And given this propensity, the reduction in global contacts during the period of isolation/quarantine	0 NA	Uniform, 0 - 0.5 Uniform, 0.4 - 0.6
Propensity for missing a day of LFA testing And given this propensity, the daily probability of missing an LFA test each day*	0 NA	Uniform, 0 - 0.5 Uniform, 0.5 - 1
LFA test sensitivity multiplier	1	Constant across the sensitivity curve, 0.8 - 1.1. This corresponds to *peak* sensitivity of 52% to 72%.

**If nodes who are DCT are not also isolating, it is assumed that when they miss an LFA test they are NOT isolating. This is intended to represent error/non-adherence, not a missed test by design (eg weekend break) nor a logistical issue for which individuals could be instructed to isolate.*

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References

[1] Fearon E, Fyles M and the TTI Modelling Group. On the use of LFA tests in contact tracing: preliminary findings. SAGE 68, Nov 16 2020. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/950771/s0897-testing-of-traced-contacts.pdf

[2] Fyles M, Fearon E, et al. Using a household structured branching process to analyse contact tracing in the SARS-CoV-2 pandemic. https://www.medrxiv.org/content/10.1101/2021.02.03.21250992v1.full.pdf

[3] Mossong J, Hens N, Jit M, Beutels P, Aurenen K, Mikolajczyk R et al. et al. Social Contacts and Mixing Patterns Relevant to the Spread of Infectious Diseases. PLoS Med. 5, e74 (2008). https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.0050074

[4] Hellewell J, Russell T, The SAFER Investigators and Field Study Team, The Crick COVID-19 Consortium, CMMID COVID-19 working group, Beale R et al. Estimating effectiveness of frequent PCR testing at different intervals for detection of SARS-CoV-2 infections. Preprint. 2020.https://cmmid.github.io/topics/covid19/pcr-positivity-over-time.html

[5] Preliminary report from the Joint PHE Porton Down & University of Oxford SARS-CoV-2 test development and validation cell: Rapid evaluation of Lateral Flow Viral Antigen detection devices (LFDs) for mass community testing. November 13, 2020. https://www.ox.ac.uk/sites/files/oxford/media_wysiwyg/UK%20evaluation_PHE%20Porton%20Down%20%20University%20of%20Oxford_final.pdf (accessed 15 November, 2020).

[6] Pellis L, Scarabel F, Stage HB, Overton CE, Chappell LHK, Lythgoe KA et al. Challenges in control of Covid-19: short doubling time and long delay to effect of interventions. 2020. Preprint arXiv:2004.00117 Q-Bio.

[7] Overton CE, Stage HB, Ahmad S, Curran-Sebastian J, Dark P, Das R et al. Using statistics and mathematical modelling to understand infectious disease outbreaks: COVID-19 as an example. Infect. Dis. Model. 5, 409–441 (2020). https://www.sciencedirect.com/science/article/pii/S2468042720300245

[8] Ferretti L, Wymant C, Kendall M, Zhao L, Nurtay A, Abeler-Dorner L et al. Quantifying SARS-CoV-2 transmission suggests epidemic control with digital contact tracing. Science 368, (2020). https://science.sciencemag.org/content/368/6491/eabb6936

[9] Madewell ZJ,Yang Y, Longini IM Jr, Halloran ME, Dean NE. Household transmission of SARS-CoV-2: a systematic review and meta-analysis of secondary attack rate. 2020. medRXiv Preprint doi: 10.1101/2020.07.29.20164590

[10] Lopez Bernal J, Panagiotopoulos N, Byers C, Garcia Vilaplana T, Boddington N, Zhang X et al. Transmission dynamics of COVID-19 in household and community settings in the United Kingdom. 2020. medRXiv Preprint doi: 10.1101/2020.08.19.20177188

[11] Buitrago-Garcia D, Egly-Gani D, Counotte MJ, Hossmann S, Imeri H, Ipekci AM, et al. Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: A living systematic review and meta-analysis. PLOS Medicine. 2020; Sept 17(9)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7508369/pdf/pmed.1003346.pdf

[12] Fancourt D, Bu F, Mak HW, et al. Covid-19 Social Study Results Release 28. 2021.https://b6bdcb03-332c-4ff9-8b9d-28f9c957493a.filesusr.com/ugd/3d9db5_bf013154aed5484b970c0cf84ff109e9.pdf (accessed 20 Jan 2021).

[13] West LE et al. Adherence to the test, trace and isolate system: results from a time series of 21 nationally representative surveys in the UK (the COVID-19 Rapid Survey of Adherence to Interventions and Responses [CORSAIR] study). https://www.medrxiv.org/content/10.1101/2020.09.15.20191957v1